Semantic Memory Impairments in Schizophrenia: a Neuropsychological Study to Evaluate Competing Theories.

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Abstract

People with a diagnosis of schizophrenia have been found to perform poorly on tasks assessing semantic memory, and these impairments have been proposed to be related to certain symptoms, in particular Formal Thought Disorder (FTD). A systematic literature review and meta-analysis identified the need a) to determine whether semantic memory is a primary impairment in schizophrenia and not secondary to other cognitive impairments and b) what cognitive models could provide the best explanation for the impairment. With these aims, Studies One and Two compared the performance of a group of people with schizophrenia across a battery of semantic memory tests (Hodges, Salmon and Butters, 1992). In order to eliminate confounding variables, two clinical control groups were recruited for comparison, one with a probable degraded semantic memory arising from Alzheimer's Dementia (AD) and the other with a primary dysexecutive syndrome caused by acquired brain injury (ABI). From these comparisons, it was possible to profile the semantic memory impairment in schizophrenia with the conclusion that any deficits are task-specific. Unlike the AD group, the impairment did not seem to arise from a loss of stored knowledge but nor did a retrieval problem, in its simplest terms, offer the best explanation. Since the ABI group performed normally on the battery it is clear that a dysexecutive syndrome does not necessarily explain poor semantic memory performance.

Qualitatively, the associations and categories formed by people with schizophrenia on tasks of semantic categorisation e.g. the Category Generation Test (CGT) (Green, Done, Anthony, McKenna and Ochocki, 2004) often resemble loosening of associations and psychotic speech. In order to understand more about the processes involved in the formation of these bizarre categories, I compared performance on the CGT of groups of people with schizophrenia, AD and ABI. I found that the people with AD performed fairly similarly to the people with schizophrenia in that they sorted cards in an idiosyncratic way but the ABI group performed normally, adhering to taxonomic categories. Although this result might suggest that the bizarre associations on the CGT in people with schizophrenia are caused by a deficit in semantic memory (and not a dysexecutive syndrome), further analysis found important differences between the AD and the schizophrenia group in the way the card sorts were formed. In addition, both these groups showed intact semantic memory knowledge of the items they mis-sorted, indicating that categorisation problems do not necessarily arise from a degraded memory store.

The difficulties people with schizophrenia appear to have on tests of associations and categorisation (e.g. CGT) could arise from a disorganised semantic memory i.e. differences in the way in which concepts are interconnected. On the CGT, patients with schizophrenia were far more likely to sort items on the basis of thematic (situational) information suggesting a preference for thematic over taxonomic associations. To test this, participants were tested using a triadic comparison task which requires choosing whether an item is best associated with a taxonomic, thematic or perceptually related item. On this test patients performed comparably to controls suggesting that their semantic memory is organised normally and that the abnormalities in the way in which items are associated on some semantic memory tests, including the CGT, are task-specific.

It has been proposed that one of the core problems in schizophrenia is that there is "an aberrant assignment of salience" (Kapur 2003) to contextually inappropriate concepts due to a dysregulated dopamine system (Kapur 2003; Kapur et al 2005). It is possible that this could also explain the semantic memory impairments in schizophrenia i.e. certain less relevant concepts/ associations are chosen because they are experienced as more salient. To test this, a group of patients with schizophrenia were assessed using a test of semantic salience. Compared to controls, the patients made significantly more errors of salience including significantly more errors where large aberrant attributions of importance were given to items. The tendency to make errors on the salience test was highly correlated with errors on the CGT and also the semantic association tests, indicating a common underlying mechanism. Therefore, it can be concluded that the semantic memory impairments in schizophrenia are task-specific, not caused by a loss of semantic knowledge or a dysexecutive syndrome, but due to an aberrant assignment of salience to less relevant semantic concepts. More work is needed to understand the cognitive processes underlying this aberrant attribution process, and also the biological substrates involved.

Thesis

The semantic memory and categorisation deficits in schizophrenia are task-specific, once the effects of IQ are controlled for. They are not caused by a loss of semantic knowledge or a dysexecutive syndrome but by an aberrant assignment of salience to semantic concepts/ associations that are less contextually relevant.

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Chapter 1: Introduction

1.1. Schizophrenia

The term schizophrenia refers to a range of different symptoms which include hallucinations, delusions, thought disorder, autistic behaviours, avolition and emotional disturbances. The symptom profiles that occur amongst different individuals with schizophrenia are widely heterogeneous and it is difficult to see at first how a diagnosis of schizophrenia can be all-encompassing. Despite this, international diagnostic guidelines such as DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, American Psychiatric Association, 1994) and ICD-10 (The International Classification of Diseases and Related Health Problems, 10th Revision, World Health Organisation, 1992) have outlined agreed definitions of schizophrenia to which the majority of psychiatrists subscribe. In order to be given a diagnosis of schizophrenia, DSM-IV states that the patient needs to present with a combination of two of the following; delusions/ hallucinations/ catatonia/ disorganised speech or negative symptoms (decreased volition, speech and emotional expression) for at least one month, with subtler signs of the illness being present for a six month period. In addition, all other related conditions such as schizo-affective disorder must also have been ruled out and the individual must report a substantial degree of social or occupational dysfunction. The ICD- 10 criteria emphasise that certain symptoms such as experiences of passivity/ control, termed first rank symptoms (Schnieder 1959) should be present for a diagnosis of schizophrenia to be given. The signs and symptoms of schizophrenia affect language, thought, emotion, movement and volitional processes. It is perhaps no surprise, therefore, that people with schizophrenia have been shown to perform badly on neuropsychological assessments, and a multitude of studies have found evidence of significant cognitive impairment. Although it does not feature as a diagnostic criterion in DSM-IV or ICD-10, the evidence for a cognitive impairment in schizophrenia is overwhelming (Heinrichs and Zakzanis 1998) leading to suggestions that its inclusion should be reconsidered (Tsuang and Faraone 2002, Lewis 2004). At any one time, 1 % of the population (on the whole, internationally) is diagnosed with schizophrenia.

Since Kraepelin (1899) and Bleuler (1911/1950) defined the condition, extensive research has been carried out with an aim of discovering more about schizophrenia, the antecedents, phenomenology and neurological profile. Although traditionally viewed as a functional psychosis only, numerous findings from neurophysiological, brain imaging and neurochemical studies have identified abnormalities in the brains of people with schizophrenia, and a general consensus has prevailed that schizophrenia is an organic condition (Shenton et al 2001, Zakzanis et al 2000). Advancements in the development of effective anti-psychotic medication in the last 50 years have revolutionised the way in which people with schizophrenia are treated and with much success. Nevertheless, antipsychotics tend to alleviate mainly the positive symptoms of schizophrenia (e.g. delusions and hallucinations) meaning that the negative symptoms (avolition, alogia) and the cognitive impairments (e.g. poor performance on tests of cognition) often remain present (Leucht et al 1999, Sharma and Antonova 2003). By discovering more about the neuropathology of schizophrenia a more effective or even preventative treatment could be developed. Nevertheless, after a century or more of research, Plum (1972) stated that “schizophrenia is the

graveyard of neuropsychology" because of the lack of progress in understanding the brain abnormalities and how they affect functioning. Despite the slow progress however, with the advancement of brain imaging technology, Kraepelin's and Bleuler's early conviction that schizophrenia is a "disease of the brain" is upheld. Two comprehensive reviews of imaging studies in schizophrenia (Harrison 1999, Shenton et al 2001) reported moderate to substantial evidence for brain abnormalities in schizophrenia including abnormal hemispheric lateralisation, decreased whole cortical volume, ventricular enlargement, damage to the medial temporal lobes, superior temporal gyrus, the frontal lobes, parietal lobes and subcortically. It is difficult, however, to marry the theory of structural deficits in schizophrenia to what is known about the impermanent nature of the illness, with symptom severity peaking in episodes. Nevertheless, a neuropathological explanation could explain some of the cognitive impairments. On a neurochemical level, much research has identified deficits in the dopaminergic system in schizophrenia (e.g. Abi-Dhargham 2004). Because of the more transient nature of the neurochemical system, a neurochemical abnormality, rather than a structural deficit may provide a better explanation for symptoms in schizophrenia.

1.2. The Neuropsychology of Schizophrenia

IQ scores tend to be one to two standard deviations below the norm in a schizophrenia population (Blanchard and Neale 1994). Despite this, there are many people with schizophrenia who have achieved high standards of education prior to becoming unwell and it would appear to some (e.g. Bilder et al 1992) that there is a decline in intelligence resulting in the most severely cognitively impaired being the most chronically unwell patients. Nevertheless, there are many who argue (Asarnow 1999, Goldberg and Gold 1995) that this seeming deterioration often appears pre-morbidly and is an intrinsic part of the organic development of the condition. Importantly it has consistently been shown that at the time of initial assessment, the degree of cognitive impairment in an individual with schizophrenia, rather than the severity of their symptoms is the strongest predictive marker for prolonged incapacity and reduced functioning throughout their lifetime (Green 1996, Liddle 2000). Therefore it is important to help ongoing rehabilitation that we attempt to understand the typical nature of these impairments.

People with schizophrenia rarely perform as well as controls on neuropsychological assessments and widespread cognitive impairment is often reported (e.g. Mohamed et al 1999). Reflected in slow information processing with difficulties maintaining attention and motivation, this generalised cognitive deficit is likely to impair performance on the majority of neuropsychological assessments. A number of studies have looked at the typical neuropsychological profile in schizophrenia, usually across an extensive battery of different assessments. The majority (e.g. Heinrichs and Zakzanis 1998, Bilder et al 2002) report a widespread cognitive impairment, and, of those, many report additional relatively selective impairments in certain areas, namely memory/ learning and executive functioning (Bilder et al 2000, Barch 2005, Liddle and Morris 1991, Shallice et al 1991, Rushe et al 1999).

A consistent finding in the literature is that people with schizophrenia tend to perform poorly on tests which tap into "frontal" functions or executive processes such as

forming plans and strategies and switching between ideas (Morrison–Stewart et al 1992, Johnson-Selfridge and Zalewski 2001, Shallice et al 1991). Tasks in which poor performance has been frequently reported include the Wisconsin Card Sorting Test (WCST) (Abbruzzese et al 1996, Laws 1999), the Stroop (Barch et al 2004) and Verbal Fluency (Henry and Crawford 2005). Specifically, difficulties in inhibition (Volk and Lewis 2002), perseveration (Crider 1997) and an inability to utilise context correctly (Hemsley 2005) have been reported, all functions which fall under the general category of executive function. Nevertheless, it is difficult to say whether these test deficits are selective impairments, e.g. primarily affecting memory, or due to an overall diffuse generalised cognitive impairment; many have suggested this latter explanation to be the case (Dieci et al 1997, Laws 1999). Neuroimaging and neuropathological studies however have identified the Pre-Frontal Cortex (PFC) as abnormal in schizophrenia (Shenton et al 2001, Harrison 1999) and some of the first neurological data reported reduced functioning in the frontal lobes, termed hypofrontality (Williamson 1987, Andreasen et al 1992). To some extent, hypofrontality in schizophrenia has been disproved (e.g. Gur and Gur 1995) but there is still strong evidence to suggest that certain areas of the frontal cortex are affected in schizophrenia, which could explain the executive failings (Weinberger et al 1996).

Recently, Tyson et al (2005), in a longitudinal analysis, concluded that people with schizophrenia have "deficits in multiple aspects of memory which remain stable over long periods of time". A meta-analysis by Aleman et al (1999) which drew upon 70 studies focusing on the neuropsychology of schizophrenia concluded that long term memory in schizophrenia in particular is disproportionately affected. McKenna et al (1990) went as far as to say that the selective long term memory impairment in schizophrenia resembles that of classic amnesia (Baddeley 1982), namely that long term memory is affected but short term memory remains intact. This claim has been refuted however because unlike amnesiacs, it has been reported that people with schizophrenia also have a selective impairment in semantic memory as well as episodic memory (Tamlyn et al 1992, Clare et al 1993, Duffy and O'Carroll 1994). In fact, Duffy and O'Carroll (1994) found that compared to people with Korsakoff's dementia, people with schizophrenia demonstrated superior episodic memory but with relatively poorer semantic memory. Challenging these studies, a comprehensive neuropsychological analysis by Heaton (1994) in which people with schizophrenia were compared to those with Alzheimer's dementia and also controls found that out of all the many cognitive domains which were assessed, people with schizophrenia were no different from controls on general memory tests but were much worse on all other areas including attention, learning and verbal skills.

1.3. Symptoms and Neuropsychology in Schizophrenia

There are many researchers who believe that cognitive impairments and behavioural symptoms in schizophrenia go hand in hand and that difficulties in language, planning or reasoning could contribute to symptoms of thought disorder, avolition or delusions respectively (e.g. Frith 1992, Goldman-Rakic 1994, Bell et al 2006). Peter Liddle attempted to match the three groups of symptoms; positive (to include mainly delusions and hallucinations), negative (apathy, avolition, alogia, reduced affect) and disorganisation (mainly thought disorder), to particular neuropsychological deficits and their associated brain regions (Liddle 1987). Although he found moderate

correlations, subsequent studies (e.g. Simon et al 2003) have not been able to replicate any clear divisions and there is little strong evidence to suggest that certain symptoms do consistently relate to specific cognitive impairments (Elvevag and Goldberg 2000). Of all the findings, the strongest relationships have been reported between negative symptoms and problems with executive functions arising from a frontal lobe abnormality (Berman et al 1997, Capleton 1996, Gold et al 1999, Nieuwenstein et al 2001). One early review by Goldberg (1985) confirmed the association between negative symptoms and PFC abnormalities (specifically in the dorsolateral area) and furthermore linked positive symptoms with orbitofrontal dysfunction. Clinically, there are phenomenological similarities between the negative symptoms of schizophrenia and the behaviour seen in people with frontal lobe damage arising from brain injury, including avolition, disorganisation and flat affect. In addition, performance similarities have been reported between people with frontal lobe damage and schizophrenia on many tests of executive functioning such as planning, response inhibition, set switching and forming strategies (e.g. Benson and Miller 1997, Joyce et al 2002).

1.4. Semantic Memory

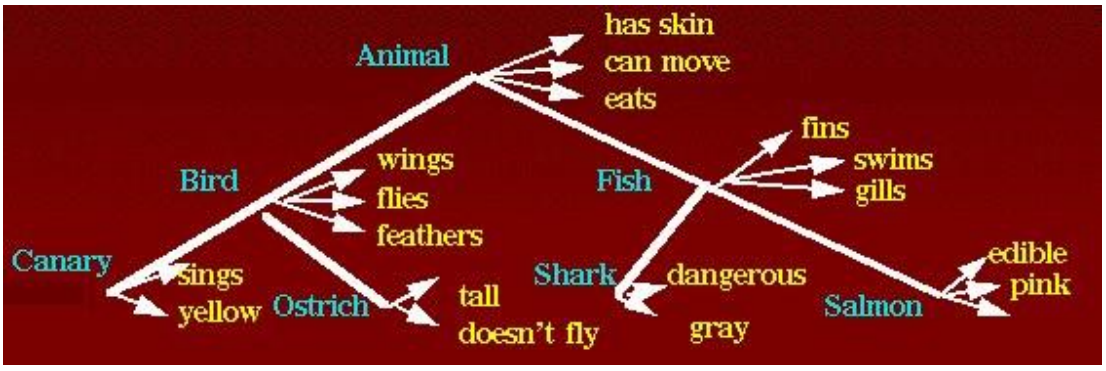
Upon embarking on this research, an aim was to focus in on the semantic memory impairments in schizophrenia. There are several reasons that semantic memory is a particularly interesting topic to investigate in schizophrenia. Firstly, there is evidence that semantic memory is selectively impaired in schizophrenia (e.g. Tamlyn e al 1992, Clare et al 1993) over and above a generalised cognitive impairment. Secondly, as highlighted by Heinrichs and Zakzanis (2000) in their meta-analysis, most studies that report cognitive impairments in schizophrenia tend to report quantitative differences, rather than qualitative ones, which may reflect a degree of illness severity rather than a specific cognitive deficit (Lewis 2004). With semantic memory however, qualitative differences between the semantic memory performance in schizophrenia and controls have been reported (e.g., Chen et al 1994, Green et al 2004), for example, in the structure of semantic categories, suggesting idiosyncrasies in the way in which semantic memory is organised in schizophrenia. Furthermore, Cutting and Murphy (1988) stated that a form of disordered thinking, which they termed, "deficient real world knowledge" could explain many of the symptoms of schizophrenia. It has been suggested by some, in fact, that tests of semantic memory can actually elicit Formal Thought Disorder (FTD) (Cameron 1939) and semantic memory impairments in schizophrenia have been shown to be linked to the presence and severity of FTD (Goldberg et al 1998, Kerns and Berenbaum 2002, Barrera et al 2005) and also delusions (Rossell et al 1999). Although these findings are inconsistent and far from conclusive, it is hard to shake the conviction that a dysfunctional semantic memory would also lead to difficulties with thought and language, as semantic memory forms the basis of what we mean when thinking and talking about everyday concepts.

Tulving (1972) was the first to subdivide the concept of long-term memory into semantic memory and episodic memory. Episodic knowledge is autobiographical and consists of memories of events which occurred at specific time points in life e.g. memories of a wedding. Separate from this, Tulving saw semantic knowledge as restricted to the meanings of words, their referents and the relations between them, e.g. knowing that a dog is an animal with four legs which chases cats. The literature

on semantic memory in schizophrenia is based largely upon Tulving's traditional definition and the common neuropsychological measures which assess semantic memory assume that semantic knowledge representations consist of a discrete concept of an object and its properties. It is worth bearing in mind, however, that the concept of semantic memory is polymorphous; there is a wide range of diverse measures which claim to assess semantic memory. Whilst the majority of the studies investigating schizophrenia do adhere to Tulving's definition, there are numerous theoeretical papers (e.g. Funnell 1992, Barsalou 1983) which posit that semantic memory should be far more inclusive as a concept.

Cognitive psychologists have provided theories or models which pertain to how semantic memory is structured and processed in the brain. Early research was based around data from semantic memory assessments such as the Tip of the Tongue test (describe what partial information is recalled for words on the Tip of the Tongue e.g. Brown and McNeill 1966), the Sentence/ Category Verification task (timed ability to verify whether a sentence is correct/ whether an item belongs to a certain category) and Lexical Decision tasks (timed ability to identify words from non words). From the speed with which these tests are performed, information can be derived about how concepts are stored, which concepts are related in memory and how people retrieve semantic information. Underlying this early work was the assumption that concepts are defined by a set of attributes or properties (e.g. Tversky 1977). Classical models of semantic memory describe a network of interconnecting concepts (called nodes) which are clustered together depending on how conceptually similar concepts are. These clusters pertain to semantic categories such as a category of vehicles where vehicles are clustered together based on the fact that they share properties. According to these models, the number of properties two items have in common determines their perceived similarity, and thus how closely they are spatially connected together in the network. The most famous of these models is the Hierarchical Network Model (Collins & Quillian, 1969), see Figure 1.

Figure 1: The Hierarchical – Network Model of Semantic Memory (Collins & Quillian, 1969) (taken from www.mtsu.edu/~sschmidt/Cognitive/semantic/c&q.jpg)



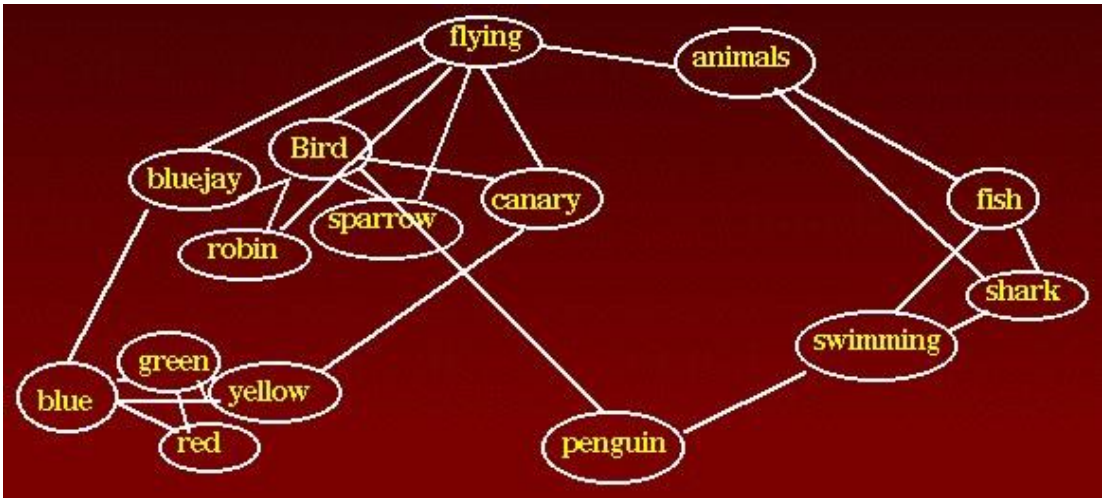
This model assumes that semantic memory is organised hierarchically. So for every taxonomic category, information about similar items is stored at one level and then more specific information for individual items is stored at a lower level. Rosch et al (1976) also proposed that there are three basic levels of knowledge representation; superordinate (general category level), basic (the individual item) and subordinate

(information about the properties of the concept). Rosch et al (1976) believed that most people use representations from the basic level of knowledge (i.e. fish) when thinking and utilising information and that this way of hierarchically storing information has an evolutionary advantage, for example when finding food or avoiding predators. In patients with neurodegenerative illnesses e.g. fronto-temporal dementia (the temporal variant, semantic dementia) and Alzheimer's dementia (AD) it has frequently been reported that as semantic memory becomes more and more impaired, representations deteriorate hierarchically in what is called "bottom-up deterioration" (e.g. Troster et al 1989). For example, Martin and Fedio (1983) asked a group of people with AD to list items that they would find in a supermarket. They found that they were less able to list individual items but could provide the overall category names. This finding was also replicated by Chertkow and Bub (1990) and Hodges et al (1992).

Despite evidence supporting a hierarchical semantic network, the network model of semantic memory has been criticised for a number of reasons. Firstly, although this model seems to work well for items from the natural world, not all types of knowledge are structured in a natural hierarchy. In addition, category effects (e.g. quicker reaction times (RTs) for verifying items in the same category) disappear when participants are given negatively framed sentences e.g. a robin is not a bird. In addition, the hierarchical model states that representations are clustered together based on similarity which is defined as the shared number of features (Tversky 1977). More contemporary theories propose that the way in which items appear closer together in semantic memory reflects more the association between items in a situational context and less their perceptual similarities (Goldstone 1994). Lastly, the hierarchical model is not able satisfactorily to explain typicality effects e.g. that it takes less time to verify that a robin is a bird over an ostrich is a bird. Despite these criticisms, much of the semantic memory research which is undertaken with people with neurodegenerative illnesses or acquired brain injury is still based around the position that semantic memory has a hierarchical structure.

Another network model which does not assume concepts are hierarchically stored was proposed by Collins and Loftus (1975) and is called the Spreading Activation Model.

Figure 2: The Spreading Activation Model (Collins & Loftus 1975) (taken from www.mtsu.edu/.../Cognitive/semantic/spread.jpg)



The theory of spreading activation states that activation, by thought or perception, of a certain concept automatically activates associated concepts, so that they are brought to mind quicker. The further in distance from the initial concept that a representation is stored in the network, the weaker the amount of activation e.g. the concept cow strongly activates other farm animals which are stored close to the cow but wild animals are stored further away and therefore are less strongly activated. Much of the thinking behind this theory is based on the semantic priming literature which is where response times for identifying a word (lexical decision) are compared following exposure to a related word or to an unrelated word. The spreading activation model is therefore able to explain typicality effects because links between concepts are based on everyday associations and not solely a taxonomic hierarchy. In this model, cognitive inhibition ensures that only associations which are relevant to the present context are attended to. The theory of spreading activation has influenced much of the literature on semantic memory in schizophrenia. In particular, studies have linked an abnormal/ hyper spreading activation with the presence of FTD. It has been found (Spitzer et al 1993a, Spitzer et al 1993b) that activation of the semantic network in people with thought disorder spreads faster and further to less related concepts. This is believed to lead to the formation of more tangential associations, in a similar way to Bleuler's concept of "loosening of associations" which he proposed underpinned psychotic thought (Bleuler 1911).

Another debated issue that concerns our understanding of semantic memory revolves around how semantic knowledge is represented on a neurological level. Throughout the literature a distinction is traditionally made between how memories are stored and how they are retrieved from storage. It is often assumed that memories are stored almost in library form with a separate retrieval mechanism which selects and utilises these representations. In neuropsychology, criteria have been proposed for distinguishing between a semantic memory impairment caused by a loss of stored knowledge and a semantic memory impairment caused by difficulties with retrieval (Warrington and Shallice 1979). Based on the test performance of two individuals with acquired semantic dyslexia, the criteria for a storage disorder proposed by Warrington and Shallice consists of 1) a consistent loss of knowledge representations

across all measures of semantic memory so that for example if you cannot name a robin you will also not be able to describe its features, 2) bottom up deterioration so that detailed item knowledge deteriorates first but more general category names such as birds or animals remain, 3) no improvement with cueing so that providing verbal clues for example the name of an animal will not trigger knowledge, 4) a frequency effect where people perform worse when presented with items which are less frequently encountered i.e. ostrich compared to robin. If the error pattern for an individual, on tests of semantic memory, met the four criteria specified then it would be assumed that their semantic knowledge had degraded and they had a storage disorder. If someone's performance met the opposite criteria e.g. inconsistent responses (so on some tests an item is named correctly and on others it isn't), no evidence of bottom up deterioration, improvement with cueing (thought to aid successful retrieval) and no frequency effect then it is assumed that their knowledge is not degraded but that their semantic memory impairment arises from difficulties with knowledge retrieval.

Table 1: Storage and Access Criteria (Warrington and Shallice 1979)

Storage Disorder	Access/ Retrieval Disorder
Error consistency across items and across time	Inconsistency of errors
Bottom up deterioration – detailed items are lost first	No evidence of bottom up deterioration
No improvement from cueing	Performance is aided by cueing
Frequency Effect – more errors on low frequency items	No frequency effects – errors are almost random

Therefore an individual with a semantic memory impairment could have a storage disorder or an access disorder. In addition, there is a school of thought that states that rather than a storage or access disorder, the semantic memory network of people with schizophrenia is idiosyncratically organised (Goldberg et al 1998, Sumiyoshi et al 2001, Elvevag et al 2002, Green et al 2004). An idiosyncratic semantic memory is thought to lead to less coherent semantic categories and atypical associations between concepts. This theory conceptually overlaps with the theory of disturbed access/ retrieval in that it proposes that item representations are not lost but merely organised differently. It is unclear, for example, whether an idiosyncratically organised semantic memory in schizophrenia is caused by developmental processes which lead to differences in how semantic networks are formed or whether a dysfunctional retrieval system means that concepts are retrieved in an unconventional way.

Chapter 2: A Systematic Literature Review and Meta-Analysis of the Semantic Memory Impairments in Schizophrenia

2.1. Introduction

There are several different tests of semantic memory, all of which vary in the demands they place upon general information processing, executive functioning, visual-perceptual and phonological processes. Semantic tasks involving a high working memory or executive load, e.g. verbal fluency, tend to make greater demands on executive processes (Hagoort 1997, Price 1998). However, tasks such as confrontation naming (i.e. naming pictured objects), make few demands on executive processes but greater demands on phonological processes (Price 1998). People with schizophrenia frequently report with a generalised intellectual deficit (e.g. Heinrichs and Zakzanis 1998, Bilder et al 2000), which means in general slower information processing and poorer cognitive abilities. Selective impairments in memory have been reported in schizophrenia (e.g. Aleman 1999), in particular long term memory, leading to some studies suggesting that there is an amnesia-like (Baddeley 1982) (e.g. disproportionately impaired long term memory) profile in schizophrenia (Tamlyn et al 1992, Clare et al 1993). However, the long term memory deficit in schizophrenia does not fit the profile of amnesia, since an executive dysfunction, which strongly influences long-term memory performance (Bilder et al 2000), is also frequently reported (Morrison-Stewart et al 1992, Wang et al 2005). It is important therefore to consider whether an impairment on a specific measure of semantic memory is due to a deficit in semantic knowledge or other cognitive abilities.

In neurodegenerative conditions where semantic memory is impaired, deficits are seen on all measures of semantic memory (e.g. Chertkow and Bub 1990, Hodges 1992) indicating that errors are due to a profound damage to semantic memory knowledge rather than a general cognitive impairment affecting tasks with higher processing demands only. In contrast, studies which have assessed patients with schizophrenia on more than one semantic memory measure have often reported that performance is relatively preserved on a number of tests e.g. naming or word-picture matching whilst on other tests such as semantic association tests performance is impaired (e.g. Al-Uzri et al 2004, Barrera et al 2005). Furthermore when semantic memory is assessed alongside other neuropsychological measures, the evidence for a selective semantic memory impairment is equivocal. For example, several studies have found the semantic memory impairments in schizophrenia to not differ in severity to other cognitive impairments (Koh 1978, Broga and Neufeld 1981, Blanchard and Neale 1994, Zanello et al 2006). In fact according to Blanchard and Neale (1994) the semantic memory impairment in schizophrenia is "best described as indicating diffuse and non localizable impairment". One study by Bilder et al (2000), using a fairly large sample (n = 94) even found that whilst there was a generalised intellectual deficit with marked memory and executive dysfunction, people with schizophrenia actually performed comparably better on tests of semantic memory. Nevertheless, other studies, although acknowledging the fact that the semantic memory impairment is influenced by deficits in other cognitive domains, have found semantic memory to be primarily impaired above and beyond the level expected by a

generalised impairment (e.g. Saykin et al 1991, Holthausen et al 2003). In the Saykin et al (1991) study a group of patients who were not currently on medication were recruited but this study used only one measure of semantic memory, the Logical Memory Passages test which is more a measure of semantic learning than recall. A more recent paper by Holthausen et al (2003) aimed to establish whether long term memory was primarily impaired in schizophrenia and, like the Saykin et al (2001) study, included only limited measures of semantic memory functioning, the Category Fluency test and the California Verbal Learning Test (CVLT). Holthausen et al (2003) looked at the amount of variability between the groups on tests of long term memory that could be explained by additional cognitive factors such as slowing of processing speed, education levels or executive functioning. They found that a fair but nevertheless modest amount of variance could be attributed to these other cognitive factors especially in the case of semantic memory but that there was a strong case for a specific long term memory deficit in schizophrenia. However in this study only one clear assessment of semantic memory was used and only education and not current IQ was taken as a measure of intellectual functioning. Two seminal studies (Tamlyn et al 1992, Clare et al 1993) also concluded that long term memory, and specifically semantic memory, was selectively impaired in schizophrenia. Nevertheless, like the Holthausen et al (2003) study, neither of these studies controlled for levels of current intellectual functioning when comparing groups.

In conclusion, of the studies that used a wide range of neuropsychological tests there is a fairly strong indication that long-term memory (e.g. episodic and semantic) is selectively impaired in schizophrenia over and above a generalised cognitive deficit. However, this does not meet the criteria for an amnesia in schizophrenia as there are also several reports of a selective impairment in executive functioning (e.g. Wang et al 2005) Where semantic memory is assessed a mixed picture emerges and conclusions are limited by the fact that usually only one semantic memory test is utilised. In the study by Clare et al (1993) which reported disproportionately impaired semantic memory, a battery of semantic memory tests were employed and this study therefore perhaps has more weight. Nevertheless, results from recent studies, e.g. Bilder (2000) and Blanchard and Neale (1994), point to relatively intact semantic memory performance in schizophrenia. Whereas single studies have explored this issue, no meta-analysis has yet looked at semantic memory performance in schizophrenia across a range of different measures. In this review and meta-analysis, studies featuring the most frequently used tests of semantic memory i.e. naming, word-picture matching, categorisation, priming, verbal fluency and associations are described in turn and also there is a section devoted to miscellaneous tasks which also primarily assess semantic knowledge.

The presence of a generalised cognitive impairment in schizophrenia means that on tests of semantic memory where processing demands are high, performance is likely to be low, irrespective of whether semantic knowledge is affected. Therefore, when reporting quantitative differences between groups, the relative contribution of semantic memory and overall intelligence must be considered. Controlling for current intellectual ability is especially problematic in the case of semantic memory as verbal IQ measures e.g. the WAIS (Wechsler Adult Intelligent Scale, Wechsler et al 1999) often include semantic memory tasks for example measures of vocabulary. One of the challenges to this area of research therefore is how to adequately control for

current IQ, firstly in order to tease apart the degree of semantic memory impairment in schizophrenia specifically and secondly to help adequately match patient and control groups on the basis of cognitive impairment. Because people with schizophrenia tend to always perform poorer than controls on cognitive tasks, when mentally well controls are used in studies it is difficult to say for sure whether semantic memory is primarily impaired in schizophrenia or is merely part of a constellation of cognitive deficits. The effect of confounding variables, largely IQ, will be reviewed here.

Semantic memory impairments have been put forward as a good model for explaining loosening of associations and FTD in schizophrenia (e.g. McKenna 1994; Payne 1973; Spitzer et al 1993a, Spitzer et al 1993b) as idiosyncrasies in the way in which people with schizophrenia form associations between concepts on cognitive tasks have been frequently reported (e.g. Green et al 2004; Chen et al 1994). In fact, phenomenologically, deficits in "real world knowledge" (Cutting, David and Murphy 1987) "loosening of associations" (Bleuler 1911/1950) or "overinclusive thinking" (Cameron 1939) were cited as key to explaining the symptoms and psychotic thought of schizophrenia. However despite some studies which have reported a positive relationship between symptoms and semantic memory impairments (e.g. Goldberg et al 1998), the evidence for this relationship is equivocal and it is not certain exactly how a cognitive deficit in semantic memory is related to symptoms in schizophrenia. This review will consider the accumulated evidence for a relationship between formal thought disorder (FTD) and semantic memory impairments in schizophrenia.

2.2. Systematic Literature Review and Meta Analysis – Semantic Memory in Schizophrenia

2.2.1. Aims of the Literature Review

The key questions that are addressed in this review are:

- Is semantic memory primarily impaired in schizophrenia (over and above a generalised cognitive impairment)?
- What is the typical profile of the impairment, if there is one, across the range of different tests of semantic memory?
- How does the semantic memory impairment relate to symptoms?

2.2.2. Inclusion Criteria/ Search Strategy

The inclusion criteria for this study were fairly wide including all research which assessed people with schizophrenia on any measure of semantic memory providing the following criteria were met:

- Participants must have a primary (DSM-IV/ ICD-10/ Research Diagnostic Criteria) diagnosis of schizophrenia – not schizotypy or schizoaffective disorder.
- The assessments must measure semantic memory directly and not learning/ encoding of semantic information, Tulving (1972) believed that learning words reflected episodic memory and also must involve working memory.
- Participants must be over the age of 18
- Participants must have no known secondary deficits i.e. brain injury, alcohol abuse
- Participants must be under the age of 65 (semantic memory in general worsens with age)
- Papers must be written in English
- Papers must come from a peer-reviewed journal
- The study must have a control group (or use norms)
- Studies must recruit groups of schizophrenia of 5 or more participants
- Means, standard deviations or t test, F test data must be available for patient and control groups.

The search engines Pub Med and Psych Info were used and the search was conducted firstly in 2004 but then recently extended (in order to prepare the review for publication) in October 2007. Therefore a paper by Lawrence et al (2007) was also included which was based on Studies Two and Four.

2.2.3. Search Results

The main search term was *semantic memory and schizophrenia* which resulted in 212 hits on Pub Med (Limits: Human Participants, Adult, English Language) and 15 on Psych Info. Certain secondary search terms were then used (see Table 2). All retrieved articles were then hand searched for relevance. Appendix A contains tables

which include the effect sizes and study details for all the studies included in this review. There were also 12 other papers which were included because they were cited in the articles mentioned above and were clearly pertinent. For a list see Appendix B. The total number of papers retrieved therefore was 96.

Table 2: Search Terms and Results from the search engines

Search Term	Results Pub Med	Results Psych Info	Final Number Included (excluding duplicates)
Semantic Memory and Schizophrenia	212	15	41
Semantic and Schizophrenia	380	43	8
Naming and Schizophrenia	68	6	1
Boston Naming Test and Schizophrenia	5	0	1
Categorisation and Schizophrenia	12	0	0
Semantic Categorization and Schizophrenia	16	0	0
Semantic Fluency and Schizophrenia	64	3	10
Pyramid and Palm Trees and Schizophrenia	0	0	0
Camel and Cactus and Schizophrenia	0	0	0
Word-Picture Matching and Schizophrenia	0	1	0
Storage, Access and Schizophrenia	6	0	0
Semantic Priming and Schizophrenia	81	10	23

2.2.4. Data Collection and Analysis

Separate meta-analyses were conducted for each measure of semantic memory. From each paper returned by the search, the relevant data were extracted in order to derive effect sizes. Where possible, effect sizes were derived from a calculation, recommended by Cohen (1992); the difference between the means for the clinical and control groups, divided by the pooled standard deviation. However where this raw data was not available, effect sizes were derived from t or f values and calculated using Thalheimer and Cook's (2002) formula. Cohen's (1988) d was used for the estimate of effect size with the following interpretations, d = .8 > = large, d = .5 - .79 = medium, d = .2 - .49 = small (Cohen, 1992). Homogeneity of effect size variance (within each measure of semantic memory) was assessed using the Q test of homogeneity (refs). This test assesses whether the variance within in each study is similar across studies. Where variances differ significantly it is assumed that there are substantial differences between the studies contributing to the mean. Therefore a random effects model (Shadish and Haddock, 1994) was employed, which allows for this heterogeneity. The meta-analysis was conducted using the software package Comprehensive Meta-Analysis Version 2 (Biostat 2007). For each study an effect size was calculated with standard error and 95% confidence intervals. Following this each study was weighted according to the inverse of the variance which roughly equates to sample size and a weighted effect size (Pettiti, 2000) for each measure was derived with variance and 95% confidence intervals. This enabled the assessment of the relative contribution of each included study in consideration of sample size. A fail safe N was also calculated to take into account publication bias; this estimates the number of unpublished studies which would need to have accepted the null hypothesis in order to reverse the claim that there is a significant difference between groups (Wolf, 1986).

2.3. Conclusions

A wide range of neuropsychological tests are used to assess semantic memory in schizophrenia. This variety reflects the need to assess different modalities i.e. visual and non visual, different task demands i.e. comprehension vs. production and also the level of task difficulty (implicit in this requirement is varying the degree of executive functioning i.e. retrieval required).

A key aim of the literature review was to ascertain whether there was a typical profile of semantic memory impairment in schizophrenia. Therefore, the most commonly used tests and a summary of research findings are reported below:

2.3.1. Naming in schizophrenia

The inability to name an object, referred to as anomia/ dysnomia is commonly seen to reflect a semantic memory impairment (e.g. Hodges et al 1992) once other cognitive processes (e.g. visual-perceptual) are controlled for. Tests of naming usually refer to those assessing confrontation naming, where the participant names a picture of an object, and these studies will be reviewed here. However there are other tests of naming, for example naming to description, which are less frequently used. There are several tests of confrontation naming frequently used in the literature, mainly the Boston Naming Test (BNT; Kaplan, Goodglass, & Weintraub, 1983), the Graded

Naming Test (GNT, McKenna & Warrington, 1983) and the McKenna Naming Test (McKenna 1997), all of which involve orally naming pictures of objects. As with many tests of semantic memory, IQ correlates highly with naming ability (e.g. Hawkins et al (1993) found a .83 correlation between the BNT and a measure of verbal IQ and McKenna and Warrington (1983) found the National Adult Reading Test (NART, Nelson 1982) test of pre-morbid IQ correlated strongly with the GNT (*r* = .73) and in fact the Boston Naming Test and the Graded Naming Test are used as rough measures of pre-morbid IQ in adults and children. Nevertheless, despite this caveat, naming tests do require relatively few additional cognitive processes aside from phonological retrieval and semantic memory and are thought to provide a fairly pure measure of semantic knowledge (Hart et al 1988).

In the meta-analysis of verbal fluency in schizophrenia by Henry and Crawford (2005) they often provided data on object naming on the BNT, concluding that although naming is impaired in schizophrenia, in comparison to verbal fluency the impairment is relatively minor. However, it was unclear exactly how many papers were used to derive the effect size for the BNT measure because this was not an integral aim of the paper. Therefore despite a certain level of overlap with the studies included in the Henry and Crawford meta-analysis, it was decided that only the studies identified in our literature search that related to confrontation naming impairments in schizophrenia would be included here. From the search it was found that several (15) studies have investigated naming ability in schizophrenia and that ten (66%) have provided evidence to suggest that naming is quite severely impaired (Giovannetti et al 2003; Leeson et al 2005a; Joyce et al 1996; Gourovitch et al 1996; Leeson et al 2006; Laws et al 2000; McKay et al 1996; Hoff et al 1992; Lawrence et al 2007, Laws et al 2006). Five (33%) studies found preserved naming ability in schizophrenia (Barrera et al 2005; Stirling et al 2006; Al-Uzri et al 2004; Goldberg et al 1998; Faber and Reichstein 1981). Despite this, in all studies the effect size was medium to large and therefore some of the non significant findings could reflect heterogeneity or problems with sampling.

Table 1 in Appendix A provides the effect sizes for the 15 studies included in the naming meta-analysis. All but one study (Goldberg et al 1998 for the FTD group – there was a small effect size) produced a large effect size. For all 15 naming studies, the random model meta-analysis produced a weighted effect size of -1.45 (variance = 0.044) which is a large effect with 95% confidence intervals of -1.86 - - 1.04. The fail safe N indicated that one would need 2005 studies which accepted the null hypothesis in order to say there is not a significant effect of naming in schizophrenia. The Q test of homogeneity was significant at $p < .0001$ ($Q(21) = 177.69$) indicating that the studies were heterogeneous.

Of the potential moderators for explaining poor naming performance in schizophrenia three are most apparent; chronicity, IQ and symptoms. Typically, the majority of the "naming" studies reported here recruit chronically ill patients e.g. Laws et al 2000, Lawrence et al 2007, Joyce et al 1996. Only two studies however compared groups of chronic with acute/ first episode patients (Hoff et al 1992 and McKay et al 1996) and both found greater errors in the chronically ill patients. Where data on chronicity was available (n = 13) this was entered as a moderator in the meta-analysis. For studies which recruited acute patients (or subgroups of studies) ($n_= 7$) d = -1.85 (variance =

0.27) and for chronic patients (n = 11) d = -1.27 (variance = 0.07), both large weighted effect sizes. This difference was significant (t (15) = 3.12, *p* = .007) but counter to the claims of Hoff et al 1992 and McKay et al 1996, the direction of the difference suggests that there is a greater difference between the naming performance in acute patients and normal controls.

To address the issue of IQ separately to chronicity, it is worth noting that of all the studies reviewed here, 10 studies used the NART or Wide Range Achievement Test (WRAT, Wilkinson 1993) measures of pre-morbid IQ as their only measure of intellectual functioning and 3 studies only used educational level. Although a common strategy, using the NART as a substitute for assessing current IQ is unreliable for two main reasons. Firstly it assumes there is no cognitive decline in schizophrenia (perhaps wrongly: see Crow 1987, Bilder et al 1992, although see Kurtz 2005) and that a measure of pre-morbid ability will be equivalent to current status. Secondly the NART has been shown to be an overestimation of current IQ (e.g. Russell et al 2000). By only matching groups on the NART therefore, groups will most probably differ significantly on current intellectual ability. Even where studies did use measures of current IQ (Giovannetti et al 2003; Barrera et al 2005; Lawrence et al 2007 and Stirling et al 2006) patient and control groups were not matched (i.e. were significantly different in terms of current IQ performance). In two studies (McKay et al 1996; Leeson et al 2006) when IQ was added as a covariate, differences between groups remained significant on the naming test. However in one study, (Lawrence et al 2007) differences became non significant after IQ was used as a covariate. Two studies (Lawrence et al 2007 and Giovannetti et al 2003), where there was a purposeful matching of current IQ in schizophrenia to non psychotic groups with neurological conditions (patients with Acquired Brain Injury in Lawrence et al 2007 and patients with Temporal Lobe Epilepsy (TLE) in Giovannetti et al 2003), found no significant difference between these matched groups on measures of naming. Furthermore, in the Giovannetti et al 2003 study, whilst both clinical groups performed poorer than the healthy controls on the BNT, the TLE group actually were significantly worse at naming than the group of patients with schizophrenia who shared their level of IQ. This suggests that the naming impairments in schizophrenia are relatively less than would be expected given their level of cognitive ability. In support of this, two studies which assessed people with schizophrenia on a number of neuropsychological measures (Hoff et al 1992 and Stirling et al 2006) found that despite impairments on a range of cognitive tests including semantic fluency and semantic association tests there was no difference in performance between patients and controls on tests of naming.

2.3.1.1. Symptoms and Naming

Of all the naming studies reviewed here, of those that have analyzed symptoms (n = 11), the majority (n =8) have found no significant correlation between clinical symptoms and naming test performance. However, in a small number of studies where FTD was analysed separately, the weighted mean for FTD patients (n = 4) was -1.195 (variance 0.099) and non FTD (n = 4) = -0.728 (variance = 0.039). A t test showed significant differences between these studies (t (6) = 2.51, *p* = .046) suggesting that naming is frequently reported to be more impaired in patients with FTD.

2.3.2. Word-Picture Matching in schizophrenia

The traditional test of Word-Picture Matching is called the Peabody Picture Vocabulary Test (Goldberg et al 1998) but there is a revised version called the British Picture Vocabulary Scale (BPVS, Dunn and Dunn 1997). The BPVS is frequently used to measure current IQ and therefore there is again some circularity logically in the fact that the construct being measured here can be taken both as a measure of semantic memory and of verbal IQ performance. Another test of Word Picture Matching is included in the Hodges et al (1992) Semantic Memory Test Battery. All these tests involve pointing to a picture from a number of similar alternatives, following a verbal cue. The Word-Picture Matching test is seen as a test of recognition (Marshall et al 1990) as opposed to recall which is assessed in naming tests. There are two different types of Word-Picture Matching task one of which uses semantically related foils (e.g. items of the same category) as distracters and another which uses distracters which are semantically unrelated to the target. This distinction is important because in people with semantic memory disorders, e.g. Alzheimer's Dementia (AD), depending on the severity of the dementia, errors occur only when related distracters are used (Chertkow and Bub 1990).

The search identified five studies that have looked at Word-Picture Matching in schizophrenia (Al-Uzri et al 2004; Barrera et al 2005; McKay et al 1996; Gurd et al 1997; Lawrence et al 2007). All (80%) but one (20%) (Gurd et al 1997) have found that people with schizophrenia are unimpaired on the Word-Picture Matching task. This supports claims that people with schizophrenia have greater difficulties on tasks of recall (e.g. naming) than recognition (e.g. Aleman et al 1999; Koh 1978; Gold et al 1992). In the one study by Gurd et al (1997) which reported a word-picture matching impairment, a word-finding test was given to a group of people with schizophrenia. When asked to find a member of a category e.g. any dog, patients with schizophrenia performed normally but when asked to find a specific item e.g. an Alsatian, there was a significant impairment suggesting that the ability to differentiate within-category exemplars is most impaired in schizophrenia.

Effect sizes were derived for these five studies (see Table 2 in Appendix A). The Q test of homogeneity ($Q(7) = 14.73$, $p = .04$) was significant and therefore a random effects model was again used. The combined weighted mean effect size was medium at -0.58 with a variance of 0.03, 95% confidence intervals of-0.92 – -0.24 and a failsafe N of 41. The heterogeneity of the findings may be due to cognitive deterioration in different samples for example the elderly group recruited for the McKay study did show a large effect size difference on this measure compared to the mild group who performed at the same level as controls. As previously mentioned differences in the design of the study could also explain sample variability (i.e. the Gurd study employed a slightly different measure of WPM and was the only study to report a significant impairment). Nevertheless in sum, WPM does not seem to produce impairments consistently in schizophrenia although this is not always reflected in the effect sizes which range from small to large.

2.3.2.1. Symptoms and Word Picture Matching

In three studies there was no significant correlation found between symptom severity and WPM test performance (Barrera et al 2005; Al-Uzri et al 2004 and Lawrence et al 2007) suggesting that FTD is unrelated to poor performance on tasks of WPM.

2.3.3. Semantic Fluency in schizophrenia

Verbal Fluency tasks involve recalling as many words as possible from a given category within a time limit. There are two versions of the verbal fluency task; phonemic fluency (e.g. (Controlled Word Association Task COWAT – FAS) (Benton et al 1983) where the categories are the letter F, the letter A and the letter S and the category fluency task (categories are animals, transport etc). Both are often used to assess executive functioning as they require search and retrieval through memory (Butler et al 1993). Because of the multifaceted nature of fluency tasks, it is difficult to partial out the influence of semantic memory from executive processes. Controls do relatively better on semantic fluency tasks than phonemic fluency because they are able to utilise semantic organisation (Martin et al 1994). There is also some evidence that completing the phonemic fluency task may make greater demands on executive processes such as retrieval and strategic searching because of the absence of a semantic organisation (Martin et al 1994). A comparison of semantic and phonemic fluency therefore allows for assessment of whether a semantic memory impairment is influencing poor fluency performance. A strength of comparing within patient groups on semantic vs. phonemic fluency is the fact that this obviates the methodological problem of interpreting a comparison between patients and unmatched healthy controls.

