7 _____

OLFACTION AND HIGHER COGNITIVE FUNCTIONS

MIKISHA DOOP, CHRISTINE MOHR, BRADLEY FOLLEY, WARRICK BREWER AND SOHEE PARK

> The scent was so heavenly fine that tears welled into Baldini's eyes. He did not have to test it, he simply stood at the table in front of the mixing bottle and breathed. The perfume was glorious. It was to Amour and Psyche as a symphony is to the scratching of a lonely violin. And it was more. Baldini closed his eyes and watched as the most sublime memories were awakened within him. He saw himself as a young man walking through the evening gardens of Naples; he saw himself lying in the arms of a woman with dark curly hair and saw the silhouette of a bouquet of roses on the windowsill as the night wind passed by; he heard the random song of birds and the distant music from a harbor tavern; he heard whispering at his ear, he heard I-love-you and felt his hair ruffle with bliss, now! Now at this very moment! He forced open his eyes and groaned with pleasure. This perfume was not like any perfume known before. It was not a scent that made things smell better, not some sachet, some toiletry. It was something completely new, capable of creating a whole world, a magical rich world, and in an instant you forgot all the loathsomeness around you and felt so rich, so at ease, so free, so fine. . .
>
> -from *Perfume* by Patrick Süskind

INTRODUCTION

As Süskind has reminded us in his evocative description of the power of scent, the slightest hint of perfume can transform the present into the past; it can recreate entire sensory experiences by providing an emotional link between past events initially experienced through separate senses; it can make memories seem real and tangible. In the *Remembrance of all Things Past,* Proust's description of dipping a mnemonically-rich Madeleine into his tea and being completely transported by its aroma back to his childhood, is one of the most frequently cited passages of literature. These experiences illustrate the unique power of scents, odours, smells or

aromas as mnemonic cues that can revive, refresh, retrieve and recreate entire episodes of one's life.

In this chapter, we parse the nature of olfactory memory in an attempt to understand its uniqueness and richness. We briefly summarize neurobiological underpinnings of olfactory memory before discussing specific issues pertaining to components of the olfactory memory system including a discussion of the relationship of olfactory memory to olfactory sensitivity, an evaluation of the nature of olfactory memory encoding (conscious and explicit vs. unconscious and implicit), an integration of the role of other sensory modalities in olfactory memories, an examination of the fidelity of olfactory memory over time and an assessment of the relationship between emotion and olfactory memories.

THE PROUST PHENOMENON

The Proust phenomenon has been defined in several ways. Formal definitions include the principles that memory for odours do not deteriorate as quickly as memories for other sensory modalities (Engen & Ross, 1973), that odours evoke older memories (Rubin *et al*, 1984), and that memories evoked by odours are more emotionally loaded (Herz & Cupchik, 1995). Likewise, a growing body of evidence lends strength to claims that a discrete memory system may exist for olfaction, and that memory systems may differentiate into a diverse array of component subsystems (Lehrner *et al,* 1999).

Olfactory stimuli are more potent cues of autobiographical memories than stimuli presented to other sensory modalities (Chu & Downes, 2000). However, it is not clear whether this effect is accounted for by ease of retrieval or variance in encoding and consolidation. Two hypotheses have been presented: *the differential cue affordance hypothesis* and *the differential encoding bias hypothesis* (Chu & Downes, 2002). The first hypothesis is defined in terms of its associated affordance value, which is a hypothetical measure of how efficiently episodic details can be accessed. According to the differential cue hypothesis, the Proust phenomenon is accounted for by the higher cue affordance values assigned to olfactory cues as compared to other cue types. The second hypothesis supposes that autobiographical memories differ in terms

of the number of episodic details that have been encoded and consolidated to form memory representations. It is hypothesized that the more complex a memory representation may be, the more likely that peripheral details are also encoded and consolidated. In this context, the Proust phenomenon may be explained by supposing that olfactory details of a particular episode are peripheral but integral parts of complex autobiographical memories. Thus, olfactory cues will result in recovering more detailed autobiographical memories (Chu & Downes, 2002).

