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Neuropsychological functions implicated in obsessive-compulsive behaviour: a review
Clinical features of Obsessive-Compulsive Disorder

Obsessive-Compulsive Disorder (OCD) is characterized by recurrent obsessions and/or compulsions. Obsessions are intrusive and unwanted thoughts, images or feelings which elicit considerable anxiety and discomfort. Commonly recurring themes in obsessions are aggression, blasphemy, death and (unacceptable) sexual urges. Compulsions are repetitive, ritualistic behaviours or mental acts that are performed to reduce or neutralise the anxiety that is elicited by the obsessions. The most frequently encountered compulsions are ordering, counting, checking and washing. When the patient resists carrying out the compulsions, anxiety usually increases. Patients generally recognize that the obsessions and compulsions are excessive and irrational. Nevertheless, the obsessions and compulsions cause marked distress, are time-consuming (i.e. take more than an hour a day, American Psychiatric Association, 1994) and interfere significantly with the person’s social or occupational life. Many patients experience both obsessions and compulsions; only a minority presents with either obsessions or compulsions (Foa & Kozak, 1995). OCD is classified in DSM-IV as an anxiety disorder, although not all clinicians agree on this categorization (Nelson & Chouinard, 1995).

The onset of OCD is typically during adolescence or early adulthood (Rasmussen & Tsuang, 1986). Its life time prevalence is 2.5–3% (Bland et al. 1988) and appears to be slightly elevated for women (Weissman et al. 1994). OCD is often accompanied by other psychiatric disorders such as major depression, social phobia and substance abuse (Douglass et al., 1995). A high psychiatric comorbidity was reported by Yaryura-Tobias and colleagues (2000) who reported that 32.2% of a total of 409 OCD patients developed one or more other axis-I diagnoses. There is also a high incidence of OCD, namely 30–50%, in patients with Gilles de la Tourette syndrome (motor and phonetic tics) (Rubin & Harris, 1999). However, there is evidence that OCD patients present with more severe depressive and obsessive symptoms and more frequently suffer from personality disorders (Cath et al., 1992).

Nowadays, the most effective way to treat OCD is to combine psychopharmacological with cognitive-behavioural treatment strategies. With respect to the first, OCD responds best to serotonin reuptake inhibitors (SSRIs), which block the serotonin transporter and increase synaptic availability of serotonin in the brain. SSRIs would lead in 60–70% of the cases to a considerable reduction of obsessive-compulsive symptoms (Den Boer et al., 2001). Although the precise mechanism of action is unknown, the efficacy of SSRIs may be accomplished by down-regulation of terminal auto receptors (in particular the 5-HT1d subtype).
Neuropsychological functions in OCD

in the orbitofrontal cortex (Rauch et al., 1998). Cognitive-behavioural therapy (CBT) and behaviour therapy with exposure and response prevention (ERP) are validated treatment strategies as well (Chambless & Ollendick, 2001). CBT is firmly based on the cognitive theory of obsessions (see below) whereas behaviour therapy with ERP is especially effective for changing behavioural rituals such as compulsive cleaning and checking (Marks, 1981).

In cases of severe, incapacitating OCD, neurosurgical interventions are performed during which extremely small cortical lesions are made in circumscribed brain regions (Haaijman, 1990). Bilateral lesions of the medio-orbitofrontal cortex, the cingulate cortex and the capsula interna are followed by a considerable reduction of OCD symptoms (60–80%) (Insel, 1992) which seems to have a permanent character (Haaijman, 1990).

Most investigators currently agree that OCD is accompanied by, or even due to, abnormalities in brain function. The aim of this chapter was to investigate the evidence for altered brain functionality in OCD, and to see to what extent such abnormalities can explain the specific symptoms of the disorder. To this end, we review studies on both cognitive and neural function in OCD, and combine this with recent insights in the functions of the brain areas that are afflicted in OCD. In the final section of this chapter, an attempt is made to integrate these findings into a neuropsychological model of OCD.

