Olfactory hallucinations in schizophrenia and schizoaffective disorder: A neuropsychological investigation.

Deborah Arguedas (BSc – Psych) Hons

Macquarie Centre for Cognitive Science (MACCS)

Faculty of Human Sciences

Macquarie University

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Declaration

The research reported in this thesis is my original work. It has not been submitted for a higher degree in any other university or institution. Formal ethics approval was obtained from the Macquarie University Human Ethics Committee prior to commencement of the current research: Final approval reference number HE25NOV2005-D04388. The research reported in this thesis was conducted under the supervision of my principal supervisor, Associate Professor Robyn Langdon and associate supervisor, Associate Professor Richard Stevenson.

Deborah Arguedas
General Abstract

**Purpose:** The primary aim of this research was to address the current gap in knowledge of olfactory hallucinations (OHs), specifically within the schizophrenia population. This aim was addressed by employing a symptom-focused approach that combined clinical neuropsychological and cognitive neuropsychological perspectives to inform the understanding of the neural, neuropsychological and cognitive causes of OHs. **Method:** Two groups of clinical patients (one comprised of those self-reporting recent OHs (n = 11) and another self-reporting auditory verbal hallucinations (AVHs - with no lifetime history of OHs; n = 10)), in addition to a group of healthy controls (n = 18) completed a battery of neuropsychological tasks tapping into executive and amygdala functioning. An odour source discrimination task and an auditory verbal source monitoring task was also completed. **Results:** Evidence of smell identification impairment and aspects of general executive dysfunction was found in both clinical groups relative to controls. However, a pattern of dysfunction that particularly implicates OFC and amygdala neural circuitry (and disruption to their associated higher level neuropsychological skills) was also found that was specific to patients experiencing OHs. On tasks of source monitoring, preliminary evidence was found on the odour source discrimination task suggestive of a sensory specific source monitoring bias for patients with schizophrenia who experience OHs. In addition, a specific source monitoring deficit for auditory-verbal information was also found in patients that experience AVHs. **Conclusion:** The obtained results suggest that the generation of OHs may be underpinned by a combination of specific neuronal and related source monitoring dysfunction. This finding has implications for therapy in individuals with schizophrenia who experience OHs.
General Introduction

Schizophrenia is a major disorder affecting approximately 0.5–1.5% of the world’s adult population. Overall, the age of onset for the disorder typically occurs between the late teens and early 30s, with the modal age of onset being 18-25 years of age for males and 25-35 years of age for females (APA, 1994).

The etiology of schizophrenia is yet to be fully elucidated. However, in addition to an environmental contribution to the development of this disorder, strong evidence has also been found that supports a genetic association. In individuals that have first-degree biological relatives diagnosed with schizophrenia, the lifetime risk for developing the illness has been found to be increased by approximately 8-12-fold (Ivleva, Thaker, and Tamminga, 2008). Schizophrenia is distinguished from other psychotic illnesses predominantly by the course of the illness rather than purely by the presence of symptoms. While in some individuals symptoms are chronic and unremitting, in others symptoms may occur episodically. However, in those with remitting symptoms, full interepisode recovery tends to be uncommon (APA, 1994; Ivleva, Thaker, and Tamminga, 2008).

Symptoms associated with the disorder are broadly categorized into positive and negative clusters. Those categorized into the positive cluster include delusions, hallucinations, and thought disorder, and are generally not experienced within the healthy normal population. Negative symptoms are typically associated with the absence of normal functions, and include, for example, flat affect and deficiency in the content or quantity of speech (APA, 1994).
The primary focus of this research is hallucinations in schizophrenia, specifically hallucinations of smell, or olfactory hallucinations. However, before focusing on olfactory hallucinations in schizophrenia the following section presents a more general introduction to research into hallucinations, with a primary focus on hallucinations in schizophrenia.

1. Hallucinations

Hallucinations are involuntary sensory experiences that occur despite the lack of external stimuli (Silbersweig, Stern, Frith, Cahill, & et al., 1995), and they can occur in any modality. The estimated prevalence of hallucinations in schizophrenia has been reported as ranging from 50-80% for auditory hallucinations, 30-70% for visual hallucinations, and 20-50% for somatic and tactile hallucinations. Olfactory hallucinations have been reported as occurring less frequently, with an estimated prevalence of only 10-30% (Kopala, Good, & Honer, 1994; Mueser, Bellack, & Brady, 1990; Murphy, Wittkower, Fried, & Ellenberger, 1963).

Researchers of hallucinations have adopted a variety of theoretical perspectives. Some researchers seek to elucidate the neural underpinnings of these phenomena (Badcock, 2010; Hoffman, Fernandez, Pittman, and Hampson, 2011), while other researchers consider the involvement of more general psychological factors such as metacognitive beliefs (Lobban, Haddock, Kinderman, and Wells, 2002; Smith, et al, 2006). Yet other researchers (Bentall, 1990; Jones, 2010; Seal, Aleman and McGuire, 2004) explore possible cognitive processes involved in the generation of hallucinations in schizophrenia. These different theoretical perspectives will therefore be briefly considered in turn in the subsequent sections.
1.1. **Neural processes involved in hallucinations**

The investigation of auditory hallucinations has lead to theories about the involvement of language-specific neurobiological processes. For example, a recent study from Hoffman and colleagues (2011) has used functional MRI to investigate the activation of neuronal circuitry during auditory-verbal hallucinations experienced by individuals diagnosed with schizophrenia, compared to non-hallucinating patients and healthy controls. Evidence was found for elevated functional connectivity along a corticostriatal loop involving Wernickes area, which is normally involved in the comprehension of spoken and written language, the left inferior frontal gyrus and the putamen in the auditory-verbal hallucinating group relative to the other groups. In a recent review of the auditory hallucination literature, Badcock (2010) has also examined the generation of these hallucinations in the context of the neural organization of distinct pathways involved in auditory processing. This author proposed that abnormal activation within the dorsal, (localization or “where”) and ventral (identification or “what”) auditory processing pathways may contribute to the experience of auditory hallucinations as non-self-generated voices. It was further suggested that this neural disturbance, might be combined with current cognitive theories of auditory hallucinations (see below) to provide a more integrated cognitive neuropsychological model of auditory hallucinations.

Some more general psychological accounts of hallucinations have also been proposed, as discussed briefly below.

1.2. **More general psychological contributions**

Empirical evidence has been found supporting a contributory role for emotion in the development of auditory hallucinatory experiences in schizophrenia. For example, using a variety of scales
measuring different positive and negative symptoms, mood, self-esteem and evaluative beliefs about the self and others, Smith et al (2006) examined the relationship between these variables in patients diagnosed with schizophrenia or schizoaffective disorder. Results indicated that auditory hallucinations containing negative content of greater intensity were more associated with depressive mood disturbance, low self-esteem, and negative evaluative self beliefs. An independent trend was also found for a general association between depression and auditory hallucinations. These findings were interpreted to suggest that auditory hallucinations are driven by a circular process by which low mood contributes to hallucinations which, in turn, also increase the ensuing level of negative affect experienced.

Metacognitive beliefs have also been suggested as playing a role in the occurrence of auditory hallucinations. In a study conducted by Lobban et al, (2002) this possibility was specifically explored within the schizophrenia population by using a metacognitive beliefs questionnaire, anxiety questionnaire and depression scale. The responses of patients with schizophrenia who were currently experiencing auditory verbal hallucinations were compared to those made by a non-hallucinating patient group and a non-patient control group. An additional group of people experiencing elevated levels of anxiety (and no psychotic symptoms) were also included in the study as a control for anxiety. The hallucinating group was found to report a significantly lower level of cognitive confidence (specifically, confidence with aspects of their memory) relative to the non-hallucinating schizophrenia group, after controlling for depression and anxiety. The hallucinators were also found to score higher than the anxiety group in the level of importance they placed on the consistency of their thoughts. This pattern of findings was interpreted as suggesting that lower levels of cognitive confidence and a stronger belief in the importance of consistency of thoughts may contribute to the experience of auditory hallucinations. This pattern
of results was also thought to be consistent with a suggestion made by Bentall et al (1990) that beliefs and expectations play a role in the generation of auditory hallucinations.

A more general integrative model explaining psychotic symptoms (including hallucinations) has been suggested by Morrison (2001), who incorporates a combination of cognitive, psychological and behavioural components. He proposes that psychotic symptoms reflect intrusions into awareness, of cognitive, somatic, emotional or externally based information, which are misinterpreted and misattributed. The types of misinterpretations and misattributions are thought to be influenced by a combination of personal experiences, beliefs and defective self and social knowledge. The content of the intrusions is likely to be of a culturally unacceptable nature and to cause associated distress. The misinterpretations and misattributions are subsequently thought to be maintained by a combination of mood, associated physiology, and various cognitive and behavioural conditioned responses such as selective attention, avoidance behaviours and inefficient thought control strategies.

Evidence for disturbances to more specific cognitive processes in the generation and maintenance of hallucinations has also been found and will be described in the following section.

1.3 Cognitive theories of hallucinations

Bentall (1990) was a pioneer in this area of research and carried out an influential review of early studies conducted in this area. He subsequently proposed a general framework for the creation of hallucinations whereby they arise from an impaired ability to discriminate between real and self-generated imagined events. Bentall argued that inaccuracies in judging the source from which incoming perceptive information comes (i.e., in making reality discrimination judgments) may
give rise to a bias towards attributing this information to external rather than internal sources. He suggested that reality discrimination judgments made by people with schizophrenia may be highly influenced by the contextual nature of the information perceived, and that the diversity of hallucinations experienced could be driven by the type of associated discrimination errors being made.

A more recent systematic literature review, which focused specifically on auditory-verbal hallucinations (AVHs), was conducted by Seal, et al (2004). Seal and colleagues assessed the empirical evidence for the prevailing models of hallucinations, which typically implicated dysfunction within the individual cognitive mechanisms of various sorts of self-monitoring. Specifically, they described the ability to accurately identify internal self-generated speech (i.e. inner speech) as distinct from the externally generated speech of someone else. Dysfunction of this ability was said to be reflected in the misattribution of inner speech to an external source rather than to the self, resulting in the experience of ‘hearing voices’. Auditory verbal imagery refers, instead, to the process of subjective mental imagery for voices. Abnormally vivid or even reduced auditory imagery may reflect dysfunction within the process leading to the misattribution of self-generated auditory imagery to an external source. Finally, episodic memory refers to the recollection of specific events or experiences, and which typically incorporates associated sensory and perceptual information, such as the recollection of hearing voices. Disturbance to this memory process during retrieval of auditory episodic memories may result in confusion in the monitoring of the source from which the auditory memory arose, thus resulting in auditory-verbal hallucinations.
Overall, Seal and colleagues concluded that a one-dimensional model involving dysfunction within only one individual component of self-monitoring was insufficient in itself, to adequately explain the heterogeneous nature of AVHs. Instead, a multi-dimensional neurocognitive working model was proposed. This model incorporated the suggestions of aberrant self-monitoring of inner speech and of an impaired ability to source the involuntary memory of speech. However, the proposition was also made that these aberrant processes may be further moderated by inefficiency in top-down processing (i.e. via expectations and appraisals), thus influencing the specific content, meaning, location and affective prosody of the voices being heard. It was further proposed that, a general externalising response bias might also be in operation.

In a similar vein, Jones (2010) has since proposed that research needs to examine the possibility that dysfunction within different neurocognitive processes may be driving the phenomenological diversity seen within AVHs (e.g. ‘voices commenting’ versus ‘voices conversing’). He argues the case that different mechanisms need to be considered for different individual voice-hearers if we are to increase the efficacy of therapeutic treatments for AVHs.

As indicated by the above comments, auditory hallucinations, particularly AVHs (or hearing voices), have attracted most research interest to date, a fact that most likely reflects the high prevalence of this kind of hallucination within the schizophrenia population. This notwithstanding, the broadening of research to include the examination of less frequent but nonetheless characteristic types of hallucinations within schizophrenia (and also within other disorders) may assist in extending current knowledge about the heterogeneity of symptoms within the wider clinical group of interest (Jablensky, 2001). With regard to schizophrenia, new knowledge may be found that assists in elucidating the different underlying processes that drive the generation of hallucinations across different modalities. Moreover, different underlying
processes of this type might even help to further elucidate those mechanisms which drive
different subtypes of AVHs. Hallucinations within the olfactory modality (ie. olfactory
hallucinations; OHs) are of particular interest in this context since these symptoms have been
shown to have particular clinical significance for people with schizophrenia, despite being
generally less prevalent, as discussed in the following sections.

2. Olfactory hallucinations (OHs) in schizophrenia

2.1. The prevalence of OHs in schizophrenia

Relative to hallucinations in other sensory modalities (e.g. auditory and visual), OHs appear to be
less common. However, the frequency of OHs may be under-estimated to some extent since OHs
are under-represented in formal diagnostic instruments and in clinical symptom scales (Langdon,
McGuire, Stevenson and Catts, 2011). Consequently, there is a lack of specific probing about
these experiences by most clinicians.

Prevalence rates have been reported to vary from as little as 1% (Alliez and Nosida, 1925) up to
35% (Kopala et al., 1994), with an overall average incidence estimate of approximately 14%
(Stevenson, Langdon and McGuire, 2010). Langdon et al. (2011) recently conducted an
examination of past-month prevalence rates for OHs (ie, experienced in the past month), using
two pre-existing datasets: the World Health Organisation 10 Country (WHO-10) Study, which
used the Present State Examination (Jablensky, et al., 1992) to rate symptoms and symptom
ratings from various Australian studies which have used the Scales for Assessing
Positive/Negative Symptoms of Schizophrenia (SANS/SAPS)). The results from these two
relatively large datasets indicated the presence of OHs in 13% and 17%, of people with
schizophrenia respectively.
While OHs have been reported to be more common in female schizophrenia patients relative to males (Kopala, et al, 1994; Langdon et al, 2011), Stevenson et al., (2010) suggest that any gender difference may be more marked for OHs with a negative valence. It is the negative OHs which will most often come to the notice of clinicians because of their negative impact on the patients’ lives, as discussed below.

2.2. The clinical significance of olfactory hallucinations in schizophrenia

While previous reports (Kopala et al, 1994; Meats, 1988) have highlighted the general unpleasant quality and intrusive and distressing nature of OHs, more detailed accounts of the diverse characteristics of OHs has been elusive until more recently. Stevenson, et al., (2010) have attempted to provide a more comprehensive description of OHs by conducting a phenomenological survey of 51 participants with schizophrenia or schizoaffective disorder who self-reported experiencing recent OHs. Their findings offered support for the general assertion that OHs tend to be predominately negative in valence. However, a mix of pleasant and neutral OHs was also reported to be experienced by a significant number of participants. The range of different OHs experienced by patients also tended to be relatively small. However, the OHs were reported to be experienced repeatedly. In light of the above, elucidation of the mechanisms driving the generation of OHs may have important implications for the targeted treatment and management of hallucination of this type. This is especially so since OHs may be more clinically significant than has previously been considered.

The clinical significance of OHs has typically been considered to be minor relative to hallucinations in other modalities (Meats, 1988). However, Kwapil, Chapman, Chapman and
Miller, (1996) have previously highlighted the importance of OHs with regard to their predictive value. For example, they found evidence suggesting the predictive utility of aberrant olfactory experiences in non-psychotic (i.e. healthy) individuals in the subsequent development of clinical psychosis. The consensus since has generally been that the presence of OHs in patients with schizophrenia is indicative of more serious psychopathology and a poorer prognosis. Despite this, recent studies (Langdon et al, 2011; Stevenson et al, 2010) that have examined the relationship between OHs and variables such as age of symptom onset and length of illness in patients with schizophrenia experiencing current OHs have found little evidence to support the predictive utility of OHs in schizophrenia patients who are already diagnosed with the disorder.

Regardless of the prognostic value of OHs, a number of clinical correlates have been recently highlighted, emphasising the clinical importance of OHs. Specifically, Langdon et al., (2011) found evidence of a significant association between OHs and negative mood (depression and anxiety) and self-deprecation, and also between OHs and delusions of reference/control. Other strong correlates of OHs were as expected and included somatic/tactile/gustatory hallucinations, a finding that is consistent with previous studies (e.g. Mueser, Bellack, & Brady, 1990) and also auditory hallucinations (Langdon et al, 2011; Stevenson et al, 2010). The finding of an association between OHs and negative mood was of particular concern since this association suggests that these hallucinations impact negatively on patients’ quality of life. The association with delusions of reference/control is also clinically significant since it suggests that these particular types of hallucinations fuel delusions of this type.
The link between OHs and tactile hallucination was considered more informative with regard to the possible role of peripheral sensory neural abnormalities. The different putative neurological contributions to OHs are discussed in the following subsection.