These two hypotheses do not consider the role of working memory in Proust phenomenon but mounting evidence suggests that there are distinct olfactory long-term and working memory systems (White *et al,* 1998). In order to re-live the past in the manner of Proust or Monsieur Baldini, just retrieving multiple fragments of an autobiographical episode may not be sufficient for a Proustian moment. Working memory may provide the glue that integrates bits and pieces of the past that are retrieved into a Gestalt so that the past can be re-experienced here and now. To understand the Proust phenomenon and olfactory memory in general, evidence from encoding and retrieval studies as well as working memory and priming data should be considered in the context of neuroanatomy.

NEUROANATOMY OF OLFACTORY MEMORY

The first clue to the olfactory system's involvement in memory is the neuroanatomic overlap between the structures and circuits involved in memory encoding, recognition, and retrieval and the pathways involved in olfaction (see Chapter Two for further detail). From the olfactory bulb, where chemical receptors detect environmental odorants, olfactory signals are sent through the lateral olfactory tract to the pyriform cortex, which constitutes the primary olfactory cortex as outlined further in Chapter One. From the pyriform cortex, the system bifurcates to transmit information to both the lateral hypothalamus and the dorsal medial thalamus. A final level of convergence arrives in the orbitofrontal cortex (OFC), where taste and olfactory sensations from the tongue and nose create unified perceptions of flavour. Therefore, the olfactory system is widely distributed, involving preprocessing of olfactory information in the olfactory bulb, thalamus, and pyriform cortex prior to reaching the OFC (Jones-Gotman & Zatorre, 1988). Although case studies have identified olfactory memory deficits resulting from orbitofrontal and temporal cortices (Savage *et al*, 2002), it is the particular heteromodal

characteristic of the OFC that results in the blending of olfactory information with that from other sensory modalities.

Developmentally, like the rest of the prefrontal cortex, the OFC is derived from two separate moieties, and its structure and function in mature primates is reminiscent of its dual beginnings (Sanides, 1969). The OFC developed out of olfactory and hippocampal cores. The olfactory-derived subsections are generally concerned with stimulus recognition, while the hippocampal areas are generally concerned with spatial localization functions (Zald & Kim, 2001). Anatomic connectivity studies with primates have identified the lateral regions as being comprised of these olfactory generated areas, while the medial regions of the orbital surface are generally related to the areas derived initially from the hippocampus (Sanides, 1969). The gyrus rectus of the OFC is an association area between the medial and orbital frontal cortices, but its dense connections with the medial OFC give it a prominent role in the orbitofrontal functional system (Zald & Kim, 2001). Cytoarchitectonic and neurophysiological investigations of the OFC (Hof *et al*, 1995) have elucidated a relatively high degree of cellular specificity and functional demarcation within these ventral regions of cortex (Carmichael & Price, 1995; 1996; Chiavaras *et al*, 2001; Frey & Petrides, 2000; Price *et al*, 1996; Schoenbaum *et al*, 1998).

The OFC receives very little unprocessed information directly from sensory receptors. Instead, it receives sensory information from other brain centers that has already undergone essential stages of primary and secondary processing (Baylis *et al*, 1995; Carmichael & Price, 1994; Rolls *et al*, 1996). Gustatory, olfactory, auditory, and visual inputs arriving in areas of the OFC show an unparalleled level of specificity, and specific cells have been found within each modality that respond to certain specific stimuli, but not to others (Rolls, 2000; Thorpe *et al*, 1983; Zald & Kim, 1996a). Efferents from the OFC are widely distributed as well, and its influence on other areas of the brain is substantial. The OFC projects to many of the areas whence it receives projections, including limbic, frontal, and temporal cortices as well as subcortical nuclei (Carmichael & Price, 1995; 1996; Cavada *et al*, 2000; Frey & Petrides, 2000; Price *et al*, 1996). This pattern of connectivity signifies that the OFC is a convergence area for limbic and sensory structures. This is especially important in terms of mediating emotional and mnemonic interaction with the environment (Yamamoto *et al*, 1984). The OFC is also involved

in certain types of affective decision-making. Previous research with the OFC has indicated that its functional significance arises from its unique position in the frontal executive system (Fuster, 1997) and as an association area for sensory and emotional information as discussed above (Carmichael & Price, 1995; Frey & Petrides, 2000; Zald & Kim, 2001).

