

### EVENT-RELATED POTENTIALS IN OBSESSIVE-COMPULSIVE DISORDERS: ELECTROPHYSIOLOGICAL CORRELATES OF ABNORMAL COGNITION

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Individuals with an obsessive-compulsive personality disorder show certain abnormalities of cognition which may be characterized by "rigidity" (Shapiro, 1965). This may be a result of the specific "neurotic" character or of a primary deficit of the information processing.

Event-Related Potentials (ERPs) offer the possibility to investigate the functional aspects of cognitive and emotional processes. To investigate some aspects of thinking in obsessive-compulsive individuals we chose a continuous word recognition ERP-paradigm. In these experiments brain responses to repeated items ("old" words) are characterized by more positive waveforms of the ERPs mainly due to a reduction of the N400 and an enhancement of the P600 compared to the ERPs for the first presentation of the words ("new" words). This recognition-effect has been referred to as the 'old/new-effect' (e.g., Rugg et al. 1995) and has been shown to be sensitive to various cognitive and emotional factors.

In the present experiment we investigated non-medicated obsessive-compulsive patients (ICD10: F42.X; n = 8) and normal controls (n = 12). The words were presented visually with some words being repeated. The subjects had to decide whether a given item was presented for the first or the second time. For the normal controls the ERPs for the correctly detected 'old' words (recognized words) showed an increased positivity, beginning approximately 250 ms post stimulus. This effect appeared to be much smaller in the obsessive-compulsive individuals, but the N400-components for the first presentation, as well as for the second presentation were significantly enhanced compared to the normal controls. As N400 amplitude has been shown to covary with the ease of contextual integration of a stimulus we suggest that this aspect of verbal behavior is altered in obsessive-compulsive individuals and might be related to their core deficit.

### EFFECTS OF CHALLENGE WITH META-CHLOROPHENYLPIPERAZINE (mCPP) AT BEHAVIOR AND CEREBRAL BLOOD FLOW IN OBSESSIVE COMPULSIVE DISORDER

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In patients with Obsessive Compulsive Disorder (OCD) symptoms can be provoked with the non-selective serotonin-2C receptor agonist mCPP. Functional imaging studies indicate the involvement of the (pre-)frontal cortex and basal ganglia in OCD. We hypothesized that a challenge with mCPP in OCD would provoke OCD-symptoms and simultaneously increase the regional cerebral blood flow (rCBF) in the frontal cortex and basal ganglia, measured with <sup>99m</sup>Tc-HMPAO SPECT (Single Photon Emission Computed Tomography).

We performed a placebo-controlled, double-blind, randomized cross-over challenge-procedure with 0.5 mg/kg mCPP p.o. in 7 patients with OCD and 7 controls. Each challenge was followed by a SPECT-scan. Regional cerebral blood flow measurements were obtained with the cerebellum as well as whole brain as reference regions.

Preliminary results show no significant increase in behavioral effects of mCPP on obsessive-compulsive or anxiety symptoms in OCD and controls compared with placebo. In OCD, mCPP causes a significant decrease in rCBF of whole brain (p = 0.023) and cerebellum (p = 0.022) in comparison with placebo. No effects are seen in other regions of interest. In controls, mCPP causes no effect in rCBF of the cerebellum. A slight increase in the rCBF of whole brain (p = 0.068) and a significant increase in rCBF of the caudate nucleus (p = 0.04) and putamen (p = 0.027) in mCPP compared with placebo is seen. The rCBF of whole brain in OCD following placebo, but not after mCPP, was higher than in controls.

It is concluded that the mCPP decrease of rCBF of the whole brain in OCD is for the most part accounted for by the decrease of rCBF of the cerebellum. In controls the cerebellum was not affected by mCPP. The slight increase seen in whole brain is probably accounted for by the caudate nucleus and putamen. mCPP therefore appears to have a differential effect on rCBF in OCD and controls. The surprising finding that the rCBF of the cerebellum in patients with OCD is lower than in healthy controls warrants further studies into the role of this brain region in the pathophysiology of OCD.