Cognitive theories of OCD

The most comprehensive cognitive analyses of OCD were formulated by Rachman (1997, 1998) and Salkovskis (1985). Their cognitive theory of obsessions emphasizes the role of dysfunctional beliefs and the associated appraisal of threat. This theory states that obsessions have their origin in normal intrusive cognitions, that occur in at least 90% of the general population (Rachman & De Silva, 1978). Intrusive cognitions are ideas, thoughts, doubts, images or impulses that intrude in the sense that they interrupt the person’s current stream of consciousness. Furthermore, the content of these intrusions are usually experienced as upsetting, unacceptable or otherwise unpleasant (Salkovskis, 1999). The crucial factor in the development of obsessions lies with the evaluation that is made by the patient on the content or the frequency of the intrusions (Salkovskis, 1985). In particular, subjects who are vulnerable for developing obsessions tend to believe that they are personally responsible for the possible consequences of the intrusion. For the OCD patient, having an intrusion is meaningful because they are evidence
for beliefs such as ‘I am in danger of becoming a child molester’ or ‘I have contaminated things so that they may be dangerous’. The cognitive theory further states that these incorrect appraisal processes of OCD patients lead to depressed mood and increased discomfort, but also to a greater accessibility of the intrusive thoughts into consciousness, and an attentional bias towards stimuli that are related to the thought. Indeed, there is empirical support for a selective bias in attention and memory towards obsession-related stimuli (Lavy et al., 1994; Tata et al., 1996; Constans et al., 1995; Radomsky & Rachman, 1999).

As OCD patients feel personally responsible for the consequences of the obsessive thought, they usually take action to prevent the dreaded event from happening. These actions can consist of either neutralising behaviours (performing rituals or seeking reassurance) or counterproductive safety strategies such as thought suppression and avoidance. These actions not only lead to maintenance of the faulty beliefs but can also cause an increasing frequency of intrusive thoughts (Salkovskis, 1999). Therapeutic strategies that are based on the cognitive theory aim to teach the patient how to re-appraise their intrusive thoughts. This turns out to be far more effective than directly challenging the content of the obsessive thoughts (Emmelkamp, 2001).

**Functional neuroanatomy of OCD**

**Functional imaging studies**

Most functional imaging studies in OCD were performed with Positron Emission Tomography (PET). This technique makes use of radioactive tracers that emit positrons to produce images reflective of brain function or chemistry. Although there are multiple tracers, the basic principle of PET is nearly always identical. A radioactive tracer is injected, which diffuses through the body (including the brain). The PET camera detects the signal that is emitted by the radioactive substance, allowing maps to be made that reflect regional tracer concentrations. The most commonly used tracers are $^{18}$Fluorodeoxyglucose ($^{18}$FDG) as a measure for cerebral glucose metabolism and $^{15}$O-labelled water ($\text{H}_2^{15}$O) to measure cerebral blood flow. A more recently developed neuroimaging technique is functional MRI (fMRI), which takes advantage of the different magnetic properties of oxygenated and deoxygenated haemoglobin to detect subtle changes in brain blood flow and blood volume (Rauch et al., 1998). An important advantage of fMRI is
that subjects are not exposed to ionising radiation, implying that multiple studies can be performed within the same subject.

Findings of PET resting studies that were performed in OCD patients are rather consistent. Untreated OCD patients show significantly elevated glucose metabolic rates or cerebral blood flow within the orbitofrontal cortex, right prefrontal areas and the anterior cingulate cortex (Baxter et al., 1988; Swedo et al., 1989; Nordahl et al., 1989; Sawle et al., 1991). The different location of abnormal activation may be due to a variable definition of regions of interest (Baxter & Mazziotta, 1993) or to differences in patient characteristics, such as comorbid diagnoses of depression (Saxena et al., 2001). Increased levels of activation have also been observed in the caudate nucleus and thalamus (Baxter et al., 1987, 1988; Benkelfat et al., 1990; Nordahl et al., 1989; Perani et al., 1995; Swedo et al., 1989; but see also the meta-analysis by Aylward et al., 1996).