The role of the OFC in processing information from food stimuli is well established, and this system forms a model for the simultaneous representation of several sensory modalities, including olfaction, into a salient mnemonic representation. Object recognition processes from the ventral visual stream arrive in both the medial and lateral aspects of the OFC (Cavada *et al*, 2000; Frey & Petrides, 2000). Taste, smell, and flavour are also represented in distinct areas of the OFC, often with a high degree of specificity (Yamamoto *et al*, 1984). Pre-processed olfactory information from the pyriform cortex is projected to the agranular posterior regions, and these areas project to more anterior aspects within the OFC (Carmichael & Price, 1994), providing a region of extensive associative olfactory processing. Gustatory information arriving from frontal and insular cortices also project to the posterior regions of the OFC (Baylis *et al*, 1995), providing close associations between olfactory and gustatory processing cells. In fact, the proximity with which olfactory and gustatory cells process information provides specific processing of either smell or taste information, or shared processing of both modalities for specific stimuli (Rolls & Baylis, 1994). This polymodal association is responsible for experiencing flavour, the mixing of smell and taste that is so important in hedonic processing of appetitive stimuli such as food.

Experiencing all of the sensory and emotional aspects of food would require perceiving its visual, olfactory, gustatory, and tactile (and sometimes even auditory) characteristics. The polymodal association attributes of the OFC make it an ideal location for processing these inputs. Does the OFC, however, require the complete consort of sensations in order to process the emotional associations given by food stimuli? The data show that just the taste of food (Yamamoto *et al*, 1984), or even only its visual presentation (Thorpe *et al*, 1983) activate similar, specific cells in the OFC. These studies have shown that even though bimodal input activates single cells in the OFC, separate sensory signals from food processing areas are not required (Zald & Kim, 2001).

Given the OFC's high degree of sensory specificity and its role as mediator between stimulus input and behavioral output, many studies have investigated the unique role of the OFC in stimulus association learning and memory (Rolls *et al*, 1996). Single OFC neurons have been found to activate responses to stimuli only after they have been associated with negative affective outcomes, such as unpleasant taste (Thorpe *et al*, 1983). This finding indicated that orbitofrontal neurons are somehow engaged in associating stimuli with their outcomes after this outcome has become learned or expected (O'Doherty *et al*, 2002; Rolls, 2000; Thorpe *et al*, 1983; Watanabe, 1996). OFC neurons have even been examined that associate a stimulus with a certain spatial location (Lipton *et al*, 1999) because they respond when the animal is taken back to the location of stimulus presentation. This suggests that these neurons encode information about stimulus associations in memory for future retrieval. The olfactory system is further recognized in human emotional regulation and dysfunction because of its relationships with the limbic and frontal systems (Arnold & Trojanowski, 1996). The olfactory system is linked to hedonic evaluations (Royet *et al*, 2000), given that we have a well-developed process for recognizing scents, and deciding whether they are either pleasant or unpleasant. More recent primate data on error recognition (Rosenkilde *et al*, 1981), learning (Watanabe, 1998), and relative reward and preference decisions (Tremblay & Schultz, 1999) have implicated the OFC in these behaviours, so it is important to examine the specific role of olfaction in these behaviours in order to produce more specific models of olfactory influence on OFC emotional inference.

There is a further specialization of the OFC in relation to hemispheric laterality. Lateralisation is an important factor in the neuroanatomy of olfactory memory, as the right hemisphere makes a substantial contribution to retaining olfactory percepts. Response latency, in particular to identifying olfactory memories, has been linked to enhanced performance in the right hemisphere (Olsson & Cain, 2003) and olfactory deficits are seen most often when there is a right OFC insult (Zatorre & Jones-Gotman, 1991).