There have been two fairly substantial meta-analyses investigating semantic fluency in schizophrenia. Bokat and Goldberg in 2003 included data from 13 studies with the aim of comparing semantic vs. phonemic fluency. Their meta-analysis concluded that semantic fluency is disproportionately impaired compared to phonemic fluency in schizophrenia as average effect sizes were d = 1.23 and d = 1.01 respectively; a difference which was significant. Of the thirteen studies identified by Bokat and Goldberg (2003) only 7 were identified with our search (Bokat and Goldberg (2003) used MEDLINE as a search engine which may explain this discrepancy). In 2005, a much larger meta-analysis was conducted by Henry and Crawford which included data from 84 studies. This study aimed to compare verbal fluency performance in schizophrenia with performance on other neuro-cognitive tests in order to assess the relationship between verbal fluency and an executive dysfunction. In conclusion, Henry and Crawford (2005) agreed with the earlier meta-analysis in stating that semantic fluency was disproportionately affected in comparison to phonemic fluency. The results from both these reviews therefore provide strong support for a semantic memory impairment in schizophrenia. In comparison to the Bokat and Goldberg (2003) paper, the Henry and Crawford (2005) meta-analysis employed a much wider and thorough search strategy. However, unlike our review and the meta-analysis of Bokat and Goldberg (2003), patients with schizo-affective and schizophreniform disorder were also included and in some of the included studies diagnoses were not based on published criteria. Using the research methods outlined on pages 3 and 4, the current search strategy identified 39 studies of which only 15 were included in one or both earlier meta-analyses, reflecting perhaps their larger inclusion criteria. This also means that our study included data from an additional 22 papers.

Effect sizes for all 38 papers are presented in Table 3 in Appendix A. As with naming and WPM, the Q test of homogeneity was significant ($Q(42) = 262.091$, $p < .000$) and

therefore a random effects model was employed. This gave a large weighted mean of -1.33 with a variance of 0.01 and confidence intervals of -1.15 – -1.11. The fail safe N was 8474. This result is in agreement with the two previous meta-analyses in concluding that semantic fluency is severely impaired in schizophrenia. In total, 36 (92%) out of the 39 papers, (all but Cutting, David and Murphy 1987, Vinogradov et al 2002 and Elvevag et al 2005) reported a semantic fluency impairment in schizophrenia. There are three distinct methods used to assess semantic fluency performance in schizophrenia; 1) a straightforward investigation of word production on a test of semantic/ category fluency; 2) a comparison of the number of items produced in category and phonemic fluency tasks in order to control for the executive processes required and; 3) a detailed analysis of category fluency performance to investigate whether errors are due to impairments in the word clusters available for use or in the ability to switch between clusters. Out of the 39 papers, 23 (Giovannetti et al 2003; Robert et al 1997; Chen et al 2000a; Chen et al 2000b; Zanello et al 2006; Minzenberg et al 2003; Paulsen et al 1996; Elvevag et al 2002a; Vinogradov et al 2002; Aloia et al 1996; Al-Uzri et al 2004; Sumiyoshi et al 2001; Baare et al 1999; Albus et al 2006; McKay et al 1996; Lafont et al 1998; Elvevag et al 2002b; Moelter et al 2001; Allen et al 1993: Cutting, David and Murphy, 1987: Moelter et al 2005; Prescott et al 2006; Elvevag et al 2005) used the first method to assess fluency performance. In agreement with the conclusions reached by the earlier meta-analyses, 20 of these 23 studies have reported substantial impairments on tasks of semantic fluency in schizophrenia.

Several studies (n =16) used the second method, comparing semantic fluency performance in schizophrenia to phonemic fluency. This is a particularly powerful method of establishing whether semantic memory is impaired in schizophrenia because of the within subjects design. Of these 16 studies, whilst all reported an impairment in semantic fluency, only 6 (Bozikas et al 2005; Kubota et al 2005; Kravariti et al 2005; Kremen et al 2003; Gourovitch et al 1996; Granholm et al 1998) found a disproportionate impairment in comparison to phonemic fluency (suggesting a primary semantic memory impairment). Interestingly in the Kubota et al (2005) study, phonemic fluency performance was preserved in schizophrenia whereas semantic fluency performance was highly impaired; a dissociation which provides internal validity. In contrast to the conclusions from the two previously published meta-analyses however, this review identified 10 studies (Kosmidis et al 2005; Rossell 2006; Sumiyoshi et al 2005; Woods et al 2006; Stirling et al 2006; Barrera et al 2005; Halari et al 2006; Robert et al 1998; Joyce et al 1996; Elvevag et al 2001) which reported the opposite pattern of worse phonemic as opposed to semantic fluency performance. It is worth noting that 7 of the 10 papers were published after 2005 which explains why they were not included in the two previous reviews. Nevertheless in sum the majority of these studies would suggest that the poor performance in tasks of semantic fluency may be due to a large extent to an executive dysfunction rather than a primary semantic memory impairment.

The third method of dealing with the multi-factorial nature of verbal fluency is to analyse in more detail the responses elicited by the fluency tasks. The output of fluency tasks can be broken down into two processes; clustering (the formation of meaningful semantic clusters) and switching (the ability to move between clusters) (Gruenewald and Lockhead 1980). Typically on tasks of category fluency,

participants recall words in clusters relating to subcategories e.g. when recalling animals people tend to think of animals in terms of zoo animals, domestic animals etc and there tend to be gaps in fluency output when people switch between these clusters. A reduction in the size of clusters is often used to indicate a degradation of the semantic store whereas slow switching between these clusters suggests a retrieval problem. Of the 9 studies that analysed category fluency responses, 4 have found (Elvevag et al 2002a; Elvevag et al 2005; Giovannetti et al 2003; Cutting, David & Murphy, 1987) that people with schizophrenia can produce clusters that are similar in content to the normal population i.e. in terms of idiosyncrasy and typicality (Elvevag et al 2005; Allen et al 1993). In the study by Giovannetti et al (2003), a group of patients with first episode schizophrenia (FSE) were matched by IQ to a group with Temporal Lobe Epilepsy (TLE). The TLE group were equally poor with regards to fluency output but showed impaired clustering with intact switching. The FSE group showed the opposite pattern of intact clustering and impaired switching, reflecting a dissociation. In addition, in comparison to the TLE group, only the verbal fluency scores of the FSE group correlated with some additional measures of executive functioning, leading the authors to conclude that poor verbal fluency performance in schizophrenia is explainable by an executive dysfunction and not a semantic memory impairment, which is more likely to be the case in TLE where the temporal lobes are primarily affected. Five other studies have found impaired switching in schizophrenia (Lafont et al 1998; Kosmidis et al 2005; Bozikas et al 2005; Robert et al 1998; Gourovitch et al 1996) but these also reported impaired clustering (in the study by Robert et al 1997 switching was not assessed). In the study by Allen et al (1993) whilst the patients with schizophrenia produced far fewer words that controls in the first trails, when assessed over three sessions, the words they produced were as rich in variety as those produced by controls indicating "a poorly organised search through a large word pool". Nevertheless a similar study by Chen et al (2000b) found evidence of a reduced lexicon in patients with schizophrenia when their fluency performance was assessed over a number of trials. Therefore, similarly to the conclusion drawn from the phonemic vs. semantic fluency comparisons, on the basis of the clustering/ switching approach the evidence also points to an executive dysfunction as an explanation for poor semantic fluency in schizophrenia.

The confounding factor of IQ must also not be ignored and only one study (Cutting et al 1987) managed to match their groups on current IQ. Of the remainder 11 studies where current IQ was assessed the control and schizophrenia groups were significantly different. In the 15 studies which assessed pre-morbid IQ, 10 matched their groups and 5 recruited groups that differed on this measure. The other 19 studies used measures of education; 14 studies matched their groups on this measure. Where current IQ has been controlled for either through correlations (Kremen et al 2003; Vinogradov et al 2002; Giovannetti et al 2003) or covariance analyses (Giovannetti et al 2003; Elvevag et al 2002a; Stirling et al 2006; McKay et al 1996; Elvevag et al 2001) the majority of studies (all except Giovannetti et al 2003 and Elvevag et al 2001) found that following this the difference between the groups remained significant. Nevertheless, the only study that did match their groups on a measure of IQ (Cutting, David and Murphy 1987) reported no difference between the groups in terms of fluency performance. Another explanation for the varied performance pattern in the literature could be differences in illness chronicity. For example Paulsen et al (1996) found that semantic fluency was worse in early vs. late onset schizophrenia

and suggested that this could be due to the long term effects of illness. In addition a longitudinal study by Albus et al (2006) found that 58 patients with schizophrenia tested five years after their first episode on a number of neuropsychological measures had deteriorated the most on a test of semantic fluency suggesting that semantic memory does worsen over the course of the illness (although this study only tested patients on semantic fluency and not phonemic fluency).

The meta-analysis results support those conducted previously in concluding that semantic fluency is substantially impaired in schizophrenia with 92% of studies reporting large impairments. In fact, it has been reported that semantic fluency is the most severely impaired test in schizophrenia relative to other measures of neuropsychological functioning (e.g. Stirling et al 2006; Henry and Crawford 2005; Goldberg et al 1998). Of the three methods which have been used to gauge the extent of the semantic fluency impairment in schizophrenia two have concluded that executive functioning plays a large role in poor performance. This means that semantic knowledge as evident in cluster content remains intact but deficits in switching between recall strategies lead to less items being recalled in time.

2.3.3.1. Symptoms and Semantic Fluency

Another factor which could influence fluency performance is the presence and severity of the symptoms in the sample. In total, 22 studies of the 38 reviewed here have looked at the relationship between symptoms and semantic fluency test performance. Of these, 10 found no significant correlations between symptoms and test performance including a study by Barrera et al (2005) where a FTD group performed similarly to a non FTD group on measures of semantic and phonemic fluency. Eight studies found a relationship between negative symptoms and poor semantic fluency performance and in particular alogia was seen to relate strongly to the impairment (i.e. Joyce et al 1996; Sumiyoshi et al 2001). In addition four studies (Allen et al 1993; Stirling et al 2006; Goldberg et al 1998 and Kravariti et al 2005) reported a significant relationship between formal thought disorder and semantic fluency performance in schizophrenia. For example in the Goldberg et al (1998) study, people with moderate/ severe FTD showed a greater discrepancy between semantic and phonological fluency (i.e. were worse on semantic fluency) than people with mild FTD.

2.3.4. Associations Tests in schizophrenia

Identifying relevant relationships between concepts is an important function of semantic memory and unlike the more traditional semantic memory tests, tasks of semantic association utilise knowledge of situational context as well as taxonomic information. Two typical tasks of semantic association are the Camel and Cactus Test (Bozeat et al 2000) and the Pyramid and Palm Trees test (Howard and Patterson 1992) both of which require identifying which concept goes best with the target i.e. from the 4 possible responses of apple, banana, grapes and orange, which one goes best with the target, wine?

Five studies examined the ability of people with schizophrenia to complete a semantic associations test. Table 4 in Appendix A shows the effect sizes for each study. As with the other measures, the Q test of homogeneity was significant ($Q(5) = 30.34$, $p < .0001$). The random effects combined weighted mean was 0.63, variance of 0.10,

(95% confidence intervals 0.003 – 1.25). The fail safe N was 26. Out of five studies, three (60%) (Rossell and David 2006; Barrera et al 2005, Lawrence et al 2007) reported impairments. In the Barrera et al study (2005), impairments on the Camel and Cactus test were far more pronounced than on any of the other tests of semantic memory employed such as a test of synonyms, naming and vocabulary. Similarly, in the study by Lawrence et al (2007) where the performance of people with schizophrenia was compared to a neurological control group who were matched on current IQ and executive functioning the people with schizophrenia performed far poorer on the Camel and Cactus test than the neurological group even though they had performed similarly on other tests of semantic memory. Therefore it would appear that from the Barrera et al (2005) and Lawrence et al (2007) studies, semantic association test performance in schizophrenia is substantially impaired, at a level beyond that expected by performance on other measures of semantic memory and intellectual ability. Nevertheless, two studies reported preserved functioning on tests of association (Moelter et al 2005, Stirling et al 2006). Interestingly one difference between the Barrera et al (2005) and Lawrence et al (2007) studies from the Moelter et al (2005) and Stirling et al (2006) studies is that in the former studies only chronically impaired patients were recruited.

2.3.4.1. Symptoms and Association Tests

In the study by Barrera et al (2005) the semantic memory impairment on the Camel and Cactus test was much larger in patients with FTD (64% fell below the fifth percentile) than in those without (12.5% fell below the 5^{th} percentile). This impairment stands alongside relatively preserved performance in other semantic memory tests. There is therefore some suggestion that impairments on tasks of association are related to the presence of formal thought disorder although more studies are needed to replicate this finding. Nevertheless, in the Stirling et al (2006) and Lawrence et al (2007) studies no significant correlation was found between symptoms and Semantic Association performance in schizophrenia.

2.3.5. Categorisation/ Sorting Tasks in schizophrenia

One way of measuring semantic memory is to see how people group items together to form categories. In total 11 studies have investigated this ability in schizophrenia and ten (91%) have reported impairments. Effect sizes were derived (see Table 5 Appendix A) and following a significant Q test for homogeneity ($Q(16) = 150.06$, $p < .0001$), a random effects meta-analysis was conducted. The combined weighted mean was small at 0.110 (n = 17), variance = 0.060, confidence limits = -0.37 – 0.59. The fail safe N was 0.

There are three common ways of investigating category knowledge. The first and perhaps simplest involves asking people to say whether an item belongs to a certain category or not, termed a classification task. Of the 6 studies that have investigated this, 5 have found a significant impairment in schizophrenia when compared with healthy controls (Matsumoto et al 2001; Rossell and David 2006; Chen et al 1994; Clare et al 1993; Grillon et al 1991). Nevertheless, overall accuracy is high and participants tend to score within the 90% + range. In 1994, Chen et al asked people with schizophrenia to try to identify whether certain items were members of the animal category. They found that people with schizophrenia were not only slower in general but also showed a different response time pattern from that of controls which

they described as reflecting an "outward shift of semantic category boundaries with a nevertheless preserved internal category structure" i.e. they were including less typical category exemplars in their categories which were otherwise similar in contrast to controls. However more recently (Elvevag et al 2002b) an attempt to replicate this study failed although this may be due to differences in current IQ or chronicity between this study and the Chan study which the authors themselves identify. For these 6 studies, heterogeneity was significant (Q (5) = 58.36, p <.001) and a random effects meta-analysis gave a large combined mean of -0.31 (variance = 0.19), 95% confidence intervals = -1.18 – 0.57). Fail safe N = 2.

Apart from simple classification studies, there are two other ways to measure categorisation; structured or free sorting. Tasks of structured sorting such as the sorting tasks in the Hodges and Patterson (1996) Semantic Test Battery assess category knowledge by asking participants to sort picture cards into two or more categories which vary in the level of semantic knowledge required e.g. animals vs. fruit vs. birds. Three studies (McKay et al 1996; Al-Uzri et al 2004; Lawrence et al 2007) have used this measure to assess people with schizophrenia. In the studies by McKay et al (1996), and Lawrence et al (2007) people with schizophrenia (specifically a chronic and elderly group) showed preserved performance on the superordinate level of a sorting task but relatively worse performance on the second and third levels of the task where more detailed knowledge is required (see Table 3). This pattern of responding is called bottom up deterioration and is seen by some to reflect a degradation of semantic memory representations (Warrington and Shallice 1979). Interestingly, one study (Al-Uzri et al 2004) reported a different pattern of performance errors; preserved performance on the superordinate and subordinate levels of a sorting task but impairments on the basic level (Rosch et al 1976). The reason for this is unclear but it could reflect a qualitatively different semantic organisation in schizophrenia. Of these 3 studies (divided into the different levels so n = 7), heterogeneity was significant (Q (6) = 25.45, p <.001), a random effects combined mean was large at 0.77 (0.072), 0.25 – 1.30) and a failsafe N = 60.

Table 3: Bottom up Deterioration (If bottom up deterioration occurs then errors increase as sorting requires more detailed semantic knowledge).

Level	Cards (Hodges Semantic Memory Battery (Hodges and Patterson 1996))
1. Superordinate	Living vs. Non Living
2. Basic Level	Animals vs. Birds vs. Fruit
3. Subordinate	Animals that eat meat vs. Animals that don't eat meat

Another way of assessing categorisation in schizophrenia is to ask people to freely sort objects or pictures into groups that go best together (for example the Category Generation Task or CGT to assess free sorting categorisation in schizophrenia. This involves asking participants to form groups out of 45 cards with pictures on of animals, fruit, body parts, clothing and vehicles. The lack of structure in this task enables researchers to assess individual categorisation styles and preferences with

regard to the groups formed. Unlike the structured sorting task, free sorting is likely to draw upon more executive processes such as retrieval and strategy (Shallice, 1988). In addition, free sorting categorisation tasks have been used to assess thought disorder because they are believed to capture idiosyncratic connections between concepts which resemble disordered thought. In total, 3 studies have reported abnormalities on tasks of free-sorting categorisation (Green et al 2004; Lawrence et al 2007; Cutting, David and Murphy 1987). When the card groups that were formed by a participant were analyzed, Green et al (2004) reported that many people with schizophrenia showed overinclusion mimicking early studies (e.g. Epstein 1953). Overinclusion is defined as "an inability to maintain the boundaries of the problem and to restrict ...operations within its limits. All sorts of objects from outside ... are brought into the situation" (Cameron 1939). Overinclusion is conceptually similar to the responding pattern seen in the Chen et al (1994) study of extended category boundaries. This performance pattern is not present in all people with schizophrenia however, since in the study by Green et al (2004) only 9 out of 32 patients overincluded on the CGT. On top of this, two studies have reported a pattern of underinclusion where a semantic category is subdivided e.g. car, bus and train separated to the other vehicles. In fact in the study by Green et al (2004), around a third of patients showed evidence of underinclusive thinking on the CGT. A study by Lawrence et al (2007) found evidence for both overinclusion and underinclusion, unrelated to poor performance on semantic memory tests such as naming or associations and also not seen to be determined by IQ or executive dysfunction in schizophrenia. Of these 3 studies, heterogeneity was significant ($Q(3) = 18.51$, $p < .001$), random effects weighted mean = medium at -0.39 (variance = 0.17), 95 % confidence limits = -1.19 – 0.4. Fail safe N = 3.

To conclude, tasks of categorisation do not always elicit impairments in schizophrenia and differences in task requirements can strongly shape performance. For structured categorisation tasks the majority report impairments. One problem with these studies is that they tend to test only knowledge of the animal category which is known to produce accuracy advantages over other categories (e.g. Caramazza and Mahon 2003). Nevertheless the Chen et al (1994) study, although not replicated, provides evidence of a qualitatively different semantic memory in schizophrenia. Similarly, unstructured categorisation tasks have shown that some people with schizophrenia have a qualitatively different way of grouping concepts together which could reflect a more idiosyncratic semantic memory. However, it is hard to rule out the additional cognitive processes which could be influencing this performance pattern such as working memory, strategic processes and planning.

2.3.5.1. Symptoms and Categorisation

As with many of the semantic memory tasks, not all people with schizophrenia show impairments and the heterogeneity of this group in terms of symptoms could perhaps explain these differences. On the classification tasks, whilst some studies found no relationship between FTD and categorisation ability (Matsumoto et al 2005) others found correlations to be significant (Chen et al 1994). Overinclusion on cognitive tasks was originally viewed as evidence of overinclusive thinking (Payne 1973), which is central to the concept of FTD although this relationship was not found in either the Green et al (2004), Lawrence et al 2007 or Cutting, David and Murphy

(1987) studies. In the study by Lawrence et al 2007 however underinclusion was seen to be correlated with FTD.

2.3.6. Semantic Priming in schizophrenia

Traditional models of semantic memory (e.g. Collins and Loftus 1975) see semantic memory as stored in a network of concepts. When a concept is activated, activation spreads to related concepts, stored nearby, which then have a lower expectancy threshold and are more easily brought to attention. In priming tasks the reaction times between prime and target are what are being assessed. The most common way of measuring priming is to use a Lexical Decision Task which is where participants are asked to state whether a phonemic string is a word or not by saying yes and no and pressing corresponding keys. An example of direct priming is if the prime is "doctor" then the response to the target word "nurse" should be faster than if the target was an unrelated word. Abnormalities on priming tasks are assessed by comparing the reaction times in schizophrenia to normative data for example if there is a larger (or smaller) difference in response time between the prime and the target when compared to a normative sample then this is seen as abnormal. Hyperpriming refers to when reductions in reaction times on priming measures are greater than normal and hypopriming is when reductions in reaction times are less than normal or absent. A review of the semantic priming literature in schizophrenia was carried out by Minzenberg et al in 2002 and included 19 papers. This review is extensive and based on any papers which "include all English Language reports (from peer reviewed journals) of single word semantic priming studies involving participants with schizophrenia". The authors conclude that findings are distributed fairly evenly between hyperpriming, normal priming and hypopriming. Minzenberg et al (2002) report that priming is consistently found to be abnormal where attentional/ executive demands are high and surmise that this is due to impairments in the use of cognitive strategies. Our search identified 37 papers, 14 of which were also included in the review by Minzenberg et al (2002). For the effect sizes of each study see Table 7, Appendix A. The Q test of homogeneity was again significant ($Q(82) = 477.74$, $p < .001$) and therefore a random effects model was used. The combined weighted effect size was very small at -0.021, variance = 0.006, confidence intervals = -0.18 – 0.14. The fail safe N was 0.

This review found a large number (n = 22, 59%) of the 37 studies that have found some evidence of normal levels of semantic priming in schizophrenia (i.e. Rossell 2004; Surguladze et al 2002; Besche-Richard et al 2005; Minzenberg et al 2003; Chenery et al 2004; Bullen and Hemsley 1987; Quelen et al 2005; Mathalon et al 2002; Passerieux et al 1997; Spitzer et al 1994; Narr et al 2003; Spitzer et al 1993a: Spitzer et al 1993b; Ober et al 1997; Moritz et al 2001a; Moritz et al 2001b; Kuperberg et al 2007; Aloia et al 1998; Ober et al 1995; Nestor et al 2006; Barch et al 1996; Manschreck et al 1988). Of perhaps the greatest interest among the priming studies is those that report enhanced or hyper priming especially considering the wide ranging cognitive deficits and also the evidence supporting impairments in semantic memory in schizophrenia. In their review, Minzenberg et al (2002) found 7 studies (out of 19) which reported hyperpriming in schizophrenia. In the current review 17 of the 37 studies reported some evidence of hyperpriming (Henik et al 1995: Weisbord et al 1998; Spitzer et al 1994; Spitzer et al 1993a; Spitzer et al 1993b; Moritz et al 2001a; Moritz et al 2001b; Moritz et al 2002: Gouzoulis-Mayfrank et al 2003;

Lecardeur et al 2007; Chenery et al 2004; Wagner et al 2006; Baving et al 2001; Vinogradov et al 2002; Aloia et al 1998; Manschreck et al 1988; Titone et al 2000). Eleven studies out of 37 were identified which have reported the opposite pattern, hypopriming in schizophrenia (i.e. Hokama et al 2003; Aloia et al 1998; Chapin et al 1989; Ober et al 1997; Barch et al 1999; Chenery et al 2004; Passerieux et al 1997; Vinogradov et al 1992; Fuentes and Santiago 1999; Bullen and Hemsley 1987; Moritz et al 2002).A difficulty with hypopriming results though is that often processing is generally slower in schizophrenia (Neuchterlein et al 1977) and therefore comparing RTs with unmatched controls is methodologically problematic as the relative response time differences between prime and target will be larger if responses are generally slower. Despite this due to slower processing abilities decreased reaction times would be expected in people with schizophrenia and therefore reports of hyperpriming are perhaps all the more remarkable.

Studies distinguish between automatic and controlled semantic priming. Automatic semantic priming refers to the spread of activation in the semantic network and is different to controlled semantic priming which utilises attention and expectancy mechanisms. Automatic and controlled semantic priming are generally only differentiated via the length of time between the stimulus and the target in the lexical decision task (the Stimulus Onset Asynchrony SOA). In automatic priming the SOA is short (>500 ms) and in controlled priming it is longer (500 > ms). The Minzenberg et al (2002) review concluded that impairments on priming tasks seem to occur mainly when attentional/ cognitive strategies are required i.e. usually with longer SOAs. In this meta-analysis, the length of the SOA was entered as a moderator. A t test found that there was a significant difference between the studies that used short SOAs (mean effect size (random model) = -0.22 (variance = 0.016)) and the studies that used long SOAs (mean effect size (random model) = 0.113 (variance 0.011)); t (70) = 12.18, p <.0001. Therefore it appears that under automatic conditions, semantic priming is normal or enhanced in schizophrenia whereas hypopriming is more frequently found under controlled conditions.

Consistent with the Minzenberg et al (2002) review, the 37 papers reviewed here report heterogeneous findings with a high number of studies reporting normal priming and a very small combined effect size; perhaps as an artefact of the fact that hyperpriming is frequently reported in schizophrenia. The diverse nature of the findings, Minzenberg et al (2002) suggests is due to the heterogeneity of schizophrenia and it is likely that only individuals with certain symptoms, for example FTD will display abnormal semantic priming. Although hyperpriming has not been consistently replicated, the fact that some people with schizophrenia who normally show slower reaction times and information processing on most tasks, respond quicker on priming tasks, suggests that this impairment is dissociable from diffuse cognitive impairments. As with the other tests of semantic memory, once the role of additional cognitive processes are controlled for, in this case attention and executive abilities (such as planning), the amount of evidence implicating a semantic memory impairment in schizophrenia is much reduced. This is supported by the data suggesting that priming is significantly more likely to be impaired under controlled conditions, where executive processes are required.

2.3.6.1. Symptoms and Priming

Hyperpriming has been traditionally linked to the presence of FTD (e.g. Spitzer et al 1993a, Spitzer et al 1993b, Manschreck et al 1988). A relationship between hyperpriming and Formal Thought Disorder was also reported by Moritz et al (2001a), Moritz et al (2001 b), Moritz et al (2002), Chenery et al (2004), Passerieux et al (1997) and Gouzolis–Mayfrank et al (2003) who also found that hyperpriming was only present during the acute psychotic episode indicating that it is strongly related to symptom presence (state) and not overall illness (trait). Therefore it would appear that hyperpriming in schizophrenia is directly related to disorganised thinking. Authors such as Spitzer (1997), Maher et al (1987) and Manschrek et al (1988) have explained hyperpriming as a spreading of activation throughout the semantic network causing more related concepts to become activated than is normal. Further evidence for the spreading activation theory comes from studies which found hyperpriming on indirect semantic priming tasks (e.g. Moritz et al 2001a; Spitzer et al 1993a; Moritz et al 2002) where only indirectly related associations are used between prime and target e.g. stripes as a prime and lion as a target. Hyperpriming on indirect priming tasks has not always been replicated however (Gouzoulis-Mayfrank et al 2003) and hypopriming has also been reported to occur selectively in FTD patients (Aloia et al 1998). Minzenberg et al (2002) emphasised the methodological difficulties present in studies that have reported relationships between FTD and hyperpriming and stated that "it is presently unclear how semantic priming disturbances may be related to TD as manifested clinically". Nevertheless, using FTD as a moderator, this meta-analysis found that there was a significant difference ($t(43) = 2.38$, $p = 0.022$) between the studies assessing patients with FTD (combined mean effect size (random model) = 0.132, variance = 0.021) to those without FTD (combined mean effect size (random model) = 0.043, variance = 0.008). This reflects greater differences between the performances of patients with FTD compared with normal controls although not necessarily in the direction of hyperpriming in FTD.

2.3.7. Miscellaneous Semantic Tasks in schizophrenia

Ten studies have looked at the performance of people with schizophrenia on non typical tasks of semantic memory and six (75%) reported impairments. These results are also worth noting as they may contribute to a pattern of impairment. As these studies differ substantially in terms of the measures used, a combined weighted effect size is not appropriate but Table 8 in Appendix A shows the effect sizes for each study which varied from 0.13 – 3.45.

The Concrete and Abstract Word Synonym Test (Warrington et al 1998) is typically used to measure semantic memory functioning. It involves identifying the synonyms of a number of words which are graded for difficulty. Five studies have used this task or other tasks involving synonyms; 2 (Barrera et al 2005, Tendolkar et al 2004) report preserved performance and 3 (Rossell and David 2006; Clare et al 1993; Bullen and Hemsley 1987) report impaired performance. As noted by Clare et al (1993) the retrieval demands of the synonyms task are minimal making it a fairly pure measure of semantic memory. Understanding why the results of these 4 studies oppose each other is difficult as it appears that neither illness chronicity nor IQ factors can separate the groups.

An interesting study by Assaf et al (2006) used a Semantic Object Recall task where two objects are presented which together form an additional concept for example honey and sting represent the concept bee. The people with schizophrenia tended to over-recall on this task meaning they were finding connections between objects that were not found by controls. This is similar to what was reported on categorisation tasks such as the CGT where unrelated items are linked together, resembling loosening of associations. A study by Bobes et al (1996) reported difficulties in selecting related pairs of pictures in a group of people with schizophrenia. Also a study by Low et al (2006) found that people with schizophrenia were slower in deciding whether an image was a natural or artificial object. Similarly, a study by Pelad et al (2005) found that in their sample patients with schizophrenia found it difficult to make associations between words when the context was vague.
A seminal study by Clare et al (1993) used a task called the Silly Sentences Task which involves verifying the semantic accuracy of particular sentences, some of which are nonsensical. Clare et al (1993), using a group matched to controls on the NART, reported performance deficits on this task.

A couple of studies have assessed the ability of patients to provide definitions for certain words either spontaneously or via selecting an option from multiple choice e.g. McKay et al (1996). This task is conceptually very similar to IQ measures such as the Vocabulary scale in the WAIS where participants are asked to describe what words mean. Therefore, these tasks are likely to correlate strongly with IQ. Not surprisingly people with schizophrenia perform worse than controls on this task e.g. Rossell and David (2006). In the McKay et al (1996) study, performance on the definitions task still remained significantly different from the controls even when IQ was covaried although this was only derived from NART scores and not a measure of current IQ (see previous critique of using NART as a proxy measure of IQ). In conclusion, results from miscellaneous semantic memory tasks do supplement the wealth of knowledge about the semantic memory impairment in schizophrenia. It appears that difficulties with associations between concepts are a common thread from these studies. In addition, tasks involving identifying synonyms produce mixed results and perhaps not surprisingly, considering the link with IQ, tasks involving the production of definitions elicit impairments in schizophrenia.

2.3.7.1. Symptoms and Miscellaneous tasks

In the study by Pelad et al (2005), people with FTD were more impaired on the task of association. This is similar to the fact that in free sorting categorisation tasks where context is not explicitly apparent, people with schizophrenia have problems forming coherent groups. Pelad et al (2005) believe that the results of their study are compatible with the spreading activation theory of semantic memory in thought disorder, specifically that "any shift in congruity causes a spread of activation such that the patients cannot decide whether word pairs make sense or not". Similarly in the studies by Low et al (2006) and Assaf et al (2005), also involving associations, impairments were significantly correlated with the presence of FTD.

2.3.8. Conclusions of the Literature Review/ Meta-Analysis

This review has systematically considered data from 96 papers assessing people with schizophrenia on a wide range of tests of semantic memory including naming, word-picture matching, semantic fluency, associations, priming, categorisation and also several miscellaneous tasks. The majority of papers report semantic memory impairments in schizophrenia although there are several studies that report preserved functioning. From the accumulated results one can gauge some sense of a typical profile of impairment in schizophrenia. It would appear that there is a widespread impairment but that some tests consistently elicit more impairments than others (see Table4). On tests of priming and especially word picture matching there are fewer studies which report cognitive impairments. This could be due to the less demanding nature of these tests as they measure largely pure/ automatic semantic memory processes. In fact the varied profile of impairment supports the claim that semantic knowledge is relatively intact in schizophrenia as it would appear that when task demands are minimal impairments are infrequently reported. This goes against the suggestion that there is a storage disorder in schizophrenia.

Table 4: The profile of impairment across tasks

Task	Percentage of studies that reported an impairment	Percentage of studies that found preserved performance
Naming (n = 15)	67%	33%
WPM (n = 5)	20%	80%
Semantic Fluency (n = 38)	92%	8%
Associations (n = 5)	60%	40%
Categorisation (n = 11)	91%	9%
Priming (n = 43)	61%	59%
Miscellaneous (n = 8)	75%	25%

Table 5 shows the combined effect sizes for each type of measure. The effect sizes reflect the profile seen in Table 4 where large impairments are seen in tests of naming and semantic fluency. On the associations and word picture matching tasks, effect sizes are in the medium range and in the categorisation and priming tasks, effect sizes are small. Therefore for the word-picture matching studies where impairments are not frequently reported, there may be substantial differences between groups and in the categorisation tasks, the opposite pattern may be true with frequent significant differences but small effect sizes.

Table 5: Combined Effect Sizes for each type of task.

Task	Combined Effect Size (CIs)	Fail Safe N
Naming	-1.45 (-1.86 - -1.04) LARGE	2005
WPM	-0.58 (-0.92 - - 0.24) MEDIUM	41
Semantic Fluency	-1.33 (-1.15 - - 1.11) LARGE	8474
Associations	0.63 (0.003 – 1.28) MEDIUM	26
Categorisation	0.11 (-0.37 – 0.59) SMALL	0
Priming	-0.021 (-0.18 – -0.14) SMALL	0
Miscellaneous	Range from -0.13 – 3.45 SMALL – LARGE	n/a

Because the various tests of semantic memory differ in the demands they make upon intellectual and executive abilities it is possible that on tasks where semantic memory impairments are more consistently reported this is due to a task's greater effort load. The evidence for this is equivocal. On tests of naming there appears to be some evidence to suggest that impairments are due to diffuse cognitive deficits as when multiple semantic memory tests are employed, naming ability is often relatively well preserved (e.g. Lawrence et al 2007; Al-Uzri et al 2004 and Barrera et al 2005). One problem is that mentally well controls nearly always have superior cognitive abilities and therefore it is difficult to match groups on measures of current cognitive ability. Therefore most studies are only able to use estimates of pre-morbid IQ which is known to be problematic (e.g. Russell et al 2004). Where groups have been matched to neurologically impaired comparison groups e.g. Temporal Lobe Epilepsy (Giovannetti et al 2003) or ABI (Lawrence et al 2007), this provides a better comparison group as the design permits double dissociation and removes the problem of different cognitive ability. The conclusions from these studies are that when current IQ is controlled for, performance on tasks of naming is relatively intact. Aside from the naming studies, very few studies have been able to match their groups for current IQ and the data is equivocal (based on covariance analyses largely) as to whether poor intellectual ability can explain semantic memory impairments in schizophrenia.

There is far more data available to implicate a role for an executive dysfunction in explaining semantic memory impairments. From the verbal fluency studies, a number of studies using two different methods strong in internal validity concluding that poor retrieval and the ability to switch between recall strategies provide the best explanation for poor semantic fluency performance. Furthermore in the priming studies, it was found that controlled semantic priming (where there are greater demands on attentional and expectancy mechanisms) elicited greater priming abnormalities than under automatic conditions. A study by Lawrence et al (2007) matched a group of patients with schizophrenia to a neurological comparison group on the basis of both IQ and intellectual functioning. This study found that compared to the neurological control group, people with schizophrenia were impaired on the semantic association and sorting tests on a semantic battery but not the naming and WPM tests suggesting that once executive functioning is controlled for only certain tests elicit impairments. Nevertheless the neurological comparison group, who had a selective executive dysfunction performed at ceiling on all tests of semantic memory which goes against the claim that an executive dysfunction per se leads to semantic memory impairments on these tests. Interestingly considering that we know the temporal and frontal lobes are the main brain regions involved in semantic memory processing, there are surprisingly few studies where groups of patients with frontal or temporal lobe damage are recruited for comparison purposes. In fact there are a number of similarities qualitatively with the pattern of semantic memory impairment observed in patients with Alzheimer's Dementia particularly in the priming (Giffard et al 2005) and semantic fluency literature (Henry et al 2004).

One school of thought is that schizophrenia is a heterogeneous disorder both in terms of symptoms and in terms of cognitive deficits (Kremen et al (2004)). Liddle's (Liddle 1987 a) classic symptom subtypes of schizophrenia have been linked with associated neuropsychological impairments, albeit not entirely successfully (e.g. Simon et al 2003). There have also been attempts to classify the cognitive subtypes of

schizophrenia. Proposed cognitive subtypes in schizophrenia include those with deficits on frontal/ executive tests, temporal/ memory tests and those who have a widespread impairment (Kremen et al 2004). In addition, there are several studies which have claimed that there is a neuropsychologically normal subgroup of people with schizophrenia (e.g. Palmer 1997). Heinricks and Awad (1993) believed there are 5 cognitive subtypes of schizophrenia ;1) an executive subtype, 2) a normative subtype, 3) an executive-motor subtype, 4) a dementia subtype and 5) a motor subtype. This classification however was only based on results from four tasks. Nevertheless, it could be the case that in the semantic memory literature, the reason that contradictory findings are reported is that only a subtype of patients has semantic memory problems. More research is needed to determine whether this truly is the case and if so whether this particular subtype share certain symptoms. In addition the cognitive impairments in schizophrenia have been shown to vary over time (e.g .Matthysse et al 1999) and this inconsistency could also explain sampling variations.

Few studies reviewed here have looked at the effect of illness chronicity on semantic memory functioning specifically but of those that have (e.g McKay et al 1996) and in the wider literature (e.g. Maher et al 1996; Tamlyn et al 1992; Chan et al 2000; Paulsen et al 1996) there is some evidence that semantic memory performance worsens as illness duration increases. Although like the studies assessing more generalised impairments, there are several studies (e.g Sumiyoshi et al 2005, Gouzoulis-Mayfrank et al 2003) which have also reported impaired semantic memory in acutely ill patients and data from the meta-analysis would suggest that chronicity is not necessarily related to anomia in schizophrenia. In a study by Paulsen et al (1996) it was reported that patients with early onset schizophrenia performed worse on a test of semantic memory than patients who had developed schizophrenia later in life. If semantic memory impairments are worse in early onset schizophrenia then this could imply a neurodevelopmental aetiology. It is therefore surprising that in the literature, no one has compared some of these aspects of semantic memory which are seen as interesting models of schizophrenia with other neurodevelopmental disorders.

Several studies have looked at whether semantic memory functioning in schizophrenia is affected by neuroleptic medication. Research such as by Sumiyoshi et al (2006) has claimed that semantic memory organisation in schizophrenia improves following treatments with atypical antipsychotics such as olanzapine or ziprasidone. Sumiyoshi et al (2006) found that using MDS analysis, semantic networks which were found at baseline to lack structure, became more meaningful following a course of treatment with atypical antipsychotics. Similarly, a study by Goldberg et al (2000) found that semantic priming improved in a group of people with schizophrenia who were receiving neuroleptic medication compared to a placebo group. However, other work has found no effects or only limited effects of neuroleptics on semantic memory functioning (Vinogradov et al 2002) and a study by Albus et al (2006) found that verbal fluency performance was worse in a medicated group (compared to a non medicated group) with first episode psychosis. Brebion et al (2004) found that the degree of anticholinergic medication in schizophrenia predicted memory impairment especially with regard to semantic memory although in a study by Duffy and O'Carroll (1994) the level of anticholinergic medication did not predict semantic memory performance. Despite these noted effects of medication, several studies have found severe cognitive impairments in patients who are drug naïve (Mc

Creadie et al 1997, Saykin et al 1994) or who have been taken off their medication (Blanchard and Neale 1994). In sum, cognitive impairments in schizophrenia do not seem to be explainable by medication but are nevertheless likely to be influenced by it either for better or worse. As with chronicity, there are few studies that have reported on the effects of medication on semantic memory specifically but those that have tend to present mixed findings.

Several studies have reported impairments in the way in which concepts are associated on tasks of semantic memory (e.g. Lawrence et al 2007, Green et al 2004). This performance pattern can resemble that described by Bleuler as loosening of associations, once seen as a cardinal symptom of schizophrenia. The tasks of semantic memory which elicit this type of loosening of association are categorisation, association tests, some miscellaneous tasks, and perhaps indirect semantic priming. There is some evidence to suggest that a disorganised semantic memory relates to the presence of FTD in schizophrenia especially on tests of naming and priming. However, more work needs to be done in particular to understand the relationship between loosening of associations as evidenced clinically (as FTD) and the impairments seen on tasks of semantic memory. Kerns and Berenbaum (2002) state the need for people with and without FTD in schizophrenia to be compared on a battery of semantic memory tests and perhaps this is the way forward. Although relationships between negative symptoms (Sumiyoshi et al 2005) and semantic memory and also delusions (Rossell et al 1999) and semantic memory have been reported, studies are too few in number to support the conclusion of a strong relationship.

In sum, the evidence suggests that semantic memory is impaired in schizophrenia but not in all patients and not on all tests. This inconsistency supports the claim that knowledge is not degraded in schizophrenia and difficulties lie largely with knowledge retrieval. The evidence for a confounding effect of illness chronicity or low IQ is equivocal and impeded by the limited number of studies and the difficulties with matching for IQ in patients and controls. Where studies have directly compared people with schizophrenia to neurological comparison groups, matched on current IQ, relatively intact performance on a number of measures has been reported. A strong role is implicated for an executive dysfunction as explaining some of the semantic fluency performance especially semantic priming and verbal fluency. The methods used on these tasks have a within subjects design and therefore good internal validity which bypasses the methodological problems inherent in comparing with control data. Although not consistently replicated, the meta-analysis data for the naming and priming studies support the claim that FTD is related to a semantic memory impairment although despite the traditional view of Spitzer and colleagues, the analysis suggests that FTD leads to greater deficits in impairments and not enhanced performance. Tests of categorisation and association can be seen to be cognitive measures of loosening of associations but the data supporting a link between performance on these tasks and FTD is equivocal.

From the literature review, a number of key areas have been identified, which need further research. These are:

1. Once IQ and executive functioning is taken into account is semantic memory really impaired in schizophrenia across a number of different tests?
2. Is semantic memory qualitatively different in schizophrenia as suggested by performance on categorisation tasks?
3. Does the semantic memory impairment in schizophrenia meet criteria for either a degraded store, impaired retrieval or a disorganised semantic network?
4. How do semantic memory impairments in schizophrenia relate to symptoms especially FTD?

Chapter 3: Review of the literature looking at potential explanations for the semantic memory impairment in schizophrenia. Is it due to a storage disorder, access disorder or a disorganised semantic memory?

From the meta-analysis it is apparent that the profile of semantic memory impairment in schizophrenia is inconsistent and dependent on task demands. This and also the evidence from the meta-analysis supporting a link between semantic memory impairments and an executive dysfunction in schizophrenia, would suggest that the semantic memory impairment in schizophrenia arises largely from retrieval problems and not a deficit in semantic knowledge. Warrington and Shallice (1979) developed a set of criteria (see Table 1) for distinguishing between a neurological deficit where semantic representations are degraded/ lost, from an impairment in semantic memory which arises more from difficulties retrieving stored knowledge. These criteria have been utilised to classify the semantic memory impairments present in neurodegenerative conditions such as Alzheimer's dementia (e.g. Chertkow and Bub 1990) and also have become a popular way to classify the semantic memory impairments in schizophrenia (e.g. Rossell and David 2006). Bleuler and Kraepelin both appear to have had different opinions as to whether there is a storage or access disorder in schizophrenia. Kraepelin (1919) is quoted as saying about cognition in schizophrenia; "*memory… acquired knowledge and expertness remains sometimes fairly well preserved, sometimes they undergo considerable loss*". However Bleuler stated (1911) that "*the actual amount of knowledge remains preserved… but it is not always available or it is employed in the wrong way."* A definitive conclusion is yet to be reached however as to whether knowledge is lost in schizophrenia or whether the problems are due to difficulties with retrieval. Although this distinction has been criticised as invalid as a cognitive and neurological model of semantic memory impairments (e.g. Rapp and Caramazza 1993), it is still used to assess the memory impairments in schizophrenia (e.g. most recently Rossell and David 2006).

3.1. Studies analysing Error Consistency

Probably the most important of Warrington and Shallice's 4 criteria (see Table 1, page 14), item consistency refers to the tendency of the participant to produce errors consistently for the same individual items across the different tests of semantic memory i.e. be unable to name an apple and also be unable to point it out in the Word-Picture Matching test. The implication is that if the memory representation of an item is lost/ degraded then it will be impervious to retrieval, independent of task, modality or difficulty. A problem with item retrieval is indicated by error inconsistencies, suggesting that with the correct testing paradigm, retrieval can produce the correct response.

The majority of studies which have investigated the consistency of responding in schizophrenia have found a consistent response profile (Rossell and David 2006; Leeson et al 2005a; Laws et al 2000; Leeson et al 2006). However, there are some reports of inconsistency (e.g. Al-Uzri et al 2004). One way of measuring consistency is to use the two parameter stochastic Markov chain model (Faglioni and Botti 1993) which looks at the consistency of responses across two tests or across two testing

occasions. This model provides the probability that an item is stored (s) and that an item will be retrieved from store (r) whilst taking into account chance consistency. Four studies were reviewed which have used this formula to calculate consistency of responses over time in people with schizophrenia. Leeson et al (2006) tested 32 people with schizophrenia on a picture naming task and found both reduced s values and r values in schizophrenia (limited only to those with high FTD). In addition, the 2005a study by Leeson et al which looked at naming consistency over time found both reduced s and r values in their schizophrenia sample. Leeson et al (2005a, 2006) concluded from both these studies that both storage and access is impaired in schizophrenia, concurring with a study by Laws et al (2000). Laws et al (2000) looked at naming performance over two separate occasions in 22 people with schizophrenia. They found that, based on consistency analyses, the majority of patients fitted the criteria for a storage disorder. The only study reviewed here that did not use this model to calculate consistency was Al-Uzri et al (2004) who directly compared performance across two testing sessions using t tests. This study found inconsistencies in errors suggestive of an access disorder. In sum therefore, although the majority of studies find consistency of errors in schizophrenia indicating a degraded store, there is some suggestion that when different methods of statistical analyses are employed, this result changes.

3.2. Studies analysing Cueing effects

Warrington and Shallice (1979) reason that if a person has lost stored semantic knowledge then they should not be able to access that knowledge when semantic cues are provided. As semantic cues promote better access/ retrieval of items then it is believed that if performance improves with cueing then one can conclude that retrieval mechanisms were at fault and that information had always been available. Two studies reviewed here have looked at the role of semantic cueing in schizophrenia. An early study by Joyce et al (1996) found that 80% of their sample of 50 people with schizophrenia produced more words on a category fluency task when they had been provided with a cue. Together with the evidence that they showed a normal pattern of performance on the fluency tests, in that they performed relatively better on the category fluency task compared to the letter fluency task, the authors concluded that the problem was with access and not store. A more recent study by Al-Uzri et al (2004) which tested 12 people with schizophrenia on a battery of semantic memory tasks found improvements on performance following a cue on two tasks of naming, picture naming and naming to description.

In addition, studies such as Rossell and David (2006) and Spitzer et al (1993, 1994) found hyperpriming which has also been proposed by Warrington (1975) to indicate a storage disorder. The logic of this differs greatly to that proposed by Spitzer and colleagues to explain hyperpriming. The rationale behind Warrington's claim is that as specific attributes become lost, similar concepts can overlap and become confused. This leads to faster reaction times (e.g. hyper priming). Although conceptually similar to the theory of how cueing aids recall, priming tests are methodologically different and this must be considered when comparing the two sets of results. In sum therefore, studies which have assessed cueing have found that performance is aided by cuing and therefore that semantic memory impairments are explainable by retrieval difficulties. However the recent study by Rossell and David (2006) which utilised

semantic priming found that there was some indication for hyperpriming although not quite in the way they would expect for a storage disorder.

3.3. Bottom- up Deterioration

It is believed that subordinate, detailed attribute information is more vulnerable to loss as part of a storage disorder than superordinate, general category information. Therefore one sign of a storage disorder is relative difficulties with subordinate information.

One study has reported bottom up deterioration in schizophrenia (McKay et al 1996). However, it is highly feasible that this effect could be caused by differences in the relative difficulty of the sorting tasks at the different levels as it has been found (Cox et al 1996) that tasks assessing more detailed attribute knowledge are more demanding on intelligence and executive processes. In the study by Al-Uzri et al (2004), a different pattern to bottom up deterioration was reported on a task of semantic categorisation.

3.4. Frequency

Further evidence for a storage disorder comes from studies which report that patients with schizophrenia produce more errors with low frequency words i.e. words that occur less often in common speech. Warrington and Shallice (1979) stated that words that are less typical/ frequent were more likely to become degraded as part of a storage disorder because they are used less often and have fewer connections with other concepts.

Two studies have reported a frequency effect in schizophrenia. For example Laws et al (2000) found a very significant frequency effect. Rossell and David (2006) also found a frequency effect on the majority of their semantic tests in the schizophrenia group. However this effect was also found in the controls. In a similar way to the bottom up deterioration theory however, it could be the case that less frequent words are harder to retrieve and difficulties reflect an access disorder rather than a loss of stored information (e.g. Rapp and Caramazza 1993). Furthermore, a frequency effect on reaction times is well established in normative data (e.g. Carroll and White 1973) so it is problematic to report this as evidence for a storage disorder (e.g. Rossell and David 2006). It would be preferable to analyse errors for frequency to determine whether more infrequently used words incur more errors (as in the Laws et al (2000) study) rather to assume that a frequency effect as determined by reaction times is evidence for a deficit.