When obsessive-compulsive symptoms are provoked by exposure, brain activation rates increase in the caudate nucleus, putamen, globus pallidus, thalamus and orbitofrontal and anterior cingulate cortex (McGuire et al., 1994; Rauch et al., 1994; Adler et al., 2000) and in the amygdala and insula as well (Breiter et al., 1996). The observed functional abnormalities are state-dependent, as successful treatment (either with pharmacotherapy or behavioural therapy) leads to a normalisation of activation rates in orbitofrontal (Benkelfat et al., 1990; Swedo et al., 1992; Saxena et al., 2002), anterior cingulate (Perani et al., 1995) and caudate regions (Benkelfat et al., 1990; Baxter et al., 1992; Schwartz et al., 1996; Saxena et al., 2002).

A recent fMRI study compared the neural response of OCD patients with washing compulsions (‘washers’) and patients with checking compulsions (‘checkers’) to washer relevant pictures (Phillips et al., 2000). Remarkably, although washers reported significantly higher levels of fear and disgust than checkers when confronted with washer-related pictures, it was only the checkers that showed increased activation of the orbitofrontal-striatal circuit. Future studies may provide insight in the experience of emotion at the one hand and the elicitation of obsessive-compulsive symptoms at the other hand (Phillips et al., 2000).

Finally, a few cognitive activation studies have been performed, of which the results indicate that OCD patients activate different neural patterns than volunteers when performing a neuropsychological task, whether this was procedural learning (Rauch et al., 1997–pet), verbal fluency (Pujol et al., 1999–fMRI) or the Wisconsin Card Sorting Test (Lucey et al., 1997–SPECT).
Neuropsychological functions in OCD

Contemporary neurobiological models of OCD have been shaped to a large degree by findings from functional neuroimaging studies. Generally, it is believed that OCD is mediated by a neural circuit comprising orbitofrontal cortex, the cingulate cortex and the caudate nucleus (which is the anterior part of the striatum (Insel, 1992; Graybiel & Rauch, 2000). This ‘OCD-circuit’ (Graybiel & Rauch, 2000) is one of the multiple, parallel and anatomically segregated corticostriatal circuits that connect the prefrontal cortex with subcortical structures (Alexander et al., 1986). Each circuit forms a closed loop, as there is a final link back to the frontal cortex (see figure 1). There are two pathways within each circuit: a direct and an indirect pathway between the striatum and thalamus (see figure 1) and these circuits work together to modulate input to the thalamus (Baxter, 1999).

Some researchers propose that in patients with OCD, the direct striatothalamic pathway is disproportionally strongly activated, resulting in decreased inhibition of the thalamic nuclei. As the projections from the thalamus to the cortex are excitatory, this thalamic disinhibition could eventually produce an excessive activation of the orbitofrontal and anterior cingulate cortex (Baxter, 1992; Baxter et al., 1996). Unfortunately, this account is not very explicit about how the abnormal striatal activation results in obsessive-compulsive behaviour (Baxter, 1999).

Current theoretical models of the basal ganglia suggest a prominent role for these structures in context-dependent selection or ‘set’ processes (Robbins & Brown, 1990; Houk & Wise, 1995; Wickens & Kötter, 1995). This would be the result of the capacity of spiny striatal neurons to recognize complex patterns in the environment. Anatomically, there are multiple projections from several cortical columns to these neurons, which means that different kinds of information converge on striatal neurons. Via dopaminergic reinforcement signals (Schultz, 1997), the striatum is able to recognize and register complex contextual patterns that are relevant for behaviour (Lawrence et al., 2000). Accordingly, the striatum informs the cortex about which sensory input is relevant and therefore should be attended to (Beiser et al., 1997). Although tentative, a compromised functionality of the basal ganglia in OCD could have as a result that obsession-related external stimuli, and perhaps internal stimuli such as thoughts or impulses, more easily gain access into conscious awareness of the patient.

There are also theorists that relate OCD symptoms directly to altered functionality of the orbitofrontal regions (Insel, 1992; Schwartz, 1997). Single-cell recordings in non-human primates have revealed the presence of neurons in the orbitofrontal and cingulate cortex that exclusively fire when a monkey does
not receive an anticipated reward (Thorpe et al., 1983). The excessive activation of the medial and orbitofrontal cortex in OCD would be a human analogue to these ‘error-detection cells’ and give rise to the feeling ‘that something is wrong’ (Schwartz, 1997). If the dysfunction of these brain regions is permanent, these error signals may continue to be generated, despite efforts of the patient to reduce them by performing compulsive actions (Schwartz, 1997).