Several facets of olfactory processing, such as odour detection (Eichenbaum *et al*, 1983), discrimination (Abraham & Mathai, 1983), and memory (Dade *et al*, 2002), occur in the

anteromesial temporal lobes. Some evidence suggests a distinctive role for right temporal cortex in olfactory memory (Rausch *et al*, 1977) given the left hemispheric advantage in verbal memory tasks and the right hemisphere advantage for nonverbal memory (Buchanan *et al*, 2001). However, in two corresponding studies, Dade *et al*. (2002) showed both left and right temporal lobe participation in olfactory memory. More specifically, the pyriform cortex, the entorhinal cortex, the periamygdaloid cortex, and the anterior cortical nucleus of the amygdala play a pivotal role in olfactory processes (Savic, 2001). In a study of patients with either left or right amygdala damage, Buchanan and colleagues (2003) found impaired performance on an odour-name matching task in left temporal lobectomy patients, supporting the specialized role of the left amygdala in verbal-odour associations. These findings were independent of generalized memory impairments, suggesting an olfactory-specific memory deficit following amygdala damage. However, this study did not find support for the broader role that the amygdala may play in olfactory processing, as there was no difference between normal controls and right temporal lobectomy patients in an odour-recognition task (Buchanan *et al*, 2003). Thus, there may not be a specific advantage of the right hemisphere in olfactory processing.

Lastly, in addition to the OFC and the temporal lobe, the role of the hippocampus in episodic memory (including olfactory memory) retrieval must be emphasized. Along with the frontal cortex, hippocampus provides the primary circuit where short-term memories are transferred into long-term memories. As described further in Chapter two, damage to the hippocampus (Levy *et al*, 2003) and medial temporal lobes (Mouly *et al*, 2001) impairs olfactory memory.

ENCODING OF OLFACTORY STIMULI IN RELATION TO SEMANTIC PROCESSING AND AFFECT

A growing body of evidence indicates that a discrete memory system may exist for the olfactory domain and that the olfactory memory system may bifurcate into a diverse array of component subsystems (Lehrner *et al*, 1999). In order for memories to form, encoding must occur and, considering the uniqueness of the olfactory perceptual system, it is important to understand how or if encoding of olfactory stimuli may be different from encoding in other sensory modalities.

Auditory and visual sensory information arrives at heteromodal cortex already having undergone significant preprocessing. Auditory processing initially takes place in the inferior colliculi of the brainstem, then transferring to the medial geniculate body of the thalamus. From the thalamus, the system bifurcates, as one path leads to primary auditory cortex (BA 41) and the other to secondary auditory cortices (BA 42 and 22). Although the inferior temporal gyrus is particularly specified for visual memories, visual processing occurs in the lateral geniculate nucleus of the thalamus, the superior colliculi, the occipital cortex, and then to the parietal and temporal lobes for further motion- and pattern-recognition processing. In the end, auditory and visual pathways synapse in OFC. The olfactory system is exclusive in that it has more *direct* contact to the external environment via olfactory receptor cells, and it directly projects to the brain via the olfactory bulb. Moreover, the sensory input is relayed directly to the cortex and is not initially relayed to the thalamus (Powell *et al*, 1965). Lastly, cortical olfactory areas are phylogenetically older than other sensory cortical areas. This implies both an anatomical and functional proximity to the limbic system that is much closer than other sensory modalities. Therefore, olfactory encoding process seems qualitatively different from encoding in visual or auditory modalities. Whether the perception and encoding of stimuli significantly affect how they are stored can be debated and in this context the role of language in olfactory encoding must be carefully considered. However, the picture is rather complicated.

The role of language in encoding olfactory stimuli remains to be elucidated. Moreover, it is not clear whether aspects of odour perception, such as pleasantness or familiarity, influence the labeling of odour during the encoding stage. Rosenbluth *et al.* (2000) showed that children who were blind early in childhood significantly out-performed controls on an olfactory recognition task. This study concluded that the difference in performance arose from an advantage in labeling the odours. Murphy and Cain (1986) found that blind subjects recalled 31% more odours from memory than sighted controls. This advantage is not accounted for by increased olfactory sensitivity in blind individuals. Wakefield *et al.* (2004) found that blind children named 20% more odours than their sighted counterparts and odour perception (i.e. pleasantness, familiarity) did not account for this difference. This result suggests that blind individuals may have an advantage in accessing memory for non-visual stimuli (Wakefield *et al*, 2004). Does

language facilitate olfactory memory? To begin to address this question, we need to look further into semantic processes.