Table 6 provides a summary of the studies that have assessed the semantic memory impairments in schizophrenia with regards to either or all of the four criteria specified by Warrington and Shallice to distinguish a storage from an access disorder. In sum, based on the four criteria of Warrington and Shallice, it is hard to say with any conviction whether the semantic memory impairment in schizophrenia meets the criteria for a degraded store or difficulties with retrieval. The majority of studies report a storage disorder which is evident in high consistency in the items eliciting errors on tasks of semantic memory, a loss of subordinate/attribute knowledge over

superordinate knowledge (although the evidence for this is equivocal) and a tendency to make more errors on items with low frequency of usage. This pattern suggests that there is a degradation of semantic knowledge in schizophrenia meaning that certain items or connections are lost to retrieval. This conclusion, however, does appear to depend on the criteria and further work is needed to understand whether this is attributable to specific methodology e.g. in the case of item consistency. When cuing is assessed, access disorders are reported. Nevertheless there are very few studies which have investigated this issue and more work is required in order to form a valid conclusion.

Table 6: Summary of studies investigating the storage/ access dichotomy

	Storage	Access
Error Consistency (n = 5)	4	1
Cuing (n = 2)	0	2
Bottom up Deterioration (n = 2)	1	1
Frequency (n = 2)	2	0

3.5. Evidence from Verbal Fluency Tasks

As mentioned, several studies have compared the performance of people with schizophrenia on a letter fluency task and a semantic fluency task. It is suggested (e.g. Monsch et al 1994) that a disproportionate impairment on category fluency compared to letter fluency reflects a breakdown in semantic knowledge over and above retrieval difficulties which affect performance on both tasks. A seminal study by Allen et al (1993), utilising a verbal fluency paradigm provided evidence of a normal sized word lexicon in schizophrenia refuting the claim that items become lost. Although the patients were initially impaired on verbal fluency, when the task was repeated they recalled a different set of words resulting in a total number of different words which was comparable to the control group. The authors claim that difficulties with verbal fluency are to do with initiating a search and with the retrieval of exemplars and do not reflect a loss of stored representations. This finding was replicated by Elvevag et al (2001), however an attempt to replicate the results of the Allen study by Chen et al (2000) failed and a smaller lexicon in schizophrenia was reported. Nevertheless as reviewed above the majority of studies found a disproportionate level of semantic to phonemic fluency errors (Minzenberg et al 2002) although retrieval processes were also strongly implicated in these impairments.

In sum the verbal fluency literature lends some support to the theory that there is a storage disorder in schizophrenia but as with the other studies, not enough work has been done to be able to convincingly say for sure that the semantic memory impairment in schizophrenia fits with either disorder.

3.5. Review of the literature examining whether there is a disorganised semantic memory in schizophrenia

One possible way of looking at how an individual's semantic memory is organised is through Multi-Dimensional Scaling (MDS) Analysis. Based on a person's responses from a semantic fluency or a triadic comparison task (say which 2 words out of 3 are the most similar), responses are analysed in terms of the way they are clustered together and the distances between them. This is based on their similarity/ dissimilarity in terms of the order in which they are recalled in the fluency test e.g. if cat is recalled following dog then this is seen to be similar and hence stored closer together in the semantic network (Paulsen et al 1996). A few studies have used MDS analysis or pathfinder analysis to assess the semantic networks of people with schizophrenia. Aloia et al (1996) used MDS analysis to map the category fluency responses of a group of people with schizophrenia. Unlike controls, Aloia et al found that the semantic clusters seen in the maps of the schizophrenia group were loosely clustered and not logically ordered. A study by Paulsen et al (1996) compared the semantic maps of people with early onset and late onset schizophrenia and found that only the early onset people had qualitatively different maps to the controls and were disorganised. There was even more difference when the semantic maps of the different subtypes of schizophrenia were compared, the non paranoid group's maps were more similar to the controls whereas the non paranoid maps were highly different. Of particular note was the fact that in the non paranoid group, some common animal names were linked with atypical associates equally to typical ones so that a cow was seen as having as much in common with a horse as with a zebra. In a recent study by Sumiyoshi et al (2005) MDS analysis was carried out based on verbal fluency responses. It was found that people with schizophrenia had a less clearly organised semantic map which lacked certain dimensions which controls used to group animals. There was even more difference between people with alogia and people without alogia in terms of their semantic maps. This study replicated their earlier study (Sumiyoshi et al 2001) which using a similar procedure found that certain dimensions which controls used to group animals weren't used by the people with schizophrenia. In Figure 3, an example is given of the maps generated by the MDS analysis for a group of people with schizophrenia (map b) and a group of healthy controls (map a). In the control groups' map the animals were recalled based on four dimensions (large – upper right quadrant, wild – lower right quadrant, small – upper left quadrant and domestic – upper left quadrant). In the schizophrenia group, there was a lack of meaningful dimension and animals appeared to be recalled more randomly.

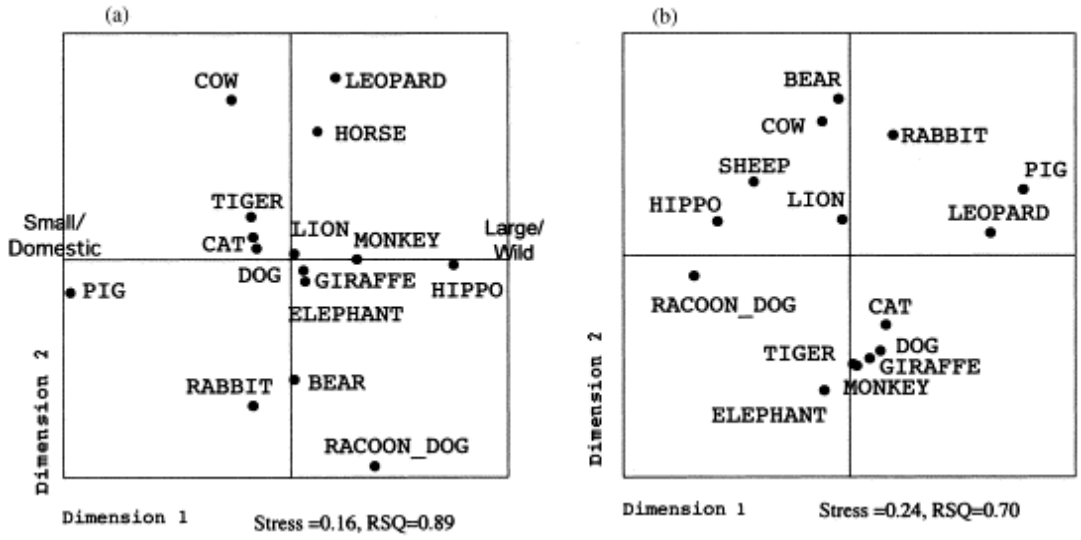


Figure 3: Semantic Maps of the animal category for controls (a) and people with schizophrenia (b) using MDS analysis (Sumiyoshi et al 2001).

In general these studies seem to provide strong evidence that semantic memory is organised differently in at least some people with schizophrenia. There is some evidence to suggest that disorganisation is closely linked to the presence of certain symptoms i.e. thought disorder is related to a disorganised semantic memory. Tallent et al (2001) compared the semantic maps of people with and without formal thought disorder following a triadic comparison task. They found that the low FTD group were like the controls in that their responses were organised into 3 clear dimensions. On the other hand, the high FTD group's semantic maps had no real clear dimensions suggesting a disorganised semantic memory is related to FTD. However, in this study the sample size was very small and the results lacked statistical power.

Nevertheless, MDS studies have been criticised on methodological grounds as they do not take into account the heterogeneity of the schizophrenia samples when creating an averaged map of semantic networks (Elvevag and Storms 2003, Storms et al 2003). Studies such as Elvevag and Storms 2003 claim that as people with schizophrenia show no inter-individual or intra – individual consistency in their individual maps of semantic similarity, then it is invalid to create an average group map. In the same vein, a recent study (Prescott et al 2006) has questioned the conclusions drawn by verbal fluency paradigms which report disorganised semantic networks in schizophrenia. By reanalyzing the data using new methods it was shown that the semantic memory networks of the people with schizophrenia actually have a similar structure of organisation to controls.

In sum these studies show that another feasible explanation for semantic memory impairments in schizophrenia is that semantic networks are disorganised. One might therefore expect that tasks involving making associations between concepts or forming categories may elicit more difficulties in schizophrenia. However, there are methodological limitations to MDS analyses. Importantly, it appears that a true investigation of semantic memory impairments in schizophrenia must not only quantitatively but also qualitatively analyse responses given.

In order to understand the semantic memory impairment in schizophrenia and consider possible explanations, it is important to understand the neurological processes involved. As it is agreed that schizophrenia is a disorder with an organic aetiology then a semantic memory impairment in schizophrenia is likely to be related to neurological abnormalities.

Chapter 4: The Neural Substrate of Semantic Memory

4.1. Introduction

The cognitive models of semantic memory (reviewed earlier), although partially supported by neuropsychological evidence are not necessarily biologically plausible. More precisely, brain imaging studies allow us to identify likely brain areas involved in tasks of semantic memory. Several theories suggest that semantic memory is a distributed process (e.g. Caramazza et al 1990) but nevertheless it is agreed that certain areas such as the temporal lobes and PFC have specific roles (Martin and Chao 2001). A comprehensive review of 275 PET and fMRI studies by Cabeza and Nyberg (2000) concluded that semantic memory processing is associated with increased activations in specifically the PFC, the Temporal Lobes, the Anterior Cingulate and the Cerebellar regions. In addition, activation was found to be lateralized to the left hemisphere in both the PFC and the Temporal Lobes. More recent research has claimed that more specific regions of the Temporal Lobes (see Figure 4) are responsible for semantic memory processing including the posterior left temporal lobe (Saumier and Chertkow 2002) and the anterior temporal lobe (Noppeney et al 2007, Saumier and Chertkow 2002). A common opinion (e.g. Barsalou et al 2003) is that semantic memory representations are stored across a number of different association areas responding to separate modalities for example visual semantic information is stored in the visual association areas. However, based on evidence largely from patients with neurodegenerative conditions, the temporal cortex is believed to be responsible in some way for culminating that information; in a way an amodal system (e.g. Damasio et al 1996).

There is some indication (e.g. Troyer et al 1998, Noppeney and Price 2002), tying in with the storage/ access distinction, that the temporal lobes are where semantic memories are stored in the brain and that the PFC and sub-cortical areas are responsible for the retrieval and effective utilisation of this information. The role of the temporal lobes in semantic memory can be demonstrated by the fact that people with Semantic Dementia (SD; the temporal variant of fronto-temporal dementia) suffer from asymmetric atrophy of the temporal lobes (e.g. Chan et al 2001, Davies et al 2004) and are specifically impaired on tasks of semantic memory (Hodges and Patterson 2007). Strong correlations have been reported between the severity of the semantic memory impairment in SD and the extent of temporal lobe atrophy (Mummery et al 2000, Levy et al 2004) confirming the importance of the temporal lobes to semantic memory. In addition, people with lesions to the temporal lobes are impaired on memory tasks (Kolb and Whishaw 1983, Saykin et al 1991). It was traditionally believed that long term memory was controlled by the medial temporal lobes (Squire and Zola-Morgan 1991), and there is recent evidence to support a role for the hippocampus in semantic memory (Davies et al 2004), for example area CA1 is believed to be involved in processing contextual information (Siekmeier et al 2007). Cabeza and Nyberg (2000) found semantic memory related activations in the temporal lobes were focused in the left middle temporal gyrus (area 21) and in the occipital-to temporal regions (area 37). Area 21 seems particularly important as it is activated independent of test modality whereas Area 37 seemed more related to processing the visual properties of objects. Data derived from people who have category specific deficits (e.g. are impaired for living things or non living things only)

have also provided evidence that different parts of the temporal lobes are involved in processing different parts of semantic knowledge (Brambati et al 2006), for example, there is substantial evidence that non-living things areas are processed in the prefrontal cortex (Devlin et al 2002). Furthermore, it is often the case that in neurodegenerative conditions such as dementias where temporal lobe atrophy is severe, a category specific deficit for living things has been reported (e.g. Laws et al 2007) suggesting that this sort of semantic knowledge is contained more exclusively in the temporal lobes than non-living knowledge.

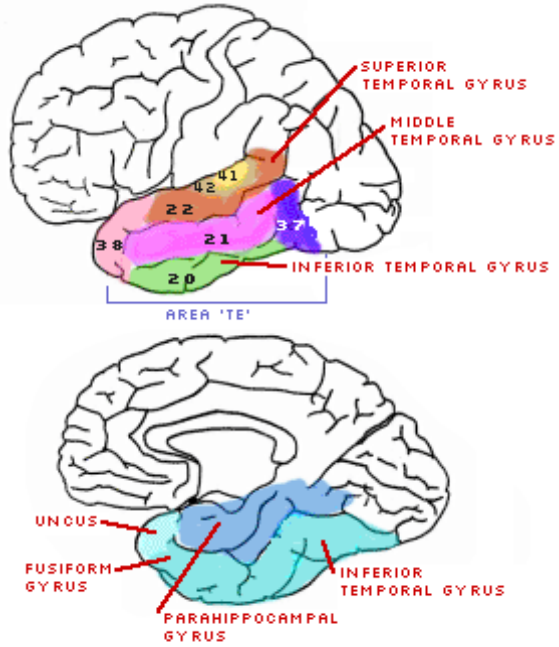


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Figure 4: Diagram of the temporal lobes.

The role of the PFC in semantic memory processing has been proposed to be related to strategic retrieval processes (Baddeley 1996, Frith 1995), whereas the temporal lobes are seen to store semantic knowledge and to be the site of automatic semantic memory processes (Troyer et al 1998). In support of this, people with damage to the frontal lobes do not typically report with a semantic memory problem where tasks do not involve strategic processes (Goodglass and Baker 1976, Baldo and Shimamura 1998), and in dissociation, people with temporal lobe excisions tend to be unimpaired on tasks where strategies are required (Iddon et al 1998). In addition, patients with a semantic memory impairment arising from frontal lobe damage tend to have an inconsistent profile of impairment suggestive of an access disorder (e.g. Jeffries and Lambon Ralph 2006, Taylor et al 2005, Hodges et al 1991). In the Cabeza and Nyberg (2000) review, semantic memory activations in the PFC were widespread and were involved in both the classification and generation of semantic information. There were more activations in dorsal areas on verbal fluency tasks suggesting that this area is involved in a working memory capacity. Although verbal fluency tasks do involve executive functioning, when compared to phonemic fluency tasks, semantic fluency tasks have been found to involve greater activation in the temporal neocortex and medial temporal cortex (Mummery et al 1996, Gourovitch et al 2001). Troyer et al (1998) compared 53 people with frontal lobe lesions to 23 people with temporal lobe lesions on the two types of fluency tests; semantic and phonemic. The frontal lobe

patients produced normal clusters on both tests but found it difficult to switch between clusters. In contrast the temporal lobe patients performed relatively normally on the phonemic fluency task but showed deficits in clustering and switching on the semantic fluency task. The Cabeza and Nyberg (2000) study also found that in Brodman's area 11, there was more activation for semantic categorisation/ classification tasks indicating a role in decision making. There was also increased activation in the anterior cingulate when selecting among responses (e.g. Assaf et al 2006).

In summary therefore, both neuroimaging studies and data from patients with neurodegenerative conditions provide strong support for the role of the temporal lobes and the prefrontal cortex in semantic memory. Not surprisingly considering the frequent reports of a semantic memory impairment, there is strong evidence to suggest that people with schizophrenia have damage to their temporal cortex (Zakzanis et al 2000, Honea et al 2005) and also their pre frontal cortex (Shenton et al 2001) which both could very well impact upon their semantic memory functioning.

4.2. Comparing the semantic memory impairments in schizophrenia with those seen in neurological groups

In order to understand the neural substrate of the semantic memory impairments in schizophrenia it is useful to contrast the performance profile against that seen in other clinical groups where semantic memory is affected. The nature of semantic memory impairments in patients with either acquired brain damage or neurodegenerative illness depends on the locus of pathology. Hence patients with prefrontal damage are likely to do poorer on tasks involving a high working memory or executive load e.g. verbal fluency regions (Hagoort 1997, Price 1998). On the other hand, anomia is commonly associated with atrophy in the left anterior/ superior temporal cortex in diverse neurodegenerative disorders (Galton et al 2001).

One neurodegenerative condition where the temporal lobes are selectively damaged is semantic dementia (SD) (the temporal variant of fronto-temporal dementia). People with semantic dementia suffer from asymmetric atrophy of the temporal lobes and are specifically impaired on tasks of semantic memory (Scahill 2005, Grossman et al 2004). The semantic memory impairment in SD typically involves anomia, a disproportionate impairment on semantic as opposed to phonemic fluency and high item error consistency. This pattern is characteristic of a storage disorder (Rosser and Hodges 1994, Garrard, et al 1997). Further support of a storage disorder in SD is the fact that there is progressive deterioration of anterior and inferolateral regions of the temporal lobe and disproportionate damage to the polar, anterior fusiform and inferior temporal gyri (Chan et al 2001, Davies et al 2004). In addition, there is evidence of atrophy of the medial temporal lobe also, in particular the hippocampal formation and the perirhinal cortex (Mummery et al 2000).

A neuro-developmental condition where the temporal lobes are selectively damaged is Temporal Lobe Epilepsy (TLE). Interestingly unlike with SD, people with TLE often behave clinically similar to people with schizophrenia in that they often experience psychosis (Blumer et al 1998), especially if the epilepsy is confined to the left hemisphere (Flor-Henry 1969). A study by Barr et al (1997) found similarities

between patients with Temporal Lobe Epilepsy and patients with schizophrenia in the fact that they both had larger ventricles and reduced hippocampal volumes. Whereas anomia is common in Temporal Lobe Epilepsy, it is not commonly reported in schizophrenia suggesting that although temporal lobe pathology may be common to both conditions there are qualitative differences. What seems to set people with schizophrenia apart is that they present with a combination of frontal and temporal lobe dysfunction (Gold et al 1992) resulting in a different cognitive profile. However, this was refuted by Mellers et al (2000) in a study where people with TLE and psychotic symptoms did not differ from patients with schizophrenia on measures of memory and executive function, suggesting that temporal lobe dysfunction could perhaps explain the cognitive impairments in schizophrenia.

Another neurodegenerative condition which features semantic memory impairments is Huntington's dementia (HD). However unlike SD, people with HD have subcortical/ frontal damage. This is reflected in their different pattern of impairment which is suggestive of difficulties retrieving semantic knowledge (e.g. Taylor et al 2005, Hodges et al 1991, Brandt 1985, Butters et al 1985). In the seminal study by Joyce et al (1996) it was concluded that unlike neurodegenerative conditions, the semantic memory impairment of people with schizophrenia resembles more that seen in patients with subcortical impairments such as HD. Furthermore a study by Pantelis et al (1997) found that when compared to people with temporal lobe lesions, frontal lobe lesions or subcortical damage, the memory profile in schizophrenia better resembled that of people with frontal/ subcortical and not temporal damage. Korsakoff's dementia also features largely subcortical damage (occurring mainly in the thalamus) which affects mainly autobiographical memory function. Of interest is a study by Duffy and O'Carroll (1994) which compared the performance of 40 people with schizophrenia to 18 people with Korsakoff's dementia on several tasks of semantic and episodic memory. A double dissociation was found in that the people with schizophrenia showed better episodic memory than the Korsakoff patients but had worse semantic memory suggesting that unlike in subcortical dementia, people with schizophrenia are selectively impaired on tasks of semantic memory and this is not wholly explainable by a retrieval deficit.

In summary it would appear that the semantic memory impairment in schizophrenia is different from that seen in SD in that there is a more inconsistent performance profile and anomia is less frequently reported. In some ways, the impairment is more similar to that in HD because there is strong evidence for a dysexecutive syndrome in schizophrenia (which although reported in SD is less severe than their memory impairment) and difficulties with knowledge retrieval. Although people with schizophrenia appear more clinically similar to TLE than the neurodegenerative conditions there are qualitative differences in the semantic memory impairments. Together with the inconsistencies in the semantic memory in schizophrenia literature and the fact that the neurological data doesn't provide much clarity, it is difficult to get a clear picture of what causes semantic memory impairments in schizophrenia.

People with Alzheimer's dementia, (AD), present with a widespread semantic memory impairment which is in many ways similar, although milder, to that seen in SD (e.g. Rogers et al 2006). This is consistent with the fact that the temporal lobes are known to be severely affected in AD (Zakzanis et al 2003). Despite what are clear

differences in the neuropathology, it has been reported that people with schizophrenia in some ways perform similarly to patients with AD on tests of semantic memory (McKay et al 1996). Patients with AD are also far more readily available than patients with semantic dementia, who in some ways appear the most suitable comparison group as they have a relatively isolated semantic memory impairment. However, there is also a need to profile the semantic memory impairment in schizophrenia against that of a comparison group with more widespread cognitive impairments which are present in AD. Therefore, in order to further understand how the semantic memory impairment in schizophrenia compares to that in AD, a direct comparison was conducted between the two patient groups. Firstly, a review of the literature on the semantic memory impairment in AD was conducted.

4.3. Semantic Memory in Alzheimer's Dementia

Alzheimer's dementia (AD) is a degenerative illness which affects mostly people over 60 years old. AD is fairly common affecting 1% of people over 60 and reaching a statistical probability of 20% once people reach the age of 80. In a relatively short time (typically 6 months to a year) people who have AD lose their long term memory and executive functioning, a state that progressively worsens leading to severe incapacity. AD is officially diagnosed at post mortem because of the presence of amyloid plaques (proteins that build up between neurons in the brain), neurofibrillary tangles (twisted bundles of fibres found inside neurons) and severe neuronal atrophy in the brain.

The DSM-IV diagnostic criteria for AD are 1) an impairment in memory, 2) at least one other cognitive disturbance (aphasia, apraxia or agnosia), 3) evidence of a significant decline in functioning, 4) a significant impairment in occupational or social function, 5) a course of gradual onset and continuing cognitive decline and 6) this decline must not be explained by another central nervous system or systematic disorder. The cognitive deterioration seen in AD is a reflection of the spreading neuropathology with impairments in episodic memory initially occurring as the hippocampus is affected and then a semantic memory impairment when damage spreads to the temporal neocortex (Cummings and Benson 1992, Smith 2002). Even when many aspects of normal day-to-day functioning are still intact, people can display a marked anomia (Huff et al 1986, Done and Hajilou 2005, Vogel et al 2005, Margolin et al 1990) and perform poorly on all tasks of semantic memory (Hodges, et al 1992, Chertkow and Bub 1990).

Since a seminal article by Chertkow and Bub in 1990, it is commonly believed that, as with SD, the semantic memory impairment in AD conforms to a pattern of lost stored knowledge (Salmon et al 1999), perhaps as a consequence of neuronal atrophy. Hodges et al (1992) designed a neuropsychological test battery to assess semantic memory function in AD. Participants were required to complete a series of tasks, including category fluency, confrontation naming, word to picture matching, card sorting and providing word definitions. Hodges et al (1992) reported that patients with AD performed significantly worse than healthy controls on virtually all sub-tests of the battery. In addition, Hodges et al (1992) reported that patients with AD showed marked item consistency across tasks, a finding that has been reported elsewhere (Huff et al 1986, Henderson et al 1990). This pattern of errors suggests that patients

with AD show a loss of semantic knowledge, rather than a failure of access. In a comparison with HD, Hodges et al (1991) analysed the errors made by people with AD on the Boston Naming Test. They found that unlike the HD patients, the people with AD made errors that indicated a loss of semantic information for example associative errors (e.g. digging for spade) or subordinate errors (e.g. musical instrument for flute). The frequency of superordinate errors supports the theory that there is bottom up deterioration in AD, which again has been frequently reported in the literature (e.g. Martin 1987, Troster et al 1989, Hough and Givens 2004, Done and Gale 1997, Alathari et al 2004, Bayles et al 1990). Further support for a storage disorder comes from studies where participants with AD show no improvement with item cuing (Delezer et al 2003, Randolph et al 1993) and also difficulties generating words on verbal fluency tasks (Binetti et al 1995, Epker et al 1999, Butters et al 1987). In addition, evidence from the priming literature has found relative hyperpriming for category knowledge over detailed knowledge in AD (Giffard et al 2001) suggestive of a preference for superordinate knowledge. Giffard et al (2001) conclude that faster priming in AD is indicative of a loss of knowledge as according to their theory it takes less processing time to traverse a depleted network. This is not the interpretation used to explain hyperpriming in the schizophrenia literature however (see review of priming literature). Similarly a study by Rohrer et al (1995) found faster response latency on verbal fluency tasks in AD for semantic but not phonemic items which they suggest implies a reduction of available items, hence a faster search. A recent review of the priming studies in AD by Laisney et al (2004) concluded that the majority of priming studies supported the assumption that there is lost semantic knowledge rather than problems with access.

As with the schizophrenia literature, multi-dimensional scaling studies have been used to assess the semantic memory networks of people with AD (e.g. Chan et al 1993 a, Chan et al 1993 b,). Although these studies have been criticised for their methodology, it is worthwhile noting that the semantic networks of people with AD appear less populated and coherent than normal controls. In the studies by Chan et al (1993a, 1993b) using an MDS analysis based on responses from a verbal fluency task, it was found that the semantic map for the AD group did differ greatly from controls in that they did not show clear groupings of objects, individual items were classed atypically and there was more of a focus on concrete information in categorisation rather than abstract information. The authors concluded this must reflect a breakdown/ disruption to the semantic network. A review of semantic memory impairments in AD was conducted by Salmon et al in (1999) which looked at the results from the consistency studies and also semantic mapping (MDS) studies. The review concluded that semantic memory representations are lost in AD. A more recent meta-analysis by Henry et al (2004) concluded that there is a semantic degradation in AD but that when retrieval demands are high (for example in the verbal fluency task), this has an additive effect and worsens the impairment. Problems on word association tasks in AD (e.g. Abeysinghe et al 1990) have also been used to illustrate a loss of semantic knowledge. Following on from the MDS studies of Chan et al, Au et al (2002) found on a triadic comparison task, that AD patients seemed to be worse at forming thematic relationships between concepts and instead demonstrated a preference for associating objects based on their perceptual qualities. This tendency increased as disease severity increased and Au et al (2002) concluded that the reliance on perceptual qualities over thematic ones is because of a loss of stored attributes in AD.

Despite what appears to be compelling evidence that knowledge representations are lost in AD, there are several studies that refute this and report evidence of the opposite performance pattern. Inconsistency of responding has been reported (e.g. Rich et al 2002, Funnell 1992, Storms et al 2003), also improvement following cueing (Martin and Fedio 1983) and priming (Chertkow and Bub 1990) and a lack of frequency effect (Johnson et al 1995). In addition, there are several reports of intact attribute knowledge in AD (Astell and Harley 2002, Nebes 1989, Nebes and Brady 1988, Nebes and Brady 1990, Bonilla and Johnson 1995, Johnson et al 1997, Smith et al 2001, Grober et al 1985, Bayles et al 1990) and also intact relations among semantic concepts (Johnson and Hermann 1995, Somners and Pierce 1990). In fact, Hartman (1991) stated that the "primary deficit in AD is an inability to initiate and maintain an organised retrieval strategy". Cox et al (1996) state that findings of lost attribute knowledge in AD could be in fact the result of impaired executive processes or the increasing difficulty of the task demands, a theory that has been mirrored by Smith et al (2001). A meta-analysis of verbal fluency performance in AD by Henry et al (2004) concluded that there is evidence of a storage disorder in AD but when retrieval demands are high, further problems accessing knowledge have an additive effect in worsening performance. In 1999, Sailor et al, using a true-false paradigm involving semantically related or unrelated attributes found no attribute knowledge loss in AD. Sailor et al (1999) theorised that the semantic memory impairment in AD was due to an inability to identify the specific nature of the relations between items. In one study by Abeysingue et al (1990), on a word association task, AD participants could offer definitions of items but were unable to find their associates indicating again that the problem is with relations between items. An inability to form associations between concepts in AD could indicate a disorganised semantic memory, a loss of interconnections or difficulties retrieving semantic information.

In sum, semantic memory is impaired in AD and there is much evidence to suggest that this is caused largely by problems arising from degradation of the semantic knowledge store but also with the additive influence of retrieval deficits. As previously mentioned there is some evidence to suggest that a storage disorder explanation may also be appropriate in schizophrenia although unlike AD, preserved functioning is reported on certain tests for example word picture matching. In addition the systematic review reported that anomia was an inconsistent finding in schizophrenia whereas it is consistently reported in AD. A direct comparison of the semantic memory impairment in schizophrenia and AD would help answer the issues raised in the review i.e. with AD patients as a cognitively matched comparison group, how does the semantic memory impairment in schizophrenia compare? Do these two conditions differ quantitatively only (by severity) or is there a qualitative difference with regards to their semantic memory performance profile? In addition, as the majority of papers report a storage like disorder in AD, how does the profile of impairment in schizophrenia compare and is there a similar neuropsychological explanation?

McKay et al (1996) attempted to compare 46 people with schizophrenia on the Hodges et al (1992) semantic battery to the 22 AD patients reported in Hodges et al (1992). The patients with schizophrenia were divided into three groups, core (severe, chronic illness), elderly (aged between 64 and 72 years) and mild (relapsing and

remitting illnesses, some degree of recovery between episodes). The study reported a substantial semantic memory impairment in schizophrenia which was present to a small degree in mildly psychotic patients but increased in severity in the chronic and elderly group. The semantic tests used were semantic fluency, naming, sorting level 1 (superordinate), 2 (base level) and 3 (subordinate), word-picture matching and a definitions tests. Whilst the AD patients performed worse than the controls on all the semantic tests, the mild schizophrenia group were only impaired on the verbal fluency and definitions test, the core group were impaired on the verbal fluency test, the subordinate sorting test, the naming test and the definitions and the elderly group were impaired on all of the tests. In fact on the fluency test, the naming test, level 2 and 3 of the sorting tests, the word-picture matching test and the definitions test, the elderly group did not perform significantly differently to the AD group. Although groups were not matched for pre-morbid or current IQ, a covariance analysis showed that significant differences remained between the groups on the semantic tests once IQ had been controlled for. This study was the first to report that the semantic memory impairment in schizophrenia can be quantitatively similar to that in AD. McKay et al (1996) speculate that the observed similarities in performance could be explained by the fact that both people with AD and people with schizophrenia have damage to the temporal lobes. Therefore a comparison between AD and schizophrenia on a battery of semantic memory tests would also allow for further speculation about the neural substrate of the semantic memory impairment in schizophrenia.

4.4. The neural substrate of semantic memory in schizophrenia and AD

Although cell atrophy is widespread in AD, there is much evidence to suggest that the temporal lobes are selectively damaged. The medial temporal lobes (Hyman et al 1984, Braak and Braak 1991) and in particular the hippocampus (Charletta et al 2003, Mentis 2000, Zakzanis et al 2003, de Leon et al 1997) whose role in memory processing is well documented (Squire and Zola Morgan 1991), have been reported to be abnormal in AD. A review by Chetelat and Baron (2003) confirmed a neuropathological deterioration in AD which primarily affects the medial temporal lobe and association cortex. The pattern of temporal atrophy does differ however from that observed in semantic dementia, where there is progressive deterioration of anterior and inferolateral regions of the temporal lobe and disproportionate damage to the polar, anterior fusiform and inferior temporal gyri (Chan et al 2001, Davies et al 2004). A meta analysis by Zakzanis et al (2003) which included results from 121 structural and functional imaging studies of AD reported substantial cell loss in several areas, in particular the temporal lobes, hippocampus, association cortices and the amygdala and thalamus. As with previous studies, the analysis concluded that damage to the hippocampus was the most reliable predictor of early AD whilst volume loss in the medial temporal lobes in general was predictive of people with AD in the later stages. This picture ties in with the clinical presentation of cognitive and social deterioration and it is widely accepted that medial temporal lobe cell loss in AD is related to deficits in long term memory (Heun et al 1997, Scheltens et al 1992).

Unlike the widespread neocortical atrophy present in AD (reaching 66% at the severest stage, Bobinski et al 1996), the structural damage in the brains of people with schizophrenia is relatively marginal (e.g. Zakzanis et al 2000) ranging from 4% to

26% in the medial temporal lobes. (Shenton et al 2001) However, it would be misleading to suggest that schizophrenia is purely a "functional" psychosis, as there are still numerous studies citing brain abnormalities to some degree. A review in 1999 by Harrison summarised the strength of the evidence for specific structural abnormalities, concluding that there is strong evidence of enlarged lateral and third ventricles in schizophrenia and decreased cortical volume with a disproportionate loss of grey matter from the temporal lobes (including the hippocampus). Similarly to in AD, CT and MRI studies agree on the finding of decreased temporal lobe volume in schizophrenia (Suddath et al 1989, 1990, Brown 1986, Vogeley et al 1998, Altshuler et al 1990, Jeste and Lohr 1989). In addition, disturbances at the microscopic level of temporal lobe neurons have been frequently reported in schizophrenia although findings are inconclusive (Harrison 1999). In the last seven years, since the Harrison (1999) review, more studies have reported reduced volumes of the amygdala and hippocampus (Suzuki et al 2005, Wright et al 2000) and the superior temporal gyrus (Onitsuka et al 2004, Highley et al 1999), although there have been several contradictory studies where no structural abnormalities in the temporal lobes have been found (i.e. Heckers et al 1991, Pakkenberg 1990). In a systematic review on structural changes in schizophrenia, Shenton et al 2001 reported that the medial temporal lobes are also a key site of damage in schizophrenia, with volume reduction ranging from 4% to 26%, particularly affecting the hippocampal complex. Studies linking temporal lobe pathology and symptomology in schizophrenia typically involve the hippocampus (Friston et al 1992, Liddle et al 1992). Specifically, a study by Shenton et al (1992) reported a correlation between temporal lobe atrophy and thought disorder. In addition, decreased superior temporal gyrus volume has also been linked with the severity of thought disorder and auditory hallucinations (Barta et al 1990, Marsh et al 1997, Onitsuka et al 2004).

As semantic memory processes typically involve the temporal lobes, it would be logical to predict that if there is temporal lobe pathology in schizophrenia then semantic memory would be affected depending on the location and type of neuropathology. Strong support for the association between temporal lobe pathology and impaired semantic memory comes from a study by Nestor et al (1993) in which performance by people with schizophrenia on semantic memory tasks such as categorisation were correlated with reduced temporal lobe volume whereas performance on visual memory tasks was not. The link between poor performance on semantic memory tasks and temporal lobe impairment in schizophrenia has in fact frequently been reported (Vita et al 1995, Gruzelier et al 1988). Despite what are similar locations of damage in both schizophrenia and AD, the difference in the level of cell atrophy suggests that semantic memory processing would not be affected to the same extent. For example the fact that anomia is more prevalent in AD than schizophrenia is perhaps a reflection of the fact that there is a more extensive and substantial structural and functional damage to the medial temporal lobes in patients with AD. In addition, neuro-imaging studies point to a qualitatively different temporal lobe pathology in schizophrenia than in AD; in AD there is reduced functioning (Fox et al 2001), in schizophrenia there are reports of hyperactivity (Gur 1978, Hazlett et al 2000, Fletcher et al 1998) reflecting perhaps increased activation of irrelevant associations. However a systematic review by Zakzanis et al (2000) reported hypoactivation of temporal and frontal structures in schizophrenia.

One finding which is often reported in schizophrenia is of increased cerebral asymmetry and in particular disproportionate left hemisphere lateralisation of functioning (Crow et al 1990). Many studies have observed disproportionate left hemisphere lateralisation of functioning in schizophrenia specifically in the temporal lobes (Brown et al 1986, Pearlson et al 1997, Buchsbaum 1990). Semantic memory and in particular categorisation has been found to rely more on the left hemisphere (e.g. Saumier and Chertkow 2002). Therefore, left hemisphere lateralisation in schizophrenia might suggest that there are some advantages in semantic memory processes in schizophrenia (perhaps backing up the hyperpriming literature). A study by Chiarello and Richards (1992) found that distant associations are inhibited in the left hemisphere and facilitated in the right so someone with damage to their right hemisphere would have difficulties forming unusual associations whereas damage to the left hemisphere would produce problems inhibiting those associations. According to the spreading activation literature based on priming tasks and also clinical accounts of formal thought disorder in schizophrenia, patients find it easy to form bizarre connections but are less able to inhibit them as controls; the opposite to what is predicted by lateralization theories if Chiarello and Richards (1992) are right. Despite this there is evidence that the right hemisphere is involved more in processing semantic context which is an area that is believed to be deficient in schizophrenia (Hemsley 2005). Interestingly naming ability has been found to rely more on the left temporal lobes (Seidenberg et al 2005, McMillan et al 2004) and this perhaps could explain why it is often preserved in schizophrenia. Despite this, the evidence for left hemisphere lateralisation has not always been replicated (Becker et al 1996, Sim et al 2006) and a study by Kircher et al (2001) reported increased right temporal cortex activation in schizophrenia during a semantic memory task.

A leading theory of schizophrenia neuropathology is that there is a disconnection between the frontal and temporal lobes (Friston 1998) leading to reduced inter-hemisphere communication. There are numerous studies supporting this claim with evidence cited of reduced frontal-temporal connectivity (Winterer et al 2003, Mitelman et al 2005a, 2005b, Ford et al 2002) and it could be that this theory explains the different performance profile in schizophrenia. On the other hand, Mitelman et al (2005a) found using neuroimaging techniques that there were stronger than normal positive inter-correlations among temporal areas in schizophrenia suggesting greater "talk" between temporal regions (theoretically similar to spreading activation theories). Distinguishing between search processes and retrieval processes of semantic memory, Granholm et al (1998) reported that people with schizophrenia showed a dysfunction of the automatic processes, controlled by the temporal lobes, resulting in a greater demand for frontal lobe involvement.

To pick apart the similarities and differences in temporal lobe neuropathology in AD and schizophrenia, we must focus in upon the specific temporal lobe regions affected. A review by Antonova et al (2004) reported 13 studies investigating whole temporal lobe volume reductions in schizophrenia and states that only one (Sanfilipo et al 2002) reported a total reduction, whereas many did not (e.g DeLisi et al 1991, Hoff et al 1992 and Vita et al 1995). In schizophrenia, reports of reduced volume or dysfunction tend to focus on the medial temporal region and in particular the hippocampus and amygdala (Davatzikos et al 2005, Wright et al 2000). A recent study by Sim et al (2006), although reporting smaller medial temporal lobe volume in

schizophrenia, did not find evidence of disproportionate damage to any specific region. As summarised by Antonova et al (2004), four studies have attempted to measure parahippocampal gyrus volume in schizophrenia (Krabbendam et al 2000, Sanfilipo et al 2002, De Lisi et al 1991 and Nestor et al 1993), none of which reported abnormal volumes. However, dysfunctions (not linked to volume) have been reported in the parahippocampal cortices (Nestor et al 1993, Prasad et al 2004, Seidman et al 2003) but this has more strongly been linked with episodic memory (Talamini et al 2005). The hippocampus itself has also been frequently listed as a specific site of malfunction in schizophrenia, although not reduced in volume necessarily (Antonova et al 2004), and this has also been linked with semantic memory functioning. Other studies report impairments predominantly in the anterior cingulate gyrus, both in prefrontal and temporolimbic regions (Yamasue et al 2004). Additionally, there is much evidence that the superior temporal gyrus is smaller in schizophrenia (Shenton et al 1992, Zipursky et al 1994, Keshavan et al 1998, Vita et al 1995, Nestor et al 1993) and that this correlates with verbal fluency and picture naming. This was not replicated though (Sanfilipo et al 2002).

In summary, despite substantial differences in the neuropathologies of AD and schizophrenia, one common feature is that there is a loss of volume in the temporal cortex which we know is associated with semantic memory processes. The main differentiating factor in the temporal lobe pathology of people with schizophrenia and people with AD seems to be the extent of the cell atrophy (e.g. O'Brien et al 1997). Evidence from functional imaging reports that there appears to be hypoactivity of areas of the temporal lobes in schizophrenia and AD although there are also reports of hyperactivity in schizophrenia. So is the difference between the two groups only one of severity, a quantitative difference or are there additional qualitative differences? Theories of temporal lobe asymmetry and frontal-temporal connectivity problems in schizophrenia do not apply to AD. In addition, the superior temporal gyrus has been cited as reduced in volume in schizophrenia although this does not appear to be the case in the early stages of AD (e.g. Frisoni et al 2007). It must be noted that there is wide heterogeneity in the pathologies of both schizophrenia and Alzheimer's dementia and that this may also reflect the varied performance profiles on test batteries. In fact it has been proposed by Allen et al (2001) that there are 2 subtypes of schizophrenia; one with frontal lobe dysfunction predominantly and one with a temporal lobe dysfunction profile, both presenting with qualitatively different impairments. Of course, despite some structural similarities, the neuropathologies of schizophrenia and AD differ in many respects, mainly on a neurochemical level (e.g. White and Cummings 1996). In AD there is a depletion of acetylcholine throughout the brain but in particular in the medial temporal lobe (Reinikainen et al 1988). In schizophrenia, a dysfunctional dopamine system is known to affect a wide range of functions, acting both cortically and sub-cortically (Abi-Dargham 2004). Furthermore although damage to the prefrontal cortex has been reported in AD, this is not as strong a finding as in schizophrenia and as was suggested from the comparisons with people with TLE, what may differentiate the neurology of people with schizophrenia and also those with HD to other neurological conditions where semantic memory is selectively impaired is that damage to the PFC and subcortex is a confirmed finding. In summary, however, there seem to be more similarities than differences in the temporal lobe pathology of people with schizophrenia and people with AD.

Chapter 5: Profiling the Semantic Memory Impairment in Schizophrenia

Study One: Comparing people with schizophrenia to people with Alzheimer's dementia on a battery of semantic memory tests

Study one has been submitted for publication in Schizophrenia Research and is being edited following comments by the review panel. A copy of the submitted paper is in Appendix C.

5.1. Introduction

Based on the systematic literature review and meta-analysis, it could be said that on certain tasks, semantic memory is impaired in schizophrenia. However, for the tasks where impairments are less consistently reported, it is likely that poor performance can be explained by a generalised intellectual deficit and not a primary semantic memory impairment. There are several different neuropsychological tests of semantic memory; however they vary in the extent to which they involve other cognitive processes, especially executive functions. Therefore, in order to ascertain the overall profile of semantic memory impairments in schizophrenia, it is important to test patients on a semantic memory battery. Although a couple of studies have assessed the semantic memory performance of people with schizophrenia across a battery of tests (e.g. Barrera et al 2005, McKay et al 1996, Al-Uzri et al 2004), none of these studies fully controlled for effects of both IQ and executive functioning. As it is well known that a feature of schizophrenia is a generalised intellectual deficit (Heinrichs and Zakzanis, 1998, Blanchard and Neale 1994), this must be considered when interpreting the results from neuropsychological assessments. In order to conclude the existence of a disproportionate impairment in semantic memory, error rates must be shown to be above the level expected from poor cognitive ability. Previous research has not been able to satisfactorily rule out the effects of IQ on how participants perform on semantic memory tests as current IQ measures have often not been taken (e.g. Al-Uzri et al 2004) and groups of participants with schizophrenia are usually compared with unmatched healthy control groups. By recruiting a group of patients with AD, matched for current cognitive ability to the schizophrenia participants, this study aims to profile the true semantic memory impairment in schizophrenia whilst controlling for intellectual ability.

In order to understand the nature of the semantic memory impairment in schizophrenia, it is useful to assess to what extent it maps on to a well known neurological model. In 1979, Warrington and Shallice theorised that the test performance of neurological patients with semantic memory difficulties conform to one of two types of disorder; degraded store or impaired access (see Table 1). This model has achieved wide-spread acceptance in the relevant literature (Storms et al 2003, Rossell and David 2005, Leeson et al 2006) although its validity has been debated. It is now fairly well established that patients with AD have a pattern of semantic memory impairment which conforms to a storage disorder. Perhaps most illustrative of this is the finding of high consistency of errors across time (Henderson et al (1990) and across tests (Huff et al 1986, Chertkow and Bub 1990). Additionally,

AD groups have shown on verbal fluency tasks (Troster et al 1989) and sorting tasks (Hodges 1992) that they are more likely to display preserved category item knowledge but impaired object specific knowledge - an error pattern which has been termed "bottom-up deterioration". This reflects the fact that more specific item knowledge deteriorates first in AD as it is less resilient to the neuropathology than everyday item knowledge (Done and Gale 1997). Furthermore, it has commonly been reported (Thompson-Schill et al 1999, Strain, et al 1998) that patients with AD demonstrate a word frequency effect on semantic memory tasks. These features have led to the conclusion that there is a loss of stored semantic memory representations in AD, potentially as a consequence of deterioration of the neocortical association areas which are believed to store these representations (Salmon et al 1999). A study by McKay et al (1996) compared the performance of people with schizophrenia to those with Alzheimer's dementia on a battery of semantic tasks. It was found that on several measures, largely in the chronic or elderly patients with schizophrenia, the severity of errors in both group was comparable. A group of people with AD make a good comparison group to people with schizophrenia as unlike healthy controls, they tend to have a lower IQ and generally poorer cognitive ability. In this ways the groups can be easily matched for current IQ. In addition, in patients with mild-moderate AD, the semantic memory impairments are relatively (i.e. compared to the other deficits in AD) severe and have been frequently shown to be consistent with a storage disorder profile. This provides a good model of comparison for people with schizophrenia. The McKay et al (1996) study used data for the AD group from a previous paper and therefore performance was not directly compared between the two groups, who were also unmatched for current IQ.

Previous studies have attempted to apply the storage-access model to the profile of errors in schizophrenia and the majority of findings point to the presence of an access disorder (Al-Uzri et al 2004, Allen et al 1993, Spitzer et al 1993, Joyce et al 1996, McKenna et al 1994, Laws et al 1999). Using a verbal fluency task, Allen et al (1993) found that their schizophrenia sample displayed evidence of an inefficient search process through a nevertheless normal sized lexicon, a finding which has been replicated (Elvevag et al 2001). Additionally, Joyce et al (1996) tested people with schizophrenia using a cueing task and found that they did benefit from cues suggesting an intact knowledge representation which was being inefficiently accessed. Additionally, other studies have reported item inconsistency in schizophrenia (McKenna et al 1994, Al-Uzri et al 2000) indicating the presence of an access disorder. A quote by Bleuler (1911) neatly summarises the fact that the semantic memory problems in schizophrenia reflect an impairment in the way in which intact concepts are accessed rather than a loss of knowledge.

"at times these patients forget and at others they know the same fact according to the circumstances involved" – "the actual amount of knowledge remains preserved.. but it is not always available or it is employed in the wrong way."

There have however been conflicting accounts of more storage-like profiles in schizophrenia (Chen et al 2000, Rossell and David 2006) and there have been suggestions that this is related to disease chronicity and the level of cognitive impairment in the individual (Laws et al 2000). In 2000, Laws et al investigated naming consistency in 22 people with schizophrenia and found that storage disorders

were more common than access disorders. It was also found (Laws et al 2000) that the patients who displayed a storage disorder were more likely to be functionally impaired and chronically hospitalised as opposed to the other patients who lived in the community. Any individuals with schizophrenia who meet the criteria for a storage disorder therefore are likely to have a more chronic, cognitively impaired profile and their performance will overlap more with the AD sample, as has previously been reported (McKay et al 1996).

The purpose of this study was to investigate thoroughly if semantic memory is impaired in schizophrenia and to pinpoint the features of that impairment. By directly comparing the performance of people who have chronic schizophrenia with people who have Alzheimer's dementia and with controls across a semantic memory test battery, it was hoped that a strong picture of the nature of the semantic memory impairment in schizophrenia, both quantitatively and qualitatively, would emerge.

The aims for Study One were to:

1. Profile the semantic memory impairment in schizophrenia across a number of tests
2. Evaluate the relative contributions of IQ and executive functioning deficits to semantic memory performance across tests
3. Compare the semantic memory impairment in schizophrenia to that found in AD and see whether the impairments differ quantitatively and/or qualitatively.
4. Assess whether the semantic memory impairment in schizophrenia is better explained by a storage disorder or an access disorder.
5. Assess the role of semantic memory in the symptoms of schizophrenia

5.2. Method

5.2.1 Participants

Sampling

An a priori power analysis was conducted based on effect sizes derived from McKay et al (1996). The effect size was calculated using the statistical difference between the core group with schizophrenia and the AD norms on the naming test. An effect size of Cohen's d = 1.06 was derived from a mean score (out of 48) in the schizophrenia group of 42.5 (s.d = 3.6) and a mean in the AD group of 35.3 (s.d = 8.9). Based on an alpha value of 0.05, an a priori power analysis recommended a total sample size (across the two clinical groups) of 40 to end up with an excellent power of 0.95.

A total of 20 people with schizophrenia, 26 people with AD and 17 controls were included in this study.

Inclusion/ Exclusion Factors

- Patients with schizophrenia

Participants in the schizophrenia group were recruited based on the following criteria. They had been diagnosed with schizophrenia according to criteria specified in the DSM-IV by a multi-disciplinary team led by a Consultant Psychiatrist. No one was included who had a current substance abuse/ alcohol problem or who had suffered from acquired brain injury or a neurological illness. People who had a diagnosis of schizo-affective disorder were also not included.

- Patients with Alzheimer's Dementia

Participants in the AD group had been diagnosed with probable Alzheimer's Dementia by a Consultant Psychiatrist according to criteria specified in the ICD-10. Patients with severe AD find it difficult to remember even the most simple of test instructions and this therefore confounds the data. Therefore in this study, only participants with AD who scored between 19-25 on the Mini Mental State Examination (MMSE, Folstein et al 1975) were included as performance in this range indicates a mild-moderate cognitive impairment. None of the AD group was reported by their psychiatrist to have shown evidence of delusions, hallucinations or formal thought disorder.

- Controls

Control participants were excluded from the sample if they had any known psychological problems, acquired brain injury, alcohol or substance abuse. They were also only selected if they had an MMSE score greater than 25.

Because of the nature of the tasks, participants who did not have a good grasp of English were also excluded.

Recruitment Strategy

Recruitment was conducted in a team alongside Verity Lawrence an MSc student.

