additionally treated with selective serotonin reuptake inhibitors (SSRI). After the end of treatment, the test battery was applied again. Also the controls were tested again after an interval of 3 months.

Results: At baseline, patients showed significantly lower performance compared with controls on tasks of nonverbal memory and fluency as well as speed of information processing and flexible, self-guided behavior. After CBT, there were no differences between groups on any neuropsychological parameter. A significant group x time interaction was found for the organization score of the Rey Figure, for verbal creativity and for speed-related tasks of set shifting with patients improving to a significantly larger extent. There was no significant association between severity and duration of illness or additional medication intake during CBT and cognitive functioning.

Conclusion: Results suggest that certain neuropsychological deficits in OCD patients are state-related and can be improved by CBT.

S-38-02

Brain imaging findings in patients with obsessive-compulsive disorder and their impact on cognitive behavioral therapy

A. Kordon, F. Hohagen. *Lübeck, Germany*

S-38-03

Pharmacotherapy of treatment resistant OCD: A summary of recent findings

D. Denys, *UMC Utrecht Dept. of Psychiatry, Utrecht, Netherlands*

Objective: Obsessive-compulsive disorder (OCD) is a common and severe, but still under-recognized psychiatric disorder. Although serotonin reuptake inhibitors (SRIs) currently are the most effective pharmacological treatment for OCD, up to 40 to 60% of OCD patients do not respond to treatment. Even after a switch to a second SRI-treatment, 30 to 40% of OCD patients fail to respond. In case of refractoriness to SRIs, addition with antipsychotics might lead to symptom improvement. It is intriguing why antipsychotics in monotherapy lack efficacy in OCD, while they are capable to induce de novo OCD symptoms in psychotic disorders, and are efficacious in addition to SRIs in some subtypes of OCD.

Methods: Results of efficacy of addition trials will be reviewed, and the possible neurobiological mechanisms of action of antipsychotic addition to SRIs will be discussed.

Results: Risperidone, olanzapine, and quetiapine were shown to be effective as add-on to SRIs in a number of studies. Changes in extracellular dopamine levels may account for the clinical efficacy of addition strategies with atypical antipsychotics in treatment-refractory OCD.

Conclusion: Addition of antipsychotics to SRIs is a safe and effective treatment option for patients with SRI-refractory OCD.

S-38-04

Cognitive treatment of OCD: Current developments

P. Salkovskis. *London, United Kingdom*

Tuesday, April 5, 2005

S-50. Symposium: Resolving the heterogeneity of obsessive-compulsive disorder

Chairperson(s): Michael Wagner (Bonn, Germany), Hans Jörgen Grabe (Stralsund, Germany)
08.30 - 10.00, Holiday Inn - Room 8

S-50-01

Disentangling the OCD phenotype

R. Delorme, M. Leboyer. *Paris, France*

Improvement in the phenotypic definition of obsessive compulsive disorder (OCD) is of crucial importance to identify genetics susceptibility factors. Identifying homogeneous forms of OCD through "candidate symptom" approach among affected subjects might yield better results (Leboyer et al, 2003). For example, clinical, neurobiological and genetic differences have been reported with respect to AAO of OCD. However, none of the various thresholds of AAO used in previous studies has been validated, and the notion that AAO is a marker for different subtypes of OCD, remains to be proven. Using an admixture analysis, we show that the observed distribution of AAO in 161 OCD patients is a mixture of two Gaussian distributions, defined by different clinical characteristics. These results validate the distinction between early- and late-onset OCD and provide an objective threshold for subdividing these two subgroups (Delorme et al, 2004). The endophenotype approach, i.e the identification of sub-clinical traits among non affected relatives, is also one of the strategies used to isolate genetic vulnerability factors in OCD. For example, peripheral serotonergic disturbances are frequently observed in OCD patients and could be used as endophenotypes. In OCD probands (n = 48) and their unaffected parents (n = 65) as compared to controls (n = 113), we observed lower whole blood 5-HT concentration, fewer platelet 5-HT transporter binding sites, and higher platelet inositol trisphosphate content (Delorme et al, 2004). Whole blood 5-HT concentration showed a strong correlation within families. Thus, the presence of peripheral serotonergic abnormalities in OCD patients and their unaffected parents supports a familial origin of these disturbances.

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S-50-02

Patterns of co-morbidity associated with OCD

S. Ruhrmann, H. J. Grabe, P. Falkai, S. Buhtz, S. Ettelt, A. Hochrein, C. Reck, R. Pukrop, J. Klosterkötter, H. J. Freyberger, W. Maier, M. Wagner. *Depart. of Psychiatry & Psycho, Cologne, Germany*

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Co-morbidity between OCD and other disorders is of major interest in terms of shared pathophysiology, impact on treatment and early recognition.

Method: Co-morbidity was investigated in 227 OCD patients and 475 of their 1° relatives as well as in 133 non-OCD controls and 396 1° relatives by direct (SADS) or indirect (FISC) interviews for DSM-IV diagnoses.