There is conflicting evidence for the role that semantic networks may play in olfactory coding. Human subjects are notoriously poor at correctly labeling olfactory stimuli. Engen (1982) reported that subjects encode the same odour differently on successive presentations. Moreover, different subjects generated different labels for the same odours (Engen 1982). It has been proposed that odours are encoded in relation to perception and independent of semantic networks (Engen & Ross, 1973). Royet *et al*. (1999) reported left inferior frontal gyrus activation when subjects made judgments regarding odour familiarity, suggesting that the encoding of odours is not independent of semantic networks. Passively smelling of odours activated the amygdala, pyriform cortex, and cingulate cortices (Savic & Berglund, 2004). Familiar odours (rated as such after the scanning session) activated the left frontal cortex and left parietal cortex (Savic & Berglund, 2004). Familiarity rating was correlated with left inferior frontal and parahippocampal activation (Savic & Berglund, 2004). Smell is similar to other modalities in that encoding of odours is dependent on semantic networks. Moreover, semantic networks are innervated by multiple sensory modalities (Savic & Berglund, 2004).
.

Magnetoencephalographic (MEG) and EEG studies provide more insight into the relationship between semantic encoding and olfaction. Lorig (1999) proposed that olfactory processes share some of the neural substrates with language processes. Furthermore, interference occurs when both processes occur at the same time. In a study investigating this possible interference, Lorig *et al*. (1998) used olfactory and visual stimuli as distractions during a verbal processing task. There were differences in both EEG responses and verbal responses when olfactory distracters were present, but not when visual distracters were present, suggesting interference between semantic and olfactory systems (Lorig *et al*, 1998). Walla and colleagues (2003) found decreased MEG performance in a semantic (deep) encoding task during chronic odour stimulation compared to performance on the same task in the absence of odour stimulation. But the authors of this study point out that it could be argued that olfactory stimulation modulated attention and the MEG results are an indication of this modulation. In a corresponding study, Walla *et al*. (2003) showed that there was no difference in activity in a non-semantic (shallowly encoded) version of the same task, suggesting that the first effect was

independent of any modulation of attention by olfactory stimulation. Together, these findings suggest that odour interferes with verbal processes differentially in that odours disrupt semantic but not non-semantic processes (Walla *et al*, 2003). The authors propose three possible reasons why odours disrupt semantic processes, even when no cognitive demands are associated with the odours. First, odours may alter cortical regions associated with semantic processes. Second, odours may modulate cortical regions associated with semantic processes. The third option is that odours may compete with cortical regions associated with semantic processes (Walla *et al*, 2003). Other studies also suggest that olfactory processes and language processes are related in an inhibitory manner. Lehrner *et al*. (1999) found that a weak relationship between naming consistency and odour recognition, whereas the relationship between odour identification and recognition was stronger, suggesting poor semantic memory underlies both poor odour recognition and identification (Parr *et al*, 2002). On the other hand, Parr *et al*. (2002) showed that recognition of wine-relevant odours by wine experts was not related to semantic memory as measured by odour identification and naming consistency, thus implying that odour recognition exists in a perceptual memory system, although this study was conducted in a contextualized setting (Parr *et al*, 2002). Melcher and Schooler (1996) propose the concept of *verbal overshadowing* as a possible explanation for the inhibitory relationship between verbal and olfactory processes. Verbal overshadowing is assumed to transpire when subjects are forced to identify complex stimuli that are difficult to capture verbally. This concept is hypothesized to increase as perceptual and verbal experience decreases (Melcher & Schooler, 1996). In other words, the relationship between verbal and olfactory processes becomes less inhibitory as experiential knowledge increases.

Affective attributes of olfactory stimuli may interact with the role of semantic networks in olfactory encoding. Olfactory stimuli invite initial automatic, affective evaluation, which may then influence verbal coding. Engen (1987) found that category labeling for odours was inconsistent when compared to other senses, and offered three conditions in which category labeling is achieved: 1) the stimulus is perceived in terms of similar smells, 2) the stimulus is perceived in terms of context, and 3) the stimulus induces the sensation of smell (Mohr *et al*, 2001; Engen, 1987). In order to rule out these confounds associated with real odours, Mohr *et al*. (2001) investigated associations with imagined olfactory stimuli and compared them to imagined

auditory stimuli. This study found that pleasant associations are more frequent in an imagined smell fluency task (i.e. generating 'smell' words) when compared to an imagined auditory fluency task (i.e. generating 'auditory' words). In conjunction with this finding, the study also found that pleasant associations were more frequent across both fluency conditions and that both of these findings were independent of fluency performance in either task (Mohr *et al*, 2001). Given that the number of associations generated in both tasks were equal, these findings suggest that there is no differential role for the frontal cortical system in accessing verbal associates to olfactory or auditory stimuli, but that the difference lies in the semantic network architecture (Mohr *et al,* 2001).