- Participants with schizophrenia

All but two of the participants with schizophrenia were recruited from a residential rehabilitation unit for chronically ill patients. Two patients were staying on the acute psychiatric ward at the time of testing. Therefore patients varied in their length of illness with a mean illness duration of 30.5 years (s.d. = 14.3) and a mean age of onset of 22.5 years (s.d. = 10.5). Suitable participants were first identified by the Consultant Psychiatrist or Mental Health Workers. Researchers then approached the individual and gave them an Information Sheet to read and made an appointment to see them. Testing took place in quiet rooms at the various locations.

- Participants with Alzheimer's Dementia

AD patients were recruited at the time of their six monthly appointments with the Consultant Psychiatrist at the outpatient clinic. Patients saw their Psychiatrist first who confirmed to the research team that they met inclusion criteria for the study. Researchers then approached participants and gave them an Information Sheet and arranged a time to call them. If patients agreed to take part they were seen in their homes.

- Control Participants

Control participants were recruited from a community centre for retired individuals. Visitors to the centre and members of staff were recruited. A control group whose members were older than the average undergraduate sample were recruited in order to control for the age of the group of patients with Alzheimer's dementia. Volunteers came from a range of social and educational backgrounds. Rather than recruit undergraduates, it was decided that these individuals would be more comparable to the group of people with schizophrenia with regards to their educational backgrounds, age and employment history. This proved to be the case as the groups were matched for current and pre-morbid IQ.

Matching Groups on IQ

Selection of AD patients with MMSE scores within the mild-moderate range would provide a likely match, in terms of general cognitive impairment with the schizophrenia group. This was confirmed using an IQ test, the WASI (Wechsler Abbreviated Scale of Intelligence, Wechsler 1999). In order to ensure the groups were matched, data from 3 people who scored the lowest on the WASI in the schizophrenia group were excluded. Also only controls who scored above 85 on the full scale WASI were included in this study.

Demographic Information

Table 7 contains demographic data for the patients who were included in the final data analysis.

Table 7: Demographic data for patients who were included in Study One.

** = p <.01

	Schizophrenia (SZ)	Alzheimer's (AD)	Controls (C)	ANOVA	Post Hoc t tests
N	20	26	17		
Age (Mean)	51(11.18)	76.27 (7.33)	61.29 (24.97)	F (2, 60) = 16.02, p < .001	AD> SZ **
Male/ Female	11 / 9	15/11	6/11	-	

The schizophrenia and the control groups were found to be matched on age (t (21) = -1.541, p = 1.38, r = .265). The majority of the patients with schizophrenia were taking antipsychotic medication; 16 were taking atypical antipsychotics, 1 was taking typical antipsychotics, 1 was taking lithium and 2 were not taking medication. All patients with AD had been prescribed a treatment of acetylcholinesterase inhibitors.

5.2.2. Design

The study is case control and cross sectional in design. Full ethical review for the study was conducted by an NHS Research Ethics Committee and approval was granted.

Study Aims

1. To profile the semantic memory impairment in schizophrenia across a battery of semantic memory tests

2. To assess whether semantic memory in schizophrenia is impaired over and above a generalised cognitive impairment

3. To compare the semantic memory impairment profile in schizophrenia to that of people with AD who are well known to perform poorly on tasks of semantic memory

4. To assess whether the semantic memory impairment in schizophrenia meets criteria for a storage or an access disorder and to compare this to the type of disorder seen in AD.

5.2.3. Materials

The three groups will be given the following assessments:

The National Adult Reading Test (NART, Nelson, 1982)

This test was designed to assess pre-morbid IQ and involves asking participants to read aloud a list of irregularly pronounced words. Word reading has been found to correlate highly with general intelligence in normal adults (Nelson and McKenna 1975) and in addition has been found to be preserved in people with dementia. The NART is commonly used clinically to assess people with dementia and other conditions where there is believed to be some level of cognitive deterioration. The NART is often used to assess pre-morbid IQ in schizophrenia although evidence suggests that it could be an overestimate of current abilities (i.e. Russell et al 2000, Kondel et al 2003). Another limitation of the NART is that it is likely to be culturally biased towards people who have grown up speaking English (although studies have found no effect of ethnicity (Boekamp et al 1995)) and also may be biased towards the older generation (e.g. Graf et al 1995). However, in schizophrenia and also Alzheimer's dementia there is a decline in IQ and therefore it makes sense to take a measure of pre-morbid ability and ideally match participant groups. This should act in the same way as matching on the basis of educational level (Bright et al 2002). Despite its limitations, the NART is commonly used to assess pre-morbid ability and frequently reported to be a reliable measure (e.g. Crawford et al 2001, Maddrey at al 1996).

The Wechsler Abbreviated Scale of Intelligence (WASI, Wechsler 1999)

As well as pre-morbid IQ, it is important to assess for current intellectual functioning. This is especially important in this study considering the fact that firstly both clinical groups are likely to have an intellectual impairment and secondly that this impairment will impact upon their performance on the semantic memory battery. The WASI is an abbreviated version of the classic Wechsler Adult Intelligence Scale (WAIS, Wechsler 1981) and features four subtests. It is believed that a measure of IQ must encompass assessment of abilities in two domains; verbal and nonverbal (i.e. performance) and therefore a Full IQ can be separated into Verbal IQ and Performance IQ. Two of the subtests in the WASI assess verbal IQ and two assess performance IQ. In order to cut down on testing time, it was decided that two of the subtests from the WASI would be used, one for verbal IQ and one for performance IQ. The results were prorated.

Vocabulary subtest

Performance on the vocabulary subtest can be used to calculate verbal IQ. The vocabulary subtest consists of asking the participant to provide definitions of 42 words which range from simple nouns to more abstract adjectives. Aside from knowing what each word means, to achieve a high score on this test participants must be able to describe what the word means using an advanced vocabulary. One problem with this test is that it does correlate with semantic memory functioning and in fact tests involving definitions are often used to measure semantic memory (e.g. Hodges et

al 1992). Nevertheless, it is believed to be the most reliable measure of verbal IQ and to correlate highly with general IQ (e.g. Jeyakumar et al 2004).

Matrix Reasoning subtest

Performance on the matrix reasoning subtest can be used to derive a measure of performance IQ. This test involves completing 35 incomplete patterns using shapes and taps into reasoning skills. One limitation of this test which applies to many tests used to assess performance IQ is that it involves executive functioning abilities and also relies heavily on processing speed, both of which are shown to be deficient in AD and schizophrenia. Therefore, as with the vocabulary subtest caution must be taken when interpreting the matrix reasoning task and I intend to use these tests as a general guide of cognitive functioning only. As with the vocabulary test the Matrix Reasoning correlates highly with general IQ (e.g. Kaufman 1994) and is therefore a good individual subtest to use.

IQ tests have been found to be biased towards Caucasians (e.g. Heaton et al 2003) and are strongly influenced by education and reading ability (Heaton et al 2003). Nevertheless they provide a good indication of general intellectual ability.

The Mini Mental State Examination (MMSE, Folstein et al 1975)

The MMSE is a general test of cognitive ability and consists of several questions and small tests which assess orientation to time and place, attention, calculation, language and immediate and delayed memory recall. This test is used frequently to inform diagnosis of AD and neuro-degeneration is often reflected in worsening scores on the MMSE. Scores on the MMSE are out of a maximum of 30. Scoring within the range of 0 -10 indicates a severe cognitive impairment, scoring between 11-20 indicates a moderate impairment and 21-29 a mild impairment. As with the other tests of cognitive impairment which assess language, results are affected by ethnicity and education (e.g. Espino et al 2001, Jones & Gallo 2002).

Using the MMSE aids the selection of both participants with AD and controls. In addition it is a useful additional measure of cognitive impairment for the people with schizophrenia.

The Positive and Negative Syndrome Scale (PANSS, Kay et al 1987)

In addition the people with schizophrenia will be assessed using the PANSS. This is a measure of symptom severity in schizophrenia and involves a 30 item interview which lasts around an hour. The PANSS is used widely clinically. Information from the interview is used to derive ratings of a wide range of positive symptoms and negative symptoms. It is recommended that two researchers are present when the PANSS is administered and that each separately codes the responses to get a measure of inter-rater reliability. When individual items are scored, collective measures for positive symptoms, negative symptoms, thought disorder symptoms and general symptom severity can be derived.

Because of potential links between symptoms and semantic memory functioning, assessing patients using the PANSS will allow for analysis of any such relationships and also give an overall idea of the type of symptoms the patients with schizophrenia have.

The Hodges et al Semantic Memory Battery (Hodges et al 1992)

The Hodges et al (1992) Semantic Memory Battery was originally designed for use in patients with AD (Hodges et al 1992) and consists of five subtests; naming, word-picture matching, sorting (in three levels), fluency and word definitions. In addition to these standard tests of semantic memory, two tests of semantic associations were included as part of the battery. Therefore a recently developed test, the Camel and Cactus test (Bozeat et al 2000) was also included in the test battery. However, the length of time it takes to assess participants is always a consideration and therefore the fluency and word definitions tests were removed from the battery to be replaced by a Camel and Cactus test, a picture and word version. The rationale for removing the fluency and word definitions tests were that the fluency test, out of all the tests of semantic memory has probably been investigated the most in schizophrenia and also is complicated by demands on executive functions. In addition, the definitions test is conceptually similar to the vocabulary subtest of the WASI and therefore probably out of all the tests makes the greatest demands on IQ.

The same 64 items are used in each of the tests of the Hodges et al (1992) semantic battery. Half the items fall into the category of living things (animals, birds and fruit) and half into non living things (vehicles, household items and tools). Pictures of the items were taken from the selection of black and white drawings by Snodgrass and Vanderwart (Snodgrass & Vanderwart 1980). A list of items can be found in Appendix D.

Each subtest will now be described in more detail:

- The Naming Test

Pictures of the 64 items were printed onto cards which were then laminated. Cards are approximately 15 cm in width and 11 cm in height.

- The Word-Picture Matching Test

This test consists of a folder containing 64 pages. On each page is 10 items from the same taxonomic category e.g. all household items or all fruit.

- Sorting

As with the naming test, pictures of the 64 items were printed onto laminated cards. In addition laminated cards with category labels on were used. In Level 1 and Level 2 of the sorting task, all 64 items were used but in Level 3 only the animal and bird cards (n=24) and the household item and tool cards (n=24) were used.

- Camel and Cactus Pictures Test

A folder containing 68 pages of coloured pictures was used in this test. On each page a target item is positioned above 4 items which are to some extent associated with the target. One of the items is strongly associated with the target. The first four pages are for the purposes of practice.

- Camel and Cactus Words Test

This test takes the same format as the Pictures version but instead of pictures words are used.

5.2.4. Procedure

After participants had read the information sheet and once they had had the opportunity to ask questions, written informed consent was obtained. Testing usually lasted around two to three hours and was held over at least a couple of sessions.

In order to ensure the participants were matched cognitively, the MMSE, NART and WASI were the first tests to be performed. Tests were therefore administered in the following order.

1. MMSE
2. WASI
3. NART
4. Naming Test

Participants were handed the pack of cards and asked to say the name aloud of each item as they turned through the pack.

5. Word Picture Matching

Participants were given the folder of stimuli and asked to point to the named item on each page. The researcher would name each item out loud as the pages were turned.

6. Camel and Cactus Pictures

Participants were given the folder of stimuli and for each page asked to select which one out of the four pictures went with the target item. Participants either pointed or said aloud which one. There were four practice items at the beginning; if an error was made the participant was corrected and shown the correct choice.

7. Sorting Task

There are three levels to this task. For each level the category labels were set out on the table in front of the participant, spaced apart. Participants were then instructed to sort the cards into the various categories in piles underneath the labels. Each pack of cards was shuffled prior to testing.

8. Camel and Cactus Words

This test involved the same procedure as the Camel and Cactus Pictures test.

9. PANSS

Researchers were initially trained and then supervised in administering the PANSS.

5.2.5. Data Analysis

Effect Sizes
As the majority of tests are non-parametric, Pearson's product-moment correlation coefficient, *r*, is used as a measure of effect size (large, *r* >. 371, medium, *r* = 0. 1 - .371, small, *r* <. 1) following the recommendations of Cohen (1988). The *r* correlation coefficient is a measure of the linear relationship between the dependent and independent variables for example mean scores on a test of naming and the group variable.

Performance Profiles
Test scores, particularly for the controls, consisted of too many "zero error" scores and therefore departed too far from normality, even after log linear transformation, to permit a classical MANOVA profile analysis. Following the guidelines of Delucchi and Bostrom (2004), non parametric alternatives were employed, using medians as the measure of central tendency. The performance profiles of each group were plotted across the seven tests of semantic memory, and a Kruskal Wallis between groups non-parametric ANOVA was calculated for each subtest separately. Where significant group differences were found, post-hoc Mann Whitney U tests were calculated to see if the schizophrenia group differed significantly from either the controls or the AD patients.

Covariance Analysis
Performance on semantic memory tasks correlate with IQ (e.g. Leeson et al 2005a). As the control data was skewed, it was not possible to conduct an ANCOVA. Therefore in order to perform a covariance analysis a sub-sample of 13 schizophrenia patients (mean IQ = 94.7 (13.4)) were matched for IQ (t (24) = -1.544, p = .136, r = -.213) with 13 non psychiatric controls (mean IQ =102.77 (13.04)), blind to their semantic scores. For psychometric details and demographics see Table 8.

Table 8: Psychometric details for the IQ matched subgroup of people with schizophrenia and controls.

	Schizophrenia	Controls
N	13	13
Male/Female	9/4	4/9
Mean Age (s.d)	50.8 (11.97)	68.69 (19.1)
Mean NART (s.d)	109 (5.4)	99.45 (33.54)
Mean Verbal IQ (s.d.)	91.7 (14.6)	99.85 (18.76)
Mean Perf IQ (s.d)	100.54 (16.05)	104.77 (13.42)
Mean Full IQ (s.d)	94.77 (13.38)	102.77 (13.04)
Mean MMSE (s.d)	28.23 (1.36)	n/a
Mean PANSS Gen (s.d)	30.92 (6.67)	n/a
Mean PANSS Pos (s.d)	17.77 (6.07)	n/a
Mean PANSS Neg (s.d)	14.31 (6.17)	n/a
Mean PANSS TD	10 (3.76)	n/a

Mann Whitney U tests were conducted to compare the profile across the 7 semantic memory subtests for the IQ matched groups.

Correlates of semantic memory impairment
Spearman's rho correlations were conducted to compare errors on each subtest with current IQ (WASI) and symptom profiles (PANSS).

Storage vs. Access disorder analysis:
Warrington and Shallice's (1979) Method, each of the four criteria were calculated as follows:

1. **Item Consistency**: Taken from a method designed by Hodges et al (1992), a paired samples t-test was used to calculate whether the percentage of consistent pairs (i.e. correct-correct or incorrect-incorrect) was greater than the percentage of inconsistent pairs (i.e. correct-incorrect and vice versa) across two subtests (with similar error rates) for each participant group. The subtest comparisons were: Naming vs. Word-picture Matching; Semantic association tasks – Pictures vs. Words; and Sorting (Level 2) vs. Naming.
2. **Word Frequency**: Word frequency norms were used (Yoon et al 2002). A correlation between word frequency and the number of errors for each item was derived for each participant. The mean group correlations were then compared using an Independent *t* test.
3. **Cuing**: Cuing improvement was measured by comparing the error scores for the Naming (un-cued) and the Word-picture matching (cued) subtests. Following a log-linear transformation the data fitted a normally distributed model. Hence, a mixed between-within ANOVA was used to compare the error rates for the two patient groups. The scores for the controls were too skewed to be analysed parametrically.
4. **Bottom – Up Deterioration**: Friedman's trend tests were used to assess the extent to which performance differed in each group between the three sorting levels. A bottom-up deterioration occurs if a) there is a significant trend revealed by the Friedman test, b) the trend of the error rate is subordinate > base level > superordinate. Post-hoc Wilcoxon tests for all 3 groups were used to compare error rates for i) superordinate (Level 1) with base level (Level 2); and ii) base level (Level 2) with subordinate (Level 3).

Stochastic Method (Faglioni and Botti 1993)
This method is based on a 2-parameter Markov stochastic model and permits the calculation of two values: i) probability that an item is in store (s) and ii) probability of retrieval of that item from store (r). For details of how this score is calculated see Faglioni and Botti (1993).

The model is limited to a calculation based on errors across a maximum of 4 subtests. The subtests included were: Naming, Sorting (level 2) and Semantic associations Pictures and Words, given that these subtests produced relatively high error rates. The group means, for the probability that the item is in store and the probability of retrieval, were then compared using Independent *t* tests.

5.2.6. Results

Baseline Tests

Table 9 shows the performance of all three groups on the different baseline measures.

Table 9: The results of the baseline tests for participants in Study One.

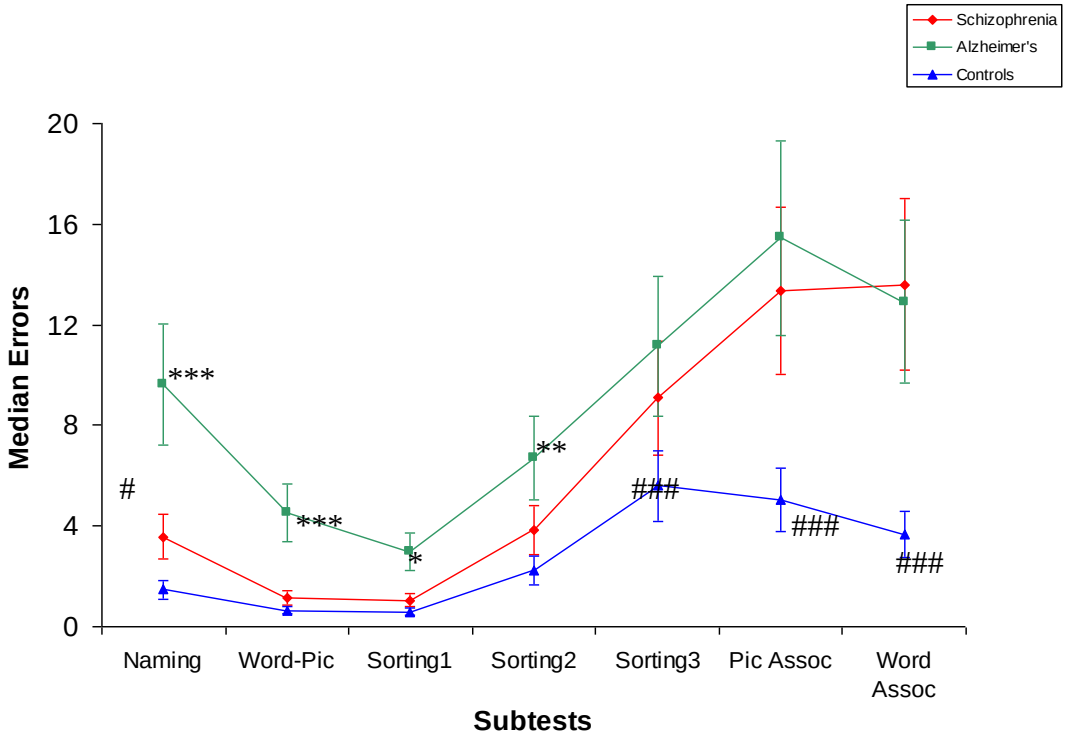
	Schizophrenia (SZ)	Alzheimer's (AD)	Controls (C)	ANOVA	Post Hoc t tests
N	20	26	17		
MMSE	27.8 (1.74)	22.27 (2.07)	-	t (44) = 9.62, p <.001	
Current IQ (WASI) - Full Scale - Verbal - Performance	85.15 (17.491) 83.2 (17.121) 90.55 (19.44)	88.16 (16.59) (n =19) 88.21 (15.82) (n =24) 93.95 (19.90) (n =21)	107.88 (14.86) 103.24 (17.72) 111.35 (17.04)	F (2,55) = 10.08, p <.001 F (2,60) = 6.96, p =.002 F (2,57) = 6.24, p =.004	C >AD** C>SZ** C >AD** C>SZ** C >AD** C>SZ**
Pre-Morbid IQ (NART)	100.5 (24.76)	103.15 (22.69)	102.27 (28.18)	F (2,58) = .065, p = .938	
PANSS (general)	30.40 (6.236)	-	-	-	
PANSS (conceptual disorganisation)	10.15 (3.167)	-	-	-	
PANSS (positive)	17.75 (5.077)	-	-	-	
PANSS (negative)	15.45 (6.778	-	-	-	

Both the patient groups were cognitively impaired, scoring within the bottom 20% of the population on current IQ. All three groups were matched on NART performance and the clinical groups were matched on all measures of current IQ (although significantly different to the controls). The severity of cognitive decline in the two patient groups was comparable as shown by the difference in pre-morbid (NART) and current (WASI) IQ scores (for the schizophrenia group, mean difference = -15.35 (25.8); for the AD group, mean difference = -19.21 (12.89); t (37) = .585, p = .562).

Semantic Memory Battery, group comparisons over the 7 semantic tests

The Kruskal – Wallis ANOVA found a significant difference in all 7 subtests between the three groups (p <.001). Each subtest revealed significant differences (p<.001) between the AD group and the controls which is illustrated in Figure 5

Figure 5: Profile of errors across the semantic memory battery for the schizophrenia (n = 20), AD (n = 26) and control (n=17) group.



AD vs. schizophrenia comparisons: * = $p<.05$
** = $p<.01$ *** = $p<.001$
Schizophrenia vs. controls comparisons: # = $p<.05$
= $p<.01$ ### = $p<.001$
Error bars indicate upper and lower quartiles.

Test-wise group comparisons between the schizophrenia and AD patients.
There were significant differences between the two groups on the Naming, Word-picture Matching and both Sorting Levels 1 and 2. For the two Semantic association Tests and Sorting Level 3 there were no significant group differences. Effect sizes were: large for Naming (r = .481), Word-picture matching (r = .478), Sorting Level 1 (r = .305) and Sorting Level 2, (r =.409), medium for Sorting Level 3 (r = .238); and small for Semantic association Pictures (r =.150), Semantic association Words (r =-.043).

Test-wise group comparisons between the schizophrenia group and the controls
There were significant differences between the schizophrenia group and the non psychiatric controls on Sorting Level 3, and the Semantic association tests, Pictures and Words. The groups performed similarly on the Naming test, Word-picture matching test and Sorting Levels 1 and 2. Effect sizes were: large for Sorting Level 3 (r = -.482), Semantic association Pictures (r = -.612) and Words (r = -.654); medium for Naming (r = -.294) and Sorting Level 2 (r =-.333); and small for Word-picture matching (r =-.166), Sorting Level 1 (r = -.103)

Semantic memory impairment in schizophrenia and IQ
The correlations between IQ and subtest error rates for the people with schizophrenia and the non psychiatric controls were very similar. For each group, there was a small-moderate correlation for each subtest.

Controlling for the effects of IQ
When the two IQ matched sub-samples from the schizophrenia and the non psychiatric control groups were compared, the pattern of performance differences were qualitatively similar, but less marked, compared to the previous analysis. The schizophrenia group produced more errors to the controls, on the two association tests: Pictures (Z = -2.578, p =.010, r = -.512) and Words (Z = -2.854, p = .004, r = -.520) and Sorting Level 3 (Z = -2.370, p =.018, r = -.399). On all other subtests the group difference did not reach the criteria for statistical significance. Therefore, controlling for the effects of IQ didn't alter the general profile of the participants with schizophrenia.

Semantic memory impairment in schizophrenia and symptomology
Neither PANSS Positive symptom ratings (max r <.26, p > .25 for all correlations, average r = 0.07), nor Negative symptom ratings (max r <.107, p > .29 for all correlations, average r = -0.10) correlated with performance on any of the 7 subtests. However there was a significant correlation between PANSS general scores and scores on the Level 2 Sorting task (r = .539, p = .014)

Applying the storage and access criteria
Method 1: The 4 criteria specified by Warrington and Shallice (1979):

1. Item Consistency
The AD group were consistent for the pair-wise comparisons of Naming vs. Word-picture matching (t (22) = 3.690, p = .001) and Semantic association, Pictures vs. Words (t (25) = 6.073, p <.001) but were inconsistent for the pair-wise comparison of Sorting Level 2 vs. Naming (t (25) = 1.336, p = .194).

The schizophrenia group were inconsistent in their responses for the pair-wise comparisons of Naming vs. Word-picture matching (t (10) = 1.64, p = 1.31), or Sorting Level 2 vs. Naming (t (16) - = 1.179, p = .256) but were consistent in the Semantic association, Pictures vs. Words comparison (t (19) = 4.805, p <.001). In summary there is some dissociation between the AD and the schizophrenia groups as consistency of error scores appeared to be more robust in AD, than in schizophrenia.

2. Frequency
There was a significant difference in the AD and schizophrenia groups in the extent to which word frequency influenced test performance. Of the participants in the AD group, 46% displayed a significant frequency effect (p<.05) in comparison to 14% in the schizophrenia group and 10% in the control group.

The AD group made more errors on items with low word frequency relative to high frequency than the schizophrenia group (t (44) = -2.809, p =.007) and were therefore significantly more affected by word frequency.

3. Cuing Effect

All three groups improved significantly when cued although there was only a minimal significant improvement in the control group (Z= -1.956, p = .05). Surprisingly the AD group showed the greatest improvement when cued (Z = 3.576, p >.001) but the schizophrenia group also improved significantly (Z = -3.509, p >.001).

4. Bottom – up Deterioration

All three groups showed a significant "bottom-up" effect, including the controls (Table 7), in that there was a significant deterioration in performance between Superordinate Sorting (Level 1) and Base Sorting (Level 2) (p <.01 for all groups) and then a further deterioration for Subordinate Sorting (Level 3) (p <.001 for all groups).

Method 2: The 2 parameter stochastic method (Faglioni and Botti 1993)

The probability that an item was stored in semantic memory did not differ significantly between the two patient groups (t (44) = .041, p = .968, r = -.097). Both groups had a mean storage capacity of at least .998 (schizophrenia s.d = .0046, AD s.d = .010).

The probability of retrieving an item from store did not differ significantly between the two groups (t (44) = 1.87, p = .068, r = -.262) but nevertheless the schizophrenia group were better at retrieving stored items having a mean r value of .867, (.063) compared to the AD group, .826, (.084).

Table 10: To what extent do the performances of the groups meet the criteria for a storage disorder?

	Item Consistency?	Frequency Effect?	An absence of improvement after cueing?	Bottom – up Deterioration?	Storage Disorder (as classified by Faglioni and Botti 1993).
AD	High	Yes	No	Yes	No
SZ	Low	No	No	Yes	No

SZ = schizophrenia

As is evident from Table 10, although neither group met all the criteria for a storage disorder, the AD group met 3, whereas the schizophrenia group met only one of the 4 criteria.

For the schizophrenia group, correlations between the storage-access parameter and the MMSE scores were significant (r (20) = -.57, p = .009). There were no significant correlations with either pre-morbid or current IQ, disease chronicity or any of the symptom measures.

5.2.7. Discussion

This study was designed to investigate the profile and underlying causes of semantic memory impairments in schizophrenia. AD participants provide a useful comparison group since the literature indicates a loss of stored semantic representations (Chertkow and Bub 1990). In the current study, the semantic memory profile for AD was consistent with a storage disorder with widespread impairments across the spectrum of subtests. This is perhaps because semantic representations in AD are degraded to the extent that retrieval is impossible, irrespective of the test used. People with schizophrenia however, appear to have no, or minimal impairments on naming, word picture matching, superordinate and base level sorting tasks, whereas they performed similarly poorly to the AD group on tasks requiring access to semantic associations, or using a subordinate sorting category. A number of other studies (McKay et al 1996, Barrera et al 2005, Leeson et al 2005a, Rodriguez-Ferrera et al 2001) also report that people with schizophrenia are only impaired on certain tests of semantic memory and have intact performance on others. Therefore, the AD and schizophrenia groups appear to not only differ quantitatively with higher error rates in the AD group but also qualitatively as they do not show the same profile of impairment across tests. This therefore suggests that there are different explanations behind the semantic memory impairments in the two groups.

I used two methods of assessing whether the semantic memory impairments in schizophrenia were caused by a loss of stored knowledge or difficulties with knowledge retrieval. The AD patients met 3 of the 4 criteria specified by Warrington and Shallice (1979) as typifying a storage disorder; consistency of errors across tests, more errors on low frequency words and bottom up deterioration. However the AD group did perform better on the word-picture matching task in comparison to the naming task which suggests that word recall in AD is facilitated with cues. Using the same model it was found that the patients with schizophrenia met only one of the four criteria stipulated for a storage disorder. They did show "bottom up deterioration" on the category sorting task but the controls also showed this pattern. Neither clinical group showed a storage impairment using the stochastic parameter model which may have been due to the relatively small amount of errors each group made.

Whether store and access are separable processes, rather than interacting ones, has however been brought into question (Forde and Humphreys 1997, Rapp and Caramazza 1993). Secondary analyses suggest that the Warrington and Shallice (1979) classical neuropsychological model is not critically or theoretically robust and is maybe limited in what it can tell us about semantic memory impairments in schizophrenia. The fact that the two criteria for a storage disorder that were met by our schizophrenia group (bottom – up deterioration and cueing) were also met by the non psychiatric control group indicates that the model is limited in validity for these particular criteria. For example the pattern of bottom up deterioration in all three groups is more likely to be a reflection of the fact that the sorting task becomes more difficult as more detailed knowledge is required (something that has been commented on before in the literature e.g. Cox, et al 1996). Variations in task difficulty may also explain the fact that all groups were able to identify items better when provided with a cue. Another issue is whether the storage/ access dichotomy reflects two distinctive neurological disorders as has been proposed (e.g. Warrington and Cipolotti 1996) or

disorders on a continuum. Work by Laws et al (1999) found that in a group of people with schizophrenia, the most severely cognitively impaired, chronically ill patients were those who presented with a storage disorder. Similarly, in the McKay et al (1996) study, the elderly and chronically ill patients in this study were those who most resembled the AD group in the severity of their semantic memory impairment. In addition MMSE scores were correlated with the presence of a storage disorder in the schizophrenia group. This suggests therefore that the notion of an access disorder being neurologically separate to a storage disorder is misleading and that there is far more of an overlap. For example it could be the case that as an access disorder worsens it resembles a storage disorder as retrieval becomes impossible for certain items.

The differences in performance profile between the schizophrenia group and the AD group suggest that there are different mechanisms underlying their semantic memory impairments. Anomia in dementia is consistently linked with pathology in the temporal cortex (e.g. Knibb and Hodges 2005, Galton et al 2001), most commonly the inferior temporal region (e.g. Mummery et al 1999, Hirono et al 2001). In schizophrenia, language impairments have not been linked to temporal lobe abnormalities in the same way and there are suggestions that language processing deficits in schizophrenia arise more from hippocampal damage (Suzuki et al 2005) or impaired frontal –temporal connectivity (Friston 1998). The different pattern of temporal lobe pathology in schizophrenia and AD (see Chapter 3) may well explain the intact naming and word-picture matching in schizophrenia and the widespread deficits in AD and perhaps future studies could confirm this fact using neuro-imaging techniques. It may however simply be a case of differing severity of neuropathology with the more widespread impairment in AD reflecting the greater and more prolific pathology.

There are several limitations to this study. Firstly mainly chronically impaired patients were used and therefore impairments may be part of an overall picture of cognitive difficulties and be unrelated to psychotic symptoms. This was supported by the lack of correlations between the PANSS and the semantic memory subtests. Nevertheless, where semantic memory impairments have been found in the literature, the most severe impairments have often been those in patients with a chronic illness and therefore this was a good comparison to the patients with AD. The fact that despite this there were clear differences between the clinical groups showed that even in patients with schizophrenia who do have a more debilitating illness their semantic memory impairment does not match that of a group of patients with mild-moderate AD. Another limitation is that the control group varied largely in age and although they were matched statistically to both clinical groups, the standard deviation was large. It may have been preferable to have two groups of controls, one matched to the schizophrenia group by age and one matched to the AD group by age just to determine if age really was a factor in determining semantic memory performance. However, there were no significant correlations between age and semantic memory subtest scores in either group. A further limitation, statistically, is that there are inherent difficulties in using multiple comparisons e.g. comparing the groups on a number of different measures of semantic memory, as this weakens the statistical power. Despite these limitations, however, this study is the first to directly compare

an IQ matched group of patients with chronic schizophrenia to a group of patients with AD across a battery of semantic memory tests.

In summary, the profile of semantic memory impairments in people with chronic schizophrenia is different in several ways from that of patients with AD. Unlike AD, there is little evidence for any degradation in the semantic memory store in schizophrenia and it is more likely that poor performance on some tests of semantic memory is due to difficulties retrieving knowledge. People with schizophrenia appear to have difficulties on certain tasks of semantic memory specifically and future studies should attempt to understand more about why this is. One possible explanation is that the Camel and Cactus tests and the higher level of the sorting task all made greater demands on executive functions, that are well known to be deficient in schizophrenia (e.g. Shallice et al 1991). It may be the case that semantic memory per se is not impaired in schizophrenia, but that on certain tests, when IQ and executive functioning demands are high, patients encounter difficulties. This hypothesis is addressed in the next study.

Chapter 6: Is an executive dysfunction responsible for the semantic memory impairments in schizophrenia?

Study Two: Comparing a group of people with an acquired brain injury resulting in a dysexecutive syndrome to a group of people with schizophrenia on the Hodges et al (1992) semantic memory battery.

6.1 Introduction

A publication based on Studies Two and Four is included in Appendix E.

An executive dysfunction is characterised by impairments on tasks involving planning, strategy, working memory, context and organisation. Executive functions have been found to involve specifically the prefrontal cortex, and patients with selective damage to this area often present with an executive dysfunction. Semantic memory processes are believed to depend on healthy executive functioning, as processes such as search, retrieval and verification of semantic information rely heavily on prefrontal functions (Baddeley 1990, Fletcher et al 1998, Wiggs et al 1998). In fact some neuropsychological assessments that aim to capture semantic memory impairments are also used as a measure of the dysexecutive syndrome, for example Verbal Fluency (Crawford et al 1993, Kolb and Whishaw, 1983, Gourovitch et al 2000). It is therefore likely that people with an executive dysfunction will perform poorly on tasks of semantic memory. In fact it has previously been suggested that errors on semantic memory tasks are due in part to executive problems, namely with retrieving information (Robert et al 1997, Frith 1992). In support of this, patients with frontal lobe damage or neurodegenerative conditions that affect the frontal lobes often display semantic memory impairments (e.g. Jefferies and Lambon Ralph 2006, Taylor et al 2005, Hodges et al 1991).

It is well known that executive functioning is profoundly impaired in schizophrenia (Shallice et al 1991, Evans et al 1997, Zalla 2000). In fact, some would go as far as to state that "all chronic schizophrenics have problems with processes tapped by "frontal" tests" Shallice et al (1991). It is therefore important that we determine whether the semantic memory impairments in schizophrenia are secondary to an executive dysfunction. Clinically, the symptoms and behaviours seen in schizophrenia have been compared to those occurring in people with damage to their frontal lobes (e.g. Morrison-Stewart et al 1992) especially negative symptoms (Liddle and Morris 1991). On neuropsychological tasks people with schizophrenia have also been found to have an executive dysfunction (e.g. Crespo-Facorro et al 2007). In a comprehensive study, Barrera et al (2005) found that people with schizophrenia performed poorly on several tests of executive function, over and above that of semantic memory. Whereas the schizophrenia group with formal thought disorder were found to be impaired on all executive function tests employed, they were only found to perform abnormally on 'higher-order' semantic associative tasks rather than lexical tasks such as naming. Barrera et al (2005) surmised that tasks assessing semantic memory vary substantially in terms of i) task difficulty and ii) demands placed on executive processes, and semantic memory impairments in schizophrenia occur where demands are placed on executive processes. It is therefore possible that the semantic memory impairments in schizophrenia could be explainable in part by executive failings.

The Camel and Cactus tests and level 3 of the sorting task were the tests that elicited the greatest numbers of errors in the people with schizophrenia. The Camel and Cactus tests require participants to select which item "goes best" with the target out of a number of competing alternatives and these tests place high demands on context processing, an area of executive functioning which has well been shown to be dysfunctional in schizophrenia (Hemsley 2005, Cohen et al 1999). There is some evidence that the Camel and Cactus tests rely more on frontal structures than some other tests which make greater demands on the temporal lobes. For example, in a study by Giovagnoli et al (2005) patients with temporal lobe epilepsy (TLE) were tested on a battery of semantic memory assessments including a semantic association test, the Pyramid and Palm Trees Test which is almost identical to the Camel and Cactus test. It was found that the TLE patients were impaired on the majority of semantic memory tests apart from the Pyramid and Palm Trees tests where their performance was intact. Conversely, when the performance of patients with Lewy body dementia (location of neurological damage is frontal-striatal) were compared to that of patients with Alzheimer's dementia on a battery of semantic memory tests, the Lewy body patients did worse on the Camel and Cactus tests and sorting tests compared to the AD patients who performed relatively better on these tasks (Lambon-Ralph et al 2001). The other subtest in which the group of people with schizophrenia were impaired was Level 3 of the Sorting Task which requires people to sort items into categories such as "bigger than a man" and "smaller than a man", a test which is conceptually similar to the Cognitive Estimates Test (Shallice and Evans 1978) used to assess executive functioning. In the other subtests of the battery which produced no impairment, there is little doubt over the accuracy of the answer given, with information either known or not known. However in the Level 3 sorting task, participants must make a decision which involves retrieving detailed semantic information and reasoning about that information, for example deciding if a particular animal eats meat or not. Therefore it could be argued that the 3 subtests on the Hodges et al (1992) semantic battery which did show much higher levels of impairment in schizophrenia are not only the most difficult (although as IQ was controlled for, this cannot wholly explain the impairments on these 3 tests) but also place greater demands upon executive abilities. In order to test this hypothesis, it was decided to a) assess the level of executive functioning in schizophrenia and perform correlational analyses to determine the relationship (if any) between semantic memory and executive functioning and b) assess a group of patients with a dysexecutive syndrome caused by acquired brain injury on the Hodges et al (1992) semantic memory battery and compare their performance profile. Following a similar line of reasoning to study one, a neurological control group were recruited in order to a) provide a well matched (on the basis of IQ) non –psychotic control group and b) attempt to isolate the cause of any impairment by investigating whether a group of patients with a dysexecutive syndrome but no semantic memory impairment could successfully complete the Hodges et al (1992) battery.

6.2. Method

6.2.1. Design

In the same way as the previous study, this study was case control in design. The research hypotheses are:

- There will be a relationship between poor performance on tasks of semantic memory and poor performance on measures of executive functioning in schizophrenia.
- The patients with ABI will show a similar pattern of semantic memory impairment to the patients with schizophrenia and will do worse on the tasks that make greater demands on the executive system.

6.2.2. Participants

The same participants with schizophrenia that were recruited in Study One were included in this study. In addition, the same control group was used.

The patients with ABI were inpatients at a regional rehabilitation unit and had no known history of psychiatric illness or drug or alcohol misuse. The locus of their brain lesions varied but people in this group were identified as presenting with a dysexecutive syndrome as the principle neuropsychological disorder (i.e. not secondary to a memory/ attentional/ other neuropsychological abnormality). This was assessed using the Behavioural Assessment of the Dysexecutive Syndrome (BADS) (Wilson et al 1996). Table 11 shows details of the exact nature of the brain injury for each participant. The length of time between the date of the trauma and the time of testing varied for each participant. Nevertheless, the executive functions of each participant were assessed over a period of a maximum of two weeks so any improvement, deterioration with regards to their executive function abilities would have been minimal. Therefore the BADS scores reflect the executive functioning of the ABI group at the time of testing.

Table 11: Information on the nature of the acquired brain injury for the ABI group

Participant	Nature of Injury
HF1	Data Unavailable
HF2	Data Unavailable
HF3	Large (80%) MCA nfarct in right hemisphere – loss of grey/ white differentiation
HF4	Right hemisphere infarct – compression of right lateral ventrical. Left hemiparesis.
HF5	Staphyloccal septicaemia. Multiple cerebral lesions – heamorrhogic septic emboli in left cerebral hemisphere in both occipital lobes.
HF7	Large right fronto-parietal intracerebral haematoma.
HF9	Right basal ganglia infarct
HF10	Dermatomyositis
HF11	Severe traumatic brain injury – cerebral oedema – fractured temporal and parietal bones.
HF12	Right cerebellum infarct

Table 12: Demographic and psychometric information for groups of participants in Study Two.

	SZ	ABI	Controls (C)	ANOVA / t tests	Post Hoc t tests
Age	51.20 (11.18)	42.60 (13.32)	53.50 (23.84)	F (2, 47) = 1.29, p = 0.28	
Male/Female	11/9	8/2	11/9		
NART Pre-morbid IQ	100.50 (24.76)	106.43 (12.59)	112.88 (8.04)	F (2, 47) = 2.12, p = 0.13	
WASI Full Scale IQ	85.15 (17.49)	77.63 (15.00)	119.90 (16.78)	F (2, 47) = 28.63, p < 0.01	C >SZ** C >ABI**
WASI Verbal IQ	83.20 (17.12)	84.88 (13.95)	114.20 (19.63)	F (2, 47) = 17.18, p < 0.01	C >SZ** C > ABI**
WASI Performance IQ	90.55 (19.44)	68.50 (18.49)	121.60 (15.76)	F (2, 47) = 30.23, p < 0.01	C > SZ** SZ >ABI* C > ABI**
MMSE	27.80 (1.74)	27.00 (2.49)	-	t (28) = 1.03, p = 0.31	
BADS	12.90 (5.68)	12.20 (3.05)	-	t (28) = 0.36, p = 0.72	

** = p <.01 * = p <.05

As is clear from Table 12, the clinical groups were matched on age, MMSE scores, NART scores, BADS scores and also verbal and full scale IQ scores. However the two patient groups were more cognitively impaired than the control group although all groups were comparable in terms of their pre-morbid IQ and age.

6.2.3. Procedure

As before, I worked alongside Verity Lawrence, an MSc student, in collecting data for this study.

The patients with ABI were given the same assessments as the people with schizophrenia (apart from the PANSS) as outlined in Study One. In addition both clinical groups were assessed using the BADS.

The Behavioural Assessment of the Dysexecutive Syndrome (BADS) (Wilson et al 1996)

There are many tests of executive functioning but the more traditional measures tend to only capture the cognitive impairments and not the day to day problems encountered by patients with a dysexecutive syndrome. The BADS was therefore developed as an ecologically valid measure of the dysexecutive syndrome. It consists of 6 tests; Rule Shift, Zoo Map, Action Program, Six Elements, Temporal Judgement and Key Search.

Rule Shift Test

This task was designed to assess a patient's ability to inhibit newly learnt responses. Participants are given a book of playing cards and told to say "Yes" or "No" as they turn each page depending on a rule. There are two rules and the participant's performance is assessed whilst adhering to the second rule as they must inhibit what they have learnt from the first rule.

Zoo Map Test

Participants are given a map of a Zoo and asked to plan their trip around the Zoo whilst visiting certain animals and taking in certain rules. This assesses the ability to plan whilst considering a lot of information.

Action Program Test

Participants are given a set of apparatus and are instructed that they must find a way of using the different tools to achieve a goal which in this case is to get a cork out of a tube without touching it.

Six Elements Test

Participants are given ten minutes to complete as much as they can from 6 different tasks. This task assesses time management as there is far too much to do in the set time and in order to complete as much as possible from all 6 tasks participants must switch tasks in a timely way. Adherence to a rule is also assessed as part of this task.

Temporal Judgement Test

This task consists of a set of questions pertaining to how long everyday tasks take e.g. "How long does it take to blow up a balloon?" The participant must estimate these times.

Key Search Test

Participants are told to imagine they have lost their keys in a field and must plan a search strategy in order to ensure they are found.

The patients with ABI were assessed using the full BADS. The participants with schizophrenia were assessed using two of the BADS subtests; the Rule Shift and the Six Elements. This was because of time constraints (the ABI group had already been assessed using the BADS as part of their clinical assessment). The BADS has been used in people with schizophrenia and found to be a reliable measure of their executive abilities, over and above any intellectual difficulties (e.g. Evans et al 1997). These two subtests were chosen as they appeared to be the two tests that best represented a full assessment of executive functioning, covering inhibition, task switching, planning, strategy skills and time management. A BADS score was derived for the ABI group based on the two subtests that were used to assess the people with schizophrenia. Using this information, a sub-analysis also found the groups to be still matched on prorated BADS scores ($t(28) = -.923$, $p = .364$). The mean prorated BADS score for the ABI group was slightly higher than when derived from all 6 tests at 14.1, (s.d = 2.84).

6.3. Results

Table 13: Semantic memory test results for the schizophrenia, ABI and control groups

	Sz	ABI	Controls			
Naming	3.20 (3.46)	2.40 (2.95)	0.70 (1.13)	*F* (2, 47) = 4.57, *p* = 0.02	SZ >C*	*F* (1, 28) = 2.68, *p* = .114
Word-Picture matching	1.15 (1.90)	1.50 (3.06)	0.40 (0.68)	*F* (2, 47) = 1.43, *p* = 0.25		
Sorting	3.85 (2.87)	1.00 (0.94)	2.40 (1.43)	*F* (2, 47) = 6.60, *p* = 0.03	SZ> ABI**	*F* (1, 28) = 6.89, *p* = .015
Semantic Association (pictures)	13.35 (6.95)	7.90 (4.07)	4.70 (2.87)	*F* (2, 47) = 14.56, *p* < .01	SZ >ABI* SZ >C**	*F* (1, 28) = 8.48 , *p* =.007
Semantic Association (words)	13.60 (7.17)	5.90 (3.21)	2.55 (3.40)	*F* (2, 47) = 4.56, *p* < .01	SZ >ABI* * SZ >C**	*F* (1, 28) = 17.92, *p* <.001

Table 13 shows the scores for all three groups on the tests of semantic memory. Scores on 4 of the 7 subtests correlated significantly with BADS scores in patients with schizophrenia (Naming, r =-.466, p = .038; Word-picture matching, r =-.588, p =.006; Semantic association Pictures, r = -.658, p =.002: Sorting Level 3, r = -.4, p =.08), indicating a role for executive functioning in semantic memory test performance. However it should be noted that on two subtests (Naming and Word-Picture matching) which correlated highly with BADS scores, the error rate for the schizophrenia group was similar to the controls. This indicates that semantic memory impairments are not only found on semantic memory subtests that correlate highly with a measure of executive dysfunction.

Surprisingly there was also a strong negative correlation between the BADS scores and the number of criteria met for a storage disorder (r (20) = -.49, p = .030), indicating that participants with a dysexecutive problem were more likely to have a storage disorder. Those meeting criteria for a predominant access disorder had significantly higher scores on the BADS, indicating a relatively intact executive system, whereas those meeting criteria for a storage disorder were more likely to have an executive dysfunction. This is counter intuitive, given the role of executive functions in retrieval from long term memory (Nathaniel-James et al 1996).

6.4. Discussion

This study found that an executive dysfunction does not fully explain poor performance on semantic memory tests in schizophrenia. Although there was a relationship between BADS scores and performance on some of the tests of semantic memory in schizophrenia, this was not consistent with the pattern of errors across tests. Therefore, although it could be said that an executive dysfunction is likely to be a contributing factor to poor semantic memory test performance it clearly cannot account for it fully. In addition, the ABI group who had a severe executive dysfunction were able to perform well on the semantic test battery suggesting that the tasks don't require intact executive abilities. The fact that the group of schizophrenia, who were also severely impaired on the BADS showed intact performance on a number of tests suggests either that their executive dysfunction does not impede their semantic memory performance on a number of tests or that for these tests, the executive function demands were minimal. This therefore implies that the other tests e.g. Camel and Cactus tests perhaps made more demands upon the executive functions. The lack of significant correlations, however, between BADS scores and the performance on these tests, and also the fact that they were completed at a normal level in the ABI group goes against this theory however.

However extrapolating from the behaviour of the ABI group to the neuropsychology of the people with schizophrenia is perhaps unwise. Although this goes some way towards ruling out the need for intact executive functioning for successful completion of these tasks , it is nevertheless possible that the ABI group compensated by relying on different processes that obviated their dysfunctional executive system e.g. the use of semantic associations. Furthermore the executive abilities of the schizophrenia group were only measured using two of the subtests of the BADS. As with semantic memory the concept of the executive functions, whilst traditionally pertaining to inhibition, working memory and self governance (i.e. strategy and planning) has also been proposed to include contextual processing, emotional processing, risk taking and attentional processing (REFS). Executive functions are believed to be fractionated (Shallice and Burgess, 1991). This has also been shown to be the case in schizophrenia (Chan et al 2006) and within individuals; it was found that whilst there could be failures on one domain e.g. initiation or sustained attention, performance was often reported to be intact on tasks assessing other domains e.g. switching and flexibility, disinhibition and attention, allocation and planning. The type of executive functions measured by the BADS may only target a small selection of these abilities and therefore one cannot generalise from this to executive abilities in general, especially as the group of patients with schizophrenia were only assessed on two subtests. Another limitation of this study is that data were unavailable regarding the exact nature of the brain damage for two participants in the ABI group. In addition, the time between trauma and the date in which the executive functions of the group were assessed, varied for each participants. Therefore, although the ABI group had a primary diagnosis of an executive dysfunction, the type, locus and time since damage for each participant varied widely and therefore this group are heterogeneous.

Despite these caveats however this study does go some way towards ruling out the explanation that an executive dysfunction can explain poor semantic memory test performance. However this does not necessarily justify the conclusion that semantic memory is a primary impairment in schizophrenia. As the more contemporary models

of semantic memory imply, semantic memory processes do not just involve accessing a store of knowledge representations but also rely largely on contextual knowledge and automatic attentional processes. These “top down” abilities are not necessarily captured by the traditional tests of executive functioning.