Figure 1 — Schematic illustration of a number of parallel cortico-striatal-thalamico-cortical circuits (adapted from Rauch et al., 1998). The paralimbic cortex is composed of the posteromedial orbitofrontal cortex, the cingulate cortex, the anterior temporal parahippocampal cortex and the insula. The striatum consists of the putamen, the caudate nucleus, and the nucleus accumbens (not shown here). The sensorimotor cortex projects to the putamen, the dorsolateral prefrontal cortex to the dorsolateral part of the caudate, the anterolateral orbitofrontal cortex to the ventromedial part of the caudate nucleus and the paralimbic cortex to the nucleus accumbens. In OCD, there would be a disruption of both the anterolateral OFC circuit as the paralimbic circuit. For every circuit, there is a striatothalamic connection consisting of a direct and an indirect route. The direct system (straight line) travels via the globus pallidus interna (not shown here) to the thalamus and exerts an excitatory influence (+) on the thalamus. The indirect system (curved line) goes from the globus pallidus externa and the subthalamic nucleus (not shown here) to the thalamus and has an inhibitory (−) influence on the thalamus.
Neuropsychological studies in OCD

In this section, we consider the evidence for functional brain impairments in OCD as has been found with the neuropsychological approach. We will concentrate on executive function, which is the set of cognitive functions that serve to optimise performance in complex situations requiring the operation of a number of cognitive processes (Baddeley, 1986). The major executive functions are planning, switching to alternative task sets, strategy use and inhibition of inappropriate responses. However, recent approaches consider the monitoring of motivational state to be one of the executive functions as well (Stuss & Alexander, 2000). This function is increasingly associated with the orbitofrontal and ventromedial parts of the prefrontal cortex (for reviews see Dolan, 2002; Krawzyk, 2002) and thus could play an important role in OCD. We first review studies on executive function in OCD that were performed with traditional neuropsychological tests. After this, we consider to what extent theories and empirical work on the functions of the orbitofrontal and ventromedial cortex are relevant for the symptoms of OCD.

Executive function in OCD: traditional neuropsychological tests

There is some evidence that OCD patients have more difficulties in set shifting than normal controls (Harvey, 1986; Head et al., 1989; Veale et al., 1996). However, it is possible that these impairments are caused by the presence of comorbid depressive symptoms, as patients suffering from major depression usually perform poor on set shifting tasks (Purcell et al., 1997; Beato et al., 1996) and OCD has one of the highest comorbidity rates with major depression (Rasmussen & Eisen, 1992). In fact, studies that carefully controlled for depressive symptoms observed normal set-shifting behaviour in OCD patients (Boone et al., 1991, Zellinski et al., 1991; Cavedini et al., 1998).

One conventional test for planning ability is the Tower of London (TOL) test (Owen et al., 1990). Subjects are presented with three columns in which coloured balls are arranged in a certain way. They are requested to select the most efficient way to move the balls in order to achieve a pre-specified arrangement. OCD patients perform normally on the TOL, although it should be noted that they need more time than controls to execute the subsequent moves (Christensen et al., 1992; Veale et al., 1996; Schmidtke et al., 1998).

Studies using tests for working memory capacity produced divergent results as well. For instance, the Self Ordered Pointing Task (SOPT, Galderisi et al., 1995) requires subjects to search through an array of different objects, without
touching the same object twice. OCD patients perform normally on these tasks (Galderisi et al., 1995; Martin et al., 1995); however, they are impaired on working memory tests that require the manipulation of nonverbal material (Purcell et al., 1998ab; Smidtke et al., 1998; but see Barnett et al., 1999). Other memory functions that are associated with the prefrontal lobe are temporal ordering and frequency estimation, and there is evidence that OCD patients have impairments in both (Jurado et al., 2001; 2002).