2.3. Peripheral and central neurological contributions to olfactory hallucinations

In attempting to account for the generation of OHs, the possible contribution of peripheral and/or central neurological disturbance requires some consideration. In reviewing the literature in this area, Stevenson and Langdon (2011) have recently reported a number of possible peripheral causes for OHs involving various degrees of olfactory receptor abnormality, such as inappropriate activation of olfactory sensory memories, misattributions and adaptation failures resulting in the misperception of odours. Their suggestions are generally consistent with previous research (see Moberg et al., 1999; Stedman and Clair, 1998; Kopala et al., 1994) in which participants with schizophrenia were reported to experience elevated odour detection thresholds and odour identification difficulties, both of which were reported as being sensitive to peripheral nerve damage.

Given the association found between OHs and tactile hallucinations, Stevenson and Langdon further proposed that the act of sniffing (in the absence of an odour) may cause a form of tactile hallucination from nasal airflow, subsequently activating olfactory pathways adequately enough to generate an OH in individuals with schizophrenia.

In terms of central neurological contributions to OHs, possible amygdala and orbitofrontal cortex (OFC) involvement was also proposed given the amygdala’s role in processing affective reactions to odours, the role of the OFC in processing olfactory hedonics, and known dysfunction
within these central neural areas in the schizophrenia population (Stevenson and Langdon, 2011). The present research will follow on from these suggestions to explore neuropsychological evidence for the specific involvement of different central neurological contributions to OHs (see below). The present research will also aim to address difficulties with using current models of hallucinations to explain OHs, as discussed below.

2.4. The inadequacy of accounting for OHs using current cognitive models of hallucinations

The number of studies that have specifically focused on OHs in the schizophrenia population is limited. One such study (Stedman & Clair, 1998) focused on the identification of impaired olfactory identification and other aspects of cognitive dysfunction in schizophrenia, in addition to the possibility of an association between olfactory identification deficits and OHs and other clinical characteristics (e.g. ahedonia). Kopala et al. (1994) also investigated olfactory identification ability and the presence of OHs in schizophrenia, but also examined other psychiatric conditions (i.e. depression and eating disorder). Results from both studies found evidence for olfactory identification deficits in patients with schizophrenia. However, there was no significant relationship found between olfactory identification impairment and the presence of OHs. These findings suggest that general odour processing deficits do not appear to be specifically associated with OHs.

More recent research interest in OHs has lead to the detailed exploration of the phenomenology of hallucinations of this type (Stevenson, et al., 2010) as well as the clinical correlates of OHs in schizophrenia and schizoaffective disorder (Langdon et al., 2011), as described in previous sections. However, to date, potential cognitive accounts for the generation of OHs are generally
lacking. For example, difficulties with monitoring the generation of inner speech may make for a plausible account of auditory-verbal hallucinations but can hardly be applied to explaining OHs. Stevenson et al., (2010) also suggest that the generation of OHs is unlikely to be accounted for by difficulties with source monitoring of odour imagery or of olfactory memories since olfactory images and memories are difficult to self-generate. This suggests that OHs in schizophrenia are not adequately explained by current cognitive theories attempting to explain hallucinations within other modalities (e.g. visual and auditory). Focused research further investigating the possible underlying mechanisms involved in the generation of OHs is therefore warranted.

3. The current research

In light of the above, the present research will attempt to address the apparent gap in the current literature concerning knowledge of the neurological and cognitive mechanisms that contribute to OHs. This will be done by using a symptom-focused approach that combines clinical neuropsychological and cognitive neuropsychological perspectives to inform understanding of the neural and cognitive causes of OHs.

To achieve this, Paper 1 will explore the neuropsychological characteristics specifically associated with OHs, as well as making inferences about the neuroanatomical structures (both cortical and sub-cortical) and the neural connections that might be specifically related to OHs. Comparison of performances will be made on a series of neuropsychological tasks administered to two groups of clinical patients, one comprising those self-reporting recent OHs and another self-reporting AVH (with no lifetime history of OHs), in addition to a group of healthy controls. Tasks will be specifically selected to tap functions thought to be associated with the areas of neural circuitry involved with the olfactory system (i.e. the orbitofrontal cortex and the
amygdala). It is hypothesized that clinical participants experiencing OHs will demonstrate greater deficits on tasks reflecting orbitofrontal and amygdala functioning, compared to clinical participants experiencing auditory-verbal hallucinations and healthy controls.

Paper 2 will then examine the cognitive processes underlying the generation of OHs in schizophrenia. Using the same groups of participants recruited for Paper 1, this study will draw upon previous research (Bentall, Baker and Havers, 1991) investigating the role of defective source monitoring in the generation of AVHs. In addition to attempting to replicate the findings of Bentall at al (1991), the current study will employ a novel olfactory source discrimination task. It is anticipated that, when compared to clinical participants experiencing AVHs and healthy controls, clinical participants experiencing OHs will demonstrate an impaired performance on tasks of source discrimination that is specific to the olfactory modality.

Overall, findings from studies of this nature may assist in better identifying neural aspects of the schizophrenia disease process that are specific to OHs. Furthermore, the identification of possible disrupted cognitive processing in patients experiencing OHs may contribute to the design of OH-specific cognitive treatments. Moreover, findings may subsequently allow for a greater understanding of the processes that underlie hallucinations more generally.
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Paper One

An exploratory study of the neuropsychological characteristics associated with olfactory hallucinations in schizophrenia.

This paper has been prepared for publication and was submitted to Journal for the International Neuropsychological Society (JINS).

Candidate’s Contribution: The candidate has played a major role in organising the protocols and setting up the paradigms for this paper. In addition, the candidate has collected all the data, conducted all initial analyses and has acted as senior author.
Abstract

Purpose: The focus of this research was to identify distinct neuropsychological characteristics associated with olfactory hallucinations (OHs) in schizophrenia, and to subsequently inform the understanding of associated neuroanatomical structures and neural circuits implicated in the generation of OHs. Methods: Twenty one clinical participants diagnosed with schizophrenia or schizoaffective disorder, were recruited into the study. Two clinical groups were formed according to recently experienced modality specific hallucinations: OHs (n = 11) and auditory verbal (AVHs; n = 10). A group of healthy controls were also recruited (n =18). Using an exploratory approach, all participants underwent a battery of standardised and experimental neuropsychological tasks measuring aspects of executive and amygdala functioning. Results: Significant group differences were found between clinical groups (OHs vs AVHs) on one task associated with the orbitofrontal cortex (OFC) (ie. the object alternation task), with participants in the OH group generating a significantly higher percentage of perseverative errors than those in the AVH group. Performance by the OH group on the Faux Pas task, which is presumed to tap into both the orbitofrontal cortex and amygdala, was poorer relative to the AVH and control groups. No significant differences were found between the OH and AVH groups on any other administered tasks. However, controls performed significantly better than both OHs and AVHs on the following tasks assessing aspects of executive functioning: University of Pennsylvania Smell Identification Test (UPSIT); Wisconsin Card Sorting Test (WCST); Controlled Oral Word Association Test (COWAT); Delis Kaplan Executive Function System (DKEFS) - Colour Word Interference Test; and Minds Eyes Test Conclusions: The study found preliminary evidence suggestive of compromise to both the orbitofrontal cortex (OFC) and amygdala specific to schizophrenia patients experiencing OHs. Evidence was also found to support a pattern of general executive dysfunction in schizophrenia.
1. Introduction

Olfactory hallucinations (OHs) refer to the false perception of an odour that occurs in the absence of a real odour in the environment (Myers, 2006). OHs have been reported to occur (albeit relatively rarely) in a range of conditions including temporal lobe epilepsy (Chen, et al., 2003; Elliott, Joyce & Shorvon, 2009; Neppe, 1981), migraine (Fuller & Guiloff, 1987; McAbee, Sagan, & Winter, 2000) and psychiatric conditions such as schizophrenia (Kopala et al., 1994). OHs have generally been associated with negative valanced sensations of smell. These include odours such as smoke, burning and decaying flesh. However, recent work conducted by Stevenson, Langdon and McGuire (2010) exploring the phenomenological nature of OHs within the schizophrenia population has revealed evidence to suggest that positive valanced sensations of smell such as perfume and flowers are also commonly experienced.

While hallucinations have long been recognized as a characteristic feature of schizophrenia, the prevalence rates of hallucinations for each sensory modality within this population has been reported to vary considerably. Auditory and visual hallucinations have typically been reported as occurring with the greatest prevalence, followed by somatic and tactile hallucinations. Olfactory hallucinations have been reported as least prevalent (Murphy et al. 1963; Mueser et al., 1990; Kopala et al., 1994).

Compared to other modalities, auditory hallucinations have attracted the majority of research interest to date. However, Jablensky (2001) raised concerns about the trend to focus predominantly on prevalent symptoms, and argued that research into less frequent but characteristic symptoms may also yield knowledge about the broader disease group. In light of this, it is proposed that the investigation of possible differences between patients who experience
olfactory hallucinations and those who do not may assist in informing about the processes that underlie hallucinations generally, in addition to informing about abnormalities that may be specific to olfactory hallucinations. For example, while olfactory identification deficits have been found to be a common feature of schizophrenia, previous research has found no evidence to support a specific link between odour processing impairments and the presence of olfactory hallucinations (Kopala *et al*., 1994).

Using a neuropsychological approach, the present study will therefore explore the characteristics of olfactory hallucinations within the schizophrenia population. In particular, the study will attempt to identify a distinct neuropsychological profile of executive dysfunction that is specifically associated with olfactory hallucinations. This will be done by exploring differences in patterns of executive functioning (ie. functions associated with the orbitofrontal versus dorsolateral regions of the frontal lobes) for individuals who experience olfactory hallucinations relative to those who experience auditory verbal hallucinations. Given the above described focus of the present study, consideration of the neuroanatomical features of the olfactory system is necessary to establish a basis for the selection of tasks thought to tap into the areas of functioning specifically associated with the olfactory system. A review of the neuropsychological features associated with schizophrenia generally (particularly the pattern of executive dysfunction) is also warranted so that the pattern of obtained results can be delineated in terms of specificity to olfactory hallucinations. These will be considered in turn below, commencing with the neuroanatomy of the olfactory system.
1.1. Neuroanatomical Organisation of the Olfactory System.

The olfactory system is comprised of both direct and indirect (ie. dual route) neurological pathways. While the indirect pathway of the system runs via the medial dorsal nuclei of the thalamus to the orbitofrontal cortex, the direct pathway runs straight to the orbitofrontal cortex without first relaying through the thalamic nuclei. The organisation of a direct pathway within the brain has therefore rendered the olfactory system distinct from those of other human sensory systems (Hawkes & Doty, 2009). The direct olfactory system pathways within the brain are depicted in a schematic representation in Figure 1.

Olfactory receptors that are located within the nasal cavity have fibres that project into the olfactory bulb (OB) within the brain. They then travel along the olfactory tract, and for the direct pathway, run straight into the primary olfactory cortex (POC). The POC is a heavily myelinated region of the brain which is located on the basal area of the frontal lobe and the medial temporal lobe (Carmichael, Clugnet & Price, 1994). It is comprised of the piriform cortex, which receives most fibres projecting from the OB; the anterior olfactory nucleus; olfactory tubercle; periamygdaloid complex and the rostral entorhinal cortex. Fibres from the POC mainly project directly into the orbitofrontal olfactory area of the frontal cortex, while others project into several additional secondary olfactory areas (Blumenfeld, 2002; Hawkes & Doty, 2009; Lezak, 2004).

Although the olfactory system has the most direct access to the hippocampus, relative to other human sensory systems, there are no direct pathways from the piriform cortex within the POC to the hippocampal formation. There are, however, heavy projections of olfactory tract fibres that connect the piriform cortex to the basolateral amygdala (Blumenfeld, 2002; Hawkes & Doty, 2009). In addition to this, animal studies that have mapped the olfactory system in mice (Kang,
Baum & Cherry, 2009; Miyamichi, et al., 2011) and the macaque monkey (Carmichael, Clugnet & Price, 1994) have found evidence that the amygdala has strong reciprocal fibres connecting it to the olfactory bulb. This pathway therefore provides another direct pathway within the olfactory system (Blumenfeld, 2002; Hawkes & Doty, 2009).

Figure 1. Schematic representation of the direct pathways within the olfactory system.
It can be seen from the organization of the olfactory system that the orbitofrontal cortex and amygdala are involved in the processing of olfactory information via direct pathways from the olfactory bulb. This suggests that the inclusion of tasks tapping into orbitofrontal and amygdala functioning would be prudent for the current study given that hallucinations within the olfactory modality are the focus of the study. However, since this study is also specifically centered around the schizophrenia population, consideration of the areas of frontal lobe pathology and amygdala functioning associated with schizophrenia generally, is also necessary in guiding task selection. A review of the literature examining the neuropsychological profile of schizophrenia is therefore presented in the following sections.

1.2. Neuropsychological Profile of Schizophrenia

A vast body of literature has accumulated over the years in an attempt to delineate a distinct profile of cognitive dysfunction associated with schizophrenia. Neuropsychological studies investigating cognitive functioning in this population has shown consistent support for a pattern of generalized cognitive impairment across a range of cognitive domains including verbal learning, memory, attention, processing speed and aspects of executive functioning (eg. impulse control, working memory, phonemic verbal fluency) (see Heinrichs & Zakzanis, 1998 and Reichenberg & Harvey, 2007 for a review). The severe level of executive dysfunction demonstrated in schizophrenia studies has been considered to be a reflection of the extent of frontal lobe pathology in patients who have schizophrenia (Bilder et al., 2000; Heinrichs & Zakzanis, 1998). In addition, neuroimaging studies have provided evidence of frontal lobe involvement with cerebral magnetic resonance imaging (MRI) showing reduced volume (Convit, et al., 2001) and grey/white matter differentiation (Crespo-Facorro et al., 2000; Gur et al., 2000;
Wible, et al., 2001) within the frontal lobes of patients with schizophrenia. This is of particular interest to the present study given the dominant role of the frontal lobes in olfactory processing.

Aspects of executive dysfunction that have typically been reported within the schizophrenia literature have predominantly emphasised functions thought to be associated with the dorsolateral prefrontal cortex (DLFPC) and associated hippocampal and striatal connections. This emphasis has primarily evolved from the common use of testing batteries that include tasks such as the Wisconsin Card Sorting Test (WCST), Controlled Oral Word Association Test (COWAT), Tower of London (TOL) and Delayed Response Task (DRT), which tap into skills such as planning, set shifting, problem solving, generativity and working memory (Pantelis & Brewer, 1995; Pantelis et al, 1997; Shallice, Burgess & Frith, 1991). However, in reviewing the schizophrenia neuropsychology literature, Pantelis and Brewer (1995) discussed possible involvement of another frontal system that has a distinct pattern of executive dysfunction to that of the DLPFC. This other system reportedly involves the orbitofrontal cortex (OFC) and circuitry to the limbic system. It is thought to be characterised by a pattern of functioning that includes utilisation behaviour, disinhibition and olfactory identification deficiencies, reflected in studies that have employed tasks such as the Stroop, Go-no go Task, Delayed Alternation Task (DAT), Object Alternation Task (OAT) and odour identification tasks such as the University of Pennsylvania Smell Identification Test (UPSIT). It was subsequently asserted by Pantelis and Brewer (1995) that the heterogeneity of executive dysfunction seen in individuals with schizophrenia may reflect abnormalities within these two distinct frontal subsystems, involving specific neural circuitry and associated subcortical structures.
While DLPFC dysfunction in schizophrenia has been well established, OFC dysfunction has received relatively little research interest by comparison, despite the suggestion of OFC associated cognitive deficits within the schizophrenia population. However, of the limited number of studies that have been conducted (Kopala, Good, & Honer, 1994; Saoud, Hueber, Mandran, Dalery, & d'Amato, 1998; Seidman, Talbot, Kalinowski, McCarley, & et al., 1991; Stedman & Clair, 1998), olfactory identification deficits within this population have been the primary research focus. Studies of this type have typically employed the UPSIT as a reliable standardised neuropsychological test of odour identification which is believed to be associated with OFC functioning due to the neuroanatomical pathways that project from the olfactory bulb to the OFC. Results of these studies have provided evidence for impaired olfactory identification (olfactory agnosia) in individuals at ultra-high risk of developing schizophrenia (Brewer, Wood, McGorry & et al., 2003) and in individuals diagnosed with schizophrenia (Kopala et al., 1994; Stedman & Clair, 1998), reflected in significantly lower scores on the UPSIT relative to controls. Interestingly, in those studies of olfactory identification deficits in schizophrenia conducted by Kopala et al. (1994) and Stedman and Clair (1998), a proportion of participants were reported to experience elevated levels of olfactory hallucinations (OHs). However, these studies failed to find a significant association between deficits in olfactory identification and the presence of OHs. Based on these findings, Kopala et al., (1994) raised the possibility that both overlapping and distinct neural circuits may be involved in olfactory identification deficits and in the generation of OHs in schizophrenia.