Chapter 7: Abnormal categorisation in schizophrenia

Traditional models of semantic memory posit that concepts can be grouped into categories based on their taxonomic similarity. The most basic categories tend to concur with natural taxonomies e.g. animals, fruits and body parts and are believed to facilitate an evolutionary advantage for information processing purposes. In addition, ad hoc categories (i.e. not natural/ taxonomic categories) can be formed around specific situational contexts or goals e.g. things to take on a picnic (Barsalou 1983). Nevertheless, it is assumed that within (and largely across) cultures people's semantic memory is organised similarly with concepts grouped according to well defined categories. Tasks of semantic categorisation assess the structure of a person's semantic memory, in particular whether concepts are organised normally i.e. in standard taxonomic categories e.g. animals.

One potential explanation for the increased abnormalities on tasks of semantic memory in people with schizophrenia is that their semantic memory is organised differently from that of people without schizophrenia. As is evident from the literature review/ meta-analysis, there is much data to support the view that semantic memory in schizophrenia is organised qualitatively differently (e.g. Paulsen et al 1996), resulting in, for example, an extension of category boundaries (Chen et al 1994) and a tendency to overinclude (i.e. to group unrelated concepts together into the same category) (Green et al 2004). Similarly to an access disorder, a disorganised semantic memory is likely to produce an inconsistent profile of impairment with problems on tasks of association and categorisation, idiosyncrasies in how concepts are related, difficulties recalling items in sequence on verbal fluency tasks and perhaps a lack of priming. All of these performance patterns have been cited in groups of people with schizophrenia as illustrated by the literature review.

The view that semantic categories are largely structured based on taxonomic information has somewhat been outdated by contemporary theories of how people form judgements of similarity between concepts. Traditionally, similarity was seen as a process of attribute matching based largely on perceptual features or perhaps on prototypes of category exemplars. However, more recent models stress the role of contextual knowledge and flexibility in how concepts are grouped together in our minds (e.g. Medin et al 1993). Goldstone (1994) discusses the different "respects of similarity" that people use in different situations and states that the "respects" we use are governed by the situational context. For example in certain situations where there is a clear situational goal e.g. planning a picnic, a more ad hoc (Barsalou 1983) respect of similarity is used to group concepts. A qualitative analysis of the strategies behind any abnormal categorisations should therefore shed some light on the different respects of similarity used.

Overinclusion has been traditionally referred to as the hallmark of psychotic thinking (Payne, 1973) and is conceptually similar to "loosening of associations" (Bleuler 1911) where speech becomes tangential and derailed e.g.

"C.I.A. Loves, wants Al-Qaeda, one family, they can't tell you about the C.I.A, conversation is in your head, you see and hear what's in your head, I put rooms in rooms, surfaces over surfaces and people in people, everything has a twin, nothing in

seen, everything has been seen, hell's angel, imagines, one mind in hell" (Extract from speech of a patient with F.T.D).

In many ways assessing overinclusion on categorisation tasks such as the CGT is a means of operationalising the concept "loosening of associations". With the traditional tests of semantic memory, performance is measured quantitatively, according to error rates. Free sorting categorisation tasks on the other hand appear to elicit qualitative differences in the way in which concepts are associated and the bizarre nature of the sorts appear to resemble "psychotic thinking". Although the link between FTD and overinclusion in schizophrenia has not been consistently reported, early research did suggest that overinclusion lies at the heart of understanding both the semantic memory impairments (e.g. McKenna et al 1994) and also the symptoms (Payne 1973) in schizophrenia. An aim of this study was to explore how the abnormalities on tasks of categorisation in schizophrenia relate to semantic impairments on the more traditional tests. A further aim was to investigate the relationship between clinical symptoms (in particular FTD) and cognitive impairments in schizophrenia in relation to categorisation performance.

Study Three: Semantic categorisation in schizophrenia

7.1. Introduction

It has been shown that people with schizophrenia perform differently to controls on tasks of semantic categorisation, for example the Category Generation Test (CGT), with a tendency for overinclusion and underinclusion (where categories are subdivided) (e.g. Green et al 2004). This was traditionally seen (e.g. Payne 1973) to be a reflection of disordered thinking processes, a loosening of associations between concepts, defined by Bleuler (1911/ 1950, p. 14) as:

"If the disease is marked, the personality loses its unity....Often ideas are only partially worked out, and fragments of ideas are connected in an illogical way to constitute a new idea. Concepts lose their completeness, seem to dispense with one or more of their essential components; indeed, in many cases they are only represented by a few truncated notions.... the process of association often works with mere fragments of ideas and concepts. This results in associations which normal individuals will regard as incorrect, bizarre, and utterly unpredictable."

Although abnormal categorisation is well documented in schizophrenia, it is not clear whether this is related to the symptomatology of schizophrenia or is just part of the constellation of semantic memory impairments. Therefore what was traditionally viewed as a fundamentally psychotic phenomenon could in fact be arising from a peculiarity of semantic memory. In order to test this possibility, a group of patients with Alzheimer's dementia, who have a profound semantic memory impairment, were assessed on the CGT. If a semantic memory impairment does explain overinclusive thinking in schizophrenia then, depending on the nature of the impairment, one might expect the AD group to also overinclude on the CGT.

Subtle differences in the semantic memory impairments in AD and schizophrenia may affect the way in which both groups sort on the CGT. The category generation test (CGT) used in this study features a set of everyday items which fall under five

superordinate category labels (Rosch et al 1976). In schizophrenia, overinclusion is reported despite the fact that detailed item knowledge has been found to be relatively intact (e.g. Barrera et al 2005, Al-Uzri et al 2004) and the internal category structures are also reported to be preserved (Chan et al 1994). Whereas general category (taxonomic) information is often intact in patients with mild AD (Martin and Fedio 1983, Chertkow and Bub 1990, Done and Gale 1997), many studies have reported that more detailed attribute knowledge is the first to become degraded (Hodges et al 1992). Bonilla and Johnson (1995) predicted that a loss of specific item knowledge in AD would result in the likelihood of sorting items on a categorization task into multiple dimensions, often termed underinclusion. One might therefore expect that the AD group would sort taxonomically on the CGT because of their preserved taxonomic categories but with perhaps some underinclusion (i.e. forming multiple groups out of one category). In contrast, one would expect overinclusion in schizophrenia due to overextended category boundaries/ spreading activation i.e. a disorganised semantic memory. A qualitative analysis of the reasons given for any unusual card sorts will cast light on further differences in the types of semantic memory impairments.

Any differences between the groups would be illustrated by their performance on two supplementary tasks assessing category knowledge and attribute knowledge. It is expected that the AD group would have lost knowledge of semantic attributes so will perform worse on a semantic probes task whereas attribute knowledge will be intact in schizophrenia. In addition it is expected that both groups would perform well on a task assessing taxonomic knowledge (a sort to label task) reflecting their intact category knowledge.

7.2. Method

7.2.1. Participants

The same participants who took part in Study One were tested using the CGT for Study Three. In addition, data from another 2 patients with schizophrenia was included. These patients had been unable to complete the full Hodges et al semantic memory battery and several of the baseline tests because of fatigue but could complete the CGT.

Therefore, the demographic and psychometric data for the schizophrenia group is shown in Table 14:

Table 14: Demographic and psychometric data for three groups in Study Three

	Schizophrenia (SZ)	Alzheimer's Dementia (AD)	Controls (C)	ANOVA	Post Hoc t tests
N	22	26	17		
Age	50.82 (11.66)	76.27 (7.34)	61.29 (24.97)	F (2, 64)= 17.18, p <.001	AD>SZ**, AD>C*
Gender (M/F)	11/11				
MMSE	27.8 (1.74)	22.27 (2.07)	-	t (44) = 9.62, p <.001	
Current IQ (WASI) - Full Scale - Verbal - Performance	85.15 (17.491) 83.2 (17.121) 90.55 (19.44)	88.16 (16.59) (n =19) 88.21 (15.82) (n =24) 83.90 (34.04) (n =21)	107.88 (14.86) 103.24 (17.72) 111.35 (17.04)	F (2,60) = 10.87, p =.007 F (2,60) = 5.40, p <.001 F (2,60) = 9.43, p <.001	C >SZ** AD>SZ*, C>SZ** SZ>AD*, C>SZ**
Pre-Morbid IQ (NART)	100.5 (24.76)	103.15 (22.69)	102.27 (28.18)	F (2,58) = .065, p = .938	
PANSS (general)	30.40 (6.236)	-	-	-	
PANSS (conceptual disorganisation)	10.15 (3.167)	-	-	-	
PANSS (positive)	17.75 (5.077)	-	-	-	
PANSS (negative)	15.45 (6.778	-	-	-	

7.2.2. Materials

The Category Generation Test (CGT) was designed by Green (Green 2002) and consists of 45 picture cards which make up 5 taxonomic categories; animals, fruit, body parts, clothes and vehicles. Data taken from a normal population (provided in Appendix F) shows that controls are constrained sufficiently by these categories to sort in this way. The cards (approximately 6 x 4 inches) contain pictures of drawings which were chosen from the Snodgrass and Vanderwart (1980) selection and an equal variety of high, medium and low typicality items were included in each category. In fact items in the five taxonomic categories were matched for typicality using Battig and Montague's (1969) category norms and a one way ANOVA found them not to differ significantly (f (4, 25) = 0.006, p = 1.0).

A set of semantic probes was created to assess detailed attribute knowledge of the items on the CGT. For each item a set of 5 questions was devised such as "Which animal has a mane?" or "Which fruit makes wine?" Ten mentally healthy controls were asked to answer these questions and only the questions which were answered correctly by at least 90% of the controls were included in the probe task. In the end, there were 3 questions for each item. The probe questions were printed on laminated cards of the same dimensions as the CGT cards.

7.2.3. Procedure

The CGT

Participants were given a set of shuffled cards and asked to sort them into groups of items that they "feel go together best". They were told that there were no restrictions on the number of groups they made or the number of cards in each group and they were given no time limit. When it was clear that the participant had finished sorting they were asked to provide a name for each of their groups. For a selection of groups that were abnormally sorted participants were asked to provide an explanation for why they had formed the group and why they had put certain cards together. Their responses were recorded verbatim.

The Probes Task

For people who had sorted abnormally on the CGT, two cards were selected which belonged in the same taxonomic category e.g. apple and banana but had been placed in separate piles by the participant. The participant was then asked to answer 6 questions about the two items. So for example if the two items were Camel and Tortoise the participant was asked "Which one of these has a hump?" These questions target detailed, subordinate information which is needed to distinguish between items of the same taxonomic category. The order of the 6 questions was randomised. This procedure was carried out for a maximum of 6 mis-sorts (questions were limited to six because the duration of testing for each participant was already fairly long).

Sorting to Label Task

Where cards had been sorted abnormally participants were also asked to complete a Sorting to Label Task. For a category that had been mis-sorted, participants were asked to then find all the cards for that category for example "find all the animal cards". The cards were shuffled prior to this task. If all 9 cards in that category were found, the participant's response was marked as correct.

7.4. Results

Quantitative Analysis

A participant was said to have overincluded if they placed items from two or more taxonomic categories into the same pile. A participant was said to have underincluded if they placed cards from a single taxonomic category into two or more piles. Proportions of overinclusion and underinclusion were then measured and can be seen in Table 15. This refers to the percentage of people in each group who overincluded or underincluded at least once on the CGT.

Table 15: Proportions of people who abnormally sorted on the CGT (overincluded and/or underincluded).

Group	Abnormally Sorted	Overincluded	Underincluded
Schizophrenia	64%	50%	55%
AD	65%	38%	62%
Controls	23%	6%	18%

People who abnormally sorted could overinclude and underinclude therefore there is an overlap in the percentages.

Chi square analyses were conducted to compare performance within each category, between groups e.g. a comparison of the number of people in each group who underincluded. The schizophrenia group differed from the normal controls for abnormal sorting (x2 (1) = 6.21, p = .013), overinclusion (x2 (1) = 8.76, p =.003) or underinclusion (x2 (1) = 5.52, p = .016). The AD group differed from the normal controls for abnormal sorting (x2 (1) = 7.21, p = .007), overinclusion (x2 (1) = 5.73, p = .017) and underinclusion (x2 (1) = 8.03, p = .005). Chi square analysis showed that the patient groups did not differ on the degree to which they abnormally sorted (x2 (1) = .016, p = .900), the degree to which they overincluded (x2 = .645 (1), p = .422) or the degree to which they underincluded (x2 (1) = .240, p =.624). In addition, each participant was given a score of i) overinclusion and ii) underinclusion on the CGT using the following formulae (Green 2002).

$$\text{Overinclusion} = \frac{\sum (\text{Taxonomic categories in each "sort category"})}{\text{Total number of "sort categories" formed by the participant}}$$

$$\text{Underinclusion} = \frac{\sum (\text{Number of "sort categories" each taxonomy is divided into})}{\text{Number of taxonomic categories (5)}}$$

For example, consider a participant sorting as follows:

1. car, bus, airplane, train, bicycle, helicopter, horse, cow, camel, elephant
2. cat, tiger
3. shirt, sock, coat, dress, hat, belt
4. orange, pear, banana, grapes, lemon, pineapple
5. arm, eye, foot, ear, hand, lips

Using the above formula, the overinclusion score is calculated as follows. Firstly the numerator is the sum of the number of taxonomic categories in each sort formed, so in this case there are 2 taxonomic categories in sort 1 (vehicles and animals) and only 1 in each of sorts 2-5. The sum is therefore 6. The denominator is the total number of sorts formed which is in this case 5. Therefore the overinclusion score for this participant is 1.2.

To calculate the underinclusion score, the numerator is the sum of the number of sorts each taxonomic category is divided into. In this case all categories are sorted together into one sort apart from the category animal which is split into two sorts. Therefore the sum is 6. The denominator is the 5 taxonomic categories that can be formed. Therefore the underinclusion score for this participant is 1.2.

For the schizophrenic group the mean overinclusion score on the CGT was 1.13, the mean underinclusion score was 1.89 and the mean total CGT score was 3.01. For the AD group the mean overinclusion score was 1.11, the mean underinclusion score was 1.62 and the mean total CGT score was 2.73. A Kruskal-Wallis non parametric test found there to be no statistically significant difference between the two groups on the basis of their overinclusion scores ($x = .427$, $p = .514$), their underinclusion scores ($x = .041$, $p = .840$) or their total CGT scores ($x = .112$, $p = .737$).

Qualitative Analysis

The reasons each participant gave for the abnormal sorts made were coded according to the following codes:

- Thematic (based on relations among objects and events that co-exist in time or space (D. R. Denney (1975) e.g. because they are all found in the kitchen)
- Functional (grouped together because of functional relationships between items e.g. because they fit together)
- Perceptual (based on physical features) e.g. because they are both long
- Subordinate (based on detailed attribute features e.g. flying vehicles)
- Phonemic (based on sound of word e.g. they both end in "T")
- Experiential (autobiographical e.g. when I was five I used to be terrified of dogs and horses)
- Unmediated (did not know the reason e.g. I don't know)

Two researchers (who were not involved with the study) independently rated the protocols, blind as to diagnosis. An inter-rater reliability analysis produced a Kappa value of .814, p <.001.

Table 16: Percentage of abnormal sorts for each category for the two groups

	Thematic	Functional	Perceptual	Phonemic	Subordinate	Unmediated	Experiential
SZ	42	45	6	9	22	9	1
AD	14	11	3	2	52	12	0

Table 16 shows the percentage of abnormal sorts for each group which fell within the categories. There was a significant difference in the proportions of thematic sorts between the two groups ($x2$ (1) = 15.03, p <.001) i.e. the group with schizophrenia were significantly more likely than the AD group to give thematic explanations for their sorts. The people with AD were more likely to give subordinate explanations (e.g. by attribute features) than the people with schizophrenia ($x2$ (1) = 14.616, p <.001). There was no difference in the degree to which the groups sorted perceptually (p = .327), functionally (p = .363), phonemically (p = .165), experientially (p = .372) or gave unmediated responses (p = .453).

Semantic Probes Task

In the AD group, 24 people (92 %) answered all their semantic probes correctly compared to 18 people (82 %) in the schizophrenia group who answered all their semantic probes correctly. A Fisher's Exact Probability Test found that there was no difference in the number of people in each group who made errors on the probe questions, ($x2$ (1) = 1.19, p = .392).

If differences in semantic feature knowledge between the groups are related to poor performance on the CGT one would expect a positive correlation between CGT scores and errors on the semantic probes task. In the schizophrenia group there were no significant correlations (using a point-biserial correlation) between the semantic probes task and overinclusion scores (r = .399, p = .066), underinclusion scores (r = -.091, p = .688) or overall CGT scores (r = -.021, p =.927). The lack of significant correlations was replicated in the AD group for correlations (again using a point-

biserial correlation) between the semantic probes task and; overinclusion scores (r = .037, p =.857); underinclusion scores (r = .369, p = .063) and overall CGT scores, (r = .311, p = .122). Therefore for both patient group no significant relationship was found between CGT performance and the ability to answer questions about semantic attributes.

Category Sorting to Label Task

In the AD group, 21 people (81%) were unable to form the complete taxonomic category for mis-sorted items, compared to 19 people (87%) in the schizophrenia group. A Fisher's Exact Probability Test showed that there was no significant difference between the performance of the two groups on this task, ($x2$ (1) = .269, p = .710).

Point-biserial correlations were taken between the participant's overinclusion, underinclusion and overall CGT scores and their ability to complete the sorting to label task. In this case, if there was a relationship between poor CGT performance and poor performance on the sorting to label task one would expect a negative correlation. For the schizophrenia group, no correlations reached significance for either overinclusion scores (r =.071, p = .753), underinclusion scores (r = .079, p = .726) or CGT scores in general (r = .087, p = .700) and sorting to rule task performance. For the AD group however, there was clearly more of a relationship between CGT performance and the ability to utilise taxonomic information; the correlation between overinclusion scores and strategy scores wasn't significant (r = .174, p = .395), underinclusion scores were significant (r=.389, p = .050) and there was a trend for significance between overall CGT scores (r = .365, p = .067) and the ability to sort when provided with a label. So, for the group of people with schizophrenia, CGT performance was unrelated to the ability to form coherent taxonomic categories in a structured task. However in the AD group a stronger relationship between the two tasks was found.

Correlations with other tests of semantic memory

Overinclusion on the CGT was not found to be correlated with any of the semantic memory tests for the group with schizophrenia, for naming, r = 0.27, p = .24, word-picture matching, r = 0.20, p = .40, sorting level 1, r = .15, p = .54, sorting level 2, r = .16, p = .51, sorting level 3, r = 0.25, p = .29, semantic associations pictures, r = 0.13, p = .58, and semantic associations words r = -0.02, p = .93. Underinclusion on the CGT was also not found to be correlated with any semantic memory test for the group with schizophrenia, for naming, r = 0.12, p = .59, word-picture matching, r = 0.08, p = .73, sorting level 1, r = 0.10, p = .67, sorting level 3, r = .34, p = .15, semantic associations pictures, r = -0.02, p = .93 and for semantic associations words, r = -0.33, p = .16. However there was a significant correlation between underinclusion and performance on sorting level 2, r = .45, p = .05.

In the AD group, there was also a lack of a significant correlation between CGT performance and performance on the Hodges et al semantic memory battery. Overinclusion was not significantly correlated with naming, r = -.125, p =.541, word picture matching, r = .010, p = .960, sorting level 1, r = -.197, p = .333, sorting level 2, r = .019, p = .926, sorting level 3, r = .056, p = .786, semantic associations pictures,

r = .093, *p* = .651 or semantic associations words, *r* = .157, *p* = .443. Underinclusion was also not significantly correlated with either naming, *r* = -.251, *p* = .216, word picture matching, *r* = -.034, *p* = .868, sorting level 1, *r* = .083, *p* =.686, sorting level 2, *r* = .157, *p* = .443, sorting level 3, *r* = .202, *p* =.323, semantic associations pictures, *r* = .160, *p* = .435 or semantic associations words, *r* = .067, *p* = .747. Semantic memory impairment does not therefore provide an explanation for abnormal sorting on the CGT.

Case Studies

Tables 17 and 18 present four case studies of the abnormal sorts participants made and their reasoning behind their groupings which is clear in both the title of the categories and more detailed explanations.

The first two case studies are participants with schizophrenia. Participant HS9 formed 8 categories, the majority of which contained a mixture of overinclusive and underinclusive groupings. HS9 sorted largely thematically. HS9 scored 30 on the PANSS general and 4 (moderate) on conceptual disorganisation. She was a patient with a long history of schizophrenia, aged 63, with an IQ of 77. Participant HS31 formed 15 groups on the CGT therefore showing a high degree of underinclusion. Again HS31 sorted thematically but also sorted subordinately. HS31 was also a patient with a long history, aged 59 with an IQ of 78. He scored 23 on the PANSS general and 4 (moderate) on conceptual disorganisation.

The following two case studies (see Tables 17 and 18) show the sorts of two participants' with Alzheimer's dementia. Participant SD18 made 9 groups on the CGT. He tended to underinclude based on subordinate information but he also overincluded in one instance. SD18 was aged 81 with an MMSE score of 19 and an IQ of 82. Participant SD22 made 7 groups. In many ways his sorts are very similar to HS9 and he overincludes on one occasion. SD22 was aged 73, with an MMSE score of 22 and an IQ of 99.

Table 17: Details of the abnormal sorts for two individual studies with schizophrenia

Participant HS9				
Category Name	Cards	Question	Answer	Coding
Something to Eat	Ear, Lips, Apple, Pineapple, Pear, Grapes, Melon, Strawberry, Orange, Banana	*Why did you put the ear in this group?* *Why did you put the lips in with this group?* *Why did you put all these cards together?*	1) You hear a person asking if they want fruit 2)You eat and you ask for fruit 3) The ear is here (points to ear), mouth is here (points to mouth) – deaf and dumb	1) Thematic 2) Thematic 3) Perceptual
Eye to see putting on hat	Foot, elbow,eye			Thematic
Food Delivery	Lorry			Thematic
Pancakes	Lemon			Thematic
Trousers	Trousers, Arm, Sock, Hand, Leg, Shoe			Unmediated
Clothes	Coat, Dress, Belt, Waistcoat, Shirt, Hat			Superordinate
Participant HS31				
Travelling	Bicycle, Roller Skate			Functional
Transport	Train, Bus, Lorry, Car			Superordinate
Sky Vehicles	Helicopter, Plane			Thematic
Animals in Forest, Desert and Grass	Tiger, Monkey, Camel, Cow, Cat			Thematic
Human Hand	Hand, Arm, Thumb			Thematic
Make up – speaking	Lips	*Why did you form this category?*	Lips are for make up and for whispering	Thematic
Hat	Hat	*Why did you form this category?*	To protect the head	Functional
Belt	Belt	*Why did you form this category?*	To tighten trousers	Functional
Senses of hearing and seeing	Eye, Ear	*Why did you form this category?*	When we see, we hear, they go together	Thematic
To put on leg	Shoes	*Why did you form this category?*	It's a leather thing and leg is a human leg	Thematic
Skating	Sledge			Thematic
Human Leg	Foot, Sock, Elbow, Leg			Subordinate
Clothing	Waistcoat, Dress, Shirt, Jacket, Trousers			Superordinate
Tame Animals	Dog, Horse, Tortoise, Elephant			Subordinate
To put on leg	Shoes			Functional

Table 18: Details of the abnormal sorts for two case studies with AD

Participant SD18				
Category Name	Cards	Question	Answer	Coding
Transport on Wheels	Lorry, Skate	*Why did you put the lorry in this group?*	1) It has wheels. I suppose I could have put it in with the road but I'll leave it.	1)Subordinate
Air transport	Plane, Helicopter			Subordinate
Transport	Bicycle, Sledge			Superordinate
Transport (Road)	Car, Train, Bus			Subordinate
Animals and Leg	All Animal cards, Leg, Elbow	*Why did you form this category?*	The Leg and Elbow are part of an animal or a body.	Functional
Limbs	All other body parts	*Why did you form this category?*	They are pieces of the body	Subordinate
Man's	Hat, Shoe, Belt	*Why did you form this category?*	A man would wear them	Thematic
Clothing	All other clothes			Superordinate
Participant SD22				
Face	Lips, Eye, Ear	*Why did you form this category?*	If someone speaks you need ears to hear	Thematic
Limbs	All other body parts			Subordinate
Domestic Animals	Cat, Dog			Subordinate
Farm Animals	Cow	*Why did you form this category?*	Gives Milk	Thematic
No name	Monkey			
No name	Tortoise			
Transport	Elephant, Camel and all transport cards	*Why did you form this category?*	The Elephant and Camel are both means of transport	Functional

7.5. Discussion

Overinclusive thinking has traditionally been seen to be a hallmark characteristic of psychosis because it epitomises disorganised and tangential thought and speech. The CGT is a task which elicits overinclusion and appears to be a good neuropsychological measure of what Bleuler (1911) described as "loosening of associations". This study found that overinclusion is not unique to psychosis and that a group of patients with AD showed loosening of associations on the CGT to a similar degree as a group with schizophrenia. The unusual explanations given by both groups for their categories were similar in style and showed evidence of loosening of associations; irrelevant connections were formed. The fact that the non-psychotic AD group overincluded and the lack of correlations between PANSS scores and overinclusion in schizophrenia suggest that overinclusion does not explain FTD as has previously been suggested (Payne, 1973). A relationship was found between underinclusion in schizophrenia and FTD which counter intuitively suggests that whilst a tendency to see unusual similarities between concepts (overinclusion) is unrelated to FTD, the tendency to focus in on the differences between them (underinclusion) could be related. However as the AD group also underincluded, the presence of underinclusion is not enough to explain FTD alone and some further critical impairment in schizophrenia is required in order to explain symptoms. In sum therefore, whilst on the CGT the two groups are producing similar patterns of behaviour, the AD group was not psychotic and showed no sign of loosening of associations clinically. This suggests a dissociation between the cognitive impairments which manifest themselves on tests of semantic memory and the clinical symptom of formal thought disorder. Therefore this study goes some way towards refuting the evidence that models of semantic memory impairment in schizophrenia can explain symptoms (e.g. Goldberg et al 1998; Payne 1973).

One aim of this study was to see if a semantic memory impairment in schizophrenia could explain overinclusion. A group of patients with AD who have a semantic memory impairment (see Study One) were therefore also assessed on the CGT and were found to perform similarly to the people with schizophrenia. This suggests that an explanation for abnormal sorting on the CGT can be found in a cognitive deficit that both groups share; namely a semantic memory impairment. Nevertheless the lack of any significant correlations between performance on the CGT and on tasks of semantic memory would suggest that a deficit in semantic knowledge may not be the most appropriate explanation after all. This is supported by the fact that especially in the schizophrenia group, both knowledge of taxonomic categories and also detailed attribute knowledge are preserved as Chen et al (1994) and others have previously suggested.

Although in some ways the CGT performance of both the AD and the schizophrenia group are quantitatively similar, on a qualitative level there are differences. In the schizophrenia group, items were mostly sorted based on thematic information, so categories became contextualised (linked to scenarios and incidents rather than taxonomies) and ad-hoc (Barsalou 1983). Hemsley (2005) in a review of the literature stated that there is a deficit in contextual knowledge in schizophrenia. In a similar vein, Kapur (2003) and Kapur et al (2005) stated that an aberrant assignment of attentional salience to contextually irrelevant concepts explains psychotic delusions. It is likely that a disinhibited spread of what is seen as contextually relevant (Mathalon

et al 2002) in schizophrenia could explain their tendency for both overinclusion and underinclusion on the CGT. When controls complete the CGT their sorting strategies are constrained by the relevant context of the task, what Goldstone (1994) terms the "relevant respects for similarity" between concepts. These constraints are not apparent in schizophrenia (and maybe also to a certain extent in AD) and their ability to pick out these relevant respects is impaired. The majority of patients with schizophrenia underinclude as frequently as they overinclude. This inconsistency seems to reflect a constant switching between sorting strategies so that sometimes certain relationships appear relevant and other times different relationships between concepts guide sorting behaviour.

Understanding more about the reasons behind the abnormal sorting in AD will allow for speculation about explanations in the schizophrenia group. There is a theory that the status of a person's semantic network is a result of his/ her possessed knowledge (Schvaneveldt et al 1985) so that if there are fewer stored semantic memory representations in the network then this will result in unusual connections between items (e.g. Chan et al 1995). As it is well known that semantic memory is degraded in AD, as was reported in Study One, it may be the case that loss of knowledge representations could also cause abnormal sorting, despite the fact that taxonomic knowledge is likely to be intact (Martin and Fedio 1983). If it is assumed that semantic memory is organised in a network of interconnected concepts (e.g. Gonnerman et al 1997, McRae et al 1997), then a random deletion of information within the network could destroy some typical semantic representations whilst leaving more unusual ones preserved i.e. instead of seeing the link between the monkey and the other animals, the relationship with the banana is more prominent. This theory does not necessarily go against the traditional view that semantic memory representations are arranged in a hierarchy (i.e. Collins and Quillian 1969), with category knowledge being better preserved than item specific knowledge, as it may be the case that although the category knowledge is intact, knowledge of the relations between items in those categories are impaired. So a participant with AD may be able to correctly identify the lemon as a fruit but they may not so easily be able to find its connection to the orange and because sorting is unstructured then this may prevent the lemon being placed with the other fruits.

Aronoff et al (2005) propose that in theory a random deletion of semantic knowledge representations would result in a deviant semantic network with atypical associations being formed between items. Several studies have shown that the semantic memory networks in AD are organised differently and that patients with AD use different criteria to group concepts (e.g. Chan et al 1993, Chan et al 1995, Au et al 2003) which could be a result of a degraded semantic store. It has also been found however that people with AD often have problems making appropriate connections between concepts even when their knowledge is relatively intact (Grober et al 1985, Cronin-Golomb et al 1992). Bonilla and Johnson (1995) used a free sorting task similar to the CGT with AD patients and found that AD patients were more likely to use multiple dimensions (underinclusion) than controls when forming categories. AD patients also incorporated less relevant information into their sorts. Bonilla and Johnson (1995) concluded that more semantic information is preserved in AD than has previously been suggested but that abstract information is not utilised in the same degree as with controls. In 1984, Gewirth et al found that compared with controls AD patients were worse at forming taxonomic associations, similar at forming thematic associations and

produced more idiosyncratic associations. This was replicated in 1985 by Santo Pietro and Goldfarb. However some studies have found that people with AD find it relatively easy to categorise items according to superordinate categories even when they are unable to name them (Martin 1987). This fact was confirmed by the consistent ability of the AD group in Study Three to form taxonomic categories when provided with the superordinate label. Therefore it is likely that unusual sorts occur due to difficulties connecting individual items at the base level due to a degraded semantic store.

Alternatively, a disproportionate difficulty in AD using rule based rather than similarity based categorisation was found by Grossman et al (2001) and this could well be a reflection of an impaired executive system in AD. Other executive failings could include problems inhibiting irrelevant information, a theory that has been proposed by Johnson et al (1995), Grande et al (1996) and Balota and Duchek (1991). Therefore although semantic knowledge is degraded in AD this may not be the only explanation for their bizarre sorting on the CGT. Difficulties forming coherent strategies or inhibiting irrelevant items could explain poor performance. Similarly, perhaps a more likely explanation for CGT performance in schizophrenia is that the processes which are involved in the correct retrieval and utilisation of this knowledge are dysfunctional. There are many cognitive processes that will impact upon categorization, aside from the need to utilise semantic knowledge, including working memory, the use of strategy, context processing, inhibition and attention. All of these areas have been found to be impaired in both schizophrenia (Goldman-Rakic 1994, Hemsley 2005, Volk et al 2002) and AD (Perry and Hodges 1999, Braver et al 2005). It is likely to be the case that a combination of cognitive difficulties in both groups are leading to what appears to be in many ways a strikingly similar pattern of results on the CGT task. In the same way as with Study One, it would appear that certain semantic tasks elicit disproportionate errors in schizophrenia and that an explanation of degraded semantic knowledge store is not appropriate. Despite the lack of significant correlations between an executive dysfunction and performance on the Hodges et al (1992) semantic battery, research would benefit from further exploration of the impact of an executive dysfunction on CGT performance in schizophrenia.

Chapter 8: Is abnormal categorisation in schizophrenia caused by an executive dysfunction?

Study Four: Exploring the relationship between an executive dysfunction and abnormal categorisation in schizophrenia

8.1. Introduction

Although an executive dysfunction in schizophrenia did not appear to explain the errors on the Hodges et al (1992) semantic memory battery in Study Two it may be the case that difficulties maintaining a categorisation strategy are responsible for abnormal groupings on the CGT. Tasks of categorisation involve the use of strategy and working memory, both areas that fall under the domain of executive functioning. In addition, difficulties understanding contextual information or being able to adhere to contextual constraints are also believed to fall under the domain of a dysexecutive syndrome (Cohen and Servan-Schreiber 1992). It has been previously reported that people with schizophrenia do poorly on tasks of semantic categorisation (e.g. Chen et al 1994, McKenna et al 1994, Green et al 2004) and this has been attributed to an executive dysfunction (e.g. Zalla et al 2001). For example Zalla et al (2001) reported that overinclusion of irrelevant items on a task by people with schizophrenia was due to the "inability to select an internal action schema and use it to generate a plan of action" i.e. an executive dysfunction. Processing of category relationships and also associative relationships between concepts have been found to activate frontal brain regions (Khatab et al 2003) and also the actual task of sorting cards into categories has been found to involve frontal regions (Koenig et al 2005, Grossman et al 2002). It is feasible that the dysexecutive syndrome that features in schizophrenia could lead to difficulties completing the CGT.

Furthermore, it has been proposed that there are two ways in which people categorise objects; using similarity processes and rule-based categorisation (e.g. Smith and Sloman 1994). Rule based categorisation is based on deciding whether an exemplar belongs in a given category depending upon a process of selecting and prioritising features and then with this information deciding if the exemplar satisfies a rule for membership of the category. This rule-based categorisation is more likely to rely on executive processes as it utilises strategies (Hough and Givens 2004). Exploring the influence of a dysexecutive syndrome on semantic categorisation in schizophrenia will allow for further speculation about the underlying processes. I therefore decided to test the ABI patients using the CGT and also perform correlational analyses between BADS scores and CGT performance in the schizophrenia group.

8.2. Participants

The schizophrenia participants from Study One and the ABI group from Study Three were recruited for this study.

8.3. Method

Participants were tested using the CGT. Data from the schizophrenia group has already been reported.

8.4. Results

Comparing the ABI group and the schizophrenia group on the CGT

Table 19: The number of people who overincluded and underincluded on the CGT in each group

		Over		Under	
		Yes	No	Yes	No
Schizophrenia	Count	11	11	12	10
	%	45	55	50	50
ABI	Count	1	9	1	9
	%	10	90	10	90
Control	Count	1	19	2	18
	%	5	95	10	90

Table 19 shows the percentages of over and underinclusion in all three groups on the CGT. The mean overinclusion score (s.d) for the schizophrenia group = 1.18 (.24), for the ABI group = 1.04 (.13) and for the controls = 1.01 (.06). The mean underinclusion score (s.d) for the schizophrenia group = 1.84 (1.5), for the ABI group = 1.06 (.13) and for the controls = 1.06 (.18).

Overinclusion

A significant difference was found between the number of people found to overinclude in the three groups, χ^2 (2) = 12.8, p = .002 (see Table 25). The group with schizophrenia were found to be significantly more likely to overinclude than both the healthy controls, χ^2 (1) = 10.39, p = .001, and the ABI groups, χ^2 (1) = 4.69, p = .030. The ABI and healthy control groups did not differ, χ^2 (1) = .27, p = .61.

Underinclusion

A significant difference was also found between the number of people who underincluded in the three groups, χ^2 (2) = 10.19, p = .006. The ABI and healthy control groups did not differ, χ^2 (1) = .00, p = 1 and the difference was therefore due to the schizophrenia group showing a higher incidence of underinclusion than both the healthy controls, χ^2 (1) = 7.14, p = .008 and the ABI groups, χ^2 (1) = 5.66, p = .017.

Correlations between BADS scores and CGT performance

Overinclusion

No correlation was found between performance on the CGT and scores on the BADS for the group with schizophrenia, r = -0.13, p = .58. In the ABI group, overinclusion was not significantly correlated with BADS scores, r = -.54, p = .11.

Underinclusion

There was however a significant negative correlation between underinclusion scores and BADS scores in schizophrenia, r = .619, p = .002. Underinclusion also didn't significantly correlate with BADS scores in the ABI group, r = -.32, p = .27.

8.5. Discussion

As with the Hodges et al semantic memory battery, semantic memory impairments on the CGT do not appear to be due to an executive disorder. People with Acquired Brain Injury (ABI), featuring a prominent executive dysfunction, performed similarly to controls on the CGT, neither overincluding nor underincluding. This suggests that, as people with an executive dysfunction can successfully complete the CGT, intact executive functioning is not an essential requirement for this task. In comparison the majority of the schizophrenia group (and the AD group) were found to perform abnormally on this task, with 45% overincluding and 50% underincluding. Nevertheless it is possible that the ABI group utilized an effective strategy that obviated their dysfunctional executive system e.g. the use of automatic semantic associations. Of interest is the fact that underinclusion in the schizophrenia group was significantly correlated with BADS scores. However as the correlation was negative, meaning high levels of underinclusion were related to high scores on the BADS (indicating intact executive functioning), this goes against the hypothesis that an executive dysfunction in schizophrenia is responsible for poor CGT performance. Nevertheless the same caveats apply to this study as for study two, namely that only a limited number of executive functions were measured and the ABI group are heterogeneous in terms of neural damage. It is wrong, therefore, to generalise from the results of this study to claim that an executive dysfunction in schizophrenia is not responsible for differences on tests of semantic categorisation. Nevertheless, the fact that a group of patients with a severe executive dysfunction (as measured on the BADS) were able to complete this task in the same way as healthy controls does suggest, at least, that the presence of an executive dysfunction does not necessarily lead to poor performance on the CGT.

Chapter 9: Exploring the conceptual preference in schizophrenia

Study Five: A comparison between people with schizophrenia and people with AD on a triadic comparison task.

9.1. Introduction

In a further attempt a) to understand the semantic memory impairments in schizophrenia and b) to see how they compare to those present in AD, I decided to compare the two groups on a further measure of semantic memory, a triadic comparison task. This task, unlike other measures of semantic memory, does not assess knowledge or record errors but looks at a person's preferences for associating certain items. In this way it is a good measure of how someone's semantic memory is organised and has been used (e.g. Tallent et al 2001, Chan et al 1995) to feed into further analysis, for example Multi-Dimensional Scaling (MDS) analysis which generates semantic maps of a person's semantic network. It has been argued (e.g. Soriano et al 2007) that unlike other measures of semantic memory, a task assessing similarity between pairs does not greatly involve retrieval processes or make high demands on information processing but represents the organisation of semantic knowledge. For the purposes of my research, using a triadic comparison task would allow me to see if people with AD and people with schizophrenia associate concepts in the same way as controls and also whether any difference is related to unusual card sorting on the CGT seen in Study Three. I hoped as well that this would shed light on some of the other semantic memory impairments in schizophrenia for example difficulties on association tasks in Study One.

A triadic comparison task asks participants to choose which one out of two options "goes best" or is "best related" to a target. For example, if the target is "carrot" would "bugs bunny" or "a tomato" go best with it? It has traditionally been used to assess whether people tend to prefer taxonomic or thematic associations, what is termed the "conceptual preference" for a particular relationship. Early evidence suggested that adults tend to connect concepts together on the basis of taxonomic associations (e.g. Lamberts and Shanks 1997), work that influenced theories such as Rosch et al (1976), which emphasise the importance of categories to how we conceptualise the world. Seminal work by Smiley and Brown (1979) which used triadic comparison tasks with children found that this taxonomic preference tended to be something that occurred only in adulthood, as children were found to link concepts using thematic/ situational associations. This led to the concept of the taxonomic/ thematic shift (Smiley and Brown 1979) which is when at a certain age children begin to use generalised taxonomies to connect concepts rather than using the contextual, situation- specific knowledge that forms the basis of newly learnt semantic concepts. The evidence for this shift is equivocal however and more recent work has found evidence for taxonomic categorisation in young children (e.g. Hashimoto et al 2007) and thematic categorisation in adults (Lin and Murphy 2001). In addition to a person's age, other factors have been found to influence an individual's conceptual preference, including situations (Baldwin 1992), word familiarity (Chaffin 1997) the specific exemplars used (Osborne and Calhoun 1998), the salience of the exemplar (Lin and Murphy 2001) and the individual's cultural background (Luria 1976).Whilst thematic

associations rely on an individual's experience of the context/ schema related to the concepts, taxonomic associations are in general formed around the perceptual similarity of the concepts (Medin and Ortony, 1989). Therefore different factors are involved and an abnormal reliance on forming either type of association could indicate a deficit in the type of information processing involved in the other. For example, if a person with schizophrenia was less likely to choose thematic associations then this could suggest a deficit in contextual processing/ episodic memory.

Triadic tasks have been used to assess semantic memory in both schizophrenia and AD. In 2001, Tallent et al used a triadic comparison task to assess the "semantic space" of individuals with schizophrenia. In this context, semantic space refers to the way in which semantic memory representations are organised and interrelated. Previous literature has proposed a disorganised or idiosyncratic semantic network in schizophrenia (e.g. Paulsen et al 1996) reflected in extended category boundaries. In the study by Tallent et al (2001) it was found that people with formal thought disorder conceptualised concepts differently from controls and people with schizophrenia with FTD on a triadic comparison task. Further analysis suggested that this was due to a disorganised semantic network. In AD, triadic comparison tasks have been used more frequently than in the schizophrenia literature (e.g. Chan et al 1995, Rich et al 2002). Similarly to people with schizophrenia, people with AD have been found to have abnormally organised semantic memory networks with less coherent categories and more sparse networks.

A study by Au et al (2003) utilised a triadic comparison task to assess the conceptual preferences of people with AD. Previous studies had reported that people with AD tend to associate concepts based on visual perceptual characteristics such as size rather than more abstract characteristics such as domesticity (Salmon et al 1999, Rich et al 2002). This trend has been proposed to reflect a deterioration of abstract associations/ attributes and a preservation of concrete feature knowledge. In the Au et al (2003) study participants were asked to choose which item out of two "was most related" to the target. The choices varied between items that were taxonomically, thematically or perceptually related. In comparison to a control group, the patients with AD were far more likely to choose perceptually related items and this trend increased as disease severity worsened. The authors concluded that this provided further evidence for a storage disorder in AD, where semantic memory representations deteriorate progressively.

In order to find out more about the semantic memory/ categorisation process in schizophrenia the conceptual preference of both patients with AD and patients with schizophrenia was assessed. In addition, by replicating the Au et al (2003) study, it was possible to build upon what had been learnt in Study One about how the semantic memory impairment differed in AD from schizophrenia and whether either/ both met criteria for a storage disorder. Based on the qualitative analysis carried out on the results of Study Three, one would expect that the AD group would form more perceptual/ lower level associates but the schizophrenia group would form more thematic associates on the triadic comparison task.

9.2. Participants

A total of 45 people took part in this research; 19 patients with a DSM-IV (as confirmed by their psychiatrist) diagnosis of schizophrenia, 13 mentally healthy controls and 13 patients with an ICD-10 (as confirmed by their psychiatrist) diagnosis of probable Alzheimer's dementia. The AD group all scored between 19-25 on the Mini Mental State Examination (MMSE), which indicates a mild to moderate level of dementia severity. The patients with schizophrenia came from a variety of settings within the NHS trust including acute care units, outpatient clinics and rehabilitation residential homes. All patients were taking anti-psychotic medication. The controls were recruited from community centres for retired people and church groups. The patients with AD were recruited from a memory clinic. For psychometric and demographic information please see Table 20:

Table 20: Psychometric details for participants recruited for Study Five

Participants	Schizophrenia	Alzheimer's Dementia	Controls
Number	19	13	13
Age (mean (s.d))	42.6 (13.9)	84 (4.7)	78.9 (6.6)
Male/ Female	12/7	4/9	3/10
NART (mean (s.d))	107.6 (7.6)	109 (7.5)	111.3 (7.7)
MMSE (mean (s.d))	28 (1.81)	21.4 (1.83)	28.9 (1.0)
Verbal IQ (mean (s.d))	93.7 (26.6)	90.08 (11.2)	97.6 (17.7)
Performance IQ (mean (s.d))	93.5 (24.5)	93.85 (15.7)	116.15 (14.5)
Full IQ (mean (s.d))	93.2 (26.9)	91.1 (11.5)	107.5 (14.4)
PANSS general	31.05 (7.8)	n/a	n/a
PANSS positive	17.05 (5.3)	n/a	n/a
PANSS negative	18.7 (7.41)	n/a	n/a

One way ANOVAs showed that all 3 groups were matched on their pre-morbid intelligence (as assessed by the NART), F (2 = .843, p =.438), their current level of verbal intelligence, F (2) = .431, p =.652 and their full intelligence level (both were assessed using the WASI), F (2) = 2.63, p = .084. However, groups did differ on performance IQ, F (2) = 6.06, p = .005, their MMSE scores, F (2) = 81.45, p <.001 and their age, F (2) = 83.16, p <.01. Nevertheless post hoc Tukey t tests did find that the AD and control groups were matched for age, p =.39 and the schizophrenia and control groups were matched for MMSE scores, p = .31. Overall, therefore the participants recruited provided a good sample for comparison.

9.3. Method

9.3.1. Materials

As the original materials used in the Au et al (2003) task were unavailable, a new version of the triadic comparison task was developed. By including the same items that were used in the CGT this enabled the assessment of item consistency and also whether conceptual preference is related to abnormal sorting. Thematic and perceptual associations were already available for all items on the CGT.

9.3.1.1 Collecting a set of attribute norms

With the help of an MSc student, Alexandra Bailey, 10-20 attributes were collected from 10 people for each of the items on the CGT; 5-10 thematic (or situational) and 5-10 perceptual. Participants were asked to write down the attributes as they came into their heads. So in a fairly crude way this provided a measure of attribute typicality. However the next step was to assess typicality more systematically. In order to narrow down the potential attributes, 6 were chosen for each item, 2 which were very frequently chosen, 2 which were in the middle, and 2 which were chosen fairly infrequently by participants (the same was done for the taxonomic norms). Next a further 10 participants were asked to rank the typicality of these attributes on a line where highly typical was at one end and highly atypical was at the other. This then provided not only ranked data for this list of attributes but also relative measurements of where people placed the items on the scale of typicality. This relative value was important because it permits development of a set of comparably typical attributes for each item. An example follows:

STEP 1: Participant generates a set of 5-10 features which they associate with the target word. This was done twice for each target (the target word here is apple):

- Thematic Features

Sauce, Tree, Toffee, Pie, Crumble, Cider, Leaf, Wood, Farm, Picker, Supermarkets, Farm Shops, Horses, Pigs, Goats, Sheep

- Perceptual Features

Red, Green, Hard, Crunchy, Juicy, Leaves, Shiny

STEP 2: The data were analysed and 6 attributes were chosen for each item, 2 that were most frequently chosen, 2 in the middle and 2 that were least frequently chosen. For apple the following attributes were chosen:

- Thematic Features
  - Tree
  - Juice
  - School Boys
  - Bowl
  - Goats
  - Snow White

- Perceptual Features
  - Green
  - Round
  - Yellow
  - Core
  - Heart Shaped
  - Leaf

STEP 3: Participants were asked to rank these attributes on a scale of 1-5 where 1 is the most typical and 6 is the least typical. Then they were asked to put the attributes in order on a line ranging from highly typical to highly atypical.

STEP 4: This data was analysed and this enabled us to have typicality data for a set of 12 attributes for each item, 6 thematic and 6 perceptual.

For the taxonomic norms a similar process was taken to when the other norms were collected apart from there was no need for Step 1 because lists of common associated items are readily available for the five common taxonomic categories used in the CGT; animals, vehicles, clothes, body parts and fruit.

Therefore using these norms (8 for each category), 10 control participants were asked to rate the typicality of each item to the taxonomic category and place each on a line relative to how typical they were to the category. As with the thematic and perceptual norms, the taxonomic norms also varied on typicality and could be used in the triadic task. For the triadic task the most commonly associated exemplar was used for all 3 types of category so that each preference was matched on the basis of typicality.

9.3.2. Procedure

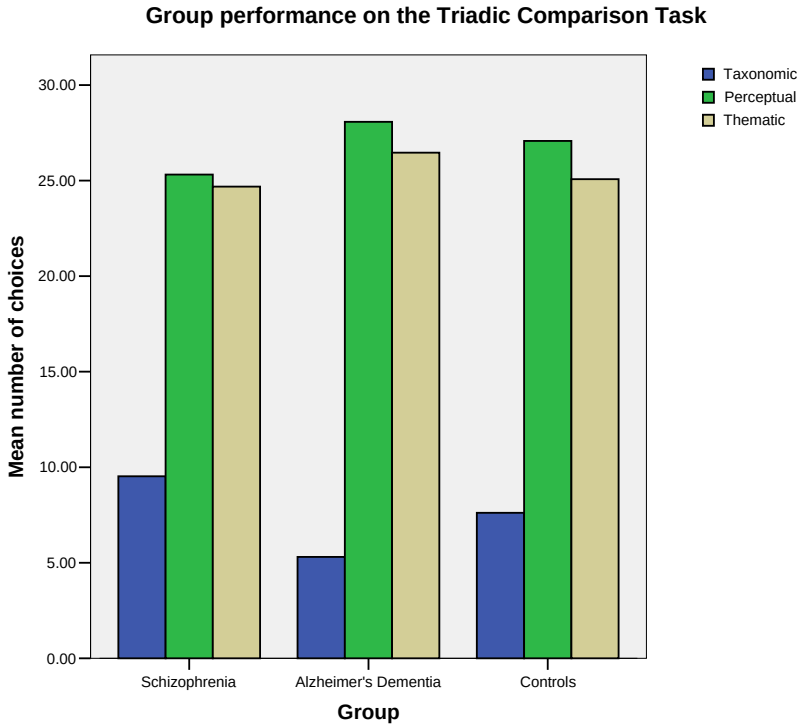
For the 20 selected items, participants were asked to complete three tasks on the triadic task; perceptual vs. thematic, thematic vs. taxonomic and taxonomic vs. perceptual. For the purposes of time, only 20 items were used in the final version. Therefore participants were given a folder containing 60 pages. On each page there was a target item and two choice items. Participants were asked to choose which one of the choice items went best with the target item.