The ability to perform a strategic search through semantic memory is usually assessed with verbal fluency tasks. These tasks typically involve the generation of word exemplars from a given category in a limited period of time. Studies using verbal fluency tasks in OCD have produced inconsistent findings (Christensen et al., 1992; Schmidtke et al., 1998; Boone et al., 1991; Martin et al., 1993). One methodological drawback is that these tasks are timed, which may have lowered scores of some OCD patients who suffer from motor slowness and meticulousness (Tallis, 1997).

The Stroop Colour Word task is presumed to assess interference control and the ability to inhibit a premature response (Schmidtke et al., 1998). OCD patients perform normally on the Stroop task (Boone et al., 1991; Aranowitz et al., 1994; Schmidtke et al., 1998). However, when the content of the stimuli is related to the obsessions, naming latencies slow down, suggesting that patients are distracted by the meaning of the word (Lavy et al., 1994; Tata et al., 1996).

Finally, studies assessing sustained attention (using continuous performance tasks) have so far not found abnormalities in OCD (Rapoport et al., 1981; Zielinski et al., 1991; Milleiry et al., 2000).

**Cognitive functions of the orbitofrontal cortex: studies in non-human primates**

The dorsolateral and orbital regions of the prefrontal cortex would subserve different cognitive functions (Alexander et al., 1990). The dorsolateral prefrontal cortex (DLPFC) occupies the upper and side regions of the prefrontal cortex and comprises Brodmann’s areas 9 and 46 (see figure 2). Due to its strong anatomical connections with the parietal cortex, which subserves the processing of spatial information, the DLPFC would control the execution of behaviour in relation to spatial context. The orbitofrontal cortex (OFC) is defined as the cortex on the orbital surface of the frontal lobe (Elliott et al., 2000). The most caudal part of the OFC is delineated as area 25, and extends to area 10 towards the frontal pole (see figure 2). At the lateral side, the OFC comprises area 47, 12 and 11 (Petrides &
Figure 2 — Brodmann's map of the cortical areas of the human brain based on their cyto-architectonic properties. Lateral view of the left hemisphere (top) and medial view of the right hemisphere (bottom). Adapted from Brodmann, 1909.
Pandya, 1994). At this point, we note that the term ‘ventromedial prefrontal cortex’ is often used interchangeably with that of orbitofrontal cortex, although not all authors agree that these regions are essentially the same. Generally, the term orbitofrontal refers to the underside of the prefrontal cortex, while ventromedial may be designated as the innermost medial areas of the ventral frontal lobe (Krawzyk, 2002), comprising areas 11, 12, 13, 25, 32 and 10 and the white matter subjacent to all of these areas (Bechara et al., 2000; see figure 2).

The medial and orbital regions of the prefrontal cortex are densely connected with the limbic system, the amygdala, the basal ganglia and the insula. There are also direct inputs from visual association areas, somatosensory cortex and the temporal pole (Petrides & Pandya, 1988). Sensory information about taste and smell is directly projected from the sensory cortex to the lateral and medial orbitofrontal cortex respectively (Elliott et al., 2000). Both humans and animals do not have to acquire the reinforcing properties of taste and smell, due to which these stimuli are ‘primary reinforcers’ (Rolls, 2000). Neurons in the orbitofrontal cortex (OFC) can contain a very detailed representation of the reinforcing properties of a stimulus. These representations are influenced by the behavioural and motivational significance of the stimulus. For instance, single-electrode recordings in monkeys reveal that the firing rate of taste-sensitive OFC neurons fades away when the animal is fed to satiety (Thorpe et al., 1983; Critchley & Rolls, 1996; Tremblay & Schultz, 1999). Interestingly, recent functional neuroimaging work in humans support these findings (O’Doherty et al., 2000; Small et al., 2001). Orbitofrontal neurons would also be involved in associating a visual stimulus with reward, which is possible because the orbitofrontal cortex receives information about its visual properties (colour, form) from the inferior temporal cortex. These details can be related to representations about the motivational importance of the stimulus. Moreover, OFC neurons are able to register changes in the rewarding properties of the stimulus. There are even populations of OFC neurons that specifically fire when an expected reward does not occur (Thorpe et al., 1983). In addition, lesions to the OFC of macaque monkeys cause profound impairments in the ability to reverse a previously established relationship between a visual stimulus and a response (Butter, 1969; Jones & Mishkin, 1972). Finally, the orbitofrontal cortex contains neurons that respond selectively to the presentation of faces (Rolls, 2000). Although face-sensitive neurons have also been detected in the temporal cortex, the neurons in the orbitofrontal regions are specifically sensitive to the expressions and identity of faces (Hasselmo et al., 1989). It is possible that the perception of a friendly smile or an angry expression is associated with positive and negative reinforcement, and these af-
ffective associations might be crucial for the development of adequate social skills (Rolls, 2000).