Typical practice in research attempting to investigate distinct patterns of executive dysfunction within a diverse range of clinical populations, including schizophrenia, has been to administer batteries that predominantly include widely used standardised neuropsychological measures (eg.
WCST, TOL and COWAT). However, increasing use of the more experimental comparative neuropsychological tasks (CNT) (which will be described in detail later) has also been shown to yield compelling results. Studies (Freedman, Black, Ebert, & Binns, 1998; Freedman, 1990; Oscar-Berman and Bardenhagen, 1998; Oscar-Berman and Zola-Morgan, 1980a, b) that have employed subtests of the CNT within a variety of human populations such as individuals with bilateral frontal lobe lesions and clinical populations including schizophrenia, Alzheimer’s Disease, Parkinson’s Disease and Korsakoff’s Disease, have consistently provided strong support suggesting that the tests that comprise the CNT are sensitive measures tapping into functions associated with damage within specific prefrontal systems, thought to be associated with the OFC and DLPFC regions of the frontal lobes.

The Comparative Neuropsychological Tasks

The Comparative Neuropsychological Tasks (CNTs) are comprised of a set of tasks which includes the delayed alternation task (DAT), object alternation task (OAT) and delayed response task (DRT). These tasks were originally based on the WCST, and were adapted from the non-human primate lesion study literature for use within human neurological patients (Freedman, 1990; Oscar-Berman and Bardenhagen, 1998). Two subtests of the CNT that are thought to tap into the OFC are the DAT and the OAT. Specifically, the DAT is thought to tap into the reward pathways in addition to measuring the cognitive functions of working memory, perseveration and the ability to shift set. As such it is considered to be associated with both the DLPFC and OFC regions of the frontal lobes. The OAT, however, is considered to predominantly measure the ability to inhibit responses whilst also tapping into the reward pathways of the frontal lobes. It is therefore thought to be the CNT task most sensitive to OFC functioning (Freedman et al., 1998; Oscar-Berman and Bardenhagen, 1998). Of particular relevance to the schizophrenia population
is a study conducted by Seidman, Oscar-Berman, Kalinowski, Ajilore, et al. (1995) which examined prefrontal cognitive impairments within the population by employing the subtests that comprise the CNT. Results found that patients with schizophrenia were significantly impaired on both the OAT and DAT, thus suggesting greater involvement of OFC versus DLPFC compromise. However, Seidman and colleagues did not consider whether these impairments were associated with OHs in their clinical group, which is something that will be considered in this study.

While the CNT tasks were originally based on the WCST, some important distinctions have been noted by Freedman (1990). Specifically, he pointed out that although elevated scores of perseveration on the WCST has typically been associated with DLPFC dysfunction, elevated scores of perseveration on the OAT task have been found to be more associated with lesions to the OFC. Freedman proposed that while the processes involved to complete both the CNT and WCST tasks appear to be relatively similar, they are most likely accessing different aspects of perseveration and subsequently different underlying neuroanatomical regions. The basis of this assertion was made based on fundamental differences between the cognitive functions utilised on the two tasks. For example, while both tasks require that individuals establish and maintain set, on the OAT individuals are required to establish set by alternating between object location, and subsequently need to inhibit making choices based on object type (ie.stimuli). Once set has been established on the OAT, individuals are not required to relinquish it. In contrast, on the WCST individuals are required to both relinquish set and to shift to an alternative set; thus impairments to one or either of these two processes can cause poor performances.
Overall, as previously discussed, findings from both odour identification studies and neurocognitive studies in schizophrenia suggest that a specific pattern of behavioural and neurocognitive impairment within this population may reflect dysfunction within a distinct neural system involving the OFC and connecting circuitry, known to feature within the olfactory processing system (Pantelis & Brewer, 1995). In light of this, the present study will therefore focus on exploring the possibility that this specific pattern of functioning is also associated with a greater incidence of OHs within the schizophrenia population. However, for this to be fully achieved, greater consideration of OFC and amygdala functioning is warranted, which will follow in the next section.

1.3. Related findings concerning the OFC and Amygdala

The OFC reportedly plays a fundamental role in adaptive behaviour and decision-making, particularly in uncertain situations that involve predicting, assessing and acting in response to rewards and punishment (Krawczyk, 2002; McClure, York, & Montague, 2004). Support for OFC involvement in reward processing has been provided from a functional imaging study conducted by Elliott, Dolan, and Frith (2000) which showed activation of the OFC during a variety of experimental tasks (such as the go no-go, unstable reward and guessing tasks), which require responses, or inhibition of responses, based on reward values of presented stimuli. Increased neural activity within the amygdala in addition to the OFC has also been observed in another fMRI study investigating the neural circuitry involved in reward processing (McClure et al., 2004). Despite this, however, studies investigating frontal lobe involvement in decision making utilising the Iowa Gambling Task (IGT), a reward task typically thought to tap into the OFC, have yielded mixed results. Ritter, Meador-Woodruff, and Dalack (2004) and Shurman, Horan and Nuechterlein (2005) found evidence supporting decision-making deficits on this task
in patients with schizophrenia - a finding which is interpreted as suggestive of OFC compromise in schizophrenia. However, other studies investigating the cognitive processes underlying decision making in participants with focal brain lesions versus healthy controls have found that damage to the DLPC interferes with performance on the IGT (Clark, et al., 2003; Manes et al., 2002). It has further been suggested that working memory (a function typically associated with the DLPC) contributes to the associative learning and decision making processes involved in completing gambling tasks such as the IGT (Dougherty & Hunter, 2003; Dunn, Dalgleish & Lawrence, 2006; Hinson, Jameson & Whitney, 2002), bringing into question, the utility of the IGT as a measure that specifically taps into the OFC versus the DLPFC.

Integration of cognitive and emotional information received from areas of the limbic system such as the amygdala, via the orbitofrontal-subcortical circuit, occurs within the OFC (Krawczyk, 2002). While dense connections between the amygdala and OFC have been implicated in the mediation of reward processing functions, evidence from lesion studies (Brothers, Ring, & Kling, 1990) suggest that these connections also play a vital role in the processing of emotional and social information required for making social judgments (McClure et al., 2004). For example, studies using fMRI have provided evidence for preferential activation of the amygdala by faces exhibiting angry or fearful expressions (see Calder, Lawrence, & Young, 2001 for a review). Judgments of social consequences concerning the emotional expressions of others (e.g. trustworthiness judgments) have also been found to be impaired in patients with amygdala damage (Adolphs, Sears, & Piven, 2001; Adolphs, Tranel, & Damsio, 1998). In addition, Blair (1995) suggested that the OFC mediated reward/punishment system has a critical role to play in the development and perhaps maintenance of moral reasoning. Consistent with this view are
studies that show activation of the OFC when participants make moral judgments (see, e.g., Greene & Haidt, 2002).

Of further relevance to this study, the ability to make assumptions regarding the feelings, intentions, or beliefs of others (referred to as “theory of mind” (ToM)) is a central underlying component of successful and appropriate social interactions (Stone, Baron-Cohen, Calder, Keane, & Young, 2003; Stone, Baron-Cohen, & Knight, 1998) and has been linked repeatedly to the OFC. Lesion studies investigating ToM deficits in individuals with frontal lobe lesions (OFC verses DLPFC) (Stone et al., 1998) and bilateral amygdala lesions (Stone et al., 2003) have found that individuals with bilateral OFC lesions and individuals with bilateral lesions of the amygdala both demonstrate impairment on tasks reflective of ToM processes. Tasks employed by Stone et al. (2003) included the Faux Pas recognition task which is a verbal task comprised of short stories containing a socially inappropriate component (ie. a Faux Pas). The task requires that participants assess the presence or absence of a Faux Pas in each story presented. Another visually based task, “Reading the Mind in the Eyes” (RME) task (Baron-Cohen, et al., 2001) was also employed. In this task the eye regions of both male and female faces are displayed in individual photographs and participants are required to make forced choice judgments regarding the person’s thoughts or feelings. Other studies (Adolphs, Baron-Cohen & Tranel, 2002; Shaw, Bramham, Lawrence, Morris, Baron-Cohen & David, 2005) using the RME task in individuals with unilateral and bilateral amygdala damage have also derived evidence specifically supporting an association between amygdala dysfunction and disturbance in the processing of social emotional expressions. Of note here, is that individuals with schizophrenia have consistently demonstrated impairments on ToM and emotion judgment tasks of this type (see, e.g., Green, Williams, & Davidson, 2003; Langdon, et al., 2006).
To date there is no known study that has attempted to systematically identify the neuropsychological processes involved in the generation of OHs in relation to what is known of the olfactory processing system. In light of this, the primary aim of this paper is to identify neuroanatomical structures and neural circuits implicated in OHs in schizophrenia, and to further identify a distinct neuropsychological profile which discriminates between patients who experience OHs and patients who experience hallucinations in other modalities (in particular, auditory verbal hallucinators), as well as healthy controls. Given the direct involvement of the OFC and the amygdala in olfactory processing and the consistent evidence provided from previous studies of aspects of executive dysfunction and ToM deficits in individuals with schizophrenia, tasks employed in the present study will primarily focus on those thought to tap into cognitive functions associated with these particular neuroanatomical structures - ie. the OFC and amygdala, whilst also including more general executive tasks commonly used in schizophrenia research. It is hypothesized that clinical participants experiencing OHs will demonstrate greater deficits on tasks associated with orbitofrontal and amygdala functioning, compared to clinical participants experiencing auditory verbal hallucinations and healthy controls.

2. Methods

2.1. Participants

Ethical clearance for the current project was provided by the relevant ethics committees. Informed written consent was obtained from participants prior to the commencement of testing. Participants for this study were initially recruited from a pool of 51 participants who had previously participated in a telephone interview investigating the phenomenology of olfactory
hallucinations in schizophrenia. Further recruitment was later conducted to supplement this pool of participants. A total of 39 participants were recruited for this study, which was comprised of 19 males and 20 females. Inclusion criteria for the study included an age range of between 18-60 years, no self-reported history of brain injury (ie. involving loss of consciousness for > 1 hour), no substance abuse within the last 5 years according to DSM-IV criteria, and fluent English. A total of 13 participants were current smokers.

Two groups of clinical participants with schizophrenia or schizoaffective disorder according to the Diagnostic Interview for Psychosis (DIP: Jablensky et al., 1999; Castle et al., 2006) were formed. Allocation of these groups was determined by the self-reported presence or absence of OHs within the last 6 months prior to testing (NB. All participants reported experiencing hallucinations within multiple sensory modalities. No participants reported experiencing OHs only). One of the groups formed consisted of participants who reported experiencing recent OHs (n=11) and the other group reported experiencing recent AVHs and no lifetime history of OHs (n=10). A healthy control group was also formed which consisted of participants who had no history of head injury or psychotic symptoms and were recruited from the general community (n=18). Each group was matched group-wise for age and gender distribution. Demographic and clinical characteristics of participants are presented in Table 2. (see results section).

2.2. Clinical Diagnosis and Characteristics

All clinical participants underwent an extensive clinical interview. The DIP was administered to obtain socio-demographic data, medical history and confirmation of diagnosis. The Scale for the Assessment of Negative Symptoms of Schizophrenia (SANS: Andreasen, 1984a) and the Scale for the Assessment of Positive Symptoms of Schizophrenia (SAPS: Andreasen, 1984b) were also
administered to assess the presence and frequency of psychotic symptoms over the current month, as well as to confirm the presence of AVHs in at least the last 6 months in the AVH group, and OHs in the OH group. The SANS and SAPS were chosen since this measure extensively probes hallucinations within all sensory modalities.

Participants within the clinical groups all met DSM-IV criteria for schizophrenia or schizoaffective disorder and reported having experienced hallucinations within the last one to six months prior to their participation in the study. At the time of testing all clinical participants were taking antipsychotic medication (typical only, n =1; atypical only, n =5; combination of typical & atypical, n =4). Five clinical participants were taking a combination of typical antipsychotics and mood stabilizers and six were taking a combination of atypical antipsychotics and mood stabilizers. There were no differences with regard to medication between the two clinical groups.

Controls underwent a semi-structured interview to obtain demographic information; medical and psychological histories; as well as cigarette, drug and alcohol histories. Participants were included in the control group if there was no evidence of recent drug and alcohol abuse or presence of psychotic symptoms using the control screen from the Structured Clinical Interview for DSM Disorders (SCID-I; First, Spitzer, Williams & Gibbon, 1997).

2.3. Apparatus and Procedure

Tasks were administered in a fixed order which was consistent across and within groups. All standardised neuropsychological tests were administered in accordance with formal standard instructions.
2.4. Neuropsychological Battery

A battery of standardised neuropsychological tests was administered to all participants. The Wechsler Test of Adult Reading (WTAR) (Wechsler, 2001) was used to derive an estimated premorbid level of intellectual functioning. Other tests making up the battery of neuropsychological measures are presented in Table 1.

Table 1. Battery of standardised neuropsychological tasks employed assessing aspects of executive functioning.

<table>
<thead>
<tr>
<th>Task (Source)</th>
<th>Score Derived</th>
</tr>
</thead>
<tbody>
<tr>
<td>• University of Pennsylvania Smell Identification Test (UPSIT) <em>(Doty, 1989)</em></td>
<td>• Total correct</td>
</tr>
<tr>
<td>• Wisconsin Card Sorting Test (WCST) - computerized version <em>(Grant &amp; Berg, 1993)</em></td>
<td>• Percent perseverative errors</td>
</tr>
<tr>
<td>• Controlled Oral Word Association Test (COWAT) – FAS and Animals total <em>(Spreen &amp; Strauss, 1998)</em></td>
<td>• Number of categories</td>
</tr>
<tr>
<td>• Trail Making Test (TMT) – A &amp; B <em>(Reitan, 1992)</em></td>
<td>• Failure to maintain set</td>
</tr>
<tr>
<td>• Tower of London (ToL) - computerized version <em>(Culbertson &amp; Zillmer, 2001)</em></td>
<td>• Total number of words generated</td>
</tr>
<tr>
<td>• DKEFS Color Word Interference Test (CWIT) – Inhibition subtest <em>(Delis, Kaplan &amp; Kramer, 2001)</em></td>
<td>• Number of repetitions</td>
</tr>
<tr>
<td></td>
<td>• Interference score</td>
</tr>
<tr>
<td></td>
<td>• Number of errors on Trails B</td>
</tr>
<tr>
<td></td>
<td>• Total number of moves</td>
</tr>
<tr>
<td></td>
<td>• Total time to complete (secs)</td>
</tr>
<tr>
<td></td>
<td>• Number of errors</td>
</tr>
</tbody>
</table>

In addition to standardized neuropsychological measures, more experimental tasks thought to tap into functions associated with the orbitofrontal cortex and the amygdala, were also administered. These included an experimental task assessing facial affect recognition and published tests consisting of the Recognition of Faux Pas Test (Stone, Baron-Cohen, & Knight, 1998), Reading the Mind in the Eyes Test (Baron-Cohen, * et al., 2001), and the Delayed Alternation Test (DAT)
and Object Alternation Test (OAT) from the Comparative Neuropsychological Task (CNT; Seidman et al., 1995). These are described in turn below:

### 2.4 (i) Emotion Recognition Task

This computerised task measures participants’ ability to accurately perceive various facial emotions. It was run using the "DMDX" software developed at Monash University and at the University of Arizona by K.I.Forster and J.C.Forster. The stimuli consisted of eight black and white standardised photographs of faces (four male and four female) which were selected from the Ekman and Friesen’s (1976) *Pictures of Facial Affect series.* The faces depicted six various emotions: happiness, sadness, surprise, fear, anger and disgust. The hair and background were removed from each photograph and morphed with neutral faces to create facial expressions depicting each of the emotions at three different intensities (50%, 75% and 100%). A total of 150 trials were administered, which comprised one block of six practice trials before six blocks of 24 trials. All testing blocks consisted of eight faces and contained each level of emotional intensity presented in a random order. For each trial, the image appeared in the centre of a computer screen with the names of the six emotions arrayed across the bottom of the screen alongside a reference to an allocated computer response key. Participants were required to judge which of the emotions was being shown by pressing the computer keyboard key allocated to the selected emotion. Scores were derived for the proportion of correct responses for each emotion at each level of emotional intensity.

### 2.4 (ii) Recognition of the Faux Pas Task

This task assesses an individual’s ability to recognise hurtful or insulting comments made unintentionally within social situations. The version of the task used in the current research was
comprised of 20 short stories, 10 of which contained a faux pas and 10 of which contained no faux pas (Stone, Baron-Cohen, & Knight, 1998). The participants were provided with a printed copy of the stories which they were requested to follow as the examiner read each story aloud. On completion of each story, participants are asked whether “there was anything in the story that shouldn’t have been said or that was awkward?” For the current study, a sensitivity score (d-prime; d’) was derived by subtracting the z-transforms of the proportion of false alarm responses from the proportion of hits (ie. correct responses).

2.4 (iii) Reading the Mind in the Eyes Task

This task measures an individual’s ability to infer the mental states of others by looking at the eye region of the face. The revised version of the task (Baron-Cohen, et al., 2001) was used for the current research, which was comprised of 36 black and white photographs of the eye region taken of 18 males and 18 females. Four different words describing how the individual was potentially thinking or feeling accompanied each set of eyes. The participants were asked to select the one word they thought to be the most applicable descriptor for the set of eyes presented. Scores obtained reflected the number of correct responses made by the participant.