The anatomical proximity of olfaction to the limbic system makes it more likely that odours are more affectively coded and coded quicker relative to the other senses. Furthermore, the prevalence of pleasant associations with olfactory stimuli can be explained with two theories of hedonic value in memory: *the mere exposure paradigm* (Zajonc, 1968) and *repression theory* (Holmes, 1970). The mere exposure paradigm supposes that repeated exposure to a stimulus shifts hedonic judgments to pleasantness. The repression theory postulates that unpleasant memories degrade faster than pleasant memories. In terms of the mere exposure paradigm, exposure in these tasks leads to increased pleasantness. But this explanation alone does not account for the difference between the olfactory fluency task and the auditory fluency task. The close proximity to the limbic system would make the olfactory system more accessible to affectively-coded information than is the case for the auditory system. In terms of the repression theory, this neuronal inhibition would push association accessibility towards the pool of pleasant memories (Mohr *et al*, 2001).

It may be impossible to tease apart the semantic networks and olfaction because this initial affective categorisation may be autonomic. Odours can induce both positive and negative affects which go on to modulate autonomic responses such as skin conductance, heart rate, and startle reflexes (Alaoui-Ismaili *et al*, 1997; Ehrilchman *et al*, 1995). Neuroimaging studies (Fulbright *et al*, 1998; Zald & Pardo, 1997) and electrophysiology studies (Kobal *et al*, 1992) have found differential cerebral activation when processing pleasant versus unpleasant odours. Moreover, differences in processing pleasant versus unpleasant odours have also been shown in

studies of response time (Bensafi *et al*, 2001). Zattore and colleagues (2000) found hypothalamic activation when subjects were asked to make hedonic judgments of olfactory stimuli. Since odours are primarily experienced in terms of affective judgments, hedonic categorisation is pivotal in odour grouping (Bensafi *et al*, 2002). Bensafi and colleagues (2002) investigated the involuntary nature of hedonic judgments of odours and found increased heart rate with exposure to unpleasant odours. This suggests that heart rate increases in the context of rejection (Bensafi *et al*, 2002). Moreover, physiological responses for judgments of familiarity differed from physiological responses for judgments of hedonic tone, suggesting that neural networks for familiarity and hedonic tones are different and that cognitive processing of odours does not inhibit autonomic responses to odours (Bensafi *et al*, 2002).

RETRIEVING OLFACTORY MEMORIES

Mounting evidence suggests that odours are more emotional and stronger memory cues than other sensory stimuli. Olfactory cues for memories may be more affective than cues presented to other modalities (Herz, 1998; Herz & Cupchik, 1992). Odour-cued memories are rated as more pleasant and are recalled less frequently than memories cued via other modalities (Rubin *et al*, 1984). Emotional potency of odour-evoked memory is correlated with specific activation in the amygdala during recall. Odour cues to personal memories elicited greater activation in the amygdala-hippocampal complex than comparable but non-personally relevant odours. These findings show that activation of the amygdala-hippocampal complex is accounted for by the emotionality of the elicited memories and is not related to olfactory artifacts (Herz *et al*, 2004). These data suggests that the amygdala-hippocampal complex may be part of the neural substrates involved in a distinct olfactory memory system