Participants were also given a naming task, a word-picture matching task and the Category Generation Task (Green 2002), all of which utilised the same items as the triadic task. In addition participants were assessed cognitively using the NART (Nelson 1982) for pre-morbid IQ, the WASI (Wechsler et al 1999) for current IQ and the BADS (Wilson et al 1996) for executive functioning. Patients with AD were assessed using the MMSE (Folstein et al 1975) to ascertain the severity of their illness and patients with schizophrenia were interviewed using the PANSS (Kay et al 1987).

9.4. Results

The total number of preferences for each of the three categories (out of a total of 40) was compared in each group using a one way ANOVA. This showed no difference between the groups in the choices they made for taxonomic, F (2) = 2.496, p =.095, for perceptual, F (2) = 2.218, p =.132 and for thematic, F (2) = .504, p = .608. All groups showed a tendency to choose perceptual associations over taxonomic and thematic as is evident in Figure 6.

Figure 6: Group performances on the triadic comparison task



Correlations were made between an individual's conceptual preference on the triadic task and their performance on the other tests of semantic memory. No correlations were found to be significant in any group. In addition the groups did not significantly differ on their performance on these tasks of semantic memory as Table 21 shows.

Table 21: The performance of the three groups on the semantic memory tasks.

	Sz (n =19)	**AD (n = 13)**	**Controls (n = 13)**	Statistics
Naming Errors	1.53 (1.93)	4.1 (3.28)	<1	F (7) = .374, p = .912
Word Picture Matching Errors	1.16 (1.61)	1.38 (1.39)	<1	F (5) = .964, p = .453
CGT Score (See Study Three)	2.43 (.65)	3.42 (.95)	2.9 (.26)	F (19) = .991, p = .500.

9.5. Discussion

This study failed to replicate the results reported by Au et al (2003), in that people with AD did not perform differently from controls on the triadic task. Nevertheless, both controls and AD patients had a high tendency to choose perceptual associates over taxonomic and thematic. In this way the results of the AD group mirror that of Au et al (2003) and it may be that the control group used in this study were non representative, perhaps because of age or education. In the Au et al (2003) study, Chinese participants were recruited and there may of course be some cultural

explanation behind the difference in performance. Nevertheless it is surprising that controls did not sort taxonomically as has traditionally been asserted (e.g. Smiley and Brown 1979) and this may be a product of the sampling or that perhaps a conceptual preference for taxonomic sorting in adults is not necessarily a completely robust finding.

What can be said with a fair degree of confidence, however, is that on this task, unlike in the study by Au et al (2003), the people with AD failed to perform any differently from controls. Taken together with the fact that this same group of people showed some performance abnormalities on the other tasks of semantic memory including the CGT one could conclude that a conceptual preference is perhaps more resilient to structural deterioration than other aspects of knowledge. The CGT abnormalities in both AD and schizophrenia that were seen in this study and also in Study Three could suggest a difference in conceptual preference, especially since once the responses were analysed qualitatively, the groups differed in the way in which they were choosing to relate concepts. It may be the case that a conceptual preference changes with age, and in fact a U shaped curve has been proposed by Smiley and Brown (1979), to explain the shift between preferences for thematic associations towards taxonomic associations. A younger control group might perhaps perform differently from the AD group; but nevertheless the fact remains that it would be age that would be the differentiating factor and not the diagnosis of AD. Some literature has claimed that in AD, the relations between concepts become impaired even when knowledge has deteriorated (Bonilla and Johnson 1995). Based on the results of this study, one can speculate that connections between concepts do remain relatively intact in AD but on certain tasks, perhaps due to working memory demands, people with AD fail to make these connections appropriately. Therefore in contrast to the structural hypothesis, it appears that knowledge remains mostly intact in AD but when recall/ information processing demands are high, this knowledge becomes inaccessible. In the next study this hypothesis will be explored.

With regard to the schizophrenia data, my prediction that they would make more thematic associates was not met. As with the AD group, the people with schizophrenia did not perform any differently from controls on this task. In some ways this result is puzzling because of the abnormal sorting that is evident on the CGT, which indicated a preference for thematic associations over taxonomic ones. As with the people with AD, it appears that the presence of a semantic memory impairment in schizophrenia is task-dependent which suggests that it is not semantic memory that is disorganised/ deteriorated per se but that there are difficulties with the cognitive processes that help retrieve and select the knowledge representations. In the triadic task therefore, people with schizophrenia show the same conceptual preference as controls. Likewise in recent studies (e.g. Soriano et al 2007) it has been reported that people with schizophrenia judge the similarity of concepts in the same way as controls. This has been put forward as evidence then when information processing demands are low, people with schizophrenia show a semantic memory network that is organised in the same way as controls. On the CGT, it would appear that people with schizophrenia are overly dependent on thematic relationships but this does not drive task performance on the triadic task. Unlike previous studies which have found widespread semantic memory impairments in schizophrenia (e.g. McKay et al 1996, Rossell and David 2006), this study used a group of controls who were matched for current and pre-morbid IQ to both clinical groups. Therefore as with Study One it

appears that, once IQ is controlled for, the semantic memory impairments in schizophrenia on several tasks disappear. Although the results of this study did not confirm the predictions, one can now say that the abnormal sorting on the CGT in schizophrenia is more likely to be explainable by task-specific factors and not by a disorganised semantic memory.

Chapter 10: How people with schizophrenia assign salience to concepts/ associations within the semantic network.

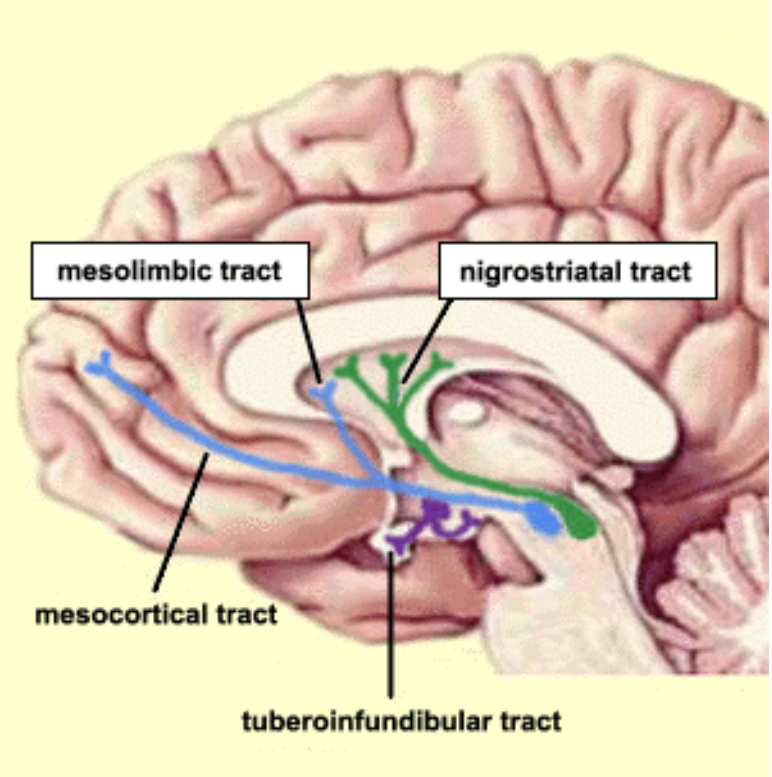
The results from Studies One to Five support the claim that semantic representations are intact in schizophrenia and that semantic memory is organised fairly normally. Differences in the way in which people with schizophrenia form semantic associations and categories appear to arise not from a deficit but more from differences in the connections that are seen as most important or relevant. This suggests abnormalities at the level of retrieval of semantic memories; however neither an executive dysfunction (Studies Two and Four) nor a generalised intellectual impairment (Study One) appear to be suitable candidates for explaining poor performance on semantic memory tasks. Neuropathological aetiologies provide an explanation for the semantic memory impairments in neurodegenerative conditions, e.g. cell atrophy to the anterior temporal lobes as an explanation for degraded semantic memory representations in semantic dementia (e.g. Davies et al 2004). In contrast to this, the semantic memory impairments in schizophrenia may be caused more by neuro-chemical abnormalities. In fact although structural and functional brain damage is frequently reported in schizophrenia, reviews have concluded that the magnitude of damage appears marginal in the temporal (Zakzanis et al 2000) and frontal lobes (Heinrichs and Zakzanis 1999). Neurochemical abnormalities, in particular a dysregulated dopaminergic system, have been found to be linked to symptom existence and severity in schizophrenia (e.g Kapur 2003, 2005). Several theories have now linked a dopaminergic dysregulation to the cognitive impairments in schizophrenia (e.g. Braver et al 1999), and one model specifying an aberrant assignment of attentional salience in schizophrenia could explain the task specific semantic memory deficits demonstrated in my previous studies.

Study Six: Is there an aberrant assignment of semantic salience in schizophrenia?

10.1. Introduction

Evidence for a link between dopamine and the symptoms of schizophrenia has been derived from three main sources; the efficacy of antipsychotics that target dopamine (D2) receptors in reducing symptom severity (e.g. Kapur and Mamo 2003); the psychotic effects of psychostimulants which increase levels of dopamine; and also via neuroimaging and anatomical data (e.g. Abi-Dhargham 2004; Winterer and Weinberger 2004). In order to understand how a dysregulated dopaminergic system can lead to the symptoms and phenomenology of schizophrenia, one must refer to what is known about the role dopamine plays in regulating normal behaviour. Dopaminergic neurons are concentrated around three main pathways in the brain; the substantia nigra (SN), the ventral-tegmental (VT) and hypothalamic pathway. The VT pathway can be divided into two; the mesolimbic and mesocortical pathway. The mesocortical pathway projects widely to the prefrontal cortex and could therefore influence a high number of cognitive functions. The mesolimbic pathway connects the prefrontal cortex with sub-cortical regions such as the striatum, amygdala and nucleus accumbens, areas believed to play a strong role in the regulation of emotions and motivations. This pathway has been strongly implicated in the neuro-pathology of schizophrenia (e.g. Winterer and Weinberger 2004).

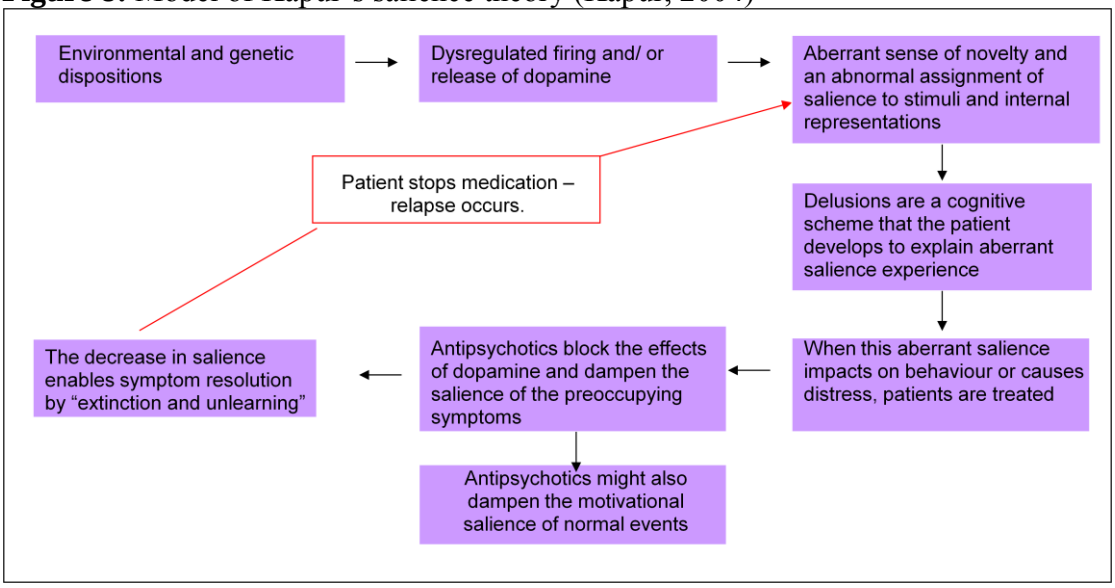
Figure 7: Dopaminergic pathways (taken from thebrain.mcgill.ca/.../a_03_cl_que_1a.gif)



Studies have found that dopamine in the mesolimbic pathway is released when a stimulus has an expected reward value according to current context and needs (e.g. Schultz 1998). The Incentive Salience theory of dopaminergic action was proposed by Berridge and Robinson (1998) and specifies that dopamine mediates the incentive salience of stimuli in order to direct attention and drive behaviour. This process is driven by external and internal context, current goals and requirements. The role of dopamine has also been referred to as differentiating signal from noise in the environment so highlighting the most relevant stimuli from many possible alternatives (e.g. Cohen and Servan-Schreiber 1992). This process also involves inhibiting stimuli which are irrelevant considering current context. Recent models of dopamine function state the role of dopamine as a combination of learning through reward expectancy as well as distinguishing task relevant information in the environment and believe mesolimbic dopamine has a unitary function as a learning/ gating mechanism (e.g. Braver et al 1999). This action is believed to take place in the prefrontal cortex and striatum. In schizophrenia, studies have found increased levels of dopamine in the striatum which has been linked to the severity of positive symptoms. In the prefrontal cortex, dopamine levels have been found to be decreased in schizophrenia; so there is hyperdopaminergia subcortically and hypodopaminergia cortically (Abi-Dhargham 2004). This dysregulation is likely to cause abnormalities in the processing of reward or signal to noise in schizophrenia. There are several dopamine-based theories for explaining the cognitive impairments and symptomatology in schizophrenia (e.g. Braver et al 1999; Gray 1995; Laviolette 2007). All seem to centre on the role of dopamine in mediating the salience of stimuli.

More recently, Kapur (2003) put forward a theory to explain psychosis, specifically the formation of delusions in schizophrenia. Observations of patients in the prodromal stage of the illness highlighted a stage of heightened awareness and anxiety before delusions and hallucinations are fully formed. Kapur's theory draws upon what is known about dopamine as a mediator of "the acquisition and expression of appropriate motivational saliences, in response to the subject's experiences and predispositions". In psychosis, Kapur proposes that a dysregulated dopamine transmission means that the release of dopamine does not coincide with relevant internal or external stimuli. This leads to the "aberrant assignment of salience to external objects and internal representations". Therefore, Kapur's theory posits that in schizophrenia, dopamine begins to become a creator of saliences rather than a mediator. This is experienced by the person with psychosis as a "novel and perplexing state marked by exaggerated importance of certain percepts and ideas". Kapur explains the formation of delusions as a way in which the person attempts to make sense of these new experiences, a top-down cognitive explanation. Delusions are therefore uniquely framed within the person's own history, cultural context and predispositions. Hallucinations are seen to be the result of an aberrant assignment of salience to internal perceptions e.g. believing that their voice is in fact the voice of an alien. Kapur also believes that the presence of cognitive biases in people with schizophrenia could explain the persistence of delusions and hallucinations despite evidence to the contrary. In this theory, antipsychotics are seen to alleviate psychotic symptoms by dampening the process of aberrant assignment of salience. This is supported by the experience of participants who state that, for example, "it doesn't bother me anymore". The reason why antipsychotics do not work instantly in resolving symptoms can be explained by the fact that the patient needs to work through their cognitive explanations/ interpretations of their experiences. For a model of Kapur's theory, see Figure 8.

Figure 8: Model of Kapur's salience theory (Kapur, 2004)



Kapur's salience theory is underspecified in several areas e.g. how the dysregulation of dopamine leads to an aberrant assignment of salience and also why delusions are so similar in type e.g. persecutory, if salience is assigned randomly. Nevertheless, this theory is the culmination of several different strands of research which have reported

difficulties using contextual information (Hemsley 2005), an inability to disattend from stimuli (Cromwell and Dokecki 1968), problems learning/ unlearning associations, difficulties on tasks of negative priming (Moritz et al 2001c), impaired latent inhibition (e.g. Gray 1995) and difficulties inhibiting irrelevant meaning in schizophrenia.

This model could offer a potential explanation for the attention to irrelevant concepts in semantic memory which may result in poor performance on certain tasks for example the associations test in Study One and the CGT in Study Three. On the CGT, the nature of the task is that it is free-sorting so there are feasibly a number of ways in which concepts could be categorised. The taxonomic categories are by far the most salient "respect of similarity" used by controls but it would appear that a more idiosyncratic way of grouping concepts was used by the patients with schizophrenia. As previously mentioned, one theory of categorisation is that concepts are associated based on the most relevant "respect of similarity" (Goldstone 1994). Therefore, it could be the case that in schizophrenia there is a problem identifying the most salient "respect of similarity". An alternative explanation for bizarre groupings on tasks of categorisation is that in schizophrenia there is an aberrant assignment of semantic salience to particular item attributes which are then used to form the basis for further categorisations. In terms of the association tests, there is also a number of different ways in which the target could be connected with the exemplars, although the most salient choice for controls is the one which is most thematically related. In the case of the people with schizophrenia, an alternative exemplar appears to become the most salient choice, leading to errors.

Although an aberrant assignment of semantic salience as an explanation for semantic memory impairments in schizophrenia is under researched there is some evidence to suggest that this is a plausible theory. For example, in 1996 Kishka et al compared the performance of a group of University students who had ingested levodopa (the precursor to dopamine) against those who hadn't on a test of direct and indirect semantic priming. They found that increased levels of dopamine led to a significant reduction in indirect semantic priming. With more dopamine there was less spreading of activation through the semantic network and attention was focussed on more directly related word meanings. Therefore it can be interpreted that the normal role of dopamine is to focus activation. In support of this, a study by Copland et al (2003) found that on a lexical decision priming task, a student population who had ingested levodopa showed greater facilitation of dominant primed words but less priming for subordinate (less typically associated) primed words.

A dopaminergic imbalance in schizophrenia, leading to less available dopamine, could explain spreading of activation or overinclusion in semantic memory. This is consistent with the findings of Abi-Dargham (2004) which implicate hypodopaminergia in the prefrontal cortex and suggest that low levels of dopamine in patients with schizophrenia lead to increased spreading activation, hyperpriming. In a similar vein, a neuro-imaging study by Laurens et al (2005) found significant functional differences between the way in which people with schizophrenia and controls reoriented their attention to novel stimuli. Patients with schizophrenia were far more prone to become distracted by irrelevant information but at the same time found it difficult to detach attention away from the most relevant stimuli. Laurens et al (2005) suggest that in schizophrenia the "salience problem" consists of both a

spreading of attention to irrelevant items but also an abnormally high level of focussed attention onto dominant stimuli. In some ways these empirical studies which are based on neuropsychological test performance support Kapur's (2003) salience theory in that in schizophrenia (or following ingestion of levodopa in controls) there appears to be a tendency for attention to be drawn to irrelevant stimuli and to be more focussed. In this respect however, the empirical studies on salience would suggest that attention is drawn towards the most dominant, task-relevant stimulus, which is difficult to marry with Kapur's theory that attention in schizophrenia is drawn towards less relevant concepts.

It must be noted here that the concept of "salience" is underspecified and appears to have various different meanings; in terms of Berridge and Robinson's (1993) "Incentive Salience" this seems to imply that a concept is salient if it motivational and relevant to the task in hand. In Kapur's (2003) model, the concept of salience seems to refer to "a process whereby events and thoughts come to grab attention, drive action, and influence goal-directed behaviour because of their association with reward or punishment". The study by Copland et al (2003) assumes that salience is where concepts in semantic memory are strongly primed or activated working in the same way as increasing the signal/ noise ratio of relevant to irrelevant concepts. In an early study by Grober et al (1985), the participants were asked to rank semantic attributes in order of how important they were to the concept. Poor performance on this test has been interpreted as due to an impairment with salience processing.

Kapur's salience theory has not yet been tested empirically. This study is the first to assess people with schizophrenia on a measure of "semantic salience" and in some ways is a pilot. As a starting point, it was decided that the salience measure should be based around the study used by Grober et al (1985), and therefore the term "importance" was used in the instructions to the participants. Although this is perhaps only one interpretation of the term salience, it was felt that the process of ranking a concept's associates by their perceived importance relies on knowledge of relevance and an association with reward. Alternative designs are not yet available and this study provides a starting point for future investigations.

10.2. Participants

Seventeen patients with schizophrenia were included in this study. They were recruited from a number of sources including outpatient clinics, residential units and acute inpatient wards from within two mental health trusts. All patients were identified by their consultant psychiatrist as having a DSM-IV diagnosis of schizophrenia. Symptom severity was assessed using the PANSS (Kay et al 1987). All patients were currently being prescribed atypical antipsychotic medication.

In addition 12 mentally well (non-psychotic) controls were tested in this study. This sample was recruited from a local supermarket as this was believed to be a good way of targeting people who were similar in socio-educational status to the schizophrenia sample. The groups were matched on age, pre-morbid IQ and current IQ with the schizophrenia sample. For demographic/ psychometric information see Table 22.

Table 22: Psychometric and demographic information for participants included in Study Six

Mean Scores (s.d)	Schizophrenia Group (N = 17)	Controls (N = 12)	Statistical Analyses
Age	37.3 (11.3)	34.42 (8.17)	t (28) = -.755, p = .457
Sex (M/F)	12/6	6/6	
NART IQ	110.31 (6.4)	111.08 (9.79)	t (26) = .253, p = .803
WASI Full	89.7 (22.7)	103.5 (14.16)	t (28) = 2.05, p = .05
WASI Verb	87.2 (21.9)	100.17 (23.14)	t (28) = .911, p = .13
WASI Perf	92.1 (23.2)	105.58 (13.01)	t (27) = 2.04, p = .051
PANSS Pos	18.4 (4.9)	n/a	
PANSS Neg	15.1 (7.9)	n/a	
PANSS Gen	28.5 (10.5)	n/a	
PANSS Conceptual Disorganisation	2.4 (1.5)	n/a	

10.3. Materials

The "salience" test was designed to be similar to that used in the study by Grober et al (1985) i.e. a target item and three attributes which varied in their perceived importance to the target item. It was important that same items that were used in the CGT also featured in the "salience" test, in order to see if there was a direct relationship between an aberrant assignment of salience (following Kapur's theory) and abnormal categorisation. With the help of an undergraduate student, Sarah Masson, a test of semantic salience was devised using the following procedure.

Originally, the same 45 items that are present in the CGT were used to generate the materials for the salience test. The norms that had been collected for the CGT (see section 9.3.1.1) were therefore used. These consisted of attributes that had been named by a normative sample as being associated with an item from the CGT. The number of times a particular attribute was cited by participants had been recorded and therefore for each attribute there was a measure of item frequency. The two most frequent, two most moderately frequent and two least frequent attributes were chosen. Six attributes were chosen in order to provide a choice. These attributes were thought to reflect attributes that were seen as very important, of medium importance and unimportant to the target item.

For these six attributes, a normative sample (n = 10) were asked to rate how important they thought they were to the target item on a 5 point likert scale which ranged from 1 (very important) to 5 (unimportant). This provided a measure of overall importance for each attribute. For an extra assurance of validity, the controls were also asked to rank the 6 attributes from 1 (most important) to 6 (least important). This gave an indication of relative importance, the reasoning being that a test could be devised with attributes, which were clearly different from each other. For a list of attributes and their rankings see Appendix G.

A pilot run of the salience study was then carried out using the same 10 controls. The target item was placed in front of the controls followed by the three attributes, which were laid out in a random order. Participants were then asked to identify the most important attribute and then which one of the remaining attributes they deemed to be the second most important. The attribute judged as most important was scored as 1,that judged second most important was scored as 2 and the remaining attribute was scored as 3 and assumed to be of least importance.

Despite the clear differences in the ratings/ ranks ascribed to the attributes in the first stage of the norming process, the results from the pilot brought up a number of inconsistencies in the placing of importance. When the normative sample judged an associative as the most important it was ascribed a mean of 1, second most important 2 and least important 3. Any attribute which had a mean value which deviated by more than .4 was replaced by another attribute as consistency was low for these items. In total 33 items were revised. The revised test was then retested on the normative sample. Agreement was still low on several items but high on many items. Only items whose attributes means were 1, 2 and 3 (+/- 0.3) were included. This left 23 items with a variation of 0.3 or less mean importance ranking.

The items and attributes were written on individual flash cards, 8.5cm x 8.5cm, in size 48, black, Times New Roman font.

10.4. Procedure

Participants were asked to complete the salience test, the NART and the WASI. For the people with schizophrenia, they were also assessed on the CGT, and a Naming and Word-Picture Matching Test containing the same items used in the CGT.

For the salience test participants were shown the target card and then the three attributes were placed in front of it. The order in which the three attribute cards appeared was randomised. Participants were asked to identify "which attribute is the most important to the target", and then when this had been selected, "which is the next most important".

10.5. Results

Data from normal raters (see materials, section 10.3) provided a benchmark against which to judge performance on the "salience" task. Therefore any decision which differed from that made by the majority of norms was deemed an error.

The two groups differed significantly in the proportion of errors in ranking that were made on any item (t (28) = 3.85, p <.001). The controls ordered the items correctly 78.63% of the time on average (s.d = 11.79) whereas the people with schizophrenia were correct only 54.5% of the time (s.d. = 19.3). It is worth noting the large standard deviation in the schizophrenia group.

Additionally, a univariate ANCOVA with verbal IQ, performance IQ and full scale IQ as covariates found that group differences on the test of salience remained significant (F (4) = 7.25, p = .001).

Further analysis was conducted to see where the groups were making errors:

The degree of difference in ranking of importance from normal raters

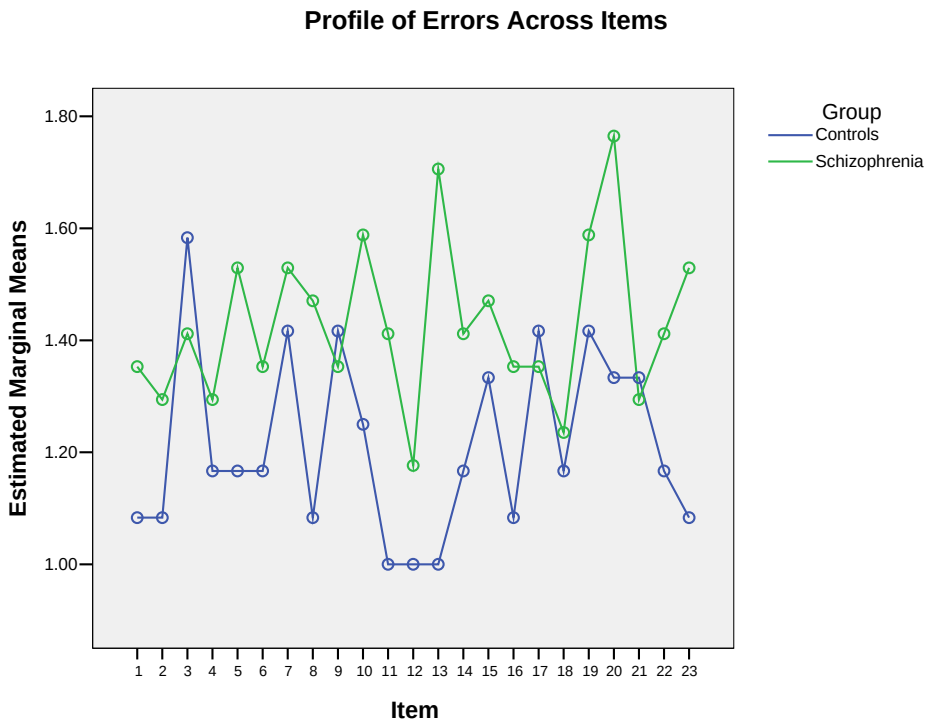
Errors of ranking differed in severity so for example an attribute seen by controls as most important could be placed differently as medium or second most important, referred to as a jump of one step. Whereas placing the most important attribute as least important is a jump of two steps. Jumps of two steps would suggest a far wider attribution of semantic salience. The two groups were compared on the number of one step jumps and two step jumps that they made.

In the control group all but one of the errors made were one jump steps (mean 4.83 one step jumps per person, s.d = 2.6) and this differed significantly (t (28) = -2.35, p =.026)) to the schizophrenia group (mean 7 one step jumps per person, s.d. = 2.43). Only two people in the control group made a two step jump compared to an average of 3.1 (s.d. = 2.4) in the schizophrenia group. Because of the skewed data, a Mann Whitney test was performed to compare the two groups who were found to differ significantly (U = 20.5, p <.001).

Did the same items produce the most errors in both groups?

Figure 9 shows the profile of errors across all the items on the salience test. For both groups the profile is fairly similar although there are clearly some items which produce relatively more errors in one group than the other group.

Figure 9: Profile of errors across items in the Salience Test



Relationships with other variables

- The CGT

Interestingly there was a strong positive correlation between errors on the salience test and the tendency to sort abnormally on the CGT in the schizophrenia group (r = .566, p = .014). The correlation between naming test performance and salience test performance in schizophrenia was not significant (r = .447, p =.063).

- IQ

In the schizophrenia group, the number of errors on the salience test was significantly correlated with IQ test performance for verbal IQ (r = -.543, p = .020), performance IQ (r = -.681, p = .002) and full scale IQ (r = -.625, p =.006). There was no significant relationship between NART scores and IQ (r = .016, p = .954). None of these correlations were significant for the control group; verbal IQ (r = -.164, p = .612), performance IQ (r = -.393, p = .206), full scale IQ (r = .091, p = .778) or NART scores (r = .342, p = .276).

- Age

In the control group there was also no significant correlation between age and salience test performance (r = -.317, p = .315) and this was the same in the schizophrenia group (r = -.117, p = .643).

- Camel and Cactus test performance

Data had been collected on 11 of the patients with schizophrenia for the Camel and Cactus tests from Study One. These patients had a mean age of 36 years (9.5 s.d), a mean NART IQ of 110.6 (6.4), a mean current IQ of 83.45 (16.9) and a mean PANSS general score of 23.7 (9.54), PANSS positive of 13.4 (9.04), PANSS negative score of 13.4 (9.04) and PANSS conceptual disorganisation score of 2.4 (1.42). This subgroup were not significantly different (p >.05) from the other schizophrenia participants on any of these variables apart from PANSS general scores (t (15) = -2.62, p = .019). A correlation analysis was performed between Camel and Cactus test performance and salience errors in this subgroup of participants. There was a highly significant correlation between Camel and Cactus picture errors and salience errors (r = .827, p = .003) and also a non significant (but borderline) correlation between Camel and Cactus words errors and salience errors (r = .583, p =.060).

A correlation analysis was conducted to relate the tendency to make large jumps of salience (i.e. a jump of two steps) with the baseline variables. Interestingly in schizophrenia there was a significant correlation between CGT performance and the tendency to make two step jumps (r = .505, p = .033). As with error rates, there were significant correlations with current IQ for performance (r = -.610, p = .007) and full scale IQ (r = -.531, p = .023) but not for significantly so for verbal (r = -.406, p = .094).

Relationship with symptoms

There were no significant correlations between any of the PANSS symptom measures (conceptual disorganisation, general, positive and negative) and salience test performance (both error rates and the tendency to make two step jumps).

10.6. Conclusions

From this study it would appear that people with schizophrenia do have an aberrant assignment of semantic salience. The groups were matched for pre-morbid and current IQ and therefore this effect can be said to be separate to what would be expected from a cognitively impaired group. The ANCOVA analysis confirmed this. In addition, the performance of the people with schizophrenia differed qualitatively in the fact that they made far more two step jumps showing that the range of their attribution of importance was much wider than the controls. This result is consistent with the salience model proposed by Kapur (2003) in that more unusual items are becoming salient to people with schizophrenia in a way that is not task-relevant.

Interestingly there were strong significant correlations between salience test performance, both in terms of errors and also two step jumps, and the tendency to sort abnormally on the CGT. This means that the people who made the most errors on the salience test and also made the highest number of two step jumps were those who tended to sort abnormally on the CGT. This provides some indication that, as predicted, there is a common mechanism involved which leads to errors in both tests. In addition, in a subsample of participants recruited for Study One, there were strong correlations between Camel and Cactus test performance and salience test performance. Therefore it appears that difficulties forming associations on the two Camel and Cactus tests and also the CGT are related to an aberrant assignment of semantic salience. The fact that the salience test only correlated with some of the semantic memory tests (largely those which elicited impairments) suggests that these impairments are due to an aberrant assignment of salience, something that perhaps does not affect performance so much on other tasks i.e. naming. Salience test performance however did not correlate with any symptom measure in schizophrenia suggesting that the cognitive impairments are perhaps unrelated to phenomenology. This could be due to the fact that our sample was from a chronically impaired population with a limited range of symptoms or whose symptoms were in remediation.

Kapur's (2003) model centres on the premise that a dysregulation of dopamine is responsible for an aberrant assignment of salience to contextually irrelevant stimuli. Therefore, following this logic, one could predict that in schizophrenia attention is being drawn to irrelevant internal/ external stimuli. In Kapur's model the nature of the stimuli which are assigned salience are underspecified, for example, this can be interpreted to mean that there is a general feeling of heightened awareness in schizophrenia, meaning that numerous concepts and experiences are seen as significant, or that certain specific ideas/ concepts become imbued with a disproportionate level of salience. The aim of Study Six was to see whether people with schizophrenia show an aberrant assignment of salience on a cognitive task using semantic concepts (e.g. objects and their attributes). Previous studies had reported that people with schizophrenia have difficulties adhering to contextual constraints when

forming associations and this could be an explanation for their impairments on the association tasks on the Hodges et al (1992) battery and also their performance on the CGT.

Based on their performance on the "salience test", it could be concluded that there is an aberrant assignment of semantic salience in schizophrenia as patients made many more errors when assigning importance to attributes, when compared to healthy controls. Further analysis suggests that the aberrant assignment of salience in schizophrenia affects a wide range of concepts as for each individual there were a number of items that were ascribed disproportionate importance (rather than just one or two). This fits in with the spreading activation theory which states that activation (determined by relevance of one concept to another) spreads further in schizophrenia to incorporate a range of less relevant concepts.

The aberrant assignment of salience did not however appear to be related to symptom severity which suggests, simplistically, that a dysregulated dopaminergic system does not explain an aberrant assignment of salience. Nevertheless, only the presence and severity of symptoms were measured. This does not necessarily permit speculation about the workings of the dopaminergic system. As Kapur hypothesises, delusions are the after-product of this abnormal attribution of salience, and therefore in chronic patients whilst delusions may be present they may not co-occur in time with poor performance on a test of semantic salience. Testing patients in the prodromal stage or directly measuring dopaminergic levels would provide better clarity on this issue. Regarding the present research, study six can support the claims of Kapur and those who have gone before him in suggesting that there is an aberrant assignment of salience in schizophrenia. In addition through the correlations with CGT and Camel and Cactus test performance, a link has been found between the semantic memory "impairments" in schizophrenia and an aberrant assignment of semantic salience.

From a cognitive perspective, it is important to consider how an aberrant assignment of semantic salience translates into what is known about semantic memory. In the spreading activation theories, related concepts are activated according to how semantically similar or associated they are and activation spreads across concepts. There are several schools of thought regarding the nature of similarity as previously discussed. It has already been proposed that there is a broader spread of activation in schizophrenia suggesting that whilst in healthy controls a concept may lead to activation of a small set of related concepts in people with schizophrenia more unrelated concepts are also activated. This ties in with the fact that on the test of salience the people with schizophrenia made many more two step jumps. If what is driving the spread of activation in semantic memory is the process of salience then an aberrant assignment of salience might lead to a less focussed, broader spread of activation. One could also say however that a primary hyper spreading of activation in the semantic memory network could lead to irrelevant concepts reaching awareness. If causality occurs in this direction then it could be the case that a disinhibition throughout the semantic network, heightened activation of the network in general or else a lack of awareness of contextual relevance could lead to an aberrant assignment of salience. Difficulties with inhibition typically fall under the domain of an executive dysfunction and have been frequently cited in schizophrenia (e.g. Leeson et al 2005b; Volk and Lewis 2002). Although underspecified by Kapur, the site of dopaminergic dysregulation is important if we are to understand the consequences in terms of

symptoms and behaviours. Winterer and Weinberger (2004) propose that the dysregulated dopaminergic system in schizophrenia consists of an imbalance between hypodopimenergia in the prefrontal cortex leading to hyperdopaminergia subcortically. Their theory states that normally, prefrontal dopamine acts to inhibit the release of dopamine subcortically, and in schizophrenia subcortical dopamine is disinhibited leading to positive symptoms. Winterer and Weinberger (2004) also state that the hypodopiminergia in the prefrontal cortex in schizophrenia could explain negative symptoms and cognitive deficits. In Kapur's model, he predicts that there is an excess of dopamine which, through an aberrant assignment of salience, leads to the formation of symptoms. This would fit in with the hyperdopaminergia subcortically in the Winterer and Weinberger model. The results from study six, however, suggest that the aberrant assignment of salience in schizophrenia is unrelated to symptoms and related to other cognitive impairments i.e. on tests of semantic memory. There is therefore an implication that the neural substrate for this may be hypodopiminergia in the PFC. The studies by Copland et al (2003) and Kischka (1996) would suggest that increased dopamine in healthy controls leads to enhanced salience processing; in this case attention became more focussed on concepts with strong meanings and less on concepts with weaker meanings. This therefore suggests that a decrease in dopamine would have the opposite effect, the assignment of salience to a wider range of less relevant concepts.

In the CGT, it is likely that, as Goldstone (1994) stated, people use "respects of similarity" (i.e. the information used to guide judgements of similarity) to group concepts together. The respects of similarity that an individual chooses depend on what is most salient to them at the time depending on the constraints of the situation and context. Therefore controls sort taxonomically as it is the most salient respect of similarity. The fact that with the people with schizophrenia CGT performance was related to poor performance on the salience test could be explained by the fact that participants see different respects of similarity as more salient for a strategy of grouping. It could also be theorised however that the aberrant assignment of salience causes a spreading of activation to unrelated concepts leading to unusual connections in the CGT, similarly to the loose category boundaries reported by Chan et al 1994. In a similar vein it could also be said that whilst performing the CGT task, participant's attention becomes drawn to loosely related concepts meaning that connections are formed ad hoc. In the same vein impairments on the association tests could be caused by attention being drawn to less related concepts. More work needs to be done in trying to understand how exactly an aberrant assignment of salience in schizophrenia is linked to their semantic memory impairments.

One limitation of this study is the fact that it is only really an indirect measure of semantic salience. In the study by Grober et al (1985), poor performance on a task where participants judged the importance of attributes to a target (identical in design to the one used here) the results were interpreted to mean a difficulty with the salience that was given to attributes. In this study therefore the word salience is seen as synonymous with importance. It may be the case that what is measured when one asks a participant to rank attributes by importance is different to the salience they give a particular attribute. One could infer from Kapur's model and the Incentive Salience model of Berridge and Robinson (1993) etc that when a stimulus becomes salient it is given extra attention and is usually associated with forthcoming reward. Although perhaps a jump, theoretically, it is not implausible to suggest that these stimuli, when

salient to a person, would also hold more importance. Whether this is importance as determined by the task demands/ situational context may be different from judging the importance of an associate to another. Nevertheless, it is useful to begin empirically testing the worth of the salience model although more work is needed in order to flesh out the theory. Future research is needed to take this work further.

Chapter 11: Summary and Conclusions

Studies 1-6 investigated the semantic memory impairment in schizophrenia across a number of tasks which were seen to target different aspects of semantic memory. In studies 1 and 2, a traditional stance was taken with regards to how semantic memory was conceptualised, mirroring the position commonly taken in the neuropsychology literature. This is where semantic memory is defined as a store of knowledge about objects and the relationships between them. Separable retrieval mechanisms are believed to be responsible for how this knowledge is accessed on cognitive tasks. Investigating performance on the CGT, however, evoked the development of a broader conception of semantic memory. Included in this, is the concept that the process of categorisation or association can depend largely on task-specific factors, current preferences and person-specific factors and not necessarily commonly held taxonomies. Furthering this, studies 5 and 6 supported the view that our semantic knowledge and how that is used is strongly influenced by what we hold to be salient at the time. How one interprets any differences (in comparison to normal controls) on tasks of semantic memory is dependent upon the task used. This research underscores the need to consider the fact that semantic memory as a concept is nebulous and appears to cover a wide range of processes, meaning that differences in performance can often be interpreted in several ways.

The task of trying to understand more about how semantic memory functions in schizophrenia is made harder by the fact that numerous cognitive deficits have been reported (e.g. unlike semantic dementia where impairments are confined largely to semantic memory). Although it is not yet an agreed diagnostic criterion, a cognitive impairment (i.e. deficits on tasks of cognition) in schizophrenia is well accepted by psychologists and psychiatrists as an intrinsic part of the condition, spanning long and short term memory, executive functions, general information processing, social and emotional processing and visual-perceptual processing. Research into the neuropsychology of schizophrenia aims to elucidate whether the cognitive impairments are separable to (e.g. Seaton et al 1999) or related to (e.g. Bell et al 2006) the symptoms of schizophrenia. The symptoms and behaviour of schizophrenia are not necessarily believed to have an organic aetiology and for this reason schizophrenia is often seen as a functional psychosis. Nevertheless, evidence from neuroimaging studies which frequently report abnormalities in brain structure and function (e.g. Shenton et al 2001), the fact that successful amelioration of symptoms relies largely on moderation of neurotransmitters and also the evidence supporting genetic abnormalities (e.g. Owen et al 2005) strongly indicate a biological basis to schizophrenia. Therefore comparisons with other non-psychotic clinical groups where the neurological aetiologies of cognitive impairments are well known allow for further speculation about the basis of the cognitive impairments in schizophrenia.

A meta-analysis and systematic literature review found evidence for an inconsistent profile of semantic memory impairment in schizophrenia. Nevertheless, it was established that more work was needed to understand the exact nature of the impairment, its severity and the likely cognitive mechanism. As with other research into the neuropsychology of schizophrenia, factors such as sample heterogeneity and the confounding influence of other cognitive deficits have slowed progress. The majority of studies reviewed did not match their schizophrenia and control groups on the basis of IQ or executive functioning. It was therefore difficult to speculate about whether semantic memory in schizophrenia was a primary impairment, above and

beyond what would be expected by a group with numerous cognitive deficits. Certain studies which employed a within-subjects design provided strong evidence for the role of a dysexecutive function in explaining some of the semantic memory impairments in schizophrenia, particularly on tests of semantic fluency and priming. Matching a group of patients with schizophrenia to clinical groups believed to have similar cognitive impairments, either generally, or in specific domains, (e.g. executive functioning or memory) means that by a process of elimination, certain hypotheses can be explored and the severity of the impairment can be compared relatively.

In Studies One and Two the semantic memory impairment in schizophrenia was assessed from a traditional neuropsychological perspective, e.g. assessing patients across a battery of tests to profile the impairment. Through comparisons with a group of patients with dementia who had a (likely) degraded semantic memory and also a group of patients with a dysexecutive syndrome caused by an acquired brain injury one could assess the influence of both types of impairment on semantic memory performance. As all clinical groups were matched for pre-morbid IQ, which is the standard in neuropsychological assessments, and also current IQ, these comparisons had an added validity. Through comparisons with the AD group, it was concluded that the semantic memory impairment in schizophrenia is task specific, once IQ is taken into consideration. On certain tasks, namely the two Camel and Cactus tests of association and the subordinate sorting task the level of poor performance in schizophrenia reached the severity seen in the AD group. Nevertheless on other tasks such as Word-Picture Matching, sorting and naming (once IQ was covaried) the group with schizophrenia performed at ceiling, whereas the AD group were substantially impaired. This was a similar conclusion to that arising from the meta-analysis, that the semantic memory impairment in schizophrenia is inconsistent and task-specific. Although the profile of impairment in schizophrenia seemed similar in some respects to that seen in AD in support of previous findings (e.g. McKay et al 1996), a profile analysis found that differences in error rates across tests meant a different profile. Whilst the AD group showed a widespread profile of impairment suggestive of degraded semantic knowledge, in schizophrenia the impairment was task-specific.

There is a traditional distinction, widely referred to in the neuropsychology literature, between disorders of memory store and retrieval (Warrington and Shallice, 1979). Until the last five years, the semantic memory impairment in schizophrenia was reported to fit the profile of an access disorder (e.g. Joyce 1996). More recently studies (e.g. Laws 2000; Rossell and David 2006) reported a storage disorder in schizophrenia. A review of the few studies which had investigated this issue found equivocal evidence for either disorder in schizophrenia. The majority of previous studies which had been reviewed had used single measures, based on only one of the criteria specified by Warrington and Shallice (1979). Using a battery of semantic memory tests, comparison with a group of patients with a degraded semantic memory and all four criteria of Warrington and Shallice (1979), Studies One and Two concluded that in schizophrenia the semantic memory impairment was not due to a degraded store. Nevertheless, fitting the data to the criteria proposed by Warrington and Shallice (1979) highlighted the fact that this distinction was not necessarily suitable for evaluating the semantic memory impairment in schizophrenia.

Although it has been reported elsewhere that semantic memory impairments in schizophrenia are related to symptoms especially FTD, this was not replicated in

studies one to six. The CGT, more than any other test of semantic memory seems to capture qualitatively a pattern of behaviour which resembles in many ways the psychotic speech of thought disorder. The bizarre sorts formed by people with schizophrenia on the CGT resemble the loosening of associations cited by Bleuler as an intrinsic part of the phenomenology of schizophrenia. Traditionally, overinclusion was seen as synonymous with psychotic thought (Payne 1973). In order to investigate the link between CGT performance and symptoms in schizophrenia it is important to see whether bizarre sorting and overinclusion occur in a group of non-psychotic people with a degraded semantic memory (i.e. with Alzheimer's Dementia).
In support of the previous literature, unusual card sorting on the CGT was reported in schizophrenia. This resembled Bleuler's definition of loosening of associations. Although overinclusion was unrelated to the presence of FTD (or any symptoms), there was a significant correlation between underinclusion and FTD. Interestingly, however, the non-psychotic AD group performed similarly to the schizophrenia group on this task, producing equal amounts of overinclusion and underinclusion. Despite this there was no indication that the abnormal sorting seen in schizophrenia was related to a semantic memory impairment and further qualitative analysis revealed differences in the way in which the two groups formed their abnormal sorts. Whilst the AD group were subdividing groups and forming connections on the basis of attribute knowledge the group of people with schizophrenia were making thematic connections and forming scenarios between items. Therefore loosening of associations represented clinically in people with FTD can be differentiated from loosening of associations represented on cognitive tasks, for example on the CGT and also tasks such as the study by Chan et al (1994) which reported spreading of category boundaries in schizophrenia. This finding therefore goes some way towards undermining the claim that cognitive impairments in schizophrenia are responsible for the development and maintenance of clinical symptoms and indicates that the two are separable.

It was apparent from studies one to four that semantic memory impairments in schizophrenia frequently occur on tasks which involve forming associations were between concepts i.e. in the CGT and Camel and Cactus test. These tasks share the common factor that rather than a simple yes/ no responses, participants are required to make choices out of a number of different alternatives. In looking at associations in semantic memory it was important to consider the different ways in which concepts can be connected in thought/ speech. In a step away from the classical library type view of semantic memory, which prevails in neuropsychology, a more contemporary line of thought sees semantic knowledge as a distributed system where context, emotions and experiences all influence how we form connections (e.g. Funnell 2001). In this way, separating concepts such as retrieval and store is inappropriate. It is possible that errors on tasks of semantic memory are due to differences in how people with schizophrenia choose to associate related concepts. In study five the aim was to assess whether the information that was being used to link concepts in schizophrenia was the same in controls. In a triadic comparison task it was reported that people with schizophrenia performed similarly to a group of patients with AD and a control group, suggesting that the tendency to make bizarre associations in schizophrenia is task specific. One could therefore conclude that semantic memory is organised normally in schizophrenia, that the same associations are available as for controls. Despite this it is evident that people with schizophrenia are choosing to make different connections between concepts on certain tasks, perhaps where choice is less constrained.

By comparing people with schizophrenia to a group with a dysexecutive syndrome resulting from an ABI and also from assessment of the schizophrenia group using the BADS, it was possible to speculate about the role of an executive dysfunction in explaining the semantic memory impairments in schizophrenia. From studies two and four, it could be concluded firstly that having a dysexecutive syndrome does not necessarily cause impairments on tasks of semantic memory and secondly that the executive dysfunction seen in schizophrenia does not provide a full explanation for their poor performance on either the tasks in the Hodges et al semantic memory battery or the CGT. Nevertheless, as only a limited aspect of executive functioning was assessed in studies two and four, it cannot be said with absolute conviction that the dysexecutive syndrome in schizophrenia and ABI were comparable and it may be the case that other aspects of executive functioning (not targeted by the BADS) have a larger influence on semantic memory processing.