2.4 (iv) Comparative Neuropsychological Tasks (CNT)

The current study replicated two subtests of the Comparative Neuropsychological Task (CNT) described by Seidman et al. (1995), the delayed alternation task (DAT) and the object alternation task (OAT). The CNT is a modified version of the Wisconsin General Test Apparatus adapted for use with human participants, which has previously been described in extensive detail (Freedman & Oscar-Berman 1986a, 1986b; Oscar-Berman, Zola-Morgan, Oberg, & Bonner, 1982; Seidman et al., 1995). In the current study for both the DAT and OAT the researcher and participant sat
opposite each other and were separated by a wooden frame (55cm high and 60cm wide). A black adjustable felt curtain was anchored to the frame so that the participants’ view of the researcher was obscured between trials. The curtain was partially raised on each trial to reveal a stimulus board (approximately 47cm x 34cm x 2.0cm) containing two reinforcement cups (10cm diameter). Only the examiner’s hands and reinforcement cups were visible to the participants on each trial. The reinforcement cups were placed approximately 20cm apart and were each lined with black felt to mute any sounds of objects being placed inside. Each cup was covered with a black square laminated cardboard cover, measuring 12cm x 12cms. For the OAT task, a three dimensional object was mounted on each cardboard cover. The objects were made of lightweight plastic and differed in shape and colour (ie. a green rectangle block and orange sphere).

Administration of the tasks was conducted as in previous studies (cf. Seidman et al., 1995). Task order was counterbalanced within and across groups. Participants were told that a five cent coin was to be placed under one of the two cups and that they were required to attempt to select the cup in which the five cent coin had been hidden. They were also told to try and get a coin on every trial because all monies that they collected during the tasks could be kept.

Delayed Alternation Task (DAT)

Participants were required to learn that the cup in which the coin was being placed was being alternated after each correct response. On trial 1 of the DAT, a five cent coin was placed in both cups. For trial 2 the coin was placed in the cup on the side that was not chosen by the participant on the preceding trial. For all subsequent trials, a correction procedure was employed (ie. the coin remained on one side until the participant made a correct response, hence completing a trial). On trials where the participant made a correct response, the coin was placed in the opposite cup on
the subsequent trial. Inter-trial interval was 5 seconds. Learning criterion was 12 consecutive correct responses. Failure criterion was 50 trials. Scores derived were percent perseverative errors and whether task criterion was able to be achieved (yes/no). Errors were considered perseverative when two or more consecutive incorrect responses were made. Percent perseverative errors were calculated by dividing the number of perseverative errors by the total number of errors made. This figure was subsequently converted into a percentage.

*Object Alternation Task (OAT)*

Participants were required to learn that the cup in which the coin was being placed was being alternated after each correct response, and that this was not dependant on the location of the object. The baiting procedure and learning criterion was the same as for the DAT. However, in this task the location of the object on each trial was determined using Gellermann’s (1933) random modified schedule (refer to Appendix 1). Scores derived were the same as for the DAT.

### 2.5. Data Analysis Plan

All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS), version 17.0 and GraphPad Prism, version 5.03.

**Preliminary analysis:** Inspection of the data was conducted and outliers with values greater than 1.5 standard deviations were examined. It was noted that an extreme outlier on one task (Trails B) was substantially impacting on the obtained mean score. This data point was subsequently removed from the analysis. It was also noted that the assumption of normality on demographic variables was not violated. Group analyses of these demographic variables were subsequently conducted using parametric analyses (ie. ANOVA and Pearson’s correlations). However, the
spread of obtained scores on most administered neuropsychological tasks was not normally distributed, violating the assumption of normality on those data. Non-parametric and parametric statistical analyses were both initially run on the data. Results were comparable across both types of analyses with no major discrepancies evident in observed areas of significance between statistical methods.

**Primary data analysis:** In light of the above, parametric analyses (ANOVA) were selected for the final analyses in preference to non-parametric methods given the robust nature of parametric analysis with small data sets, and to allow for controlling of between group differences in demographic variables. A series of analysis of covariances (ANCOVAs) was subsequently run on all administered neuropsychological tasks, except for the emotion recognition task and the “criterion achieved” scores on the CNT tasks. The analyses for these tasks will be described in detail below.

**Post Hoc Comparisons:** Post-hoc comparisons were conducted using the Ryan-Einot-Gabriel-Welsch-Q (REG-WQ) procedure due to its sensitivity in detecting significant differences between group means that may otherwise go undetected with other types of multiple comparison procedures. This procedure is reported to have good power to control for family-wise error in data that is not normally distributed (Cribbie & Keselman, 2003; Howell, 1997). Effects were judged as significant at a level of $p<0.05$, so that any potential effects could be identified, in light of the small sample sizes.

**CNT - criteria achieved scores:** Fisher’s Exact Probability Tests (2-sided) were conducted for categorical data given that some cells contained $\leq 5$ counts.
**Power Analysis:** Given the exploratory nature of this study, post-hoc power analysis using Cohen’s tables (Cohen, 1988) was carried out on significant results identified in the primary analysis. Scores obtained included effect sizes, power of obtained results and the number of participants required to test effects with 80% power. This procedure was conducted to assess the extent to which any non-significant results of the current study were potentially driven by the small sample size of the groups.

**Emotion recognition task:** A between groups repeated measures analysis was used, with group (OHs vs AVHs vs Controls) as the between subjects factor and emotion (anger, sad, fear, disgust, happy and surprise) and intensity (50%, 75% 100%) as within group factors. Pairwise comparisons were conducted on any significant effects found. Alpha was set at 0.01 to adjust for the many multiple comparisons that were made and to control for Type I error.”

**Correlation analysis:** Post hoc correlation analysis was conducted using Pearson’s correlations on tasks of interest that measured aspects of executive and amygdala functioning. This was done to further explore the potential relationship between tasks thought to primarily be associated with the neural circuits involved with OHs.
3. Results

**Descriptive Statistics**

Means and standard deviation statistics of demographic and clinical variables are presented in Table 2.

<table>
<thead>
<tr>
<th></th>
<th>OHs (n = 11)</th>
<th>AVHs (n = 10)</th>
<th>Controls (n = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>44.6 (10.3)</td>
<td>38.8 (9.6)</td>
<td>44.3 (8.5)</td>
</tr>
<tr>
<td><strong>Gender (ratio)</strong></td>
<td>Males: Females 5:6</td>
<td>5:5</td>
<td>9:9</td>
</tr>
<tr>
<td><strong>Education (years)</strong></td>
<td>11.9 (3.6)</td>
<td>11.4 (2.2)</td>
<td>14.3 (2.9)*</td>
</tr>
<tr>
<td><strong>IQ Estimate (WTAR)</strong></td>
<td>100.5 (13.3)</td>
<td>100.4 (13.3)</td>
<td>111.9 (7.2)*</td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
<td>Schizophrenia 10</td>
<td>7</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Schizoaffective Disorder 1</td>
<td>3</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Age of Symptom Onset</strong></td>
<td>23.8 (7.5)</td>
<td>22.3 (6.7)</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Length of Illness</strong></td>
<td>19.4 (8.2)</td>
<td>16.6 (12.5)</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>SANS - Total score</strong></td>
<td>11.7 (4.7)</td>
<td>10.3 (4.7)</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>SAPS - Total score</strong></td>
<td>9.4 (2.8)</td>
<td>9.9 (2.7)</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Hallucinations#</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Auditory Hallucinations</td>
<td>1.6 (2.0)</td>
<td>4.4 (0.6)*</td>
<td>N/A</td>
</tr>
<tr>
<td>Voices Commenting</td>
<td>1.7 (2.1)</td>
<td>3.3 (2.0)</td>
<td>N/A</td>
</tr>
<tr>
<td>Voices Conversing</td>
<td>1.6 (1.9)</td>
<td>2.8 (2.3)</td>
<td>N/A</td>
</tr>
<tr>
<td>Somatic or Tactile Hallucinations</td>
<td>2.5 (2.2)</td>
<td>1.0 (1.8)</td>
<td>N/A</td>
</tr>
<tr>
<td>Olfactory Hallucinations</td>
<td>4.4 (0.7)</td>
<td>0 (0)*</td>
<td>N/A</td>
</tr>
<tr>
<td>Visual Hallucinations</td>
<td>1.7 (1.9)</td>
<td>1.9 (2.1)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**Note.** *p < .05; SANS = Scale for the Assessment of Negative Symptoms of Schizophrenia; SAPS = Scale for the Assessment of Positive Symptoms of Schizophrenia; WTAR = Wechsler Test of Adult Reading; OHs = Olfactory Hallucinations; AVHs = Auditory Verbal Hallucinations; # Mean scores on SAPS items: range 0-5.
There were no significant group differences in either age \([F (2, 36) = 1.36, p > .05]\) or gender \((\chi^2 (2) = 0.07, p = 0.97)\). There was, however, a statistically significant difference between groups in terms of years of education \([F (2, 36) = 4.23, p = .02]\) and estimated premorbid level of intellectual ability \([F (2, 36) = 5.46, p = .008]\). To assess the relationship between these variables, correlation analysis was conducted which revealed a significant positive relationship between years of education and intellectual ability \((r = .57, p < .001)\). To take account of the contributory effects of premorbid intellectual ability and years of education, premorbid intellectual ability was selected as the covariate to be used in subsequent ANCOVAs since premorbid intellectual ability and years of education were inter-related and since premorbid intellectual ability was found to be the more significant predictor. Clinical participants did not differ significantly in terms of age of symptom onset \((t (19) = 0.49, p = 0.63)\), diagnosis (Fishers Test, \(p = 0.31\)), duration of illness \((t (19) = 0.60, p = 0.55)\), or severity of current positive \((t (19) = 0.48, p = 0.66)\) and negative \((t (19) = 0.70, p = 0.49)\) symptoms. However, in terms of the specific types of hallucinations experienced, the OH group experienced significantly more olfactory hallucinations relative to the AVH group \((t (19) = 20.42, p < .0005)\), and the AVH group experienced significantly more auditory verbal hallucinations than the OH group \((t (19) = 4.11, p = .001)\). There were no significant differences between clinical groups for all other types of hallucinations \((all p > .05)\).

**Primary Data Analysis**

Means and standard deviation statistics for group performances on administered tasks are presented in Tables 3 and 4. After intellectual ability was controlled for, results revealed a main effect for group on the following tasks: UPSIT \([F (2, 35) = 4.92, p = .013, \text{eta squared} = .22]\); WCST – % perseverative errors \([F (2, 35) = 4.17, p = .024, \text{eta squared} = .19]\), number of
categories [F (2, 35) = 4.85, p = .014, eta squared = .22]; CWIT – inhibition [F (2, 35) = 5.88, p = .006, eta squared = .25]; Faux Pas Test [F (2, 35) = 7.58, p = .002, eta squared = .30]; OAT – % perseverative errors [F (2, 35) = 4.97, p < .013, eta squared = .22]; COWAT – FAS [F (2, 35) = 5.14, p = .011, eta squared = .28], Animals [F (2, 35) = 3.69, p = .035, eta squared = .17]; Minds Eyes Test [F (2, 35) = 5.45, p = .009, eta squared = .24]. Results for all other administered tasks did not reach statistical significance (p > .05).

**Post Hoc Comparisons**

Results of pairwise comparisons are also shown in Tables 3 and 4. Letters (eg. A and B) show the rank of each group for each task that reached significance. Groups that show the same rank represent no significant differences between groups according to the REG-WQ procedure.

Results of REG-WQ analysis revealed that both clinical groups (OHs and AVHs) experienced significantly greater difficulty relative to controls on the following tasks: UPSIT; WCST (% Perseverative Errors & Number of Categories); COWAT (FAS & Animals); D-KEFS CWIT; Minds Eyes Test. The OAT (% perseverative errors) and Faux Pas Test were the only tasks that showed a specific effect for one of the clinical groups. On the OAT task, the OH group made significantly more perseverative errors than both the AVH and controls groups (p < .05). For the Faux Pas Test, the OH group demonstrated significantly lower sensitivity when correctly identifying a Faux Pas relative to the AVH and control groups (p < .05). No significant differences were found between the OH and AVH groups on tasks that showed significant differences between controls and clinicals (p > .05).
**Power Analysis**

Power analysis using Cohen’s (1988) tables was subsequently conducted on the means of both clinical groups to explore the strength of the above results and to examine whether the lack of significant differences between clinical groups was primarily a reflection of the small sample size in each group. Effect sizes and power of results obtained between clinical groups are presented in Table 5. The number of participants required in each clinical group to obtain significance (with probability of Type I error set at 0.05) with 80% power are also shown. By Cohen’s (1988) definition the obtained effects on the CNT-OAT % Perseverative Errors and Faux Pas tasks are large, requiring only 17 participants in each clinical group to obtain significance across these tasks with effects reaching 80% power. However, the obtained effects on standardized neuropsychological tasks tapping into aspects of executive functioning: UPSIT; WCST - % Perseverative Errors; WCST – Number of Categories; COWAT – FAS; D-KEFS CWIT – Inhibition) were of a moderate size, with at least 100 participants required in each clinical group to reach statistical significance. Small effect sizes were evident on the Minds Eyes Task and on standardised neuropsychological tasks that tap into other aspects of cognition (eg, visual attention, processing speed and semantic fluency) on the Trail Making Test-Trails A and COWAT – Animals tasks. On these tasks at least 400 participants would be required to find significant group differences between OHs and AVHs.
Table 3. Means (SD) for performance on standardised neuropsychological tests.

<table>
<thead>
<tr>
<th>Neuropsychological Test</th>
<th>OHs (n = 11)</th>
<th>AVHs (n = 10)</th>
<th>Controls (n = 18)</th>
<th>REG-WQ (P &lt; .05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olfactory Identification (UPSIT)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total correct</td>
<td>27.6 (4.4)</td>
<td>25.2 (5.4)</td>
<td>31.8 (3.2)*</td>
<td>AAB</td>
</tr>
<tr>
<td>Tower of London</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total number of moves</td>
<td>67.0 (10.1)</td>
<td>62.2 (9.4)</td>
<td>59.1 (6.8)</td>
<td>N/A</td>
</tr>
<tr>
<td>WCST</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Perseverative errors</td>
<td>26.8 (15.0)</td>
<td>19.7 (10.3)</td>
<td>10.8 (5.6)*</td>
<td>AAB</td>
</tr>
<tr>
<td>Number of categories</td>
<td>3.5 (2.3)</td>
<td>2.4 (2.0)</td>
<td>5.4 (1.5)*</td>
<td>AAB</td>
</tr>
<tr>
<td>Failure to maintain set</td>
<td>1.6 (1.2)</td>
<td>1.3 (1.4)</td>
<td>0.8 (1.0)</td>
<td>N/A</td>
</tr>
<tr>
<td>Trail Making Test</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interference Score</td>
<td>3.0 (1.0)</td>
<td>3.4 (1.6)#</td>
<td>2.85 (1.0)</td>
<td>N/A</td>
</tr>
<tr>
<td>Trails B - Number of errors</td>
<td>1.4 (2.2)</td>
<td>1.1 (1.1)</td>
<td>0.2 (0.5)</td>
<td>N/A</td>
</tr>
<tr>
<td>COWAT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FAS -Total words</td>
<td>28.1 (7.9)</td>
<td>34.1 (13.0)</td>
<td>47.5 (12.6)*</td>
<td>AAB</td>
</tr>
<tr>
<td>Number of repetitions</td>
<td>0.6 (1.4)</td>
<td>0.8 (1.0)</td>
<td>0.8 (1.3)</td>
<td>N/A</td>
</tr>
<tr>
<td>Animals – Total words</td>
<td>16.7 (4.2)</td>
<td>18.4 (5.8)</td>
<td>22.6 (3.8)*</td>
<td>AAB</td>
</tr>
<tr>
<td>Number of repetitions</td>
<td>0.7 (1.0)</td>
<td>1.0 (1.2)</td>
<td>0.3 (0.5)</td>
<td>N/A</td>
</tr>
<tr>
<td>D-KEFS Color-Word</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interference Test</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibition- time (secs)</td>
<td>67.2 (12.9)</td>
<td>61.1 (15.2)</td>
<td>46.5 (10.0)*</td>
<td>AAB</td>
</tr>
<tr>
<td>Inhibition- number of errors</td>
<td>2.2 (2.1)</td>
<td>1.6 (1.4)</td>
<td>0.9 (1.1)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Note. * = p < .05; OHs = Olfactory Hallucinations; AVHs = Auditory Verbal Hallucinations; UPSIT = University of Pennsylvania Smell identification
Table 4. Mean (SD) performance on published and experimental tasks thought to tap into frontal lobe and amygdala associated functions.