Odours may be divided into broader semantic categories (Engen, 1991) or they may be associated with places or events (de Wijk *et al*, 1995). Jonsson and Olson (2003) investigated three types of metamemory phenomena: *Feeling of Knowing* (FOK), *"Tip of the Nose" phenomena* (TON), and *Retrospective confidence judgments*. FOK can be defined as a feeling of knowing supposed information that is associated with information retrieval failures. Cain *et al*. found no predictive validity for FOK judgments about odour identity. In other words, FOK judgments are at chance level. TON occurs when subjects recognize an odour but are not able to

access the label for that odour. TON occurs involuntarily. Lastly, Retrospective confidence judgments are judgments about the correctness of already retrieved information. Jonsson and Olson (2003) found a correlation between recognition performance and FOK. This suggests that FOK judgments are associated with subsequent odour recognition.Furthermore, subjects that reported a very strong TON for subsequent odours more frequently resolved the naming of those odours. This was not found for other TON ratings. Lastly, with regards to retrospective confidence judgments, this study found that participants were overly confident in their ability identify odours (Jonsson and Olson, 2003). Taken together, these findings suggest that context may be a necessary component to identifying olfactory stimuli correctly, but context is not necessary for recognition judgments.

To elucidate the role of context in olfaction memory retrieval further, Vermetten & Bremner (2003) investigated olfactory flashbacks in a case report of three patients with Post Traumatic Stress Disorder (PTSD). Odours are more associated with affect and emotion than other sensory modalities and may underlie formation of and retrieval of content-dependent, odour-evoked memories. Memory for smells in PTSD has four features: 1) it is specific, 2) it is long-lasting, 3) it is state dependent, and 4) it is context dependent (Vermetten & Bremner, 2003). Two of the case studies showed hallucinated smells precipitated a traumatic memory with associated affect. This suggests that olfactory memories are deeply embedded and that long-term effects of memory of smells related to trauma can manifest itself upon re-exposure to cues. Moreover, this phenomenon does not extinguish with time. Vasterling *et al.* (2000) found that patients with PTSD showed olfactory identification deficits. This finding is consistent with reported dysfunction of fronto-limbic system in PTSD.

Age may modulate olfactory memory retrieval. Maylor *et al*, (2002) examined a set of young subjects (mean age 21) and a set of older subjects (mean age 84) in an autobiographical memory recall task either with or without the appropriate olfactory cues. Across the two groups, twice as many memories were recalled when accompanied with the appropriate odour than without. This study concluded that olfactory cuing is remarkably intact in old age and that memory retrieval is enhanced by exposure to associated odours.

PRIMING: SEMANTIC VERSUS PERCEPTUAL

In general, priming occurs when the processing of a previously encountered stimulus (the prime) influences the processing of a second stimulus (the target). The target can be either identical to the prime or related in some way to the target. Priming relies on a *spread of activation process*. (Koenig *et al*, 2000; McNamara, 1992). More specifically, priming can be divided into *perceptual priming* and *semantic priming.* Perceptual priming occurs when the prime and the target share perceptual qualities, whereas semantic priming occurs when the prime and the target are semantically related. It is postulated that perceptual priming and semantic priming are mediated by two discrete subsystems. Perceptual priming spreads a pattern of activation through a subsystem that stores modality-specific traces which correspond to perceptual attributes of a specific stimulus. Semantic priming activates an associative memory subsystem that stores memory traces that are independent of sensory modality (Kosslyn & Koenig, 1992; Tulving & Schacter, 1990).

Attempts to demonstrate a priming effect through the olfactory subsystem have produced conflicting results (Olsson, 1999; Olsson & Cain, 1995). Koenig and colleagues (2000) demonstrated a robust priming effect for the olfactory modality when olfactory stimuli were previously encountered in the study session. However, no priming effect was observed when the *label* for olfactory stimuli was previously encountered in the study session. Thus, intramodal (olfactory-olfactory) priming operates at a pre-semantic level and is perceptual in nature.

Some studies have shown a hemispheric effect on priming for both auditory and visual modalities. However, Olsson and Friden (2001a) did not find a hemispheric difference in an odour repetition priming task. In a related study, Olsson and Friden (2001b) found a hemispheric effect for response latencies when subject were asked to make judgments of edibility for either primed or control odours. In this study, priming was demonstrated when testing via the right nostril but not the left nostril. Furthermore, edibility judgments were more accurate when odours were presented to the left nostril. This is consistent with visual priming studies in that right hemispheric priming is dependent on perceptual similarity between the prime and the target (Olsson & Friden, 2001)