A common theme that features in the literature is that there is an impairment in the processing of relevance and contextual information in schizophrenia. Performance data on the Hodges et al (1992) battery and also on the CGT suggests that whilst people with schizophrenia are often aware of the most typical association on a task, a less typical association can often appear more relevant (at least this is assumed to underpin their choice). One further possibility is that people with schizophrenia are not aware of the social constraints of the situation. Members of the control group often pointed out the several potentially acceptable ways of forming associations between concepts on the CGT but despite this chose to sort conventionally. People with schizophrenia (and perhaps also AD) seem unable to and resist tangential alternatives and stick to the conventional sorting strategies. This tendency had been noted in the literature previously. Rosenhan and Seligman (1989) stated that "overinclusiveness results from a tendency to construct concepts using both relevant and irrelevant information" and that it arises from "an impaired capacity to resist distracting information". The classical experiments on context by Chapman et al (1964) reported that people with chronic schizophrenia had the same ability to interpret weak meanings as controls when a context was absent, proving that knowledge was intact but there were difficulties applying that knowledge. This performance pattern provides support for Kapur's (2003) "aberrant assignment of salience" model which can be seen as the culmination of these convergent lines of thinking. Kapur suggests that people with chronic schizophrenia attribute salience to less relevant concepts because of a dysregulation of the dopaminergic system. The aim of study six was to see whether an aberrant assignment of salience in schizophrenia was related to the impaired performance seen on the Camel and Cactus tests, subordinate sorting task and CGT. Using a test, based on one used previously in the literature (Grober et al, 1985) to assess semantic salience, it was reported that people with schizophrenia have an aberrant assignment of salience to irrelevant item features. Furthermore this tendency was shown to relate to abnormal performance on the CGT and Camel and Cactus tests. However, there was no link found with symptoms and it is therefore difficult to speculate on the role of dopamine in this process. Despite a number of caveats, it can be concluded that differences in the way in which people with schizophrenia process/ utilise semantic knowledge is due in part to an aberrant assignment of semantic salience, which may or may not be due to a dysregulated dopaminergic system.

The dopamine-based models also provide a plausible neurobiological model for other neuropsychological findings in schizophrenia of excess activation (Winterer & Weinberger 2004), or failure to inhibit weak semantic associations (Leeson et al 2005b) in semantic memory. Both from a cognitive, and a psycho-physiological perspective, there is some evidence to support claims that people with schizophrenia have difficulties adhering to the correct context or forming appropriate associations. Electrophysiological studies have reported abnormal brain activity within the prefrontal and temporal cortices in response to semantic associations in schizophrenia (e.g. Kuperberg et al 2007). In addition, there has been a lot of work focusing on the N400 effect in schizophrenia, which is the electrophysiological change in brain activity which occurs when a concept is unexpected or not relevant. There is a reduced N400 effect in schizophrenia (Kiang et al 2007) suggesting that either concepts appear more relevant than they should or that there is less awareness when an item is irrelevant contextually. One could say that an inability to use contextual knowledge perhaps means that meaning is interpreted literally. In fact it has previously been suggested that concrete thinking is a hallmark symptom of schizophrenia (Goldstein 1959). From studies two and four, it can be concluded that the semantic memory impairment in schizophrenia is not fully attributable to an executive dysfunction, despite the fact that the group of patients with schizophrenia scored within the lowest 10^{th} percentile of the normal population on the BADS. The dopamine based theories of schizophrenia nevertheless emphasise an executive dysfunction as a central component of their models (e.g. Winterer and Weinberger, 2004), specified largely as difficulties inhibiting information (e.g. Winterer and Weinberger, 2004). Difficulties in inhibition have also been proposed to explain anomia (Leeson et al 2005b) and spreading activation in schizophrenia (e.g. Spitzer et al 1997). The three theories of salience, context and inhibition in schizophrenia are intertwined and therefore it is difficult to sketch a coherent theoretical model. Further work is needed to understand, therefore, whether the semantic memory impairments in schizophrenia are due to difficulties inhibiting certain meanings, using contextual knowledge to correctly guide this inhibition, or else due to an aberrant assignment of salience to certain concepts.

To conclude, the semantic memory impairments in schizophrenia are different to those seen in patients with AD, in that they do not reflect a deterioration of stored knowledge and are task-specific. On certain tasks e.g. verbal fluency and priming, impairments may be due to an executive dysfunction which is present in schizophrenia. However, this did not appear to fully explain poor performance on tasks of semantic association, sorting and categorisation. Although more work is needed to define what is meant be "an aberrant assignment of salience", the salience model provides a good explanation for the fact that people with schizophrenia connect concepts in semantic memory differently to controls. Although in many ways, a pilot study, study six provided support for this explanation. A major aim of the research was to establish whether there is a link between the semantic memory impairments in schizophrenia and the presence of clinical symptoms, largely FTD. Despite a correlation between underinclusion on the CGT and FTD, the conclusion from all 6 studies is that semantic memory impairments are separate from FTD, as assessed with clinical interview.

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Appendix A

Tables of effect sizes for all studies included in the meta-analysis.

Legend for Tables:
Sz = Schizophrenia
NC = Normal Controls
RDC = Research Diagnostic Criteria
DSM = Diagnostic and Statistical Manual (Criteria)
ICD = The International Classification of Diseases and Related

Table 1: Naming studies

Study	Outcome Measure	Participants	IQ Measure	Results	Effect Size (CIs)
Al-Uzri, Laws and Mortimer 2004	Hodges Naming Test	12 Sz (DSM-IV) 12 NC	Matched for education only	There was a trend towards significance (p = .076).	-0.76 (-1.58 – 0.07) MEDIUM
Barrera, McKenna and Berrios 2005	Graded Naming Test	15 Sz FTD (RDC - chronic) 17 NC	Sz and NC matched on NART (mean SZ = 111.45 (8.15) All patients had a WAIS IQ of 85+	Tukey's HSD test Sz were not significantly different to controls (p = . 049)	-0.76 (-1.48 - -0.04) MEDIUM
		16 Sz Non – FTD (RDC - chronic) 17 NC			-0.73 (-1.44 - -0.03) MEDIUM
Faber and Reichstein 1981	Picture Naming	14 Sz FTD (Taylor and Abrams 1978 diagnostic criteria) 28 NC	Sz had similar years of schooling to controls.	FTD differed from controls (p <.01)	-1.17 (-1.85 - -0.48) LARGE
		10 Sz Non FTD (Taylor and Abrams 1978 diagnostic criteria) 28 NC			-0.89 (-1.65 - -0.15) LARGE
Giovannetti et al 2003	Boston Naming Test	47 Sz (First Episode) 31 NC	Matched on education but not WASI.	Sz significantly worse than controls (p <.001)	-1.46 (-1.97 - -0.95) LARGE
Goldberg	Boston	13 Sz Mild	Groups	Groups were	-0.23 (-

et al 1998	Naming Test	FTD (DSM-III-R) 23 NC	differed on WRAT score.	not significantly different (p = .09)	0.91 – 0.46) SMALL
		10 Sz Moderate/ Severe FTD (DSM-III-R) 23 NC			-0.76 (-1.53 – 0.00) MEDIUM
Gourovitch et al 1996	Boston Naming Test	27 Sz (DSM-III-R) 24 NC	Matched on WRAT score.	Sz were impaired (p <.05).	-0.65 (-1.22 - - 0.09) MEDIUM
Hoff et al 1992	Boston Naming Test	32 Sz First Episode (DSM-III-R) 25 NC	Different on education.	No difference between the 3 groups on ANCOVA but significant difference on post hoc test between chronic patients and controls (p >. 05)	-0.69 (-1.23 - - 0.15) MEDIUM
		26 Sz Chronic (DSM-III-R) 25 NC			-0.73 (-1.29 - - 0.16) MEDIUM
Joyce et al 1996	Boston Naming Test	50 Sz Acute (DSM-III-R) 25 NC	Groups matched on NART.	Sz were impaired (p <.001)	-6.79 (-7.98 - - 5.60) MEDIUM
Lawrence et al 2007	Naming Test (Hodges and Patterson (1996))	20 Sz Chronic (DSM-IV-TR) 20 NC	Matched on NART	Groups were significantly different (p<.05).	-0.58 (-1.22 – 0.05) MEDIUM
Laws et al 2000	Graded Naming Test	22 Sz Chronic (DSM-III-R) 100 NC (normative data)	NART within the normal range – mean Sz = 99 (12.81).	Sz were impaired (p <.01).	-2.03 (-2.56 - - 1.51) LARGE
Laws et al	Category	55 Sz (RDC)	Matched on	The majority	-1.89 (-

2006	Specific Naming Test (McKenna 1997)	22 NC	NART	of patients (76%) were significantly poorer on naming.	2.47 - - 1.32) LARGE
Leeson et al 2005	McKenna Naming Test	56 Sz (RDC) 24 NC	Matched on NART.	Sz were impaired (*p* <.0001).	-1.49 (- 2.02 - - 0.96) LARGE
Leeson et al 2006	McKenna Naming Test	16 Sz High FTD (RDC) 16 NC	Matched on NART	Both groups were impaired on naming (*p* <.001)	-2.23 (- 3.12 - - 1.35) LARGE
		16 Sz Low FTD (RDC) 16 NC			-1.15 (- 1.89 - - 0.39) LARGE
McKay et al 1996	Naming Test	20 Sz Core (DSM-III) 40 NC	All had a NART score in normal range (101.5 – 107.2)	The Core and Elderly group only were impaired on naming.	-1.69 (- 2.31 - - 1.08) LARGE
		12 Sz Elderly (DSM-III) 40 NC			-4.14 (- 5.16 - - 3.16) LARGE
		14 Sz Mild (DSM-III) 40 NC			-2.03 (- 2.75 - - 1.32) LARGE
Stirling et al 2006	Graded Naming Test	30 Sz (DSM-IV) 18 NC	Matched on NART and education level but differed in terms of current IQ (Ravens Progressive Matrices)	There was no significant difference between patients and controls	-0.55 (- 1.15 – 0.04) MEDIUM

Table 2: Word-Picture Matching studies

Study	**Outcome Measure**	**Participants**	**IQ measure**	**Results**	**Effect Size (CIs)**
Al-Uzri et	Word-	12 Sz (DSM-	Matched	Patients	-0.12 (-0.92 –

al 2004	Picture Matching	IV) 12 NC	on Education	performed at ceiling	0.69) SMALL
Barrera et al 2005	British Picture Vocabulary Scale	16 Sz Non FTD Chronic (RDC) 17 NC	Groups matched on NART and all patients had a WAIS IQ of 85+.	Neither group were impaired.	-0.35 (-1.04 – 0.34) SMALL
		15 Sz FTD Chronic (RDC) 17 NC			-0.60 (-1.31 – 0.11) MEDIUM
Gurd et al 1997	Word Finding Task	19 Sz Chronic (DSM-III-R) 21 NC	Matched on NART.	Impaired when asked to find category member but not specific item.	-0.53 (-1.16 – 0.11) MEDIUM
Lawrence et al 2007	Word – Picture Matching Test (Hodges and Patterson (1996))	20 Sz Chronic (DSM-IV-TR) 20 NC	Matched on NART	Groups were not different.	-0.65 (-1.29 - - 0.01) MEDIUM
McKay et al 1996	Word-Picture Matching	20 Sz Core (DSM-III) 40 NC	All patients had a NART score within the normal range (101-5 – 107.2).	Normal performance for all 3 groups	-0.71 (-1.26 - - 0.16) MEDIUM
		12 Sz Elderly (DSM-III) 40 NC			-1.70 (-2.4 - - 0.97) LARGE
		14 Sz Mild (DSM-III_ 40 NC			0 (-0.61 – 0.61) SMALL

Table 3: Semantic Fluency studies

Study	Outcome Measure	Participants	IQ Measure	Results	Effect Size (CIs)
Al-Uzri et al 2004	Category Fluency	12 Sz (DSM-IV) 12 NC	Matched on education	Sz produced fewer words (p = .043).	-0.89 (-1.73 - - 0.05) LARGE
Albus et al 2006	Semantic Fluency	71 Sz (DSM-III) 71 NC	Matched on education and premorbid IQ	Sz were impaired (p <.04)	-0.84 (-1.18 - - 0.49) LARGE
Allen et al 1993	Semantic Fluency	20 Sz Chronic	Matched on NART and	Sz produced fewer words	-6.4 (-8.19 - -4.61)

		(DSM-III-R) 10 NC	Education	(p <.001).	LARGE
Aloia et al 1996	Semantic Fluency	28 Sz (DSM-IV) 31 NC	Differed in terms of education but matched on WRAT	Sz produced fewer words (p <.005)	-1.39 (-1.97 - -0.83) LARGE
Baare et al 1999	Semantic and Phonemic Fluency	14 Sz Acute (DSM-IV) 14 NC	Unmatched in terms of education	Sz were worse on verbal fluency (p =.002)	-1.33 (-2.15 - -0.51) LARGE
Barrera et al 2005	Semantic Fluency	Sz FTD (RDC)	All patients had a WAIS above 85	Sz produced fewer words (p = .006)	-1.12 (-1.87 - -0.38) LARGE
		Sz Non FTD (RDC)			-0.93 (-1.65 - -0.21) LARGE
Bozikas et al 2005	Greek Verbal Fluency – Semantic and Phonemic	119 Sz Chronic (DSM-IV) 150 NC	Matched for Education	Sz generated fewer words on both tests (p <.001). They also generated fewer switches (p <.001) and clusters (p <.001).	-1.30 (-1.57 - -1.04) LARGE
Chen et al 2000 a)	Semantic Fluency	23 Sz (DSM-IV) 26 NC	Matched for years of education	Sz produced fewer words (p <.001).	-1.96 (-2.64 - -1.27) LARGE
Chen et al 2000 b)	Semantic Fluency	21 Sz (DSM-III) 11 NC	Matched for years of education	Patients generated fewer words (p <.001) and more inappropriate words (p <.011).	-2.08 (-2.97 - -1.19) LARGE
Cutting et al 1987	Semantic Fluency	20 Sz (DSM-III) 30 NC	Matched for mean current IQ	No significant difference between the groups	0.25 (-0.31 – 0.82) SMALL
Elvevag et al 2001	Semantic and	13 Sz (DSM-IV)	Matched on NART but	Sz produced fewer words	-1.24 (-2.08 - -

	Phonemic Fluency	15 NC	differed on WRAT.	(p <.01).	0.40) LARGE
Elvevag et al 2002 a)	Semantic Fluency	24 Sz (DSM-IV) 24 NC	Differed in IQ (WAIS and WRAT).	Sz produced fewer words (p <.001).	-1.59 (-2.24 - -0.94) LARGE
Elvevag et al 2005	Semantic Fluency	21 Sz (DSM-IV) 22 NC	Matched on WRAT but differed on current IQ	Number of distinct exemplars produced was similar (p =.71)	0.38 (-0.22 – 0.99) SMALL
Giovannetti et al 2003	Semantic Fluency	47 Sz First Episode (RDC) 31 NC	Unmatched on current IQ	Sz produced fewer words (p <.001).	-1.60 (-2.12 - -1.08) LARGE
Gourovitch et al 1996	Semantic and Phonemic Fluency	27 Sz (DSM-III-R) 24 NC	Matched on WRAT	Sz produced fewer words (p <.0001).	-2.24 (-2.95 - -1.54) LARGE
Granholm et al 1998	Semantic and Phonemic Fluency	15 Sz (DSM-IV) 15 NC	Matched on education but not on WAIS.	Sz were impaired (p <.05)	-0.89 (-1.65 - -0.14) LARGE
Halari et al 2006	Semantic and Phonemic Fluency	43 Sz (DSM-IV) 42 NC	Unmatched	Sz were impaired (p < . 001)	-2.11 (-2.64 - -1.58) LARGE
Joyce et al 1996	Semantic and Phonemic Fluency	50 Sz Acute (DSM-III – R) 28 NC	Matched on the NART	Sz were impaired on both tests (p <.001)	-5.27 (-6.24 - -4.29) LARGE
Kosmidis et al 2005	Semantic and Phonemic Fluency	21 Sz chronic young (DSM-IV) 21 NC	Matched on education	Sz were impaired (p <.05)	-1.89 (-2.63 - -1.17) LARGE
Kravariti et al 2005	Semantic and Phonemic Fluency	15 Sz TD (DSM-IV) 30 NC	Differed in years of education	Sz group produced fewer words (p <.05)	-1.30 (-1.97 - -0.63) LARGE
		15 Sz Neg (DSM-IV) 30 NC			-1.01 (-1.66 - -0.36) LARGE
Kremen et al 2003	Semantic and Phonemic Fluency	83 Sz Chronic (DSM-III-R) 83 NC	Matched on WRAT-R but differed on WAIS	Sz produced fewer words (p <.0001)	-1.02 (-1.34 - -0.70) LARGE

Kubota et al 2005	Semantic and Phonemic Fluency	16 Sz Chronic (DSM-IV) 19 NC	Matched for education	Sz produced fewer words (p <.001)	-2.12 (-2.95 - -1.29) LARGE
Lafont et al 1998	Semantic Fluency	26 Sz Chronic (DSM-IV) 32 NC	Matched for education and pre-morbid IQ.	Sz produced fewer words (p <.0001).	-1.53 (-2.15 - -0.91) LARGE
McKay et al 1996	Semantic Fluency (Animals only)	20 Sz Core (DSM-III) 40 NC	All Sz had a normal NART score (101-5 – 107.2 range)	All 3 groups were impaired. (p <.05)	-1.62 (-2.23 - -1.01) LARGE
		12 Sz Elderly (DSM-III) 40 NC			-1.79 (-2.52 - -1.06) LARGE
		14 Sz Mild (DSM-III) 40 NC			-1.24 (-1.89 - -0.59) LARGE
Minzenberg et al 2003	Category Fluency	57 Sz (DSM-IV) 20 NC	Unmatched on levels of education	Sz produced fewer words (p <.05).	-0.59 (-1.11 - -0.07) MEDIUM
Moelter et al 2001	Semantic Fluency	38 Sz (DSM-IV) 47 NC	Unmatched for education	Sz produced fewer words (p <.001)	-1.38 (-1.86 - -0.91) LARGE
Moelter et al 2005	Semantic Fluency	27 Sz (DSM-IV) 30 NC	Unmatched on NART	Sz produced fewer shared attributes (p <.05)	-0.53 (-1.06 – 0.003) MEDIUM
Paulsen et al 1996	Semantic Fluency	56 Sz (DSM-III-R) 28 NC	Matched for education but patients had a lower verbal IQ	Sz generated fewer words (p <.05)	-1.05 (-1.53 - -0.57) LARGE
Prescott et al 2006	Semantic Fluency	40 Sz (DSM-IV) 28 NC	Differed on NART	Sz produced fewer words (p = . 02)	-0.9 (-1.40 - - 0.39) LARGE
Robert et al 1997	Semantic Fluency	22 Sz Chronic (DSM-III-R) 22 NC	Matched for education	Sz produced fewer words (p<.0001)	-1.66 (-2.34 - -0.97) LARGE
Robert et al 1998	Semantic and Phonemic Fluency	78 Sz Chronic (DSM-IV) 64 NC	Matched for level of education	Sz produced fewer words (p <.001)	-1.64 (-2.32 - -0.96) LARGE
Rossell et	Semantic	62 Sz (DSM-	All	Sz produced	-0.27 (-

al 2006	and Phonemic Fluency	IV) 48 NC	participants had a NART score of above 90. Groups were matched for level of education but not NART scores.	fewer words (p <.001)	0.64 – 0.11) SMALL
Stirling et al 2006	Semantic and Phonemic Fluency	30 Sz (DSM-IV) 18 NC	Matched on NART and educational level but differed in terms of current IQ	Sz were impaired (p <.001)	-1.07 (-1.69 - -0.45) LARGE
Sumiyoshi et al 2001	Semantic Fluency	57 Sz (DSM-III- R or DSM-IV) 33 NC	Matched on education but different on WAIS	Sz were worse than NC (p <.01)	-1.19 (-1.65 - -0.73) LARGE
Sumiyoshi et al 2005	Semantic and Phonemic Fluency	21 Sz Alogia (DSM-IV) 38 NC	Matched on education but not the WAIS-R	Sz produced fewer words (p <.01)	-1.00 (-1.57 - -0.44) LARGE
		17 Sz Non Alogia (DSM-IV) 38 NC			-0.63 (-1.21 - -0.05) MEDIUM
Vinogradov et al 2002	Semantic Fluency	40 Sz (DSM-IV) 16 NC	Sz had fewer years of education and lower current IQ	Sz had similar output to NC (p =2) but fewer than published norms (p =.006).	-0.55 (-1.13 – 0.04) MEDIUM
Woods et al 2007	Semantic and Phonemic Fluency	22 Sz (DSM-IV) 27 NC	Unmatched on WRAT	Sz were impaired (p <.001)	-2.12 (-2.82 - -1.42) LARGE
Zanello et al 2006	Semantic Fluency	20 Sz (DSM-IV) 20 NC	Matched on two levels of education – low and high	Sz were worse than controls (p <.004)	-1.00 (-1.66 - -0.35) LARGE

Table 4: Semantic Association studies

Study	Outcome	Participants	IQ	Results	Effect Size (CIs)

	Measure		**Measure**		
Barrera et al 2005	Camel and Cactus Tests	15 Sz Non TD (RDC) 17 NC	Matched on NART. All had a WAIS IQ of above 85.	Sz were no different to NC	0.13 (-0.55 – 0.81) SMALL
		16 SZ TD (RDC) 17 NC		Sz were impaired (p =.006)	1.56 (0.77 – 2.35) LARGE
Lawrence et al 2007	Camel and Cactus Test	20 Sz (DSM-IV-TR) 20 NC	Matched on NART	Sz were impaired (p <.05)	1.63 (0.91 – 2.34) LARGE
Moelter et al 2005	Pyramid and Palm Trees	27 Sz Acute (DSM-IV) 30 NC	Unmatched NART	Sz performed similarly to NC	-0.42 (-0.95 – 0.10) MEDIUM
Rossell and David 2006	Word Association Tasks	32 Sz (DSM-IV) 32 NC	Matched on education but not NART	Sz were impaired (p <.001)	0.70 (0.19 – 1.21) LARGE
Stirling et al 2006	Pyramid and Palm Trees	30 Sz Acute (DSM-IV) 18 NC	Matched on NART and educational level but differed in terms of current IQ	No difference between Sz and NC.	0.34 (-0.25 – 0.93) SMALL-MEDIUM

Table 5: Categorisation studies

Study	**Outcome Measure**	**Participants**	**IQ Measure**	**Results**	**Effect Size (CIs)**
Al-Uzri et al 2004	Level 1 Sorting	12 Sz (DSM-IV) 12 NC	Matched on education	Sz were not impaired	0.33 (-0.48 – 1.13)
	Level 2 Sorting			Sz impaired (p =.049)	0.78 (-0.05 – 1.62)
	Level 3 Sorting			Sz were not impaired	0.16 (-0.65 – 0.96)
Chen et al 1994	Semantic Categorization Task (Wilkins et al 1971)	28 Sz (RDC) 28 NC	Matched on pre-morbid IQ	Sz were slower to respond (p =.0001)	-1.05 (-1.56 - - 0.53)
Clare et al 1993	Category Judgement Task	12 Sz Chronic (RDC) 12 NC	Matched for NART	Sz were worse (p <.0001).	-1.39 (-2.28 - - 0.50)
Cutting et al 1987	Goldstein – Scheerer Object	20 Sz acute (DSM-III)	Matched for mean IQ	Sz were more overinclusive on	-0.94 (-1.59 - - 0.28)

	Sorting Test	30 NC		non verbal test only (p <.005)	
Elvevag et al 2002 b)	Semantic Categorization Task	28 Sz (DSM-IV) 26 NC	Differed on WRAT and WAIS	Sz were slower to respond (p <.0001)	- 1.48 (-2.08 - -0.88)
Green et al 2004	Category Generation Test (CGT)	32 Sz Acute (DSM-IV) 15 NC	Not matched for NART or Quick Test for IQ	More Sz overincluded (p <.05) – derived from chi square	-0.77 (-1.41 - -0.14)
Grillon et al 1991	Semantic Categorization	17 Sz (RDC/ DSM-III) 14 NC	Matched for years of education	Sz were less accurate (p <.005) and slower (p <.006).	0.61 (-0.15 – 1.36)
Lawrence et al 2007	Sorting	20 Sz Chronic (DSM-IV-TR) 20 NC	Matched on NART	Sz were worse on sorting test (p =.03)	0.19 (-0.42 – 0.82)
	Category Generation Test - Overinclusion			More overinclusion in Sz (p =.003)	0.82 (0.18 – 1.47)
	Category Generation Test – Underinclusion			More underinclusion in Sz (p <.003)	-0.70 (-1.34 - -0.06)
Matsumoto et al 2001	Categorization Test	20 Sz 20 NC	Not matched on education	Sz were significantly slower (p = .002)and less accurate (p =.020)	0.74 (0.09 – 1.38)
McKay et al 1996	Living vs. Non Living	20 Sz Core (DSM-III) 40 NC	All Sz had a normal NART score between (101-5 – 107.2)	Sz were not different to NC	0.56 (0.014 – 1.11)
	Sorting Superordinate			Sz were not different to NC	1.18 (0.60-1.75)
	Sorting Subordinate			Sz were impaired (p <.05)	2.13 (1.47 – 2.78)
Rossell and David 2006	Categorization Test	32 Sz (DSM-IV) 32 NC	Matched on education but not NART	Sz were impaired (p <.05)	0.67 (0.17 – 1.18)

Table 6: Semantic Priming studies

Study	**Outcome Measure**	**Participants**	**IQ Measure**	**Results**	**Effect Size (CIs)**
Aloia et al 1998	Pronunciation – short SOAs	11 Sz Mild FTD (DSM-IV) 21 NC	Unmatched on WRAT	Normal priming	0.49 (-0.24 – 1.24) SMALL
		9 Sz Severe FTD (DSM-		Hypopriming	-1.03 (-1.86 –

		IV) 21 NC			0.2) LARGE
Barch et al 1996	Pronunciation 200SOA	66 Sz Non FTD (DSM-III-R) 28 NC	Differed in education	Normal priming in Sz but slower overall	-0.23 (-0.70 - 0.25) SMALL
	200 SOA	44 Sz FTD (DSM-III-R) 28 NC			0.88 (0.42 – 1.33) LARGE
	450 SOA	66 Sz Non FTD (DSM-III-R) 28 NC			0.35 (-0.13 – 0.83) SMALL
	450 SOA	44 Sz FTD (DSM-III-R) 28 NC			0.9 (0.44 – 1.36) LARGE
	700 SOA	66 Sz Non FTD (DSM-III-R) 28 NC			-0.55 (-1.03 – 0.07) MEDIUM
	700 SOA	44 Sz FTD (DSM-III-R) 28 NC			0.70 (0.25 – 1.16) MEDIUM
Barch et al 1999	300 SOA LDT	56 Sz (DSM-IV) 25 NC	Matched for education	Hypopriming	0.03 (-0.45 – 0.49) SMALL
	950 SOA LDT				-0.30 (-0.78 – 0.17) SMALL
Baving et al 2001	LDT – 800 SOA	20 SZ (DSM-IV) 20 NC	Matched for education	Hyperpriming	0.87 (0.22 – 1.52) LARGE
Besche-Richard et al 1999	LDT – 25% related words- 1500 SOA	21 Sz FTD (DSM-III-R) 20 NC	Matched for education	Normal Priming	0.05 (-0.56 – 0.66) SMALL
Blum and Friedes et al 1995	LDT – 350 SOA	10 Non FTD (DSM-III-R)	Matched for years of education	Normal priming at both levels	0.19 (-0.67 – 1.05) SMALL
		10 FTD (DSM-III-R)			0.18 (-0.68 –

					1.03) SMALL
Bullen and Hemsley 1987	Word Recognition – varied SOAs	12 Sz (ICD) 12 NC	Not matched on a synonyms test	Hypopriming	0.18 (-0.62 – 0.99) SMALL
Chapin et al 1989	LDT – 500 SOA	12 Sz (DSM-III-R) 12 NC	Matched for current IQ	Hypopriming – groups differed on response latency with	-0.99 (-1.84 - -0.15) LARGE
Chenery et al 2004	LDT 1000 SOA (high relatedness proportion word pairs)	14 Sz (DSM-IV) 12 NC	Matched on education and NART scores	Hypopriming	0.82 (0.02 – 1.62) LARGE
	LDT 250 SOA			Normal or Hyperpriming	1.14 (0.31 – 1.97) LARGE
Fuentes and Santiago	LDT – 950 SOA	16 Sz (ICD-10) 16 NC	Matched for education	Hypopriming	-0.26 (-0.95 – 0.44) SMALL
Gouzoulis-Mayfrank et al 2003	Direct LDT – 500 SOA	16 Sz FTD Acute (DSM-IV) 20 NC	Matched for education	Normal priming but also some evidence of Hyperpriming in FTD patients	0.56 (-0.11 – 1.23) MEDIUM
		17 Sz Non FTD Acute (DSM-IV) 20 NC			0.18 (-0.47 - 0.82) SMALL
	Indirect LDT – 500 SOA	16 Sz FTD Acute (DSM-IV) 20 NC			-0.13 (-0.78 – 0.53) SMALL
		17 Sz Non FTD Acute (DSM-IV) 20 NC			0.44 (0.21 – 1.09) SMALL
Henik et al 1998	LDT – combined priming effects over long and short SOA trials	16 Sz FTD (DSM-III-R) 16 NC	Matched for years of education	Hyperpriming	-0.63 (-1.34 – 0.08) MEDIUM
Hokama et al 2003	LDT – varied SOAs	18 Sz unmedicated (DSM-III-R)	Not matched	Hypopriming	0.04 (-0.61 – 0.69)

		18 NC			SMALL
Kuperberg et al 2007	Direct – 300 SOA	17 Sz Chronic (DSM-IV) 15 NC	Matched for socio-economic status	Normal priming	-2.54 (-3.51 - -1.58) LARGE
	Indirect – 300 SOA				-2.40 (-3.34 - -1.46) LARGE
Lecardeur et al 2006	LDT – 250 SOA	15 SZ Mild FTD (DSM-IV) 15 NC	Matched for education level	Sz showed hyperpriming	0.26 (-0.46 – 0.97) SMALL
	500 SOA				1.02 (0.26 – 1.78) LARGE
Manschreck et al 1998	LDT – 250 SOA	12 Sz FTD (DSM-III) 11 ND	Not matched for education	Hyperpriming	-0.01 (-1.01 – 0.98) SMALL
		6 Sz Non FTD (DSM-III) 11 NC		Normal priming	0.34 (-0.49 – 1.16) SMALL
Mathalon et al 2002	Picture-Word Matching Task (325 SOA)	18 Sz (DSM-IV) 18 NC	Matched for education	Normal priming effect	-2.4 (-3.26 - -1.54) LARGE
Minzenberg et al 2003	LDT Automatic SP 250 SOA	57 Sz (DSM-IV) 20 NC	Sz were worse on the WAIS (p <.01)	Normal priming in both conditions	0.00 (-0.51 – 0.51) SMALL
	LDT Controlled SP 1000 SOA				-0.14 (-0.65 – 0.37) SMALL
Moritz et al 2001a	Word Association – 200 SOA	30 Sz Non FTD (DSM-IV) 29 NC	Unmatched	Normal Priming	-0.004 (-0.51 – 0.52) SMALL
		15 Sz FTD (DSM-IV)		Hyperpriming	0.52 (-0.11 – 1.15) MEDIUM
Moritz et al 2001b	LDT – 200 SOA - Direct	16 FTD (DSM-IV) 30 NC	Matched for education	Hyperpriming in Sz	-0.38 (-0.99 – 0.23) SMALL

		28 Non FTD (DSM-IV) 30 NC			0.29 (-0.23 – 0.81) SMALL
	Indirect – 200 SOA	16 FTD (DSM-IV) 30 NC			-0.65 (-1.27 - -0.03) MEDIUM
		28 Non FTD (DSM-IV) 30 NC			-0.16 (-0.68 – 0.36) SMALL
Moritz et al 2002	Pronunciation – Direct 200 SOA	20 Sz Non FTD (DSM-IV) 65 NC	Matched for verbal IQ and years of education	Hypopriming in all conditions	0.13 (-0.37 – 0.63) SMALL
		12 Sz FTD (DSM-IV) 65 NC			0.13 (-0.37 – 0.63) SMALL
	Indirect – 200 SOA	20 Sz Non FTD (DSM-IV) 65 NC		Hyperpriming in FTD group	-1.07 (-1.71 - -0.43) LARGE
		12 Sz FTD (DSM-IV) 65 NC			-1.05 (-1.67 – 0.41) LARGE
Narr et al 2003	LDT – Right Hemisphere 750 SOA	34 Sz (DSM-IV) 20 NC	Matched for education	No difference in response latencies	0.59 (0.03 – 1.16) MEDIUM
Nestor et al 2006	LDT – 500 SOA	14 Sz Chronic (DSM-IV) 14 NC	Matched for parental socio-economic status	Normal semantic priming	-0.06 (-0.80 – 0.67) SMALL
Ober et al 1997	LDT 260SOA	15 Sz Paranoid (DSM-III-R) 20 Sz	Matched for education but not current IQ	Hypopriming	-0.12 (-0.79 – 0.55) SMALL
	LDT 260 SOA	16 Sz Non Paranoid (DSM-III-R) 20 Sz		Normal / Hypo priming	0.07 (-0.59 – 0.73) SMALL
	LDT 1000 SOA	15 Sz Paranoid		Normal priming	-0.09 (-0.77 –

		(DSM-III-R) 20 Sz			0.56) SMALL
	LDT 1000 SOA	16 Sz Non Paranoid (DSM-III-R) 20 Sz		Normal priming	0.16 (-0.50 – 0.82) SMALL
Ober et al 1995	LDT (superordinate prime and subordinate target) – 250 SOA	19 Sz Chronic (DSM-III-R) 22 NC	Matched for years of education	Normal priming	0.04 (-0.58 – 0.65) SMALL
Passerieux et al 1997	LDT – 50 SOA	11 Non FTD (DSM-III-R) 11 NC	Similar for socio-educational level	Normal priming	0.08 (-0.76 – 0.92) SMALL
		11 FTD (DSM-III-R) 11 NC		Hypopriming	-1.24 (-2.15 - -0.33) LARGE
Quelen et al 2005	Identify masked words following a prime – 500 SOA	20 Sz (DSM-IV) 20 NC	Matched for years of education	Normal priming	0.15 (-0.47 – 0.77) SMALL
Rossell et al 2004	LDT – 500 SOA	20 Sz Fear (DSM-IV) 20 NC	Matched for years of education and NART scores	Normal priming – slightly larger priming in fear group.	-0.09 (-0.71 – 0.56) SMALL
		20 Sz Sad (DSM-IV) 20 NC			0.07 (-0.55 – 0.69) SMALL
Spitzer et al 1993a)	200 SOA Direct	29 FTD (DSM-III-R) 20 NC	Matched for education	Hyperpriming in FTD group at short and long SOAs and non FTD group showed greater priming advantage than controls	0.37 (-0.09 – 0.83) SMALL
	200 SOA Direct	21 Non FTD (DSM-III-R) 20 NC			0.16 (-0.36 – 0.67) SMALL
	200 SOA Indirect	29 FTD (DSM-III-R) 20 NC			0.28 (-0.18 – 0.74) SMALL
	200 SOA Indirect	21 Non FTD (DSM-III-R) 20 NC			0.07 (-0.44 – 0.58) SMALL

	700 SOA Direct	21 Non FTD (DSM-III-R) 20 NC			0.27 (-0.19 – 0.73) SMALL
	700 SOA Direct	21 Non FTD (DSM-III-R) 20 NC			0.09 (-0.42 – 0.6) SMALL
	700 SOA Indirect	21 Non FTD (DSM-III-R) 20 NC			0.15 (-0.31 – 0.61) SMALL
	700 SOA Indirect	21 Non FTD (DSM-III-R) 20 NC			0.004 (-0.51 – 0.51) SMALL
Spitzer 1993 b)	LDT Direct 0 SOA	32 Sz (DSM-III-R) 32 NC	Unclear as to whether groups were matched for years of education	Normal priming at all conditions – some evidence of hyperpriming	0.45 (-0.05 – 0.95) SMALL
	LDT Direct 500 SOA				0.45 (-0.05 – 0.95) SMALL
	LDT Indirect 0 SOA				0.40 (-0.09 – 0.89) SMALL
	LDT Indirect 500 SOA				0.24 (-0.26 – 0.73) SMALL
Spitzer et al 1994	200 SOA	70 Sz (ICD-9) 44 NC	Unclear as to whether groups were matched on education	Sz were much slower at all three levels but still showed a priming effect	-1.31 (-1.73 – 0.89) LARGE
	400 SOA				-1.86 (-2.30 - -1.41) LARGE
	700 SOA				-1.40 (-1.82 - -0.98) LARGE
	Combined Priming Effects	34 Non FTD (ICD – 9) 44 NC		Normal priming in Non FTD group	0.13 (-0.32 – 0.57) SMALL
		36 FTD (ICD-9)		Hyperpriming in FTD group	0.63 (0.18 –

		44 NC			1.08) MEDIUM
Surguladze et al 2002	LDT – 400 SOA	20 Sz (DSM-IV) 26 NC	Unmatched on NART	Normal Priming	-1.91 (-2.61 – 1.21) LARGE
Titone et al 2000	LDT – Dominant Target (Moderate Context) 0 SOA	18 Sz (DSM-IV) 24 NC	Matched on years of education and pre-morbid IQ	Some evidence of hyperpriming	0.82 (0.18 – 1.45) LARGE
Vinogradov et al 1992	LDT (250 SOA)	19 Sz Chronic (DSM-III-R/ RDC) 20 NC	Matched on years of education	Hypopriming	-0.32 (-0.95 – 0.31) SMALL
Vinogradov et al 2002	LDT	40 Sz (DSM-IV) 16 NC	Unmatched for years of education and full scale current IQ	Hypopriming	0.55 (-0.04 – 1.14) MEDIUM
Wagner et al 2006	Lexical Decision Task – 800 SOA	17 Sz (DSM-IV) 20 NC	Matched for education	Hyperpriming in Sz (corrected for overall slowness)	0.87 (0.19 – 1.55) LARGE
Weisbrod et al 1998	LDT - Direct (Left Hemisphere – Right Visual Field)	24 Non FTD (ICD-9) 38 NC	Unmatched for years of education	Hyperpriming in FTD patients in both conditions	0.44 (-0.08 – 0.96) SMALL
		16 FTD (ICD-9) 38 NC			0.15 (-0.43 – 0.74) SMALL
	LDT - Indirect	24 Non FTD (ICD-9) 38 NC			0.01 (-0.50 - 0.52) SMALL
		16 FTD (ICD-9) 38 NC			2.19 (1.48 – 2.92) LARGE

Table 7: Miscellaneous studies

Study	Outcome Measure	Participants	IQ Measure	Results	Effect Size (CIs)
Assaf et al 2006	Verbal Object Recall Task	16 Sz (DSM-IV) 16 NC	Not matched for NART	Sz showed a trend toward having more false positive responses (*p* = .057)	0.56 (0.15 – 1.26) MEDIUM
Barrera et al 2005	The Concrete and Abstract Word Synonym Test	15 Sz Chronic FTD (RDC) 17 NC	Matched for NART	No significant difference between groups	1.15 (0.39 – 1.89) LARGE
		16 Sz Chronic Non FTD (RDC) 17 NC			0.63 (0.07 – 1.33) MEDIUM
Bobes et al 1996	Semantic Matching of Pictures	20 Sz Chinese (DSM-III) 20 NC Chinese	Matched for educational level	Difference between groups in ability to distinguish between congruent and incongruent pictures was highly significant (*p* <.001)	0.81 (0.17 – 1.46) LARGE
		20 Sz Cuban 20 NC Cuban	Matched for educational level		0.33 (-0.29 – 0.95) SMALL
Bullen and Hemsley 1987	The Mill Hill Synonym Test	12 Sz (ICD) 12 NC	Unmatched	Sz scored worse than controls	0.60 (-0.21 – 1.42) MEDIUM
Clare et al 1993	Silly Sentences Test	12 Sz Chronic (RDC) 12 NC	Matched for NART IQ	Sz took significantly longer to verify sentences (*p* <.0001)	- 3.45 (-4.71 - -2.19) LARGE
	Synonyms			Sz made more errors (*p* <.005)	-0.95 (-1.79 – 0.11) LARGE
Low et al 2006	Decide whether a stimulus was natural or artificial	10 Sz (DSM-IV) 10 NC	Unmatched	Sz were slower to decide	-0.93 (-1.85 - -0.01) LARGE

McKay 1996	Definitions	20 Sz Core (DSM-IV) 40 NC	Sz of normal IQ range as measured by NART	Sz made significantly more errors	1.47 (0.87 – 2.06) LARGE
Pelad et al 2005	Rate the associative relationship between concepts in a sentence	11 Sz FTD (DSM-IV) 27 NC	Unmatched for education	FTD patients found less associations compared with Non FTD and controls	- 0.16 (-0.76 – 0.45) SMALL
		17 Sz Non FTD (DSM-IV) 27 NC			0.28 (-0.43 – 0.98) SMALL
Rossell and David 2006	Synonyms Test	32 Sz (DSM-IV) 32 NC	Matched for years of education but mot for NART	Sz made significantly more errors (p <.001)	1.05 (0.52 – 1.57) LARGE
Rossell and David 2006	Definitions Test - Generate	32 Sz (DSM-IV) 32 NC	Matched for years of education but mot for NART	Sz made significantly more errors (p <.001)	1.22 (0.68 – 1.75) LARGE
Tendolkar et al 2004	Synonyms Test	12 Sz (DSM-IV) 12 NC	Matched for years of parental education	No difference in accuracy	- 0.13 (-0.93 – 0.67) SMALL

Table 8: Storage/ Access

STUDY	PARTICIPANTS	PROCEDURE	RESULTS	CONCLUSIONS
Leeson, Laws and McKenna (2006)	32 Sz (RDC) 16 FTD 16 Non FTD 16 controls	Picture Naming Faglioni and Botti's **consistency** analysis.	Impaired Naming Szgroup had impaired storage value and impaired retrieval (high FTD group only).	Impaired **Access** in FTD only Evidence of Impaired **Store** in both groups.
Al-Uzri, Laws, Mortimer (2004)	12 Sz (ICD-10) 12 controls	Hodges and Patterson (1996) Semantic Memory Battery **Consistency** analysis across time. Superordinate versus	Impaired Category Fluency, Naming to description and level 2 of sorting task only. Inconsistent on 2 tests – consistent on category fluency.	Evidence for an **access** – type disorder.

		subordinate information. Cueing Consistency across modality (verbal vs. visual).	Better with superordinate than both base level and subordinate (there was no difference). Patients improved with cueing. Inconsistent	
Elvevag, Weinstok, Kleinman and Goldberg (2001)	13 Sz (DSM-IV) 15 controls	Letter and Semantic Fluency over 3 different sessions.	Worse at fluency overall but the same amount of new exemplars were produced in the second and third times for the S groups as for the controls.	Normal sized word pool.
Rossell and David (2006)	32 Sz (DSM-IV) 32 controls	Multiple Tests Consistency Frequency Priming paradigm	Sz were impaired on all of them Sz were consistent over time. Frequency effect on most tasks (not definitions) but controls also showed a frequency effect Hyperrpriming	Evidence for a storage disorder – however current IQ was not measured. Strong evidence for consistency. Some evidence of store disorders in controls – which scored higher on NART – much greater cognitive ability. Hyperpriming could also be an indication of a disorganised/ abnormal activation not a store disorder (see below).
Leeson, McKenna and Laws (2005)	56 Sz (RDC) 24 controls	Picture Naming Task – 2 occasions F& B Consistency Analysis	Impaired Naming Lowered storage and retrieval probabilities	Characterised by both storage and retrieval difficulties. But storage related to IQ and both storage and retrieval were related to length of illness.
Laws, Al-Uzri and Mortimer (2000)	22 Sz (chronic) (DSM-III-R)	Naming – consistency analysis over 3 sessions – F& B Also frequency analysis	Mixed pattern – found more store disorders (64%) than access. Sz were more impaired on less frequent items	Evidence for a storage disorder – access and store disorders reflect differences in deficit severity.

			(p <.00001) – however this could be due to increased difficulty.	
Allen, Liddle and Frith (1993)	20 Sz (DSM-III-R) – chronic 9 depressive controls 10 controls.	Semantic Verbal Fluency	Impaired Verbal Fluency on first test but improved with cueing.	Evidence of an intact lexicon as when given further opportunity to recall words – produced same amount as controls. Concluded that intact store and impaired retrieval.
Gourovitch, Godlberg and Weinberger (1996)	27 Sz (DSM-III-R) 24 controls.	Verbal fluency – is semantic fluency worse than phonological fluency?	Sz were impaired on both fluency tasks but worse on semantic fluency	This pattern is same as in AD and reflects a breakdown in semantic store. Also BNT was correlated with the difference between semantic and phonological. However they conclude disorganisation of semantic memory.
Chen, Chen, Chan, Lam and Lieh-Mak (2000)	21 Sz (DSM-II) 11 controls	Verbal Fluency – calculated size of lexicon	Reduced lexicon size	Found store reduction. Couldn't replicate Allen's study.
Joyce, Collinson and Crichton (1996)	50 Sz (DSM-III-R) - acute 25 controls.	Category Fluency and Letter Fluency	Sz were impaired overall but showed the same pattern of improved category fluency vs. letter fluency. Performance on the category fluency task improved with cueing	Evidence for impaired access and preserved store.
Lawrence, Doughty, Al-Mousawi, Clegg and Done (2007)	20 Sz (DSM-IV-TR) 20 controls 10 ABI	Category Sorting Task	Sz showed evidence of bottom up deterioration.	Support for storage disorder in part.

Table 9: Disorganisation studies

STUDY	PARTICIPANTS	PROCEDURE	RESULTS
Tallent, Weinberger and Goldberg (2001)	10 Sz (DSM-IV) 10 controls	A Triadic Comparison Task – 3 words are presented and participants are asked to select which two are most similar – MDS analysis.	Qualitatively different semantic maps in people with high FTD vs. low FTD and controls.
Paulsen, Romero, Chan, Davis, Heaton and Jeste (1996)	56 Sz (DSM-III) 28 controls	Animal Fluency Task – MDS analysis/ Pathfinder analysis	Non paranoid early onset group had most different maps to controls.
Sumiyoshi, Sumiyoshi, Nohara, Yamashita, Matsui, Kurachi and Niwa (2005)	38 Sz (DSM-IV) 38 controls	Category Fluency and Letter Fluency – MDS analysis.	Qualitatively different semantic maps. Possibly related to alogia.
Aloia, Gourovitch, Weinberger and Goldberg (1996)	28 Sz (DSM-IV) 32 controls	Category Fluency – animals.	Qualitatively different MDS output – disorganised semantic memory in Sz.

Appendix B

List of papers found using a secondary search through the reference section of papers which were originally identified through the search engine

1. Cutting et al (1987)
2. Laws et al (2000)
3. Lawrence et al (2007)
4. Allen et al (1993)
5. Manschreck et al (1988)
6. Gurd et al (1997)
7. Ober et al (1997)
8. Elvevag et al (2001)
9. Gourovitch et al (1996)
10. Harrow et al (2003)
11. Lecardeur et al (2007)
12. Hoff et al (1992)
13. Aloia et al (1998)

Appendix C

Semantic memory impairment in schizophrenia - deficit in storage or retrieval of knowledge?

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Abstract

A group of 20 patients with chronic schizophrenia, 22 patients with AD and 15 elderly controls were compared on a semantic memory battery (Hodges, Salmon and Butters 1992, Bozeat et al 2000) to see if there was a different profile of impairment. The purpose of the study was to evaluate whether the semantic impairment in schizophrenia arises from an access disorder (e.g. executive dysfunction) or a loss of stored knowledge. The groups were matched on pre-morbid IQ (NART) and the patient groups on current IQ (WASI). Compatibility with a storage / access disorder was assessed against the 4 criteria stipulated by Warrington and Shallice (1979). As expected, the AD group showed impairment across all semantic subtests and their performance indicated a predominantly store disorder. The profile of impairment in the schizophrenia group was significantly different and they performed at ceiling on 4/ 7 tests. There was no strong evidence in favour of a storage disorder in schizophrenia and although semantic memory performance was related to IQ and executive dysfunction (BADS) a deficit in accessing knowledge also did not go far enough as an explanation for their semantic memory impairments. There are obvious neuropsychological differences in the profile of semantic memory impairments in Alzheimer's dementia and schizophrenia but we suggest that the classic storage-access dichotomy may be limited as a means of differentiating and explaining these impairments.

Keywords: Schizophrenia; Semantic Memory; Alzheimer's Dementia, Executive function, IQ

1. Introduction

Semantic memory refers to the memory store that holds general, rather than autobiographical, knowledge, most notably word meanings and object concepts. There are several different neuropsychological tests of semantic memory; however they vary in the extent to which they involve other cognitive processes, especially executive functions. Naming, or Word-Picture matching, for example, place few demands on executive processes compared to Verbal Fluency tasks (e.g. Gabrielli et al 1998, Price 1998). It is therefore important that a study investigating semantic memory impairments attempts to untangle the different neuropsychological systems and processes influencing performance on any particular task. Impaired semantic memory has been widely reported in schizophrenia (McKay et al, 1996, Chen et al, 1994) and is thought to provide a plausible cognitive model for some psychotic symptoms (Goldberg et al, 1998, Rossell et al, 1999). However, a general consensus

as to the defining features and underlying mechanisms of the semantic memory impairment in schizophrenia is yet to be reached and it is evident that gaining a clearer understanding is important in bridging the gap between cognition and phenomenology in schizophrenia.