**Cognitive functions of the orbitofrontal cortex: studies in humans**

Patients with acquired lesions of the orbitofrontal cortex present with changes in personality, such as inappropriate euphoria, a lack of responsibility and flattening of affect (Hecaen & Albert, 1978; Damasio, 1994; Anderson et al., 2000). Rolls and colleagues (1994) tested whether these behavioural changes were due to a diminished ability to detect changes in *reward value*. In their experiments, they trained patients with damage to the orbitofrontal cortex with the help of reward to select one of two visual patterns that appeared on a touch screen. Once the learning criterion had been reached, the stimulus-reward association was reversed. That is, subjects had to learn that reward could be obtained by touching the previously non-rewarded stimulus. Although the patients could verbally indicate that ‘something had changed’ in the reward contingencies, they continued to choose for the initially rewarded stimulus. One patient said “no!” to himself upon seeing the first-rewarded stimulus, then touched it, and commented “I knew I was wrong” (Rolls et al., 1994). Interestingly, impaired performance on this task was related to the degree of socially inappropriate behaviour in daily life (Rolls et al., 1994). Patients with damage to the orbital prefrontal cortex also display an impaired ability to recognize emotional expressions on faces and in voices (Hornak et al., 1996). These deficits were accompanied by altered emotional experience (as reported by the patients) and to the severity of disinhibited behaviour in daily life.

Damasio and colleagues developed another paradigm to characterize cognitive function of these patients. In their Iowa Gambling task (Bechara et al., 1994; see figure 3) subjects select cards from four decks of identical cards. For each card, subjects obtain a certain amount of (facsimile) money, and they are told to gain as much money as possible. Unknown to the subject, each deck of cards is associated with a different schedule of reward and punishment (see figure 3). Decks A and B provide high rewards and substantial penalties, whereas deck C and D provide modest rewards and lower penalties. Healthy subjects are able to find out the most advantageous strategy (i.e. selecting from decks C and D) throughout the task. However, patients with orbitofrontal damage are profoundly impaired in that they persistently chose from the ‘risky’ decks and thus lose a large amount of money (Bechara et al., 1994). The Iowa Gambling task (or modified versions) have been applied to study decision making in a variety of neurological (North
& O’Carroll, 2001; Bechara et al., 1999; Rahman et al., 1999) and psychiatric populations (Wilder et al., 1998; Rubinsztein et al., 2001; Van Honk et al., 2002; Cavedini et al., 2001, 2002; Nielen et al., 2002) and in substance abusers (Grant et al., 2000; Bechara & Damasio, 2002).