<table>
<thead>
<tr>
<th>Comparative Neuropsychological Tasks</th>
<th>OHs (n = 11)</th>
<th>AVHs (n = 10)</th>
<th>Controls (n = 18)</th>
<th>REG-WQ (P &lt; .05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delayed Alternation Task (DAT)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Perseverative Errors</td>
<td>31.3 (22.6)</td>
<td>36.7 (23.3)</td>
<td>18.8 (21.3)</td>
<td>N/A</td>
</tr>
<tr>
<td>Criterion achieved</td>
<td>Yes:6/No:5</td>
<td>Yes:4/No:6</td>
<td>Yes:16/No:2*</td>
<td>-</td>
</tr>
<tr>
<td>Object Alternation Task (OAT)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Perseverative Errors</td>
<td>43.8 (21.9)</td>
<td>23.0 (17.9)</td>
<td>14.8 (22.0)*</td>
<td>ABB</td>
</tr>
<tr>
<td>Criterion achieved</td>
<td>Yes:5/No:6</td>
<td>Yes:7/No:3</td>
<td>Yes:18/No:0*</td>
<td>-</td>
</tr>
<tr>
<td>Faux Pas Task</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d’ score</td>
<td>1.7 (1.5)</td>
<td>3.4 (1.1)</td>
<td>3.7 (1.1)*</td>
<td>ABB</td>
</tr>
<tr>
<td>Minds Eyes Task</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number correct</td>
<td>21.5 (2.9)</td>
<td>22.2 (5.9)</td>
<td>28.3 (3.7)*</td>
<td>AAB</td>
</tr>
</tbody>
</table>

*Note. * = p < .05; OHs = Olfactory Hallucinations; AVHs = Auditory Verbal Hallucinations.
Table 5. Power analysis and estimated sample size required to achieve statistical significance ($\alpha < .05$) and 80% power for differences between clinical groups (OHs versus AVHs).

<table>
<thead>
<tr>
<th>Task</th>
<th>Cohen’s $d$</th>
<th>Power (%)</th>
<th>N required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olfactory Identification (UPSIT)</td>
<td>0.48</td>
<td>13</td>
<td>100</td>
</tr>
<tr>
<td>WCST - % Perseverative Errors</td>
<td>0.55</td>
<td>18</td>
<td>45</td>
</tr>
<tr>
<td>WCST – Number of Categories</td>
<td>0.50</td>
<td>18</td>
<td>64</td>
</tr>
<tr>
<td>COWAT – FAS total words</td>
<td>0.56</td>
<td>18</td>
<td>45</td>
</tr>
<tr>
<td>COWAT – Animals total words</td>
<td>0.33</td>
<td>10</td>
<td>180</td>
</tr>
<tr>
<td>D-KEFS CWIT – Inhibition</td>
<td>0.43</td>
<td>13</td>
<td>100</td>
</tr>
<tr>
<td>CNT-OAT % Perseverative Errors</td>
<td>1.04</td>
<td>56</td>
<td>17</td>
</tr>
<tr>
<td>Faux Pas Task</td>
<td>1.32</td>
<td>71</td>
<td>12</td>
</tr>
<tr>
<td>Minds Eyes Task</td>
<td>0.16</td>
<td>6</td>
<td>400</td>
</tr>
</tbody>
</table>

Emotion Recognition Task

Initial results for the emotion recognition task revealed significant main effects for emotion [Wilkes Lambda, $F (5, 32) = 40.38$, $p < .0005$, eta squared = .86], intensity [Wilkes Lambda, $F (2, 35) = 82.07$, $p < .0005$, eta squared = .82], and group [Wilkes Lambda, $F (2, 36) = 3.45$, $p = .04$, eta squared = .16]. There was a significant emotion x intensity interaction [Wilkes Lambda, $F (10, 27) = 3.32$, $p < .006$, eta squared = .55]. However, the three-way interaction of emotion x intensity x group failed to reach statistical significance ($p = .63$). Once intellectual ability was included in the analyses as a covariate, the main effects of group and intensity and all interaction
effects failed to reach statistical significance (p > .05). The only effect that remained significant was the main effect of emotion [Wilkes Lambda, F (5, 31) = 6.15, p < .0001, eta squared = .50]. This effect was of a moderate size, by Cohen’s (1988) definition.

To further explore this main effect, pairwise comparisons were conducted. Results revealed that the only difference in emotions to reach statistical significance was between happy and disgusted facial expressions (p < .005). Inspection of the means indicated that overall participants were able to correctly identify a larger proportion of faces depicting happy emotions (M = 0.95, sd = 0.07) versus those depicting the emotion of disgust (M = 0.54, sd = 0.22). All other contrasts did not reach statistical significance (p > 0.01). Given the lack of significance between emotions other than happy and disgust, overall means were collapsed across intensity to further explore group patterns across emotion. These are shown in Figure 2. Inspection of the plot reveals a general trend for poorer performance on most negative emotions (eg. angry, fear and disgust) relative to more positive emotions (eg. happy and surprise) across groups.
Figure 2. Proportion of correct responses on the Emotion Recognition Task for each group (OHs vs AVHs vs controls) collapsed across intensity.

Given the amygdala’s involvement in processing fear, it was of particular interest to the present study to explore the results for the expression of fear in greater detail, independently of the other emotions. Therefore, a one way ANOVA was conducted with fear as the between subjects variable and group as the between subjects variable. Results revealed a lack of statistically significant group differences (p > .05). However, comparison of the OH group with the AVH and control groups combined as one group, revealed a tendency for the OH group to experience greater difficulty in correctly identifying fearful faces relative to the other participants combined (t (37), p = 0.06).
**Post-hoc Correlation Analysis**

Given the pattern of obtained results and the particular interest of the present study in tasks thought to tap in the OFC and amygdala functioning, correlation analyses was conducted on the UPSIT, Faux Pas, OAT - % perseverative errors, and the emotion of Fear on the Emotion Recognition Task. This was done to further explore the relationship between these specific tasks for each of the groups. In light of the small sample size of the groups and to normalize group distributions, the data for these tasks were transformed into z-scores. Correlation analysis was subsequently run separately for each group.

For the control group, all correlations were small (ie. < .2), and failed to reach statistical significance (p > .40). The results for the two clinical groups (ie. AVHs and OHs) are shown in Table 6. It can be seen that the only association to reach statistical significance was for the OH group. Based on Cohen’s (1988) tables, this was a strong association between the OAT (% perseverative errors) and the Faux Pas sensitivity score, with an increase in perseverative errors on the OAT associated with increasingly poor performance on the Faux Pas task. While a moderate association was also demonstrated between these same task measures for the AVH group, it failed to reach significance. All other correlations for the AVH group were weak, and non significant (p >.10) However, for the OH group, a moderate association was also found between the Faux Pas sensitivity score and fear recognition; as performance on the Faux Pas task increased so too did participants’ ability to accurately identify fearful facial expressions. While this association failed to reach statistical significance, it did, however, approach significance (p = .07). Another moderate, but non-significant association was also evident within the OH group, with an increase in perseverative errors on the OAT associated with increased difficulty in
accurately identifying fearful facial expressions (p = .18). All other correlations for the OH group were weak and non-significant (p > .4).

Table 6. Matrix of Pearson's correlations for z-scores of OHs (in shaded area) and AVHs on tasks of interest tapping into orbitofrontal cortex and the amygdala.

<table>
<thead>
<tr>
<th>TASKS</th>
<th>UPSIT Score (1)</th>
<th>Faux Pas Task ' Score (2)</th>
<th>CNT – OAT % Perseverative Errors (3)</th>
<th>Emotion Recognition Task - Fear (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>-.31</td>
<td>-.07</td>
<td>.18</td>
</tr>
<tr>
<td>2</td>
<td>.06</td>
<td>-</td>
<td>-.56</td>
<td>-.13</td>
</tr>
<tr>
<td>3</td>
<td>-.26</td>
<td>-.75*</td>
<td>-</td>
<td>.17</td>
</tr>
<tr>
<td>4</td>
<td>.08</td>
<td>.56</td>
<td>-.44</td>
<td>-</td>
</tr>
</tbody>
</table>

*significant at .05 (2-tailed); shaded area = OH Group; unshaded area = AVH Group

4. Discussion

The present study explored aspects of neuropsychological functioning within patients diagnosed with schizophrenia or schizoaffective disorder experiencing recent OHs versus those experiencing AVHs, as well as within healthy controls. Neuropsychological tasks employed in the study assessed various facets of executive functioning, with particular focus placed on standardized and experimental tasks believed to be underpinned by OFC function as well as tasks underpinned by amygdala functioning. The aim was to possibly identify a profile of distinct neuropsychological characteristics particularly within patients that experience OHs.
Findings revealed evidence of a specific association between OHs in schizophrenia (or schizoaffective disorder) and impairments on tasks associated with OFC functioning. Specifically, those patients with schizophrenia who experienced OHs made a greater number of perseverative errors on the OAT task compared to healthy controls and patients experiencing AVH and no lifetime history of OHs. The strength of this relationship was confirmed by its large effect size. Both non-human primate lesion studies and human clinical studies (Freedman, Black, Ebert, & Binns, 1998; Freedman, 1990; Oscar-Berman and Bardenhagen, 1998; Oscar-Berman and Zola-Morgan, 1980a, b) have localized performance on the OAT to the OFC.

Moreover, the current study found that the OH group performed significantly more poorly on a test that has presumed OFC and amygdala involvement, ie. the Faux Pas task. The OH group showed less sensitivity when detecting faux pas on this test. This effect was of a magnitude to have met Cohen’s definition of a large effect size (Cohen, 1988).

In addition to findings suggestive of specific OFC involvement within the OH group, a common thread of executive dysfunction was also revealed across both clinical groups. This was reflected in a relatively equal level of poor performance by the OH and AVHs groups relative to healthy controls on tasks of odour identification (UPSIT), problem solving (WCST- categories; DAT - criterion achieved; OAT-criterion achieved), phonemic fluency (COWAT - FAS) and inhibitory control (D-KEFS CWIT - Inhibition) which is in-keeping with previous evidence of executive difficulties within the schizophrenia population as described by Heinrichs & Zakzanis (1998) and Reichenberg and Harvey (2007).
The lack of significant differences between clinical groups on the UPSIT is entirely consistent with those findings of previous studies conducted by Kopala et al. (1994) and Stedman and Clair (1998), who also found a lack of significant association between odour identification deficits and OHs. Thus odour identification deficits appear to be a general feature of schizophrenia, and not specific to schizophrenia patients experiencing OHs. While the ability to accurately identify different odours has been shown to involve the OFC, it may not be a process that uniquely contributes to the generation of OHs. The presence of anosmia in schizophrenia may purely reflect one aspect of executive dysfunction that incorporates OFC involvement and thus is suggestive of a possible overlapping pathway across different symptom profiles in schizophrenia that does not appear to specifically drive OHs.

While some similarity in results were observed across the WCST, OAT and DAT, some differences were also found which warrant consideration given that the OAT and DAT administration procedures were derived and modified from those of the WCST. On all three tasks, participants in both clinical groups experienced significantly greater difficulty than controls in completing each of these tasks, suggesting that both clinical groups found the task difficult to a relatively similar degree. Differences were, however, found in the pattern of results for the amount of perseverative errors made across tasks. Specifically, as previously discussed, significant differences were found between clinical groups on the OAT task. However, this effect was not found on the WCST or DAT. The disparity in results across tasks may be explained by task sensitivity to differing facets of perseveration, such as those described by Freedman (1990), and by the nature of the OAT with regard to it also tapping into the reward pathways. Recall that the administration of this task involves positive reinforcement via monetary gain (albeit small). In
contrast, feedback on the WCST across trials is given orally and therefore fails to tap into the reward pathway to the extent that the OAT does. Although on the DAT participants also received positive reinforcement via monetary gain, this task does not also require the use of inhibitory control and therefore does not draw as heavily on OFC functioning. The WCST and DAT may also differ from the OAT in placing greater demands on working memory. Therefore the obtained results on the WCST and DAT may be reflective of a greater DLPFC involvement, while the OAT may primarily draw on functioning associated with the OFC. The pattern of results obtained on these tasks therefore support the possibility of distinct OFC involvement in OHs in addition to an overlapping compromise of frontal lobe neural network also seen in patients without OHs.

In contrast to findings on the Faux Pas task, performance by both clinical groups on another ToM task, the Minds Eyes task, was significantly poorer relative to healthy controls, with no significant differences evident between performances of the OH versus AVH groups. Power analysis indicated that for statistical significance between clinical groups to have been obtained on this task, a sample size of at least 400 participants in each clinical group would be required. The striking differences seen in performance by clinical participants on both ToM tasks may possibly be driven by differences in aspects of the cognitive load required to complete each of these tasks. Although both tasks tap into ToM processes, they do so in distinct ways that require different levels of processing. Specifically, the Faux Pas task is a language based task involving not only the attribution of others mental state, but also the ability to make higher order social inferences regarding mental state, via the integration of multiple sources of incoming information. However, as described by Baron-Cohen et al. (2001) the Minds Eyes task taps into only the first stage of processing (ie. attribution of mental state) and does not require participants
to make inferences regarding the social context of that mental state. Thus, given that performance on the Minds Eyes and Faux Pas Tasks requires the utilisation of different levels of higher order ToM processing, and in light of the difference in findings on these tasks in the current study, the pattern of data suggests that, in addition to possible OFC and amygdala involvement, there may be a higher level impairment of cognitive processing, perhaps involving social evaluations, that also contributes to the generation of OHs within the schizophrenia population.

While findings obtained on the Faux Pas task provided potential support for some amygdala involvement in the OH group, results from the Emotion Recognition task provided only limited corroborative evidence. Firstly, no significant group differences were found on the Emotion Recognition task, with healthy controls demonstrating a relatively equal ability to both clinical groups in accurately recognizing facial expressions depicting an array of emotional states. The level of emotional intensity also did not appear to significantly influence the obtained results. Despite the lack of group differences, the pattern of results indicated that participants generally found faces depicting disgusted facial expressions significantly more difficult to accurately identify than faces depicting happy facial expressions. This lack of a clear discrepancy in results between groups on current testing, most likely reflects the limited power within each group cell on this task. However, further inspection of the pattern of obtained means across each emotion revealed a general trend for participants to have greater difficulty in correctly identifying facial expression depicting a negative valance (ie. anger, disgust, fear) relative to a positive valance (happy, surprise). Additional focused exploration targeting the groups’ performance on the emotion of fear, yielded interesting results. Specifically, there was a tendency for the OH group to experience the greater level of difficulty in correctly identifying fearful facial expressions,
when compared to the other two groups. The AVH group experienced less difficulty than the OH group and controls experienced the least level of difficulty overall. This finding, although only suggestive, is consistent with a greater level of amygdala disturbance in the OH group relative to the other groups. However, these preliminary findings require replication utilizing greater sample sizes, to yield more definitive results.

Exploratory correlation analysis on the tasks that yielded significant differences between the OH and AVH groups in the main analyses (ie. UPSIT, Faux PAS, OAT-% perseverative errors and the emotion of fear on the Emotion Recognition task) also provided additional support for stronger relations between OFC and amygdala functioning within clinical participants who experience OHs. Of note, the strongest relationships were found for the OH group between the Faux Pas sensitivity score, the OAT-% perseverative errors and accuracy for recognition of fear. While a correlation of reasonable strength was also found for the AVH group between the Faux Pas sensitivity score and OAT - % perseverative errors, the strength of the relationship between these variables for the OH group was stronger than for the AVH group, and it also reached statistical significance for the OH group. This suggests a stronger association in the levels of functioning utilised to complete these tasks within the OH group, relative to the AVH group. Interestingly, the correlations between the UPSIT and other tasks, was minimal across both clinical groups. Given that the associations were strongest between tasks that utilize higher level cognitive skills, but not on the task (UPSIT) that draws on lower level functions, these findings allude to the possibility that higher level processing deficits may play a particular role in OHs.
In addition to the main findings described above, incidental neuropsychological results were also found that indicated other areas of cognitive dysfunction common to both clinical groups. This was reflected in a significantly slower performance by OHS and AVHs relative to controls on a timed psychomotor task of visual scanning (ie. TMT-A). This finding is in-keeping with processing speed deficits in schizophrenia, reported consistently throughout the literature (Heinrichs & Zakzania, 1998; Reichenberg & Harvey, 2007). A contribution to slowing in processing speed is also likely to be associated with the reported neuroleptic medications taken by the participants with schizophrenia at the time of testing. In addition, semantic fluency was significantly reduced in both clinical groups compared to controls. Given that temporal lobe involvement has been indicated by cerebral fMRI during semantic fluency tasks (Birn et al., 2010) current findings provide support implicating temporal lobe dysfunction in schizophrenia generally.