In classical neuropsychology, disorders of semantic memory are classified as either a loss of stored knowledge or a deficit in knowledge retrieval. Warrington and Shallice (1979) outlined 4 criteria for a storage disorder, all of which have been reported extensively in Alzheimer's Dementia (AD) (e.g Chertkov and Bub 1990). The semantic storage disorder profile in AD which prevails in the literature provides a useful benchmark against which the profile of semantic memory errors in schizophrenia can be compared. Only one study has compared both schizophrenia and AD on a broad range of semantic memory measures (McKay et al 1996), reporting some performance similarities. However, this study used normative data for AD, and did not match groups on the basis of some general intellectual impairment.

Against these reported similarities, there is nevertheless evidence that schizophrenia and AD lie at opposite ends of the storage-access dichotomy. Bleuler (1911) reported that in schizophrenia, "*the actual amount of knowledge remains preserved… but it is not always available or it is employed in the wrong way."* More recent neuropsychological studies have also found that the response pattern in schizophrenia on semantic memory tasks points to the presence of an access disorder (Al-Uzri et al 2004, Joyce et al 1996). For example, using a verbal fluency task, Allen, Liddle and Frith (1993) found their schizophrenia group displayed evidence of an inefficient search process through a normal sized lexicon. There have however also been conflicting accounts of storage-like profiles in schizophrenia (e.g. Rossell and David 2005) and it is suggested that this is related to disease chronicity and cognitive impairment (Laws 1998, Laws 2000). Any individuals with schizophrenia who meet the criteria for a storage disorder therefore are likely to have a more chronic, cognitively impaired profile and their performance will overlap more with the AD sample, as has previously been reported (McKay et al 1996).

Difficulties accessing semantic memory typically arise from a failure in the selection and execution of retrieval strategies (Frith 1992, Robert et al 1997). People with schizophrenia have a profound executive dysfunction (Shallice et al 1991), which could explain the fact that they have difficulties retrieving stored semantic information. The search, retrieval and verification of semantic information rely heavily on executive functions (Baddeley 1990) and it is therefore important to evaluate whether failures on semantic memory tasks are linked with an executive dysfunction in schizophrenia.

The purpose of the study reported here is to explore the pattern of semantic memory impairment in schizophrenia across a range of neuropsychological tests to see: 1) whether the profile of semantic memory impairment in schizophrenia matches that of patients with AD , 2) whether patients with schizophrenia meet the criteria for degraded semantic store or whether they have a predominantly retrieval problem, 3) whether semantic memory impairment is correlated with executive dysfunction and 4) if semantic memory impairment is related to either the positive or negative symptoms in schizophrenia.

2. Method

2.1. Participants

A group of 20 people (11 males, 9 females) with a DSM-IV diagnosis of schizophrenia participated in this study. They were all chronic inpatients (average illness duration, 30.5 years (s.d = 14.3), mean age of onset, 22.5 years (s.d. = 10.5)), living in a residential unit with no known history of brain injury, neurological illness or drug / alcohol misuse. Patients were taking the following medication: 16 on atypical antipsychotics, 1 on typical antipsychotics, 1 on lithium and 2 taking no medication.

A group of 26 people (15 males, 11 females) with a diagnosis of Alzheimer's Dementia (AD), according to ICD-10 criteria, and who scored between 19-25 on the Mini Mental State Examination MMSE (Folstein et al 1975) (indicating a mild-moderate memory impairment) participated in this study. Clinical groups were matched on the basis of current IQ and pre-morbid IQ (see Table 1) and therefore were comparable cognitively. None of the AD group was reported by their psychiatrist to have shown evidence of delusions, hallucinations or formal thought disorder. All AD participants were assessed at home and recruited from an outpatient memory clinic and the majority were taking acetylcholinesterase inhibitors.

An elderly group of 15 healthy controls (5 males, 10 females) volunteered to participate in the study. The controls were matched for age with the AD group (t (16.7) = 1.662, p = .115). All were recruited from a community centre for retired people who had no known psychological problems. Full ethical review for the study was conducted by a NHS REC and approval was granted. After complete description of the study to the participants, written informed consent was obtained.

2.2. Measures

The participants completed the following measures (see Table 1):

2.2.1.Baseline tests of general cognitive abilities.

The National Adult Reading Test (NART, Nelson, 1982) for pre-morbid IQ and two subtests (Vocabulary and Matrix Reasoning) taken from the Wechsler Abbreviated Scale of Intelligence (WASI, Wechsler, 1999) for current IQ. The group of patients with schizophrenia were also assessed for symptom severity with the Positive and Negative Syndrome Scale (PANSS, Kay et al, 2000). Executive functioning was assessed in the schizophrenia group using two subtests from the Behavioural Assessment of the Dysexecutive Syndrome (BADS, Wilson et al 1996), the Rule Shift Card Test and the Modified Six Elements Test.

2.2.2. Semantic Memory Tests:

i) Hodges Semantic Test Battery (Hodges, Salmon & Butters 1992)
This test battery, used widely in neuropsychological studies of semantic memory impairment (Bozeat et al 2000, McKay 1996), comprises 5 subtests: Picture Naming, Word-Picture Matching, Category Sorting (by 3 levels; 1, Superordinate (e.g. *living vs. non living*), 2, Base level (e.g. *vehicles vs. tools vs. household items*) or 3, Subordinate (e.g. *metal vs. not metal*)). Images of 64 items (32 living and 32 non living) derived from a corpus of line drawings (Snodgrass and Vanderwart, 1980) with names balanced for word frequency were used throughout.

ii) Semantic association tests (The Camel and Cactus Tests) (Bozeat et al, 2000) These tests assess ability to find the most salient semantic association between a target item and four possible choices, one of which shares a specific semantic feature with the target (e.g. *target = bottle of wine, possible choices = orange, grapes, strawberry and banana*). There are two versions of this test: non-verbal (using pictures) and verbal (using words).

3. Data Analysis

3.1. Performance Profiles

Figure 1 shows the performance of the 3 groups across the 7 tests of semantic memory. The elderly control group performed at ceiling on all 7 tests and therefore data violated assumptions of normality. An ANOVA was used to calculate whether there were overall differences in performance between the two clinical groups on the semantic test battery. To evaluate whether the AD patients and schizophrenia patients have different profiles of semantic impairment a multivariate (MANOVA) profile analysis was computed, since the data do not fit with strict criteria for a repeated measures ANOVA (Tabachnick and Fidell 2007). Tukey post hoc *t* tests were carried out to further explore group differences on the seven subtests.

3.2. Relationship with IQ

As there were no significant differences between the AD and the schizophrenia group on measures of verbal IQ, performance IQ and full scale IQ, there was no need to do an ANCOVA.

3.4. Correlates of semantic memory impairment

Pearson's correlations were conducted to compare errors on each subtest with current IQ (WASI), executive dysfunction (BADS) and symptom profiles (PANSS).

3.5. Storage vs. Access disorder analysis:

This comprises four criteria to distinguish access from store disorder:

5. **Item Consistency**: If an item is lost then errors will occur for this item across all tests. Based on a method by Hodges (Hodges et al, 1992), error rates on subtests (matched for difficulty) are compared using *t*-tests.
6. **Word Frequency**: Familiar (high frequency) items have more robust representations in the semantic store, than less familiar (low frequency) items. For each participant a correlation between word frequency norms (Alario and Ferrnad, 1999) and error frequency for each item was derived. Groups were compared using Independent *t*-tests.
7. **Cuing**: Items lost from store are irretrievable despite cuing which normally aids retrieval. Cuing improvement was measured by comparing errors for Naming (un-cued) and Word-Picture Matching (cued) subtests. Following a log-linear transformation the data on these two tests fitted a normally distributed model. Hence, a mixed between-within ANOVA was used to compare error rates for the two patient groups.
8. **Bottom – Up Deterioration**: Superordinate category knowledge (e.g. knowing whether an item is living or non-living), is relatively well preserved compared to subordinate category knowledge (e.g. knowing whether an item is wooden) in store disorders, since superordinate knowledge is distributed whereas subordinate knowledge is localised in semantic memory space. A bottom-up deterioration occurs if there is a

significant trend, as revealed by a Friedman trend test, of error rates increasing from superordinate > base level > subordinate.

4. Results

INSERT TABLE 1 ABOUT HERE

4.1. Baseline Measures

Both the patient groups were cognitively impaired, scoring within the bottom 20% of the population on current IQ. Additionally, the schizophrenia participants were in the bottom 10th percentile range on the two subtests of the BADS. This indicates that as a group they had markedly impaired executive function. However, individual executive impairment varied from the top 90th percentile to the lowest percentile.

4.2. Semantic Memory Battery, group comparisons over the 7 semantic tests

ANOVA produced a significant main effect for both test ($F = 62.74$, $p < .001$,) and group ($F(1, 44) = 5.63$, $p = .022$) reflecting the higher number of errors overall in the AD group. The MANOVA profile analysis produced a significantly different profile for the two groups $F(6,39)=3.8$,$p=.004$), Thus the apparent difference in profile (see Figure 1) is statistically significant.

4.3. Test-wise group comparisons between the schizophrenia and AD patients.

Post hoc tests revealed that the groups performed similarly poorly on 3 of the tests; Associations Pictures ($t(44) = -1.01$, $p = .317$, $d = .3$), Associations Words ($t(44) = .289$, $p = .774$, $d = .1$) and Sorting Level 3 ($t(44) = -1.63$, $p = .111$, $d = .5$) but the AD group produced significantly more errors on the Naming test ($t(38) = -3.64$, $p = .001$, $d = 1.1$), Word-Picture Matching test ($t(38) = -3.61$, $p < .001$, $d = 1.1$) and Sorting Level 1 ($t(44) = -2.21$, $p = .032$, $d = .6$) and Sorting Level 2 ($t(44) = -2.98$, $p = .005$, $d = .9$).

4.5. Semantic memory impairment in schizophrenia and IQ

There were strong correlations between IQ (full scale score on WASI) and semantic memory subtests for the schizophrenia group; Semantic Association Pictures ($r = -.590$, $p = .006$), Word-Picture Matching ($r = -.530$, $p = .016$), Semantic Association Words ($r=-.634$, $p = .003$) and Sorting Level 3 ($r = -.488$, $p = .029$) but only weak correlations between IQ and Naming ($r=-.268$, $p = .253$), Sorting Level 1 ($r = -.310$, $p = .184$) and Sorting Level 2 ($r = -.169$, $p = .476$).

4.6. Semantic memory impairment in schizophrenia and Executive Dysfunction

Scores on 4 of the 7 subtests correlated significantly with BADS scores in patients with schizophrenia (Naming, $r=-.466$, $p = .038$; Word-Picture Matching, $r=-.588$, $p = .006$; Semantic association Pictures, $r = -.658$, $p = .002$: Sorting Level 3, $r = -.4$, $p = .08$), indicating a role for executive functioning in semantic memory test performance. However it should be noted that on two subtests (Naming and Word-Picture Matching) which correlated highly with BADS scores, the error rate for the schizophrenia group was within the normal range.

4.7. Semantic memory impairment in schizophrenia and symptomology

Neither PANSS Positive symptom ratings (max $r < .26$, $p > .25$ for all correlations, average $r = 0.07$), nor Negative symptom ratings (max $r < .107$, $p > .29$ for all correlations, average $r = -0.10$) correlated with performance on any of the 7 subtests.

However there was a significant correlation between PANSS general scores and scores on the Level 2 Sorting task (r = .539, p = .014).

4.8. Applying the storage and access criteria, Warrington and Shallice (1979):

1. Item Consistency

The AD group were consistent for the pair-wise comparisons of Naming vs. Word-Picture Matching (t (22) = 3.690, p = .001) and Semantic association, Pictures vs. Words (t (25) = 6.073, p <.001) and showed a tendency towards consistency for the pair-wise comparison of Sorting Level 2 vs. Naming (t (25) = 1.336, p = .194).

The schizophrenia group were inconsistent in their responses for the pair-wise comparisons of Naming vs. Word-Picture Matching (t (10) = 1.64, p = 1.31), or Sorting Level 2 vs. Naming (t (16) - = 1.179, p = .256) but were consistent in the Semantic association, Pictures vs. Words comparison (t (19) = 4.805, p <.001). In summary, consistency of error scores appears to be more robust in AD than in schizophrenia indicating some dissociation.

2. Frequency

Of the participants in the AD group, 42% displayed a significant frequency effect (p<.05) in comparison to 15% in the schizophrenia group and 10% in the control group. The AD group made more errors on items with low word frequency relative to high frequency than the schizophrenia group (t (39) = -2.882, p <.05). There was therefore a significant difference in the AD and schizophrenia groups in the extent to which word frequency influenced test performance.

3. Cuing Effect

Both groups improved significantly when cued although surprisingly the AD group showed the greatest improvement when cued (t (25) = 4.75, p >.001) but the schizophrenia group also improved significantly (t (19) = 4.62, p >.001). It should be noted that this pattern was borderline significant in the control group (t (14) = 2.19, p = .044).

4. Bottom – up Deterioration

All three groups showed a significant "bottom-up" effect, in that there was a significant deterioration in performance between Superordinate Sorting (Level 1) and Base Sorting (Level 2) (p <.01 for both groups) and then a further deterioration for Subordinate Sorting (Level 3) (p <.001 for both groups). It is worth noting that the controls also showed this pattern (p <.001*)*).

INSERT TABLE 2 ABOUT HERE

Although neither group met all the criteria for a storage disorder, the AD group met 3, whereas the schizophrenia group met only 1 of the 4 criteria.

Surprisingly there was a strong negative correlation in the schizophrenia group between the BADS scores and the number of criteria met for a storage disorder (r (20) = -.49, p = .030), indicating that participants with a dysexecutive problem were more likely to have a storage disorder. There were no significant correlations with either pre-morbid or current IQ, disease chronicity or any of the symptom measures.

5. Discussion

In this study, the profile of semantic memory performance for the AD participants was similar to that reported elsewhere (e.g. Chertkow and Bub, 1990) with impairments across all semantic memory tasks. This pattern of widespread impairments and the fact that the AD group met 3 of the 4 criteria for a storage disorder suggests that their semantic representations are degraded. In the schizophrenia group however, there were only minimal impairments on 3 of the subtests; Naming, Word-Picture Matching, and Base Level Sorting. This pattern of selective poor performance across tests suggests not only that semantic memory may not primarily be impaired in schizophrenia but also that errors do not arise from a degraded store. A profile analysis showed that the groups performed differently across the battery of tests suggesting that the semantic memory impairments in AD and schizophrenia arise from different mechanisms.

Of the 4 storage disorder criteria stipulated by Warrington and Shallice (1979), the schizophrenia group only met one, bottom up deterioration, which was also met by the control group. Therefore by a process of elimination the results of this study concur with Joyce et al (1996) and Allen et al (1993) who report an access type disorder in schizophrenia. Nevertheless, the fact that the controls met the bottom up deterioration storage criterion in this study and the fact that the AD group improved with cuing questions the validity of the storage/ access dichotomy. It has been suggested (e.g. Rapp and Caramazza 1993, Forde and Humphreys 1997) that the distinction between storage and access disorders is overly simplistic and does not map on to contemporary cognitive and neurophysiological models of semantic memory. Executive functions are thought to be involved in access to long term memory (Schacter et al 1998) and it would therefore be expected that access disorders would be associated with an executive dysfunction. However, individual participants in the schizophrenia group who met criteria for an access disorder had significantly higher scores on the BADS, indicating a relatively intact executive system. Furthermore those meeting criteria for a storage disorder were more likely to have an executive dysfunction.

The semantic memory impairments in schizophrenia appear to be most marked for the semantic association tests which involve identifying the most salient association from competing alternatives. Recent dopamine based theories of schizophrenia (Kapur, 2003, Winterer and Weinberger, 2004) have explained excessive attention to contextually weak semantic associations as reduced signal: noise ratio. These dopamine based theories also provide a plausible neurobiological model for the other neuropsychological findings in schizophrenia of excess activation of weak semantic associations (Goldberg et al, 1998; Aloia et al, 1998), or failure to inhibit weak semantic associates (Moritz et al 2001a; Spitzer, 1993). One caveat to this explanation however is that in Kapur's model, hyperdopaminergia was purported to explain positive symptoms in schizophrenia and in this study we found no correlations between semantic memory impairments and positive symptom severity.

This study is the first to directly compare an IQ matched group of patients with schizophrenia to a group of patients with AD across a battery of semantic memory tests. However the study is limited by the fact that 2 of the AD patients were unable to

complete the vocabulary subtest and 5 were unable to complete the matrix reasoning subtest on the WASI.

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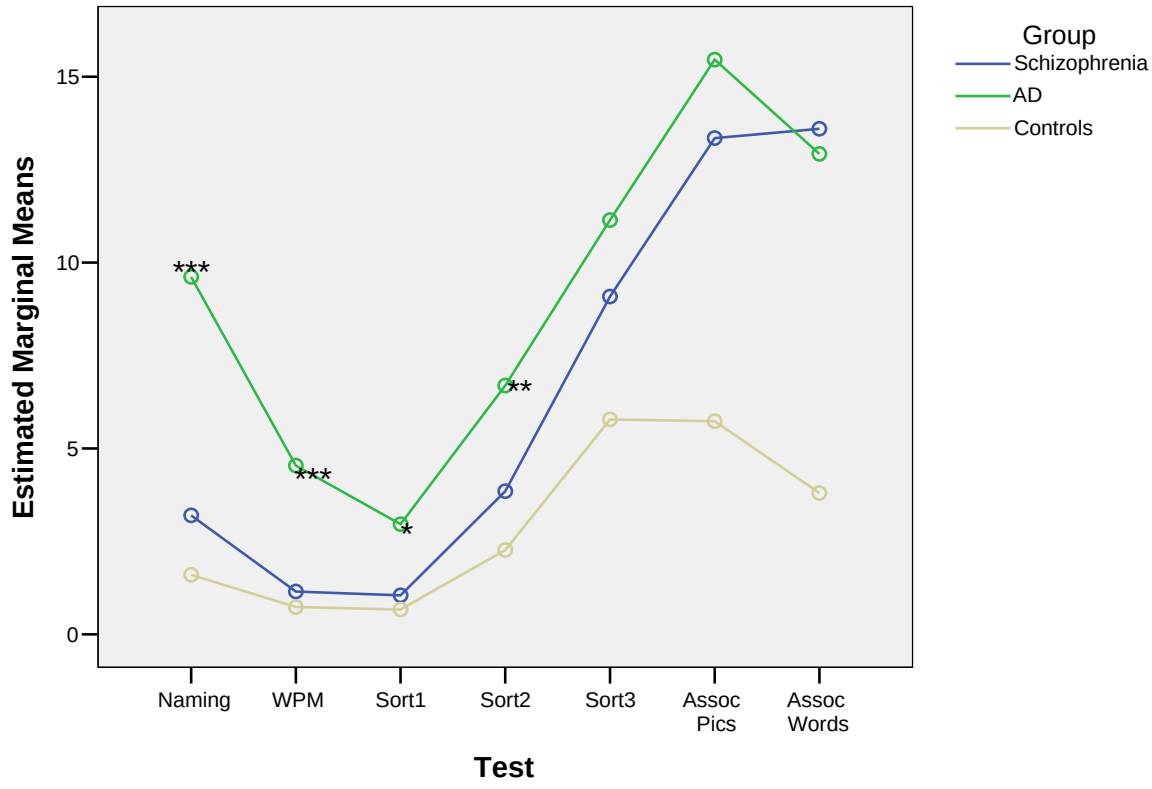
TABLES AND FIGURES

Table 1: Participant demographics and results of the baseline and semantic memory tests

	Schizophrenia (SZ)	Alzheimer's (AD)	Controls (C)	ANOVA	Post Hoc t tests
N	20	26	15		
Age (Mean)	51(11.18)	76.27 (7.33)	68.20 (17.96)	F (2, 60) = 25.3, p <.001	AD>SZ **
Male/ Female	11 / 9	15/11	5/11	-	
MMSE	-	22.27 (2.07)	-	-	
Current IQ (WASI)					
- Full Scale	85.15 (17.491)	88.16 (16.59) (n =19)	107.87 (17.25)	F (2,53) = 8.50, p =.001	C>SZ**, C>AD*
- Verbal	83.2 (17.121)	88.21 (15.82) (n =24)	103.27 (20.24)	F (2,60) = 4.66, p =.013	C>AD*, C>SZ*
- Performance	90.55 (19.44)	83.90 (34.04) (n =21)	110. 60 (17.37)	F (2,60) = 8.34, p =.001	C>AD**
Pre-Morbid IQ (NART)	100.5 (24.76)	103.15 (22.69)	102.38 (31.63)	F (2,58) = .062, p = .940	
PANSS (general)	30.40 (6.236)	-	-	-	
PANSS (conceptual disorganisation)	10.15 (3.167)	-	-	-	
PANSS (positive)	17.75 (5.077)	-	-	-	
PANSS (negative)	15.45 (6.778	-	-	-	
BADS	12.90 (5.684)	-	-	-	

N.B. Full scale IQ could not be obtained in 7 of the AD cases.
Independent t tests were conducted to compare participant groups on demographics:
* p <.05 significance ** p <.001 significance

Figure 1: Profile of errors across the semantic memory battery for the schizophrenia (n = 20), AD (n = 26) and control (n = 15) groups.



AD vs. Schizophrenia comparisons: * = p<.05 ** = p<.01 *** = p<.001

Table 2: To what extent do the performances of the groups meet the criteria for a storage disorder?

	Item Consistency?	Frequency Effect?	An absence of improvement after cueing?	Bottom – up Deterioration?
AD	High	Yes	No	Yes
Schizophrenia	Low	No	No	Yes

Appendix D

List of items included in the Hodges et al (1992) Semantic Memory Battery:

Helicopter
Mouse
Toaster
Strawberry
Suitcase
Cat
Bicycle
Apple
Rabbit
Sledge
Dustbin
Frog
Tomato
Lorry
Cow
Watering can
Pineapple
Bus
Stool
Dog
Cherry
Basket
Train
Squirrel
Pear
Horse
Motorbike
Banana
Barrel
Plane
Orange
Piano
Tortoise
Pliers
Key
Penguin
Axe
Monkey
Toothbrush
Eagle
Saw
Rhino
Plug
Chicken
Spanner
Kangaroo
Glass
Duck
Scissors

Camel
Envelope
Owl
Paintbrush
Tiger
Comb
Swan
Screwdriver
Elephant
Candle
Ostrich
Alligator
Brush
Peacock
Hammer

Appendix E

Do overinclusion and distorted semantic category boundaries in schizophrenia arise from executive dysfunction?

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Abstract

Semantic memory impairments have been reported extensively in people with schizophrenia. Inefficient search and retrieval strategies, due to an executive dysfunction, rather than a primary loss of semantic knowledge are a primary candidate for such impairments. In order to test this hypothesis we compared the performance of 20 patients meeting DSM-IV-TR criteria for schizophrenia with that of 20 healthy controls and 10 patients with acquired brain injury (ABI) with a dysexecutive syndrome. Seventy percent of the people with schizophrenia and 100% of the ABI patients in this study met criteria for executive impairment. However, the two groups performed significantly differently on a range of semantic memory tests. Whereas 45% of the patients with schizophrenia met criteria for distorted semantic category boundaries (n.b. overinclusion), this was true for only 10% of the ABI patients. In addition, no correlation was found between severity of executive dysfunction and tendency to overinclude in the schizophrenia group. This pattern of neuropsychological findings suggests that overinclusion, or disorganized semantic categorization procedures, in schizophrenia does not result from a classical executive dysfunction. Alternative explanations are discussed.

Keywords: Schizophrenia; Semantic memory; Overinclusion; Executive function

1. Introduction

It has been widely reported that people with schizophrenia perform differently on tasks of semantic memory (e.g., [Mckay et al., 1996] and [Goldberg et al., 1998]) leading many to infer that their semantic memory is organized differently or even degraded. One example of how people with schizophrenia deviate from the norm is the way in which they group objects into categories, first described by Cameron (1938) as overinclusion; the inability to maintain category boundaries, leading to the formation of vague and overextensive categories. People with schizophrenia therefore frequently fail to appropriately exclude contextually irrelevant items from the categories that they produce. Cameron (1938) considered this to be the ‘essence of schizophrenic thought disorder’. Payne and Hewlett (1960) compared overinclusion in

people with acute schizophrenia, neuroses, depression and healthy controls and found that the prevalence of overinclusion in the group with schizophrenia clearly differentiated them from the other groups.

More recently, new attempts have been made to further explain the phenomenon of overinclusion. Chen et al. (1994) asked participants to state whether or not a series of words, differing in degrees of semantic relatedness to a target category, were members of the category. It was concluded that people with schizophrenia showed "an outward shift of semantic category boundaries" (p. 193), by including items that would normally be considered to be outside of a target category. Elvevag et al. (2002), however, employed the same test as Chen et al. (1994) but failed to replicate these findings, claiming that "although patients with schizophrenia may have intact representations, "movements" between these representations...is not optimal" (p. 197). A number of authors (e.g., [Goldberg et al., 1998] and [Zalla et al., 2001]) have suggested that the performance of people with schizophrenia on semantic memory tests such as that employed by Chen et al. (1994) and Elvevag et al. (2002) may have been a result of an executive dysfunction, whereby the ability to shift between semantic categories is impaired, but knowledge of these semantic categories remains intact.

Allen et al. (1993) provided further evidence that semantic knowledge is preserved in schizophrenia. They concluded that poor performance on a verbal fluency task by people with schizophrenia was a result of difficulties in organizing their search and inefficient retrieval strategies, rather than an actual loss of semantic knowledge. This also appears to reflect impaired executive functioning rather than a primary loss of semantic knowledge.

Barrera et al. (2005) found that people with schizophrenia performed poorly on several tests of executive function, over and above that of semantic memory. Whereas the schizophrenia group with formal thought disorder were found to be impaired on all executive function tests employed, they were only found to perform abnormally on 'higher order' semantic associative tasks rather than lexical tasks such as naming. Barrera et al. (2005) surmised that tasks assessing semantic memory vary substantially in terms of (i) task difficulty and (ii) demands placed on executive processes, and semantic memory impairments in schizophrenia occur where demands are placed on executive processes.

It has therefore been suggested that the anomalies shown by people with schizophrenia on semantic categorization tasks are a result of an executive dysfunction, whereby they are unable to disinhibit inappropriate responses (e.g., [Leeson et al., 2005], [Nathaniel-James et al., 1996] and [Zalla et al., 2001]). Zalla et al. (2001) reported that overinclusion of irrelevant items into a target script in schizophrenia was due to the "inability to select an internal action schema and use it to generate a plan of action," (p. 290) i.e., an executive dysfunction. Similarly, a failure of executive processes has been implicated in tasks where patients fail to utilize a beneficial categorization strategy during encoding or retrieval from long-term memory (Brebion et al., 1997).

To summarise, dysfunctional categorization strategies in people with schizophrenia have long been thought to be a result of impaired semantic memory per se (e.g., Chen

et al., 1994). However, strategies for encoding and retrieval from long-term memory do make demands on the executive system ([Fletcher et al., 1998] and [Wiggs et al., 1998]). Since executive dysfunction is frequently reported in schizophrenia (e.g., Zalla et al., 2001), it may well be the case that a failure to categorize objects into their respective semantic categories reflects a disorder of the executive rather than the semantic system.

In order to directly test whether the unusual sorting found in schizophrenia is due to an executive dysfunction, we compared the performance of a group with chronic schizophrenia, with a group of patients, with moderate/severe executive dysfunction resulting from acquired brain injury (ABI), on several semantic memory tasks including the Category Generation Test (Green et al., 2004). It was expected that (i) if differences in sorting in schizophrenia are a result of an executive problem then a similar response profile would be observed in the ABI group, (ii) deviations in sorting in the schizophrenia group would correlate with the degree of executive dysfunction.

2. Method

2.1. Participants

Twenty (11 males, 9 females) people meeting DSM-IV-TR criteria for schizophrenia, 10 (8 males, 2 females) people with executive dysfunction resulting from acquired brain injury (ABI) and 20 (11 males, 9 females) healthy controls took part in the study. The group with schizophrenia were chronic inpatients (average illness duration, 30.5 years (SD = 14.3), mean age of onset, 22.5 years (SD = 10.5)) in a residential setting and had no known history of brain injury, neurological illness or drug or alcohol misuse. Patients were taking the following medication: 16 on atypical antipsychotics, 1 on typical antipsychotics, 1 on lithium and 2 taking no medication. The group with ABI were inpatients at a regional rehabilitation unit and had no known history of psychiatric illness or drug or alcohol misuse. The locus of their brain lesions varied but people in this group were identified as presenting with a dysexecutive syndrome as the principle neuropsychological disorder (i.e. not secondary to a memory/attentional/other neuropsychological abnormality). The healthy controls were staff and attendees recruited from a community centre for retired local residents without mental health problems. All groups were matched for pre-morbid intelligence. Ethical approval was received from the Local Research Ethics Committee and written informed consent was obtained from all participants prior to the study.

2.2. Baseline tests

All three groups were matched on pre-morbid IQ as measured by the National Adult Reading Test (NART, Nelson, 1982). The schizophrenia and ABI groups were matched on current intellectual functioning, as measured by the Wechsler Abbreviated Scale of Intelligence (WASI, Wechsler, 1999), and general cognitive functioning as measured with the Mini Mental State Examination (MMSE, Folstein et al., 1975). Both groups demonstrated severe levels of executive dysfunction as measured by the Behavioural Assessment of Dysexecutive Syndrome (BADS, Wilson et al., 1996) and mean scores for both groups fell within the bottom 10th percentile range of the normal population. The group with schizophrenia were also assessed for

positive symptoms, negative symptoms, conceptual disorganization and general psychopathology with the Positive and Negative Syndrome Scale (PANSS, Kay et al., 2000). Results of these baseline tests can be seen in Table 1.

Table 1.

Demographics and mean results of the baseline tests and Semantic Memory Test Battery for the three groups (SD)

	Schizophrenia (SZ)	**ABI**	**Controls (C)**	**ANOVA/*t* tests**	**Post hoc *t* tests**	**ANCOVA[a]**
Age	51.20 (11.18)	42.60 (13.32)	53.50 (23.84)	$F(2,47) = 1.29$, $p = 0.28$		
Male/Female	11/9	8/2	11/9			
NART pre-morbid IQ	100.50 (24.76)	106.43 (12.59)	112.88 (8.04)	$F(2,47) = 2.12$, $p = 0.13$		
WASI full scale IQ	85.15 (17.49)	77.63 (15.00)	119.90 (16.78)	$F(2,47) = 28.63$, $p < 0.01$	C > SZ **	
					C > ABI **	
WASI verbal IQ	83.20 (17.12)	84.88 (13.95)	114.20 (19.63)	$F(2,47) = 17.18$, $p < 0.01$	C > SZ **	
					C > ABI **	
WASI performance IQ	90.55 (19.44)	68.50 (18.49)	121.60 (15.76)	$F(2,47) = 30.23$, $p < 0.01$	C > SZ **	
					SZ > ABI *	
					C > ABI **	
MMSE	27.80 (1.74)	27.00 (2.49)	–	$t(28) = 1.03$, $p = 0.31$		
BADS	12.90 (5.68)	12.20 (3.05)	–	$t(28) = 0.36$, $p = 0.72$		
PANSS general	30.40 (6.23)	–	–	–		
PANSS positive	17.75 (5.08)	–	–	–		

	Schizophrenia (SZ)	ABI	Controls (C)	ANOVA/*t* tests	Post hoc *t* tests	ANCOVA[a]
PANSS negative	15.45 (6.78)	–	–	–		
PANSS conceptual disorganization	2.25 (1.52)					
Semantic memory test — mean errors (SD)						
Naming	3.20 (3.46)	2.40 (2.95)	0.70 (1.13)	$F(2,47) = 4.57$, $p = 0.02$	SZ > C ∗	$F(1,28) = 2.68$, $p = 0.114$
Word–picture matching	1.15 (1.90)	1.50 (3.06)	0.40 (0.68)	$F(2,47) = 1.43$, $p = 0.25$		
Sorting	3.85 (2.87)	1.00 (0.94)	2.40 (1.43)	$F(2,47) = 6.60$, $p = 0.03$	SZ > ABI ∗ ∗	$F(1,28) = 6.89$, $p = 0.015$
Semantic association (pictures)	13.35 (6.95)	7.90 (4.07)	4.70 (2.87)	$F(2,47) = 14.56$, $p < 0.01$	SZ > ABI ∗	$F(1,28) = 8.48$, $p = 0.007$
					SZ > C ∗ ∗	
Semantic association (words)	13.60 (7.17)	5.90 (3.21)	2.55 (3.40)	$F(2,47) = 4.56$, $p < 0.01$	SZ > ABI ∗ ∗	$F(1,28) = 17.92$, $p < 0.001$
					SZ > C ∗ ∗	

Independent *t* tests were conducted to compare participant groups: $*p < 0.05$ significance, $**p < 0.01$ significance.
[a] Comparing SZ vs. C with IQ as a covariate.

2.3. Semantic memory tests

(i) Hodges Semantic Memory Test Battery (Hodges et al., 1992).

All participants completed 5 semantic memory tests, each including the same 64 items. These were: confrontation naming, word-to-picture matching, sorting and two semantic association tests, based on the Howard and Patterson (1992) Pyramid and Palm Trees test (Howard and Patterson, 1992) which involved picture–picture matching and word–word matching (Bozeat et al., 2000). These tests were taken from a revised version of a semantic memory test battery ([Hodges et al., 1992] and [Thompson et al., 2004]) (for more details, see Doughty et al., 2007).

(ii) Category Generation Test (Green et al., 2004).

Participants were presented with 45 14.5 × 10 cm laminated cards. Each card had a black and white picture in the centre and was selected from the Snodgrass and Vanderwart (1980) set. The cards represented five taxonomic categories (fruit, vehicles, animals, body parts and clothing), with nine members in each. Controls adhere to the constraints of the task and tend to produce these five categories. Participants were given the 45 cards and asked to sort them into piles of 'things that they feel go together'. Participants were informed that they could make as many or as few piles as they wished and that there were no right or wrong answers.

A participant was said to have overincluded if they placed items from two or more taxonomic categories into the same pile, e.g., tiger sorted with vehicles. A participant was said to have underincluded if they placed cards from a single taxonomic category into two or more piles. In addition to this we also generated overinclusion and underinclusion scores to determine the magnitude of overinclusion and underinclusion (see website).

2.4. Executive function tests

The group with schizophrenia completed 2 subtests of the BADS in order to reduce the overall testing load. These were the rule-shift test, as a measure of task-switching and the modified six-elements test, as a measure of the ability to plan, organize and monitor behaviour. This test was selected as it has been found to be ecologically valid and elicit executive deficits in schizophrenia independently of any deficits in general intelligence (Evans et al., 1997). The scores from these 2 subtests were prorated to give an overall BADS score (see Table 1).

The ABI group completed the BADS test battery as part of their standard assessment procedure. The battery consists of 6 tests aimed at measuring a range of executive abilities, including task switching, novel problem solving, action planning, route planning, temporal judgement and self-monitoring.

3. Results

3.1. Performance on the Hodges semantic memory test battery

People with schizophrenia were found to make significantly more errors than both the normal control and the ABI groups on all semantic memory tests except for word–picture matching (see Table 1). Considering the role of IQ in semantic memory tasks, a covariance analysis was conducted which found that once IQ was controlled for, the significant difference on the naming test between the schizophrenia and the control group disappeared.

3.2. Performance on the category generation test

3.2.1. Overinclusion

A significant difference was found between the number of people found to overinclude in the three groups, χ^2 (2) = 10.37, p = 0.006 (see Table 2). The effect size correlation for this difference was large, Cramer's Φ = 0.46, resulting in an

excellent power value of 0.90. The group with schizophrenia were found to be significantly more likely to overinclude than both the healthy controls, χ^2 (1) = 8.53, p = 0.003, and the ABI groups, χ^2 (1) = 3.68, p = 0.028. The ABI and healthy control groups did not differ, χ^2 (1) = 0.27, p = 0.61.

Table 2.

The number of people who overincluded and underincluded on the CGT in each group

		Over		**Under**	
		Yes	**No**	**Yes**	**No**
Schizophrenia	Count	9	11	10	10
	%	45	55	50	50
	Adjusted residual	3.0	− 3.0	2.6	− 2.6
ABI	Count	1	9	1	9
	%	10	90	10	90
	Adjusted residual	− 1.1	1.1	− 1.5	1.5
Control	Count	1	19	2	18
	%	5	95	10	90
	Adjusted residual	− 2.4	2.4	− 2.1	2.1

The mean overinclusion score (SD) for the schizophrenia group = 1.12 (0.18), for the ABI group = 1.04 (0.13) and for the controls = 1.01 (0.06) and the mean underinclusion score (SD) for the schizophrenia group = 1.86 (1.6), for the ABI group = 1.06 (0.13) and for the controls = 1.06 (0.18).

3.2.2. Underinclusion

A significant difference was also found between the number of people who underincluded in the three groups, χ^2 (2) = 9.98, p = 0.007, resulting in a large effect size correlation, Cramer's Φ = 0.45, and an excellent power value of 0.89. The ABI and healthy control groups did not differ, χ^2 (1) = 0.00, p = 1 and the difference was therefore due to the schizophrenia group showing a higher incidence of underinclusion than both the healthy controls, χ^2 (1) = 7.62, p = 0.003 and the ABI groups, χ^2 (1) = 4.59, p = 0.016.

3.3. Anomalous categorization and general intelligence

3.3.1. Overinclusion

No correlation was found between any groups' performance on the CGT and their performance on the WASI, for the group with schizophrenia, $r = -0.13$, $p = 0.58$, the controls, $r = -0.06$, $p = 0.82$, or for the ABI group, $r = -0.13$, $p = 0.77$. As the clinical groups were matched for current level of intelligence, this does not seem to offer an explanation of overinclusion in schizophrenia.

3.3.2. Underinclusion

Underinclusion scores were also not found to be correlated with general intelligence, for the group with schizophrenia, $r = -0.04$, $p = 0.85$, ABI, $r = -0.34$, $p = 0.41$ or the healthy controls, $r = -0.29$, $p = 0.21$. As with overinclusion, intelligence does not seem to provide an explanation for underinclusion in schizophrenia.

3.4. Anomalous categorization and executive dysfunction

3.4.1. Overinclusion

No correlation was found between performance on the CGT and scores on the BADS for the group with schizophrenia, $r = -0.13$, $p = 0.58$. As the ABI group were found to perform similarly to the healthy controls on the CGT, an executive function problem cannot be an explanation for overinclusion on this sorting task for the schizophrenia group.

3.4.2. Underinclusion

As with overinclusion, no correlation was found between underinclusion scores on the CGT and scores on the BADS for the group with schizophrenia $r = 0.00$, $p = 1$. Executive dysfunction does not therefore seem to offer an explanation for anomalous categorization in schizophrenia.

3.5. Anomalous categorization and semantic memory

3.5.1. Overinclusion

Overinclusion on the CGT was not found to be correlated with any of the semantic memory tests for the group with schizophrenia, for naming, $r = 0.19$, $p = 0.44$, word–picture matching, $r = 0.20$, $p = 0.40$, sorting, $r = 0.16$, $p = 0.51$, picture–picture matching, $r = 0.13$, $p = 0.58$, and for word–word matching $r = -0.02$, $p = 0.93$.

3.5.2. Underinclusion

Underinclusion on the CGT was also not found to be correlated with any semantic memory test for the group with schizophrenia, for naming, $r = 0.03$, $p = 0.90$, word–picture matching, $r = 0.08$, $p = 0.73$, sorting, $r = 0.10$, $p = 0.67$, picture–picture matching, $r = -0.02$, $p = 0.93$ and for word–word matching, $r = -0.32$, $p = 0.16$. Semantic memory impairment does not therefore provide an explanation for sorting performance on the CGT.

3.6. Anomalous categorization and symptom measures

3.6.1. Overinclusion

Overinclusion in schizophrenia was not found to be correlated with any symptom measure on the PANSS, for general psychopathology, $r = -0.09$, $p = 0.71$, for positive symptoms, $r = -0.10$, $p = 0.67$, for negative symptoms, $r = 0.02$, $p = 0.95$, or for conceptual disorganization, $r = -0.03$, $p = 0.91$.

3.6.2. Underinclusion

No correlation was found between underinclusion in the group with schizophrenia and general psychopathology, $r = 0.07$, $p = 0.76$, or negative symptoms, $r = -0.22$, $p = 0.34$, as measured with the PANSS. A significant correlation was, however, found between underinclusion in this group and conceptual disorganization scores on the PANSS, $r = 0.50$, $p = 0.026$, and a moderate correlation was also found with positive symptom scores, $r = 0.41$, $p = 0.07$.

3.7. Case studies

In order to further investigate the types of sorts made by people with schizophrenia, participants were asked to name their categories and provide explanations behind their card choices immediately after they completed the CGT. Table 3 and Table 4 present 2 cases: BS11 who overincluded and HS31 who both overincluded and underincluded. Both cases met DSM-IV criteria for schizophrenia. BS11 had a NART score of 107, a WASI score of 99, a BADS score of 15 and a PANSS conceptual disorganization score of 1 referring to a lack of thought disorder. Participant HS31 had a NART score of 105, a WASI score of 78, a BADS score of 3 and scored 4 on the conceptual disorganization item of the PANSS meaning a moderate level of thought disorder.

Table 3.

Participant BS11's abnormal card sorts and her reasons for these card sorts

Name of category	Cards in category	Reason given
Fruit and hands and body	All fruit plus elbow, arm, thumb, leg and monkey	Use parts of the body to lean on and monkeys eat all the fruit
Transport	All 9 plus hand	People use the hand for public transport and ordinary transport
Animals	All except monkey	(Monkey was put in a previous category)
Parts of the body and face	Foot, eye, lips and ear	
Clothes	All 9 items	

Table 4.

Participant HS31's abnormal card sorts and his reasons for these card sorts

Name of category	Cards in category	Reason given
“Make up — speaking”	Lips	“It's make up and for whispering”
“Hat”	Hat	“To protect the head”
“Belt”	Belt	“To tighten the trousers”
“Senses of hearing and seeing”	Eye, ear	“When we see, we hear — they go together”
“To put on leg”	Shoe	“It's a leather thing and leg is a human leg”
“Travelling”	Bicycle, rollerskate	
“Transport”	Train, bus, lorry, car	
“Human hand”	Hand, arm, thumb	
“Sledge”	Sledge	“It's for skating”
“Human leg”	Foot, sock, elbow, leg	
“Clothing”	All other clothes	
“Fruits”	All fruit	
“Tame animals”	Dog, horse, tortoise, elephant	
“Sky vehicles”	Helicopter, plane	
“Animals”	Tiger, monkey, camel, cow, cat	“They are animals in the forest, the desert and the grass”

4. Discussion

People with acquired brain injury (ABI) and a prominent executive dysfunction performed similarly to controls on a comprehensive semantic memory test battery (Hodges et al., 1992) and therefore showed intact semantic memory ability. Contrary to this, there was a marked semantic memory impairment in the schizophrenia group (matched for IQ and executive dysfunction). As with the Hodges Semantic Memory Test Battery, people with schizophrenia were also found to perform differently to controls on a simple categorization test, the CGT. Sixty percent of people with schizophrenia were found to perform differently on this task, with 45% overincluding, showing a broadening of their semantic category boundaries, and 50% underincluding, by excluding relevant items from a target category. 50% of this group were found to both over and underinclude, providing evidence for a general disorganization of the semantic category boundaries in the schizophrenia group. The ABI group, however, was again found to perform normally on the CGT, indicating normal categorization procedures. Although this goes some way towards ruling out

the need for intact executive functioning for successful completion of this particular categorization task, it is nevertheless possible that the ABI group utilized an effective strategy that obviated their dysfunctional executive system, e.g., the use of semantic associations. Thus the disorganized categorization found in the schizophrenia group appears not to arise from an executive dysfunction, nor does it appear to arise from a general cognitive impairment since both the schizophrenia and ABI groups were matched on the WASI. Furthermore, performance of patients with schizophrenia on the CGT did not correlate with either MMSE, WASI or BADS scores. Disorganized semantic categorization in schizophrenia may also be separable from other semantic memory impairments, since error rates of patients on the CGT do not correlate with error rates on the Hodges Semantic Memory Test Battery.

Somewhat surprisingly, overinclusion was not found to be related to any symptoms as measured with the PANSS, including conceptual disorganization. Underinclusion was however related to conceptual disorganization and could be a result of the person attending to insignificant details of the task.

A tendency to attend to contextually irrelevant information has frequently been cited to be at the heart of the cognitive difficulties in schizophrenia (e.g., [Goldberg et al., 1998] and [Leeson et al., 2005]) and is referred to as difficulties utilising contextual information ([Cohen and Servan-Schreiber, 1992] and [Hemsley, 2005]) or inhibiting irrelevant information ([Kapur, 2003] and [Leeson et al., 2005]). An abnormality in either of these areas could result in the pattern of behaviour seen on the CGT. On a free sorting task such as the CGT, the way in which the cards are categorized is to an extent open to interpretation and what is deemed an appropriate sorting strategy to use. Normal controls show a response bias leading them to access stored representations of taxonomic categories and sort accordingly, a strategy that people with schizophrenia are not compelled to use as often. When controls do deviate from the standard taxonomic categories it is likely to involve a subdivision of categories and is qualitatively different to the overinclusion seen in schizophrenia (see website).

Hemsley (2005) in a review of the context literature claimed that people with schizophrenia are affected differently by contextual influences, meaning that "objects may acquire altered significance or implications for action". This fits in with the recent theory proposed by Kapur (2003) where a misattribution of salience results in attention being given to concepts that are contextually irrelevant. As Hemsley suggests attention may be captured by "incidental details of the environment which would not normally reach awareness" (Hemsley, 2005). In the CGT task, people with schizophrenia appear to sort on the basis of what becomes salient to them in a bottom-up, 'ad hoc' fashion which manifests itself in their bizarre card sorts (see Table 3 and Table 4).

It is important to note that the people with schizophrenia tested in this study were chronic and not highly symptomatic. The control group also varied fairly substantially in age and so therefore may not have been the best match demographically. Further research is needed in order to examine the generalisability of these findings to people in the acute phase of the disorder.

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Appendix F

Normative data is available for the CGT. 50 people were asked to complete the CGT with the instructions that they should sort the cards into piles of items that go best together. 46 people were also assessed using the National Adult Reading Test (NART) to get a rough measure of IQ. For 39 people, a measure of current IQ was also taken using the Wechsler Abbreviated Scale of Intelligence (WASI) The data can be seen in the following table:

Mean age (s.d)	55.1 (19.9)
Sex (Male/ Female)	20/30
Mean NART IQ (s.d)	106.7 (31.9) N = 46
Mean WASI IQ (s.d)	106.4 (20.3) N = 39
Number who abnormally sorted	7 (14%)
Number who overincluded	0
Number who underincluded	7 (14%)
Overinclusion Score (s.d)	1.00 (.00)
Underinclusion Score (s.d)	1.04 (.14)
CGT Score (s.d)	2.05 (.14)

A list of the 45 items included in the CGT follows:

Category	Category Members
Fruit	lemon, pineapple, melon, apple, pear, orange, grapes, banana and strawberry
Body Parts	leg, elbow, arm, thumb, hand, mouth, ear, foot and eye
Clothing	shirt, jacket, dress, sock, shoe, trousers, waistcoat, hat and belt.
Transport	Train, Car, Bus, Bicycle, Sledge, helicopter, plane, lorry and rollerskate.
Animals	Camel, Horse, Elephant, Dog, Cat, tortoise, tiger, monkey and cow

Appendix G

The following table includes a list of the items used in the salience test, with the mean importance scores given to item attributes by the normative sample. Those used in the final salience test are shaded (table constructed by Sarah Masson).

Item number	Item	Very important attribute	Mean score	Important attribute	Mean score	Unimportant attribute	Mean score	New item Number
1	Banana	Food	1.3	Custard	2.0	Comedy	2.8	1
2	Belt	Buckle	1.0	Loops	2.0	Hitting	3.0	2
3	Bicycle	Wheels	1.0	Helmet	2.3	Stabilisers	2.7	3
4	Bus	Driver	1.1	Conductor	2.1	School Kids	2.7	4
5	Camel	Hump	1.1	Water	2.1	Cigarettes	2.8	5
6	Car	Engine	1.1	Seat Belt	1.9	Booster Seat	3.0	6
7	Cow	Udders	1.1	Horns	2.2	Flies	2.7	7
8	Dog	Bark	1.0	Collar	2.0	Wolf	2.9	8
9	Dress	Clothing	1.1	Wedding	1.9	Spots	3.0	9
10	Ear	Hearing	1.2	Earring	2.1	Earphones	2.7	10
11	Elephant	Trunk	1.0	Ears	2.0	Rides	3.0	11
12	Eye	Sight	1.2	Glasses	1.9	Spying	3.0	12
13	Foot	Toes	1.3	Print	2.0	Flip-flop	2.7	13
14	Grapes	Bunch	1.1	Juice	2.1	Hospital	2.8	14
15	Lemon	Fruit	1.1	Pips	2.1	Cleaner	2.8	15
16	Lorry	Wheels	1.1	Motorway	1.9	Fluffy Dice	3.0	16
17	Pear	Tree	1.2	Juice	2.1	Apple	2.7	17
18	Plane	Wings	1.1	Airhostess	2.0	Orange	3.0	18
19	Rollerskate	Wheels	1.1	Knee Pads	2.2	Ice Skate	2.7	19
20	Shirt	Sleeves	1.3	Buttons	1.9	Cuff Links	2.8	20
21	Sock	Feet	1.0	Heel	2.1	Christmas	2.9	21
22	Tiger	Stripes	1.2	Claws	1.8	Esso	3.0	22
23	Train	Station	1.0	Ticket	2.2	Whistle	2.8	23