To explain the nature of deficits in patients with orbitofrontal damage, the ‘somatic marker hypothesis’ has been postulated (Damasio, 1994, 1996). According to this theory, damage to the orbitofrontal cortex (OFC) precludes the ability to use emotions for adaptation in complex situations. Under normal circumstances, the orbitofrontal cortex holds representations of the somatic states (‘somatic markers’) that accompany emotional states, which are coupled with facts about the situation in which the emotion occurred. The somatic markers can influence the processes of responding to stimuli, either consciously or more covertly, by signalling which option is likely to be the most advantageous. This biasing signal is most influential when the future is uncertain (Dolan, 1999). After disruption of the somatic marker system, as present after orbitofrontal damage, response options become more or less equal. The patient may resort to deciding based on the immediate benefits of an option, or even take no decision at all (Bechara et al., 2001). Although alternative explanations for the behaviour of patients with orbitofrontal damage have been proposed (Rolls, 1996; Plaisted & Sahakian,
1997), the somatic marker hypothesis has thus far been the most influential account of orbitofrontal function. Functional neuroimaging studies in humans support the role of the orbitofrontal cortex in the experience of both positive and negative emotions (Lane et al., 1997ab; Northoff et al., 2000; O’Doherty et al., 2001; Knutson et al., 2000) but also in recognition of facial expressions (Morris et al., 1996; Phillips et al., 1997) and identification of odour (Yousem et al., 1997; Fulbright et al., 1998; Zald & Pardo, 2000; Royet et al., 2000) and taste (Francis et al., 1999). Furthermore, the orbitofrontal cortex is also activated during decision making and guessing tasks (Elliott et al., 1997ab, 1999; Rogers et al., 1999; Ernst et al., 2002). The strength of the neural response in this region seems to be modulated by the extent to which subjects can predict the occurrence of reward (Elliott et al., 1999; Berns et al., 2001).

**Cognitive involvement of orbitofrontal cortex in OCD**

Recent studies examined whether the cognitive functions of the orbitofrontal cortex are involved in OCD. Sprengelmeyer and coworkers (1997) found that OCD patients had a normal ability to identify facial expressions of fear, happiness, surprise and anger, but were impaired in the recognition of disgust. Remarkably, patients with Huntington’s chorea display similar face recognition impairments (Sprengelmeyer et al., 1996), so these findings lack specificity for OCD. Lesions of the orbitofrontal cortex impair odour identification (Zatorre & Jones-Gotman, 1991), but there are inconsistent reports about odour recognition in OCD patients (Barnett et al., 1999; Hermesh et al., 1999). The object alternation paradigm originates from investigations after orbitofrontal function in non-human primates, but has been applied in humans as well (Freedman et al., 1998). Subjects are presented with two different objects, and are told that one of them hides a coin. The subject’s task is to learn that the object under which the penny was located was being alternated after each correct response. Monkeys and humans with orbitofrontal damage are unable to discover this rule (Gansler et al., 1996; Freedman et al., 1998). OCD patients perform worse than normal and schizophrenic controls (Abbruzzese et al., 1997; Gross-Isseroff et al., 1996; Spitznagel & Suhr, 2002) although the group differences in the study by Gross-Isseroff and colleagues were due to educational differences. Finally, OCD patients show increased risk taking on the Iowa Gambling task (Cavedini et al., 2001) but these results were not replicated in a subsequent study (Nielen et al., 2002).
Error processing and OCD

So far, there is no compelling evidence for cognitive involvement of the orbitofrontal cortex in OCD. One alternative approach towards the study of cognitive function in OCD may lie within the field of error processing. As proposed before, increased activation of the orbitofrontal and cingulate cortex in OCD could reflect an excessive generation of error signals (Schwartz, 1997). A more elaborate account of the error detection mechanism in OCD was formulated by Pitman (1987), who states that behaviour is controlled by a system in which environmental input is matched to an internal reference point (‘comparator’). The comparator calculates the difference between the input signal and the internal standard, and when comparison yields a mismatch, an error signal is generated. This error signal represents a level of discomfort (Pitman, 1987) and would inform cognitive, motor and affective systems of the necessity to correct the observed discrepancy. It depends on the level and motivational significance of the error message whether behavioural action is taken or not (Gehring et al., 2000). OCD patients may have an intrinsic defect in this comparator mechanism, so that this system continues to generate error messages (Pitman, 1987; Schwartz, 1997). Empirical support for this notion comes from a study demonstrating that OCD patients respond with an enhanced error-related negativity (ERN) to errors on a reaction time task (Gehring et al., 2000). The ERN is a negative-polarity, event-related potential brain component that is presumed to reflect error detection (Falkenstein et al., 1991; Coles et al., 1995) and is generated in the anterior cingulate cortex (Bush et al., 2000; Paus, 2001). Interestingly, these larger ERNs in OCD were observed on a non-symptom-relevant task, confirming there is a general dysfunction of the comparator system (Gehring et al., 2000). In line with this are recent findings by Hajcak & Simons (2002) who found that college students with subclinical levels of OCD displayed enlarged ERNs on both erroneous and correct trials of a Stroop task. This suggests that OCD is characterized by excessive error monitoring, regardless of whether or not errors have actually been made (Hajcak & Simons, 2002). It seems very interesting to pursue the study of error processing in OCD, as it offers the prospect of relating psychological models of error detection to the observed brain abnormalities in the disorder.
Integration: towards a neuropsychological model of OCD