Results: OCD patients showed significantly elevated odds ratios (OR) for agoraphobia, separation anxiety disorder, social phobia, specific phobia, hypochondriasis, major depression, tic and Tourette's disorder, trichotillomania, body dysmorphic disorder, bulimia nervosa, and as a trend for anorexia nervosa and kleptomania. In first degree relatives of OCD patients there was a significantly higher risk for OCD (clinical and subclinical) and alcohol abuse. A trend was observed for an increased prevalence of dysthymia. ORs were markedly increased for all anxiety disorders, but statistical significance ($p < 0.05$) was not achieved.

Conclusion: A broadly increased risk for co-morbid disorders was observed in OCD patients, which supports and extents earlier findings. From a clinical point of view, especially the elevated risks for depression, anxiety disorders and alcohol abuse need to be considered as potential factors that may interfere with treatment and worsen prognosis.

S-50-03

Impulsiveness in Obsessive-Compulsive Disorder - Results of a family study

S. Ettelt, H. J. Grabe, H. J. Freyberger. *University of Greifswald, Depa, Stralsund, Germany*

Objective: Although some researchers suggested Obsessive-Compulsive-Disorder (OCD) to be a disorder of impulse control, previous studies found no clear evidence of an association between impulsiveness and OCD. This paper investigates the hypotheses of an elevated level of impulsiveness in cases and their first degree relatives compared to controls and their first degree relatives.

Methods: 70 cases and their 140 first degree relatives were compared to 70 controls and their 135 first degree relatives from a German family study on OCD (GENOS). All OCD cases and controls completed the Barratt Impulsiveness Scale (BIS-11) and the PAUDA-Inventory. Direct interviews were carried out in all cases and all controls and most relatives with the Schedule for Affective Disorders and Schizophrenia – Lifetime version (SADS LA IV) for anxiety disorders (DSM-IV). A registration of obsessive-compulsive symptoms was made by the Yale-Brown-Obsessive-Compulsive Checklist and Scale (Y-BOCS).

Results: OCD was significantly associated with higher scores of cognitive and total impulsiveness. However, first degree relatives of OCD cases and of controls had comparable BIS-11. scores. Cognitive impulsiveness was significant correlated with the present Y-BOCS Score for Obsessions. In linear regression analyses, the BIS-11. total score showed significant intrafamilial associations within the families of control subjects but not within families of OCD cases.

Conclusion: OCD is a severe mental disorder that is associated with cognitive impulsiveness. Cognitive impulsiveness is associated with a number of OCD symptoms, highly with obsessions. This trait seems to be restricted to the affected subjects and is not present in their first degree relatives.

S-50-04

A neurocognitive endophenotype in OCD?

M. Wagner, F. Buhtz, A. Hochrein, S. Schulze-Rauschenbach, E. Matuschek, S. Ruhrmann, R. Pukrop, J. Klosterkötter, H.-J. Grabe, P. Falkai. *Psychiatry, Bonn, Germany*

Objective: The endophenotype approach strives to identify neurobiological features which are more proximal to the genetic or environmental causes of a disease than are its behavioural manifestations leading to diagnosis. Familiarity of these features and independence from symptomatic state in patients are two important criteria. For example, in relatives of schizophrenics, neurocognitive deficits are present which are milder than those consistently found in patients, and which may be related to susceptibiliy genes affecting brain development. In patients with Obsessive Compulsive Disorder, moderate neuropsychological deficits have often been described, but these might be partly secondary to depressive symptoms. No family study so far has explored whether some of the neurocognitive deficits seen in patients with Obsessive Compulsive Disorder are also present in their healthy relatives.

Methods: We assessed neuropsychological and oculomotor perfomance in 64 patients with OCD, 33 of their unaffected first degree relatives, and matched healthy community controls.

Results: Memory functions were unaffected in OCD patients. Deficits in word fluency, perceptual organisation, and problem solving were related to current depression. Deficits in antisaccade performance, visual working memory and cognitive flexibility were independent of depression. Relatives were impaired in visual working memory and in the antisaccade task.

Conclusion: Some neurocognitive deficits, presumably related to frontostriatal functioning, seem to be present in OCD patients independent of current depression, and can be measured in relatives as well. If replicated, this novel finding would suggest that some specific cognitive functions may serve as endophenotypes in further research on OCD.

S-50-05

The role of dopamine in obsessive compulsive disorder: Preclinical and clinical evidence

D. Denys, *UMC Utrecht Dept. of Psychiatry, Utrecht, Netherlands*

Obsessive compulsive disorder (OCD) is a frequent and chronic psychiatric disorder that has been linked closely to the serotonin system mainly because of the anti-obsessional efficacy of selective serotonin inhibitors (SRIs). A limitation of the serotonin hypothesis of OCD is that a substantial part of the patients with OCD show no significant improvement after an adequate trial with an SRI. Pros and contras with regard the serotonin hypothesis of OCD will be discussed. There is substantial evidence that patients refractory to SRIs may benefit from addition therapies with antipsychotics, suggesting that dopamine might play a role in the pathophysiology of OCD. In this review, the preclinical and clinical evidence on the role of dopamine in OCD will be summarized. Evidence for the involvement of dopamine in OCD may be obtained by preclinical data from (1) animal models, and by clinical data from (2) measurements of dopamine and metabolite concentrations, (3) pharmacochallenge and (4) pharmacotherapeutic studies, (5) neuro-imaging, and (6) association studies.

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