In conclusion, while the pattern of results obtained from the current study suggest that schizophrenic patients experience deficits associated with both OFC and DLPFC functioning regardless of whether they experience AVHs or OHS, results also provided tentative support for a pattern of functioning which particularly implicates OFC and amygdala neural circuitry involvement (and disruption to their associated higher level cognitive skills) which is specific to OHS. The overall pattern of results obtained in the current study therefore provide preliminary support for Kopala et al's (1994) suggestion of involvement for both OH-specific and overlapping non-specific neural circuits in the generation of OHS. However, additional research further exploring this possibility is clearly warranted. Future research is also likely to benefit
from incorporation of both neuropsychological tests and functional brain imaging to enhance the specificity of obtained results.
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APPENDIX 1

1. RRRLLRRLRL 23. LRRRLRLLLR
2. RRRLLRLLRL 24. LRRLLRLLLLR
3. RRRLLRLRLLL 25. LRRLLRLRRRR
4. RRRLLLRRRL 26. LRRLLRRLLLLR
5. RRRLLLLRLRL 27. LRRLLLRRLLLLR
6. RRLLRLRLLL 28. LRRLLRRRRRL
7. RRLLRLRRRL 29. LRRLLRRRLRRR
8. RRLLRRLLRL 30. LRRLLRRLLRRR
9. RRLLRRLLRL 31. LRRLLRRLLRRR
10. RRLLRLRRLLR 32. LRRLLRRLLRRR
11. RRLLRRLLLRL 33. LRRLLRRLLRRR
12. RRLLRLRRRLR 34. LRRRRLLRRRR
13. RRRLLRRRLRR 35. LRRRRRRRRRR
14. RRRLLRRLLL 36. LRRRRRRRRRR
15. RRRLLRRLLLR 37. LRRRRRRRRRR
16. RRRLLRRRRRL 38. LRRRRRRRRRR
17. RRRRRLLRLR 39. LRRRRRRRRRR
18. RRRRRRRLLR 40. LRRRRRRRRRR
19. RRRRRRRRRR 41. LRRRRRRRRRR
20. RRRRRRRRRR 42. LRRRRRRRRRR
21. RRRRRRRRRR 43. LRRRRRRRRRR
22. RRRRRRRRRR 44. LRRRRRRRRRR

Chance orders of alternate stimuli in visual discrimination tasks (Gellerman, 1933).
Paper Two

Source monitoring and olfactory hallucinations in schizophrenia.

This paper has been prepared for publication and was submitted to the journal, *Psychological Medicine* on 25th July 2011.

**Candidate’s Contribution:** The candidate has played a major role in organising the protocols and setting up the paradigms for this paper. In addition, the candidate has collected all the data, conducted all initial analyses and has acted as senior author.
Abstract

**Aim:** To explore the role of odour specific source monitoring dysfunction in the generation of olfactory hallucinations in schizophrenia. **Methods:** Twenty one clinical participants diagnosed with schizophrenia were recruited into the study. Two clinical groups were formed according to recently experienced modality specific hallucinations: those with olfactory hallucinations (OHs; n = 11) and those with auditory verbal hallucinations (AVHs; n = 10). A group of healthy controls were also recruited (n = 18). All participants completed a novel odour source monitoring task and a more traditional auditory verbal source monitoring task. **Results:** For the odour source monitoring task, a significant group effect was found. Overall the OH group had greater difficulty in correctly discriminating previous actual versus imagined odours than did the AVH group and healthy controls. The OH group generally thought that they had actually smelt the odours more times than they had. For the auditory verbal source monitoring task both the OH and AVH groups experienced greater difficulty than controls in correctly attributing the source (self vs other) from which a set of names of category exemplars were generated in response to cues. Greater difficulty was experienced by both clinical groups (but more so for AVHs) when the category exemplar was of ‘low typicality’. Significantly fewer correct attributions were made by the AVH group when words were either self generated or novel foils. **Conclusions:** Results are interpreted as suggesting that some hallucinations within particular modalities are likely to occur as a consequence of faulty source monitoring within the corresponding modality. Preliminary evidence suggests that olfactory source monitoring difficulties may underlie, or contribute to, the generation of OHs in schizophrenia.
1. Introduction

Hallucinations are multifaceted and phenomenologically diverse experiences that can occur within single or multiple sensory modalities (Laroi & Woodward, 2007). They are a characteristic and predominantly distressing feature of schizophrenia, but are also experienced by a small proportion of individuals within the non-psychiatric population (Ditman & Kuperberg, 2005; Johns & van Os, 2001). The heterogeneous nature of hallucinations has made it difficult for researchers to obtain a precise understanding of the driving mechanisms involved in the generation of hallucinations. Despite this, several reviews of the literature have adopted a cognitive neuropsychiatric approach (Bentall, 1990; Ditman & Kuperberg, 2005; Johnson & Raye, 1981; Laroi & Woodward, 2007) and have attempted to delineate the specific cognitive mechanisms underlying the generation of hallucinations and have generally concluded that disturbance to the process of ‘reality monitoring’ is a well-validated and primary feature common to most cognitive theories of hallucinations.

The concept of reality monitoring (also referred to as source monitoring in the context of hallucinations research) refers to the cognitive processes involved in discriminating between self-generated and externally-generated sources of information. It is a process that relies heavily on the ability to accurately remember, over time, the origin of the source from which the information was perceived to have come (Bentall, 1990; Bre´bion, Ohlsen, Pilowsky & David, 2008; Johnson, Hashtroudi, & Lindsay, 1993). The process is therefore thought to involve the making of judgements which are based on information utilized via memory (Johnson & Raye, 1981).
Research investigating the cognitive processes underlying reality monitoring in non-clinical individuals, has provided some insight into the possible cognitive mechanisms involved. In one such source discrimination study, Johnson, Foley and Leach (1988) investigated the ability of individuals to discriminate between the source (self vs external) of words perceived via the auditory modality versus those that were imagined. Identification of the source of words as internal rather than external was found to be more difficult when imagining words being spoken in another person’s voice compared to imagining words being spoken in one’s own voice. Judgements were further impaired when discriminating between imagined versus perceived words if the words were imagined as being spoken in a voice other than a familiar voice or one’s own voice. These findings were interpreted as being consistent with the idea that reality monitoring is affected by the extent to which sensory aspects of perceived and imagined memories are similar.

Support for the involvement of source monitoring disturbance in hallucinations has primarily come from studies directly attempting to examine this process by using psychiatric patients who experience auditory verbal hallucinations (AVHs). A study of this type was conducted by Bentall, Baker and Havers (1991) who compared psychiatric patients currently experiencing AVHs versus patients with no documented history of hallucinations (ie. psychiatric controls), and healthy controls. The task employed was an auditory verbal reality monitoring task that was based on a procedure used in an earlier source monitoring study conducted by Johnson, Raye, Foley and Foley (1981) and which incorporated a distinction between stimuli that required either high or low cognitive effort to generate spoken words. In Bentall et al’s study, participants were initially required to either generate or listen to names of category exemplars based on either easy
or difficult cues. After a one week time interval, they were provided with a list of words containing those that had been self-generated, those that had been generated and spoken by the experimenter and words that had not been part of the initial test phase. Participants were subsequently required to identify the source from which they thought the words had come. Results failed to find significant group differences in participants’ ability to discriminate between self generated and externally generated words. However, an error analysis indicated that the AVH group attributed more self-generated high cognitive effort words to the experimenter, than did the psychiatric controls and healthy controls. This was thought to provide evidence suggesting that hallucinators demonstrate an external attribution bias when uncertain about the perceived source (interval vs external) from which stimuli came and are unable to use cues of greater self-generated effort when making such attributions.

Furthermore, in a more recent source monitoring study (Bre´bion, et al., 2008) focusing on visual hallucinations, participants were comprised of two hallucinating groups - those experiencing visual hallucinations and those experiencing auditory hallucinations. Participants were required to remember words and pictures in addition to the mode of presentation. Results found that patients experiencing visual hallucinations demonstrated a response bias reflected in the misattribution of spoken stimuli (which was assumed to generate a mental image) to pictures. However, the same effect was not seen in the patients experiencing auditory hallucinations. This pattern of data was interpreted as suggesting that visual hallucinations may be associated with difficulties in differentiating the source of mentally generated visual images from those actually perceived. The results of these previously described studies raises the possibility of an association between sensory specific source monitoring difficulties with the generation of hallucinations within
particular sensory modalities (e.g. auditory verbal source monitoring difficulties for auditory verbal hallucinations and visual source monitoring disturbance for visual hallucinations). However, research that investigates the cognitive processes underlying source monitoring difficulties for hallucinations experienced in other sensory modalities, such as olfactory hallucinations (OHs), appears to be lacking.

In addition to evidence for disrupted cognitive processes involved in source monitoring, support for associated neural mechanisms has also come from research using brain imaging techniques. A recent fMRI study conducted by Kensinger and Schacter (2005) investigated the neural processes thought to influence reality monitoring errors and differences in processing of emotional versus neutral stimuli in healthy adults. Results of their study provided evidence suggesting that the OFC and amygdala are involved in the modulation of reality monitoring accuracy for emotion laden information. Activity in these regions was found to be associated with reduced probability for memory misattributions specifically for emotional stimuli, suggestive of the operation of distinct processes modulating reality monitoring for emotional versus neutral forms of information. This is of particular interest since most hallucinatory experiences, including OHs, tend to involve negative emotional content – e.g. OHs of death smells are not uncommon. Given that the amygdala and the OFC have been implicated both in olfactory processing as well as in reality monitoring concerning emotional stimuli, it is possible that OHs may reflect misattributions of olfactory information, especially with the involvement of an emotional component, to external sources instead of to internal self-generated imaginings or perhaps involuntary memories.
No study to date, has attempted to investigate the role of impaired source monitoring in the
generation of OHs within the schizophrenia population. In light of this, the aim of the current
research is to address this gap in the literature by exploring the possibility of underlying self-
monitoring dysfunction specifically for olfactory information in the production of OHs.
Employment of a novel source discrimination task for olfactory stimuli as well as a more
traditional source discrimination task for auditory verbal stimuli may provide valuable
information about the disrupted cognitive processes that specifically underlie OHs and
hallucinations in general.

It was hypothesized that relative to healthy controls and clinical participants experiencing
auditory verbal hallucinations (AVHs), clinical participants experiencing olfactory hallucinations
(OHs) would demonstrate greater difficulty in discriminating actual versus imagined odours on a
source discrimination task designed specifically for olfactory stimuli. In contrast, it was
hypothesized that the AVH group would experience less difficulty on the task relative to the
participants in the OH group.
2. Methods

2.1. Participants

Ethical clearance for the current project was provided by the relevant ethics committees. Informed written consent was obtained from participants prior to the commencement of testing. Participants for this study were initially recruited from a pool of 51 participants who had previously participated in a telephone interview investigating the phenomenology of olfactory hallucinations in schizophrenia. Further recruitment was later conducted to supplement this pool of participants. All participants underwent testing as described in Paper 1 and the current paper during the same sessions. A total of 39 participants were recruited for this study, which was comprised of 19 males and 20 females. Inclusion criteria for the study included an age range of between 18-60 years, no self-reported history of brain injury (ie. involving loss of consciousness for > 1 hour), no substance abuse within the last 5 years according to DSM-IV criteria, and fluent English. A total of 13 participants were current smokers.

Two groups of clinical participants with schizophrenia or schizoaffective disorder according to the Diagnostic Interview for Psychosis (DIP: Jablensky et al., 1999; Castle et al, 2005) were formed. Allocation of these groups was determined by the self-reported presence or absence of OHs within the last 6 months prior to testing. (NB. All participants reported experiencing hallucinations within multiple sensory modalities. No participants reported experiencing OHs only). One group consisted of participants who reported experiencing recent OHs (n=11) and the other group reported experiencing recent AVHs and no lifetime history of OHs (n=10). A healthy control group was also formed which consisted of participants who had no history of head injury or psychotic symptoms and were recruited from the general community (n=18). Each
group was matched group-wise for age and gender distribution. Demographic and clinical characteristics of participants are presented in Table 2.

2.2. Clinical Diagnosis and Characteristics

All clinical participants underwent an extensive clinical interview. The DIP was administered to obtain socio-demographic data, medical history and confirmation of diagnosis. The Scale for the Assessment of Negative Symptoms of Schizophrenia (SANS: Andreasen, 1984a) and the Scale for the Assessment of Positive Symptoms of Schizophrenia (SAPS: Andreasen, 1984b) were also administered to assess the presence and frequency of psychotic symptoms over the current month, as well as to confirm the presence of AVHs in at least the last 6 months in the AVH group, and OHs in the OH group. The SANS and SAPS were chosen since this measure extensively probes hallucinations within all sensory modalities.

Participants within the clinical groups all met DSM-IV criteria for schizophrenia or schizoaffective disorder and reported having experienced hallucinations within the last one to six months prior to their participation in the study. At the time of testing all clinical participants were taking antipsychotic medication (typical only, n =1; atypical only, n =5; combination of typical & atypical, n =4). Five clinical participants were taking a combination of typical antipsychotics and mood stabilizers and six were taking a combination of atypical antipsychotics and mood stabilizers. There were no differences with regard to medication between the two clinical groups.

Controls underwent a semi-structured interview to obtain demographic information; medical and psychological histories; as well as cigarette, drug and alcohol histories. Participants were included in the control group if there was no evidence of recent drug and alcohol abuse or
presence of psychotic symptoms using the control screen from the Structured Clinical Interview for DSM Disorders (SCID-I; First, Spitzer, Williams & Gibbon, 1997)

2.3. Experimental tasks

The following two experimental tasks (ie. the odour source discrimination task and the auditory verbal source monitoring task) were administered in a counterbalanced order within groups, matched across groups (ie. OH, AVH and healthy controls). For both tasks, there was a two hour delay between each phase of the task (ie. exposure and test). During this delay the participants completed a subset of the neuropsychological tasks described in Paper 1.

2.3 (i) Odour Source Discrimination Task

This task was used to determine the ability of participants to retrospectively discriminate between real and imagined odours.

Stimuli: The stimuli were comprised of eight odours, each contained individually in opaque plastic squeezy bottles. Four were positive odours and four were negative odours [POSITIVE: Coffee (Harris Premium Blend; 10.0g), Vicks (Vapor Rub; 50g), Baby powder (Johnson & Johnson; 50g), Lemon (Lemon Oil; 0.175g); NEGATIVE: Manure (Dynamic Lifter; 5.0g), Rotting fish (Fermented Shrimp Paste; 5.0g), Smelly Feet (Parmesan Cheese; 5.0g & Iso-valeric Acid; 0.02g), Smoke (Guaicol & Thiophene; 0.025g)]. In addition, there was one practice odour, which was Mint (Peppermint Oil; 0.075g). Prior to the commencement of the current study the hedonics of the above odours had been assessed in people within the general population who indicated less preference for the negative set of odours relative to the positive set of odours.
Procedure: At the outset, participants were advised that the task was an “odour imagery test”. They were told that the task involved smelling some real odours as well as imagining some odours.

Training: To familiarize participants with the smells, each of the eight odours were presented one at a time in the same format. To ensure participants made an accurate association between each odour and the name of the odour, participants were given three puffs from the bottle containing the odour at which time they were told the name of the smell (eg. “this is the smell of manure”). After the final puff, participants were required to clear their nostrils of the odour by taking two deep breaths and expelling the air through their nose. Presentation order of the odours was randomised for each subject within each group and yoked between groups (i.e. the first subject in each group were administered the odours in the same presentation order).

Experimental Phase: Participants subsequently received two practice trials. On the first trial, they were told to ‘Close your eyes and sniff this MINT odour’. Three puffs of the odour were administered as the participants sniffed. To present the task as an odour imagery test, they were then asked to rate how intense they thought the odour smelt, using a five point category scale ranging from number 1, representing “very weak” through to number 5 representing “very strong” (ie.1-2-3-4-5 g). Participants then cleared their head of the odour by taking two deep breaths and expelling the air through their nose. The second practice trial followed immediately. However, this time participants were asked to ‘Close your eyes and sniff, and try to imagine the odour of a BANANA’. They subsequently rated how intense the imagined odour had smelt
using the above described category scale. As before, they were asked to clear their head of the imagined smell by taking two deep breaths and expelling the air through their nose. On completion of both practice trials, participants were told ‘Now you will be presented with some real smells and you will also be asked to imagine some as well’. Twenty four experimental trials were then administered. Twelve trials involved the “real” smelling procedure and the other twelve involved the “imagine” smelling procedure. For both procedure types, four pairs of positive/negative items were formed. The four pairs formed the basis for the allocation of odours to conditions (eg. when 3 of the odours were actually smelt, participants were required to imagine 0 odours, when 2 odours were actually smelt, participants were required to imagine 1 odour etc). See Table 1. for the complete configuration of trials. At the end of the 24 trials, participants were asked to rate, overall, how easy or hard it was to imagine the odours using a 5 point category scale (ie. 1-2-3-4-5), with 1 representing “very easy”, 3 representing “average” and 5 representing “very hard”.

Table 1. Configuration of experimental trials for the Odour Imagery Test.

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>REALLY SNIFFED</th>
<th>IMAGINED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odour 1 (positive; eg, baby powder)</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Odour 1 (negative; eg, manure)</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Odour 2 (positive)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Odour 2 (negative)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Odour 3 (positive)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Odour 3 (negative)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Odour 4 (positive)</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Odour 4 (negative)</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>
Test Phase: Participants were told the following: ‘Now you will be given a surprise memory test for the odours you smelled in the odour imagery test earlier today’. One practice trial was initially conducted, where participants were asked to close their eyes and to sniff whilst three puffs of the Mint odour was administered. They were subsequently told ‘In the odour imagery test earlier today, you smelt some odours and imagined others. Some odours were smelt only once, some twice, some three times and some four times. I’d like you to tell me now how many times you think that you actually smelt this odour during the odour imagery test?’ (This count includes the familiarize phase when participants were introduced to the smell of each odour.) Participants responded on a 4 point scale: 1-Smelt it once; 2-Smelt it twice; 3-Smelt it three times; 4-Smelt it four times. Participants were told to give their best guess if they were unsure about their rating. This procedure was repeated for each of the eight target odours, which were presented in a different random order for each participant, but yoked across the three conditions of the design as described above.