CROSS MODAL INTEGRATION

The olfactory memory system may rely upon cross modal integration, and incongruent cues could attenuate olfactory memory retrieval. Morrot *et al*, (2002) found that in the absence of visual cues, subjects incorrectly described white wine odours using red wine terms. This is consistent with past studies of incongruent versus congruent cues. Identification of single odours improves when relevant semantic information is also presented (Cain, 1979). Basic properties of olfactory perception (such as intensity and thresholds) are modulated by visual and cognitive factors (Zellner & Kautz, 1990, Dalton, 1996; 2000, Distel & Hudson, 2001) suggesting multiple sites of integration. There is some evidence that olfactory information aids visual episodic memories, and that it provides a contextual salience to the memory storage and retrieval systems (Gottfried *et al*, 2004). The effect of olfactory information on verbal memory encoding and retrieval may also be modulated, in part, based on the presence or absence of associated olfactory information (Bonfigli *et al*, 2002).

As outlined by Gottfried & Dolan (2003) the hippocampus is one probable site. It can be accessed directly or indirectly from all sensory modalities. Lesion studies show that post-surgical epilepsy patients with damage to hippocampus and adjacent medial temporal structures are impaired on a variety of cross-modal odour tasks (Eichenbaum *et al*, 1983). Another possible site of integration is the OFC. The OFC has been shown to receive afferent inputs from the pyriform cortex and visual association areas in non-human primates (Carmicheal & Price, 1995). Moreover, fMRI cross-modal study showed OFC activation in an olfactory-visual associative learning task (Gottfried e*t al*, 2002). Gottfried & Dolan (2003) investigated these possible sites of integration and found that olfactory detection was faster and more accurate when presented with semantically congruent visual stimuli. They also found activation in anterior hippocampus and rostromedial OFC during congruency-specific tasks. These results suggest both the hippocampus and OFC are involved in cross-modal integration.

As discussed previously, another possible site of integration may be the prefrontal cortex. Traditionally, the prefrontal cortex is divided into two anatomical parts: the dorsolateral

prefrontal cortex ad the ventrolateral prefrontal cortex, although the functionality of these two divisions is not as clear. Goldman-Rakic (1995) proposes a functional division based on segregated areas that process a specific type of knowledge. Specifically, this model supposes that the dorsolateral prefrontal cortex is reserved for spatial functioning while the ventrolateral cortex processes verbal information. This model assumes that different sensory modalities can contribute to one informational domain. Single cell recording studies in non-human primates indicate that there is no specific division of cells responding to spatial versus non-spatial working memory (White & Wise, 1999).

Alternatively, Petrides (1995) offers a "two-level hypothesis," dividing the lateral frontal cortex with respect to its executive functions, such that the middorsolateral and midventrolateral frontal cortex are divided according to the processes being carried out. Dade and colleagues (2001) found that olfactory working memory activates dorsolateral and ventrolateral PFC, but differs from face working memory with regards to activation in parietal lobe. More specifically, overlap was found in the dorsolateral, ventrolateral and frontal polar cortices suggesting that, in general, the same functional prefrontal regions are used in visual and olfactory working memory tasks (Dade *et al*, 2001).

CONCLUSIONS

Bringing together the evidence from encoding and retrieval studies as well as incorporating olfactory working memory and olfactory priming creates a broader working definition of the Proust phenomenon and allows for a conceptualisation of the olfactory memory subsystem and how it is integrated with other memory subsystems. Neuroanatomical overlap between the structures and circuits involved in memory encoding, recognition, and retrieval and the pathways involved in olfaction suggest that components of the olfactory memory subsystem are highly integrated and may modulate one another (see Figure 7.1). Olfactory perceptual qualities, such as hedonics and familiarity are autonomic in nature and influence olfactory stimulus encoding. The context in which olfactory stimuli are encoded is likely to influence olfactory memory retrieval. In turn, olfactory memory retrieval can modulate the experience of olfactory qualities such as hedonics and familiarity.

Finally, olfactory, affect and semantic processing are intimately intertwined and perhaps disentangling the complex relationships among these three domains remains as challenging as the dark journey that Grenouille undertook to distill the essence of the human scent in Süskind's Perfume.

---------------Insert Figure 7.1 about here-----------------

Figure 7.1. A schematic diagram of the relationship among olfactory perception, encoding and retrieval