Intrusive cognitions are quite ordinary phenomena that are experienced by most people every now and then. Patients with OCD, though, experience not only more intrusions but also are more aware of them. Furthermore, these intrusions usually elicit so much anxiety and distress that they markedly interfere with the subjective well being of the patient. A neurobiological explanation for this phenomenon is that OCD patients are more vulnerable to develop obsessions because of a disrupted equilibrium between direct and indirect basal ganglia subcircuits. We have seen that this could result in a biased filtering of incoming information, due to which obsessive thoughts or OCD-relevant information in the environment gain more easily access to conscious awareness. It remains to be seen whether this defect in striatal function is already present before OCD symptoms develop (so whether it is a ‘trait’ feature), or whether it is secondary to the abnormal neural activation of prefrontal cortical regions.

The characteristic information processing style of OCD patients could subsequently facilitate the development of obsessions. According to the cognitive theory of OCD, one key factor that facilitates the development of obsessions is the way in which intrusive cognitions are interpreted. As OCD patients have beliefs about increased personal responsibility, intrusive cognitions are appraised as indicating that the patient is responsible for the harm. Interestingly, research on the cognitive functions of the medial and orbitofrontal cortex reveals that these brain regions are crucially involved in the processing of emotion-related meanings. Although admittedly tentative, it is not unlikely that the excessive activation of the orbitofrontal network in OCD somehow stands for the faulty appraisal processes that characterize OCD (see figure 4). Appraisal can be considered to be the outcome of a matching process between perceptual input and an internal reference value. For example, thinking about stabbing someone (which is an intrusion) conflicts with moral standards about how one should behave, and therefore results in a mismatch or error signal. There is evidence that OCD patients already produce stronger error signals when dealing with non-threatening (and even ‘correct’) information. These signals could intensify even further in an obsessional state, possibly manifesting themselves as the excessive neural activation in the medial and orbitofrontal regions as has been found with PET and fMRI.

In turn, the enhanced prefrontal activation helps to sustain the relative overactivation of the direct as compared to the indirect striatal-thalamic pathway. This could mean that information about relevant themes (such as contamination or loss of control) is passed on to the striatum. These nuclei can use complex pat-
tern recognition to detect significant environmental input, which is relevant for the patient and therefore should gain access to conscious processing. Such a mechanism could explain the increased access of obsession-related thoughts and themes to conscious awareness.

The model that we propose here can also explain the persistent nature of compulsive actions. In order to determine the adequacy of a compulsive action, patients have to link the visual and sensory feedback that is obtained from performing the action to an internal reference (for compulsive handwashing, this could be ‘I feel clean’). When this comparison continues to produce a mismatch, for instance because the patient uses unusually strict criteria, performing the action can no longer reduce the anxiety. This can explain why many OCD patients eventually develop a complex hierarchy of rules that must be met in order to evaluate their own actions. One clinical example is the OCD patient who can only lock the door of his house by turning the key over and over again, on the rhythm of a tune that he is humming. The instant a car drives by in the street, the ritual is interrupted and the patient has to start all over again.

Therapeutic interventions with SSRIs or CBT are usually able to break this vicious circle. SSRIs may alter the sensitivity of 5-HT receptor subtypes in prefrontal and striatal areas and the amygdala, which may help to establish a new balance within striatal subcircuits. The efficacy of cognitive behaviour therapy, with its focus on cognitive appraisal processes, may be mediated directly by changes in the comparator system.

**Figure 4** — A neuropsychological model for OCD.
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