2.3 (ii) Auditory Verbal Source Monitoring Task

This task was based on the auditory verbal reality monitoring task described by Bentall, Baker and Havers (1991). It was used to determine the ability of participants to retrospectively discriminate between internally and externally generated spoken words, each generated in response to specific category cues.

Stimuli: The task consisted of 32 items each comprising a category name and letter cue (or cues: refer to Appendix 1.). Sixteen of the items were of low typicality (ie. requiring high cognitive
effort to generate the response - eg. “a musical instrument starting with the letter S - SAXAPHONE”). The other 16 items were of high typicality (ie. requiring low cognitive effort to generate the response - eg. “a type of vehicle starting with the letter C - CAR”). Typicality of category words was determined based on Hampton and Gardiner’s (1983) norms of internal category structure. The surprise test phase consisted of an additional eight “new” words, four of which were selected from low typical category exemplars and the other four of which were high typical. The presentation order of the words was in a fixed random order which was consistent across testing groups.

Procedure: At the outset, participants were advised that the task was about category names and examples of categories, and that it involved both thinking of, and listening to, words that met a specific criteria.

Exposure Phase: Participants were instructed that for each item of the task, the experimenter would provide a category with a letter cue (or cues) for a word. They would subsequently be required to either generate (ie think of and say aloud) a word that fitted the criteria or the experimenter would generate the word that fitted the criteria (eg. as per Appendix 1.). On trials that the experimenter generated the word, the participant would be required to repeat the word aloud. Participants subsequently underwent four practice trials to ensure understanding of task instructions, prior to commencement of the experimental trials.

Test Phase: In the test phase of the experiment, a total of 40 words were presented. Thirty-two of the words had been generated in the initial phase of testing plus an additional eight new words
that had not been presented in the exposure phase, so had subsequently not been previously heard. Participants were told the following: “You will now be given a surprise memory test for the words that were said during the Category Naming Test earlier today. In the Category Naming Test you were given a category and a letter cue and then either I told you a word that met the criteria, or you produced the word. In the memory test I will just say a word. If that word is one that you produced I want you to say ‘mine’. If the word was one that I said I want you to say ‘yours’. There will also be some words that were not said during the category naming test to which I want you to say ‘new’”. The words were subsequently read aloud in a pre-allocated random order and responses of “mine”, “yours” or “new” were recorded for each item.

3. Data Analysis Plan
All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS), version 17.0.

Preliminary analysis: Preliminary inspection of the data was conducted to assess the underlying assumptions required for parametric analysis. The assumptions of normality and equality of variance were satisfied for all variables. However, the assumption of sphericity, was found not to be satisfied on some variables. Therefore, on those variables where sphericity was found to be violated, the degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity.
**Primary data analysis:** Repeated measures analysis of variance (ANOVA) was run on each task. Alpha was set at a level of .05 for each task. Given that there were significant group differences between groups for intellectual ability (refer to Paper 1) \[F (2, 36) = 5.46, p = .008\], all analyses were initially run with estimated IQ) entered as a covariate. Results indicated that intellectual ability had no significant effect on any of the variables entered in the analyses (all \(p > .1\)). Therefore, the analyses were re-run for each task without the inclusion of the intellectual ability variable.

**Post Hoc Comparisons:** Post-hoc comparisons were conducted using the Ryan-Einot-Gabriel-Welsch-Q (REG-WQ) procedure due to its sensitivity in detecting significant differences between group means that may otherwise go undetected with other types of multiple comparison procedures. This procedure is reported to have good power to control for family-wise error in data that is not normally distributed (Cribbie & Keselman, 2003; Howell, 1997). Effects were judged as significant at a level of \(p < 0.05\), so that any potential effects could be identified, in light of the small sample sizes.

4. **Results**

4.1. **Odour source discrimination task**

Group (OHs vs AVHs vs Controls) was the between subjects variable and number of times actually smelt (1 vs 2 vs 3 vs 4) and valence (positive vs negative) were the within subjects variables. The dependant variable was the rating score of the number of times participants thought they smelt each odour.
Group mean scores for the number of times participants thought they smelt the odours across each level that the odours were actually smelt are presented on Figure 1. No effects involving valence were significant. There was a statistically significant main effect for the number of times participants thought they had smelt the odours [Wilkes Lambda, $F(3, 34) = 5.22$, $p = .005$, eta squared = .32]. Trend analysis revealed a significant linear relationship ($p = .001$) for this variable, with the number of times that participants thought they had actually smelt each odour increasing as the number of times they had actually smelt the odour increased. There was also a significant main effect of group [$F(2, 36) = 4.50$, $p = .018$, eta squared = .20]. Post-hoc comparisons using REG-WQ indicated that the AVH and control group formed one homogenous subset ($p < .05$) and the OH group another. Overall, the OH group reported experiencing all of the odours ($M = 3.1$) more frequently than the other two groups (both $M = 2.5$). The interaction of times thought smelt x group failed to reach significance [Wilkes Lambda, $F(6, 68) = 1.43$, $p = .22$].

![Figure 1](image_url)

**Figure 1.** Group mean scores of number of times participants thought the odours were smelt across each level that the odours were actually smelt.
In light of the obtained results on this task, it was of interest to explore whether any potential relationship exists in the performance of the OH group on this task with their performance on three key tasks tapping into aspects of higher level (executive) functioning, from Paper 1 (ie. University of Pennsylvania Smell Identification Test (UPSIT), Faux Pas Task (d' Score) and Object Alternation Task (% Perseverative Errors)). Therefore, Pearson’s correlation analyses was conducted on the z scores of the three task scores from Paper 1 with the mean times the real odours were actually smelt (ie. across 1, 2, 3, & 4). Results revealed that there was no significant relationship between the mean number of times the odours were thought to have been smelt and any of the above three task scores from Paper 1 (all p>.05).

**Intensity Ratings**

In terms of intensity ratings, there was no significant group differences in the estimated intensity of the real odours smelt (F (2,36) = .06, p = .95) or the odours that participants were asked to imagine (F (2,36) = .36, p = .70). There was, however, a significant group effect for the level of difficulty participants found in imagining the odours (F (2,36) = 3.40, p = .04). Post hoc comparisons using REG-WQ indicated that the OH group found it significantly easier to imagine odours (mean rating = 2.5) relative to the AVH (mean rating = 3.6) and control (mean rating = 3.7) groups.
4.2. Auditory verbal source monitoring task

Group (OHs vs AVHs vs Controls) was the between subjects variable. Within subjects variables were typicality (high vs low) and source (self vs given vs new). The dependant variable was the proportion of correct attributions made, excluding those self-generated trials for which a participant failed to produce a response.

Group mean scores for the proportion of words correctly attributed to each source for high and low typical categories are presented in Table 2.

Table 2. Mean proportion of words correctly attributed to each source for high typical (ie. low effort) and low typical (ie. high effort) exemplars of the categories.

<table>
<thead>
<tr>
<th>Typicality</th>
<th>Source</th>
<th>OH</th>
<th>AVH</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self</td>
<td></td>
<td>0.6 (0.2)</td>
<td>0.6 (0.2)</td>
<td>0.9 (0.1)</td>
</tr>
<tr>
<td>Given</td>
<td></td>
<td>0.6 (0.3)</td>
<td>0.5 (0.3)</td>
<td>0.8 (0.2)</td>
</tr>
<tr>
<td>New</td>
<td></td>
<td>0.8 (0.4)</td>
<td>0.5 (0.3)</td>
<td>0.8 (0.3)</td>
</tr>
<tr>
<td><strong>High</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self</td>
<td></td>
<td>0.8 (0.3)</td>
<td>0.7 (0.2)</td>
<td>0.8 (0.2)</td>
</tr>
<tr>
<td>Given</td>
<td></td>
<td>0.6 (0.3)</td>
<td>0.4 (0.3)</td>
<td>0.7 (0.2)</td>
</tr>
<tr>
<td>New</td>
<td></td>
<td>0.7 (0.3)</td>
<td>0.7 (0.3)</td>
<td>0.7 (0.4)</td>
</tr>
</tbody>
</table>
There was a statistically significant main effect of group [Wilkes Lambda, \( F(2, 36) = 11.75, p < .0005, \) eta squared = .40]. However, the main effects of source [Greenhouse-Geisser, \( F(1.57, 56.5) = 3.08, p = .65 \) and typicality [Wilkes Lambda, \( F(1, 36) = .003, p = .96 \) failed to reach significance. In terms of interaction effects, the two-way source x group interaction was not significant \( (p = .88) \). However, there were significant two way interactions found for typicality x group [Wilkes Lambda, \( F(2, 36) = 7.60, p = .002, \) eta squared = .30] and typicality x source [Wilkes Lambda, \( F(2, 35) = 3.95, p = .028, \) eta squared = .18]. These were incorporated into a highly significant three way interaction of typicality x source x group [Wilkes Lambda, \( F(2, 36) = 4.19, p = .004, \) eta squared = .19]. To further explore the three-way interaction separate analyses were run for each source, the results of which are displayed in Figures 2, 3 and 4.

![Figure 2. Proportion of correctly attributed scores for words that were self-generated by participants.](image-url)
As seen in Figure 2, when participants were required to self-generate or “think” of words to specific categories, there was an overall main effect of group [Wilkes Lambda, F (2, 36) = 8.96, p = .001, eta squared = .33]. Post-hoc comparisons using REG-WQ revealed a significant difference between the clinical groups (ie. OHs and AVHs) relative to controls (p < .05) with the clinical groups experiencing significantly greater difficulty in correctly attributing words than did the controls. There was no significant difference between the OH and AVH groups (p > .05). This group effect was incorporated into a significant interaction of typicality x group [Wilkes Lambda, F (2, 36) = 10.51, p < .0005, eta squared = .37]. To explore this interaction, each type of typicality (ie. high and low) was entered into the analysis separately. For high typicality words (ie. when less cognitive effort was required to generate them), there was no significant differences between groups (p = .30). There was, however, a significant group effect for low typicality words (ie. when greater cognitive effort was required to generate them). Trend analysis revealed a significant linear trend (p < .0005) with the AVH group (M = .5) making fewer correct attributions than the OH group (M = .6), who made fewer correct attributions that did the control group (M = .9). Further comparisons using REG-WQ indicated that the increased difficulty of the clinical groups (ie. OH and AVH) was significantly greater than that experienced by the controls (p < .05). It is also of note that controls showed a pattern of superior performance for low typical compared to high typical exemplars (ie, for high effort vs low effort), whereas patients showed the reverse pattern.

When participants were provided with words that met the specific categories (ie. “listen”), there was a significant main effect of typicality [Wilkes Lambda, F (1, 36) = 4.42, p = .043, eta squared
Inspection of Figure 3 revealed that more low typicality words were attributed correctly to the experimenter (mean = .7) relative to high typical words (mean = .6). There was also a significant main effect of group [Wilkes Lambda, F (2, 36) = 5.39, p < .009, eta squared = .23]. Trend analysis revealed a significant linear effect (p = .002) with the AVH group attributing fewer words correctly (M = .5) than the OH group (M = .6), who attributed less than controls (M = .7). Post-hoc comparisons using REG-WQ, indicated that the AVH group experienced significantly greater difficulty in correctly attributing words relative to the control group (p < .05). While the OH group also experienced greater difficulty than controls, the difference failed to reach statistical significance (p > .05). The OH group also experienced less difficulty than the AVH group. However, the difference again failed to be of a significant magnitude (p > .05). In terms of the interaction effect for typicality x group, it failed to reach statistical significance (p = .27).

Figure 3. Proportion of correctly attributed scores for words that were given to participants.
For new words the main effects of typicality and group failed to reach significance (p > .09). However, there was a significant typicality x group interaction effect [Wilkes Lambda, F (2, 36) = 5.47, p < .008, eta squared = .23]. Inspection of Figure 4. suggests that when the words were of low typicality for a category (and these were typically less common words), the AVH group experienced significantly greater difficulty at correctly attributing the words as being new and attributed them instead to the test phase, than the OH and control groups. However, when the words were of a high typical category, the AVH group’s ability to correctly attribute the words was better and at a relatively consistent level to the OH group. Controls appeared generally able to correctly attribute new words, whether of low or high typicality, than both clinical groups.

![Figure 4. Proportion of correctly attributed "new" words.](image)

Figure 4. Proportion of correctly attributed "new" words.
Error Analysis

Further analysis was conducted to examine the pattern of misattributions made by participants, the results of which are shown in Figure 5. There were no significant group differences [Wilkes Lambda, F(2,36) = .75, p = .48] in the proportion of self-generated words that were incorrectly attributed to the experimenter. There was, however, a significant main effect for typicality [Wilkes Lambda, F (1, 36) = 6.12, p = .018, eta squared = .15]. Trend analysis revealed a linear trend with all participants demonstrating more errors on high typicality (ie. low cognitive effort) words than on low typicality (ie. high cognitive effort) words. The interaction of typicality x group was not significant [p = .80].

Self-Generated Words Attributed to Experimenter as Source

![Graph showing mean proportion of self-generated items incorrectly attributed to the experimenter as source.]

Figure 5. Mean proportion of self-generated items incorrectly attributed to the experimenter as source.

5. Discussion
The present study explored the role of source monitoring difficulties in the generation of OHs in schizophrenia. This was done by using a novel odour source monitoring task in addition to a more traditional auditory verbal source monitoring task, which had previously been described in a study conducted by Bentall, Baker and Havers (1991). The aim was to attempt to identify a pattern of sensory specific source monitoring dysfunction within patients diagnosed with schizophrenia and who experience OHs, in comparison to those who experience auditory verbal hallucinations (and no OHs), and healthy controls. In doing so, it was anticipated that a contribution to the understanding of the underlying cognitive processes involved in less prevalent modality specific hallucinations such as OHs would be made.

Overall, the study yielded an interesting array of findings. Firstly, results of the odour source monitoring task revealed preliminary evidence suggestive of a sensory specific source monitoring bias for patients with schizophrenia who experience OHs. This was reflected in a tendency for OH participants to overestimate the number of times they thought they had actually previously smelt an assortment of odours (rather than having imagined smelling them), relative to patients with schizophrenia who had no history of OH experiences (but experienced AVHs) and healthy controls. A pattern of significantly greater difficulty by the OH participants in accurately recalling the source (actual versus imagined) from which the odours originally came alludes to source monitoring difficulties that are specific within the olfactory modality for patients who experience OHs. In addition, relative to controls and AVHs, those participants who experienced OHs also reported less difficulty in attempting to imagine odours. This may also represent a cognitive vulnerability that contributes to the generation of OHs.
Further tentative evidence of sensory specific source monitoring disturbance was provided from the results of the auditory verbal source monitoring task. Overall, the AVH group experienced greater difficulty than the OH and control groups in correctly attributing the source from which words had been generated in response to specific category cues, regardless of whether the source had been self-generated, or provided by the experimenter. However, this discrimination difficulty appeared to be intensified when the words were originally self generated or when the words had not been previously heard before. In addition to this, both clinical groups experienced more difficulty in accurately discriminating source when greater cognitive effort was required to self-generate the words. This specific pattern of findings is in contrast to those found by Bentall, Baker and Havers (1991), who found that source discriminability was generally more accurate in individuals experiencing auditory hallucinations when items required greater cognitive effort (ie. low typicality), which was the pattern also seen for healthy controls when attributing the source of self-generated words in the current study. However, these distinct patterns may be reflective of differences in the samples, specifically differences in the symptomology experiences by participants in the hallucinations group of each study. Participants in the Bentall, Baker and Havers’ study who experienced hallucinations were reported to be experiencing auditory hallucinations which were not reported to necessarily have been of the auditory verbal subtype, whereas the current study used participants particularly experiencing auditory verbal hallucinations. It is also possible that the two patient samples differed in other ways – for example, the current patient sample were fairly chronic and may have had greater deficits of semantic memory, although this speculation cannot be more directly assessed.
In the current study, the extent of discrimination disturbance on the task was not as great for the OH group as the AVHs, with their overall ability to accurately identify the source from which the words were generated, being lower than for the control group. These results suggest that although both clinical groups tended to experience source monitoring difficulty for verbally generated information, patients experiencing AVHs consistently had greater difficulty than those patients experiencing OHs. Overall, these findings provide general support for Bentall, Baker and Havers’ (1991) assertion of sensory specific (ie. verbal) source monitoring difficulties in patients experiencing AVHs.

It should be noted that non-sensory differences existed between the two source monitoring tasks employed which requires consideration in light of the results obtained. Specifically, the odour source monitoring task contained odours that were emotionally valanced (ie. positive vs negative), and therefore had the potential to be emotionally salient to participants. In addition, participants had previously been exposed to all odours prior to the test phase of the task. In contrast, the words used in the auditory source monitoring task were emotionally neutral and the stimuli presented in the test phase of the task incorporated items that participants had previously been exposed to in addition to new items. While the possibility exists that the inclusion of emotionally salient odour stimuli on the odour source monitoring task and the inclusion of new items in the test phase of the auditory verbal source monitoring task might have differentially influenced performances on these tasks, these task differences are unlikely to fully account for the particular patterns of group differences for each sensory specific task.
In light of this, the combined pattern of data obtained from both the odour source monitoring task and the auditory source monitoring task of the present study could be interpreted as suggesting that hallucinations within particular modalities are likely to occur as a consequence of faulty source monitoring within the corresponding modality. Given that Brébion, et al. (2008) found evidence suggestive of source monitoring disturbance within the visual modality in patients experiencing visual hallucinations, and Bentall, Baker and Havers (1991) found evidence suggestive of verbal source monitoring difficulties in patients experiencing auditory verbal hallucinations, it is possible that olfactory source monitoring difficulties may also underlie, or contribute to, the generation of OHs in schizophrenia.

The present study provided some positive results for a defective source monitoring system in OHs. It appears that difficulty in distinguishing real from imagined odours, particularly when participants believe they have smelt the odours multiple times previously, may act as a mechanism for the generation of OHs. It is possible that this may also be facilitated in those individuals who experience less difficulty in being able to bring odours to mind. This, together with the findings from Paper 1 of disturbance to the neuronal circuitry involving the orbitofrontal cortex and amygdala in OHs, suggests that the generation of OHs may be driven by a combination of specific neuronal and source monitoring dysfunction. These findings have implications for the treatment of OHs, suggesting that a cognitive behavioural approach targeting source monitoring functioning may be of benefit in the management of these symptoms.

Some limitations of this research exist which include the relatively small sample size within each clinical group due to recruitment constraints associated with the specific inclusion criteria of the
study. Additional research is therefore warranted to try to validate the current findings. It may also be prudent for future studies to include a non-hallucinating clinical group to further explore whether monitoring of self-generated effort is impaired in all patients who experience hallucinations, or in schizophrenia generally, given that a non-hallucinating clinical group was not included in the current study. Despite this, however, the data obtained highlights the seemingly important role of sensory specific source monitoring dysfunction in the generation of hallucinations generally. It is also the first known study to extend previous source monitoring research in an attempt to explore the potential odour specific source monitoring dysfunction in the generation of OHs.
References

Andreasen, N. G., (1984a). Scale for the assessment of negative symptoms (SANS). University of Iowa, Iowa City, IA.

Andreasen, N. G., (1984b). Scale for the assessment of positive symptoms (SAPS). University of Iowa, Iowa City, IA.


## Appendix 1
Auditory Verbal Source Monitoring Task Stimulus List

<table>
<thead>
<tr>
<th>Category and Letter Cue</th>
<th>Frequency or Typicality</th>
</tr>
</thead>
<tbody>
<tr>
<td>A type of relative – starting with &quot;F&quot;</td>
<td>high</td>
</tr>
<tr>
<td>An Australian city – starting with &quot;S&quot;</td>
<td>high</td>
</tr>
<tr>
<td>A piece of furniture – starting with &quot;D&quot; ending with &quot;K&quot;</td>
<td>high</td>
</tr>
<tr>
<td>A non-alcoholic drink – starting with &quot;M&quot;</td>
<td>high</td>
</tr>
<tr>
<td>A piece of furniture – starting with &quot;C&quot;</td>
<td>high</td>
</tr>
<tr>
<td>A type of vehicle – starting with &quot;C&quot;</td>
<td>high</td>
</tr>
<tr>
<td>A type of precious gem – starting with &quot;D&quot;</td>
<td>high</td>
</tr>
<tr>
<td>A type of footwear – starting with &quot;B&quot;</td>
<td>high</td>
</tr>
<tr>
<td>A type of clothing – starting with &quot;S&quot;</td>
<td>high</td>
</tr>
<tr>
<td>A part of a building – starting with &quot;D&quot;</td>
<td>high</td>
</tr>
<tr>
<td>A type of reading material – starting with &quot;B&quot;</td>
<td>high</td>
</tr>
<tr>
<td>A four-footed animal – starting with &quot;H&quot;</td>
<td>high</td>
</tr>
<tr>
<td>A measure of distance – starting with &quot;M&quot;</td>
<td>high</td>
</tr>
<tr>
<td>A type of vegetable – starting with &quot;C&quot;</td>
<td>high</td>
</tr>
<tr>
<td>A type of insect – starting with &quot;A&quot;</td>
<td>high</td>
</tr>
<tr>
<td>A flower type – starting with &quot;R&quot;</td>
<td>high</td>
</tr>
<tr>
<td>A country – starting with &quot;J&quot;</td>
<td>low</td>
</tr>
<tr>
<td>A musical instrument – starting with &quot;S&quot;</td>
<td>low</td>
</tr>
<tr>
<td>A colour – starting with &quot;T&quot;</td>
<td>low</td>
</tr>
<tr>
<td>An alcoholic drink – starting with &quot;BR&quot;</td>
<td>low</td>
</tr>
<tr>
<td>A type of insect – starting with &quot;B&quot; ending with &quot;Y&quot;</td>
<td>low</td>
</tr>
<tr>
<td>A type of tree – starting with &quot;M&quot;</td>
<td>low</td>
</tr>
<tr>
<td>A type of carpenter's tool – starting with &quot;C&quot;</td>
<td>low</td>
</tr>
<tr>
<td>A flower type – starting with &quot;T&quot;</td>
<td>low</td>
</tr>
<tr>
<td>A body part – starting with &quot;T&quot;</td>
<td>low</td>
</tr>
<tr>
<td>A type of sport – starting with &quot;V&quot;</td>
<td>low</td>
</tr>
<tr>
<td>A type of bird – starting with &quot;O&quot;</td>
<td>low</td>
</tr>
<tr>
<td>A country – starting with &quot;N&quot;</td>
<td>low</td>
</tr>
<tr>
<td>A weather phenomenon – starting with &quot;L&quot;</td>
<td>low</td>
</tr>
<tr>
<td>A colour – starting with &quot;V&quot;</td>
<td>low</td>
</tr>
<tr>
<td>A type of fruit – starting with &quot;R&quot;</td>
<td>low</td>
</tr>
<tr>
<td>A type of food flavouring – starting with &quot;M&quot;</td>
<td>low</td>
</tr>
<tr>
<td>cat</td>
<td>high</td>
</tr>
<tr>
<td>australia</td>
<td>high</td>
</tr>
<tr>
<td>gold</td>
<td>low</td>
</tr>
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<td>jade</td>
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</tr>
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<td>nylon</td>
<td>low</td>
</tr>
<tr>
<td>salt</td>
<td>high</td>
</tr>
<tr>
<td>apple</td>
<td>high</td>
</tr>
</tbody>
</table>
1. General Discussion

Hallucinations of smell, or olfactory hallucinations (OHs), are less prevalent than other hallucinations in schizophrenia, including the most common, auditory hallucinations, which have been the focus of most research to date on hallucinations in schizophrenia. Consequently these symptoms are currently under-researched and poorly understood. This is a regrettable gap in the literature since OHs are present in a significant minority of people with schizophrenia, with past-month prevalence rates estimated at between 13 and 17% (Langdon et al., 2011). Moreover, these symptoms may be indicative of aspects of the underlying disease process(es), with unusual olfactory experiences in non-clinical individuals being predictive of the later development of schizophrenia (Kwapil, et al., 1996). Research also suggests that OHs may be of particular clinical significance to those individuals who have these experiences. For example, many OHs have an unpleasant negative quality (Kopala et al, 1994; Meats, 1988; Stevenson et al., 2010), are associated with depressed mood and self-deprecation, and may fuel delusions of reference and/or control (Langdon et al., 2011). The neural and cognitive underpinning of OHs are also in question with no evidence to suggest that these symptoms associate with the olfactory identification deficits that are also seen in schizophrenia (Kopala et al., 1994; Stedman & Clair, 1998) and little direct support that they might be explained by the current models of other hallucinations in schizophrenia; for example, questions have been raised as to whether OHs might stem from intrusions of involuntary olfactory images or memories, which are then misattributed to external reality (Stevenson et al., 2010).
The primary aim of this research project was to address the current gap in knowledge of OHs, specifically within the schizophrenia population. This aim was addressed by employing a symptom-focused approach that combined clinical neuropsychological and cognitive neuropsychological perspectives to inform the understanding of the neural, neuropsychological and cognitive causes of OHs. Patients diagnosed with schizophrenia or schizoaffective disorder, were recruited to take part in the research program. Two clinical groups and a group of healthy controls were formed for comparison. One clinical group comprised patients who had recently experienced OHs and the other comprised patients who had recently experienced auditory verbal hallucinations (AVHs), but no lifetime history of OHs. Overall, it was anticipated that the findings of this research would assist in advancing knowledge of the mechanisms involved in the generation of OHs, and hallucinations generally, addressing the afore-mentioned current gap in the literature.

1.1. Neuropsychological characteristics of OHs in schizophrenia.

The first paper examined the neuropsychological characteristics associated specifically with OHs in schizophrenia, with a view to informing understanding of the related neuroanatomical structures (both cortical and sub-cortical) and neural connections. Tasks employed in the study were selected based on neuropsychological functions thought to be associated with the areas of neural circuitry involved with the olfactory system, in particular, the orbitofrontal cortex (OFC) and amygdala. It was anticipated that clinical participants experiencing OHs would demonstrate greater deficits on tasks reflecting OFC and amygdala functioning, compared to clinical participants experiencing AVHs and healthy controls.
The pattern of results obtained was generally consistent with previous evidence of global executive deficits in people with schizophrenia, with and without OHs. Both clinical groups, those experiencing OHs and those experiencing AVHs, experienced significantly greater difficulty relative to healthy controls on the smell identification task (UPSIT), consistent with a number of previous studies that show olfactory identification deficits are not specifically associated with OHs (Kopala, et al., 1994; Stedman and Clair, 1998). Both clinical groups also showed notable executive deficits on a number of standard neuropsychological tasks, including the D-KEFS Colour Word Interference Test (D-KEFS CWIT), the Wisconsin Card Sorting Test (WCST) and the Controlled Oral Word Association Test (COWAT).

With regard to the comparative neuropsychological tasks (CNT), which was developed to tease apart the contribution of the OFC and the dorsolateral prefrontal cortex (DLPFC), there was evidence of both OFC and DLPFC dysfunction regardless of whether patients experienced AVHs or OHs, also consistent with previous findings (Seidman, Oscar-Berman, Kalinowski, Ajilore, et al. (1995). In addition, evidence of OFC functioning specific to OHs was also found on the OAT. However, results using more experimentally based tasks, such as the Faux Pas Task and the Emotion Recognition Task, also provided tentative support for a pattern of dysfunction which particularly implicates OFC and amygdala neural circuitry (and disruption to their associated higher level neuropsychological skills) which is specific to OHs.

The overall pattern of results from the first paper is thus generally consistent with Kopala et al's (1994) suggestion of involvement of both OH specific and overlapping non-specific neural circuits in the generation of OHs.
1.2. **Source monitoring dysfunction in OHs.**

The focus of the second paper was to test a ‘defective source-monitoring’ cognitive model of the generation of OHs in schizophrenia. Using the same groups of participants, who were recruited for the first paper, the main aim of this second paper was to investigate the role of impaired source monitoring of imagined versus real odours in the generation of OHs. This was done by designing a novel odour source discrimination task in which participants smelled or imagined a set of negative and positive odours. An auditory-verbal reality monitoring task, which was based on previous research (Bentall, Baker and Havers, 1991), was also used to further explore modality specific source monitoring dysfunction in different groups of hallucinators. It was anticipated that, when compared to clinical participants experiencing AVHs and healthy controls, clinical participants experiencing OHs would demonstrate an impaired performance on the task of source discrimination and reality monitoring, specific to olfactory processing. In contrast, it was hypothesized that the AVH group would experience less difficulty on the task relative to the participants in the OH group.

Results of the odour source monitoring task revealed preliminary evidence suggestive of a sensory specific source monitoring bias for patients with schizophrenia who experience OHs. This was reflected in a tendency for OH participants to overestimate the number of times they thought they had actually previously smelt an assortment of odours (rather than having imagined smelling them), relative to patients with schizophrenia who had no history of OH experiences (but experienced AVHs) and healthy controls. This effect was no more marked for negative compared to positive odours, however. In addition, relative to controls and AVHs, those participants who experienced OHs also reported less difficulty in attempting to imagine the
odours, suggesting a possible contribution from olfactory imagery in the generation of OHs, along with a source-monitoring difficulty in recalling whether smells were actual versus imagined. This set of findings, combined with the absence of a similar difficulty with monitoring the source of auditory-verbal material (see below), alluded to source monitoring difficulties that are specific within the olfactory modality for patients who experience OHs.

Results obtained from the auditory-verbal source monitoring task provided further evidence of sensory specific source monitoring disturbance in different groups of hallucinating patients. The AVH group was found to experience greater difficulty than the OH and control groups in correctly attributing the source from which words had been generated (self or other or new) in response to specific category cues. However, this discrimination difficulty appeared to be intensified when the words were originally self-generated or when the words had not been previously heard before.

In addition to this, both clinical groups experienced more difficulty in accurately discriminating source when greater cognitive effort was required to self-generate the words. While the specific pattern of findings obtained in the current research varied in specificity to those found by Bentall, et al. (1991), the differences in patterns obtained most likely reflects differences in the samples, particularly differences in the symptomology of participants in the hallucinations group of each study. The overall results of the current study were, however, consistent with the general conclusion drawn by Bentall, et al. (1991) of a source monitoring deficit for auditory-verbal information in patients that experience auditory hallucinations.
The combined pattern of data obtained from both the odour source monitoring task and the auditory source monitoring task in the second paper could be interpreted as suggesting that hallucinations within particular modalities are likely to occur as a consequence of faulty source monitoring within the corresponding modality. These results accord with previous evidence of source monitoring disturbance within the visual modality in patients experiencing visual hallucinations (Bre´bion, et al., 2008), and within the auditory-verbal modality in patients experiencing auditory hallucinations (Bentall, et al., 1991). Thus, it is similarly possible that olfactory source monitoring difficulties specifically contribute to the generation of OHs in schizophrenia.

1.3. Overall conclusion

The second paper provides some significant and interesting results that support the proposal for a defective source monitoring system that contributes to the generation of OHs. It appears that difficulty in distinguishing real from imagined odours, particularly when participants mistakenly believe they have really smelled odours much more frequently than they truly have, may act as a mechanism that contributes to the generation of OHs. It is also possible that OHs may be further facilitated in those individuals who experience less difficulty in being able to bring odours to mind.

This set of findings from the second paper, complement the findings from the first paper which suggest disturbance to the neuronal circuitry involving the OFC and amygdala, specifically in people who experience OHs. Thus the generation of OHs may be underpinned by a combination of specific neuronal and related source monitoring dysfunction. These findings therefore have
implications for the treatment of OHs. The pattern of cognitive dysfunction demonstrated by individuals with schizophrenia who experience OHs, highlights a vulnerability to experience source monitoring dysfunction which is specific to the olfactory modality. The manifestation of this is also likely to vary according to environmental triggers. As such, the use of a cognitive behavioural therapy (CBT) approach that attempts to identify such triggers and which targets interventions focused on source monitoring functioning specific to olfaction, may be of benefit in the management of these symptoms.

It is acknowledged that the relatively small sample size within each clinical group represents a limitation of the current research project. Nonetheless, some significant results were obtained, reflecting noteworthy features of the design of the research. One such strength was the recruitment of a clinical sample who reported having recently experienced OHs, increasing the likelihood that results tapped into “online processing” contributing to OHs. An additional strength of the research program was the combination of both clinical neuropsychological and cognitive neuropsychological approaches to assist with the elucidation of both the possible aberrant neural structures and connections involved in OHs in addition to the cognitive processes that may be disrupted by those aberrant neural mechanisms. This has allowed for the provision of a more multi-layered understanding of the possible processes contributing to the generation of OHs.

Given the preliminary nature of the current research program, additional research is clearly warranted to replicate and validate the current findings. It may also be prudent for future studies in this line of research to also include a non-hallucinating clinical group to further explore
whether monitoring of self-generated effort is impaired in all hallucinating patients with schizophrenia, or in schizophrenia more generally. Despite this, however, the data obtained highlights the seemingly important role of sensory specific source monitoring dysfunction in the generation of hallucinations in different modalities. Results also provide the very first extension of previous research on source monitoring in hallucinations in an attempt to explore the potential role of odour specific source monitoring dysfunction in OHs. In light of the other significant results obtained in this current research, it is also likely to be of benefit to future research on OHs to incorporate both neuropsychological tests as well as functional brain imaging to enhance the specificity of results obtained. Of particular interest would be the implementation of the above suggestions in other modalities in which hallucinations occur less frequently, such as tactile and gustatory hallucinations to explore whether similar modality specific neuroanatomical and source monitoring disturbances occur.
References