### CEREBRAL UPTAKE OF 99m-Tc-HMPAO IS STABLE IN OBSESSIVE COMPULSIVE DISORDER (OCD) DURING EXPOSURE IN-VIVO ON SPLIT DOSE SINGLE PHOTON EMISSION TOMOGRAPHY (SPET)

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Reduced caudate uptake of 99m-Tc-HMPAO has been reported in OCD (Rubin et al 1992, Edmonstone et al 1994, Lucey et al 1995). To examine the influence of acute anxiety on regional cerebral uptake of 99m-Tc-HMPAO (a marker of regional cerebral blood flow), 15 DSM III-R OCD outpatients (9 male, 6 female) were SPET scanned twice in a single session on a brain dedicated GE SPET scanner. A split dose resting 99m-Tc-HMPAO SPET scan was followed 1 hour later by a second 99m-Tc-HMPAO SPET during exposure in-vivo to a feared stimulus. Uptake of 99m-Tc-HMPAO in resting and provoked conditions was compared. Mean (SD) patient age was 39 (8) years and illness duration was 24 (1) years. Mean (SD) YBOCS score was 24 (5) and BECK depression score was 13 (7). Seven patients were drug free for at least 3 months. Patients pulse, respiratory rate and visual analogue anxiety level were recorded throughout. Scans were analyzed blindly by a single rater. Regional 99m-Tc-HMPAO uptake was expressed as a ratio of mean cerebellar uptake. Following exposure patients pulse, respiratory rate and anxiety level were significantly elevated (F = 11.6, df = 1.29, p = 0.002). Total cerebral and regional 99m-Tc-HMPAO uptake was unchanged during exposure (F = 0.29, df = 1.28, p = 0.6). The results suggest that 99m-Tc-HMPAO uptake in OCD is not altered by acute anxiety.

### THE GALWAY STUDY OF PANIC DISORDER IV: TEMPORAL STABILITY OF DIAGNOSIS BY PRESENT STATE EXAMINATION TEST RETEST

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**Background:** A long term outcome study of DSM III-R Panic Disorder included Present State Examination (PSE) at baseline and follow up 5 to 6 years later.

**Aims and Method:** PSE test retest and individual within-patient change scores on various PSE syndromes were assessed for consis-

tency with either a categorical view of panic disorder as a stable clinical entity or panic disorder as one facet only of a 'general neurotic syndrome'.

**Result:** PSE profile at baseline was virtually identical with that at follow up. Few patients had 'changed' in PSE syndrome diagnosis after 5 to 6 years.

**Conclusion:** These data, although not conclusive, are supportive of the concept of DSM III-R Panic Disorder as a stable clinical entity and are correspondingly difficult to reconcile with the view that Panic Disorder is but one facet only of a general neurotic syndrome.

#### "FEAR FIGHTER," BEHAVIOURAL SELF-HELP FOR AGORAPHOBIA ON COMPUTER MULTIMEDIA — A NEW SYSTEM

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Computer aids in medicine have been available for many years mostly to do assessment or to collect data. Computer aids for treatment are still uncommon. A behavioural self care system has been computerised and subjected to prepilot testing.

10 agoraphobic patients who were either receiving treatment or had done so previously were asked to comment on Fear Fighter and compare it to their experience of face to face behaviour therapy. All 10 patients felt that Fear Fighter was user friendly, even those who had not used a computer before. Although they could not comment on Fear Fighter's efficacy as they were not using it as a self treatment tool, all 10 patients felt keenly that "Fear Fighter" could be used for self-treatment and could have helped them. The use of multimedia, in particular female voice-over accompanying text, was seen as a great advantage in making the computer system feel friendly.

#### THE BENZODIAZEPINE ANTAGONIST FLUMAZENIL IS ANXIOLYTIC IN HIGH STATE ANXIETY AND ANXIOGENIC IN LOW STATE ANXIETY IN A STUDY OF 23 FEMALE ANIMAL PHOBICS

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**Objectives:** Flumazenil (Ro 15-1788) initially was believed to be a pure benzodiazepine receptor antagonist, exerting no intrinsic effects. Later in several studies evidence for agonistic or inverse agonistic effects of flumazenil was found. In humans flumazenil has been shown to be anxiogenic, e.g. [1], or anxiolytic [2]. On the other hand it has been asserted that "flumazenil exhibits virtually zero intrinsic efficacy" [3]. File and Hitchcott [4] explained these contradictions by suggesting that flumazenil normalizes the benzodiazepine receptor, returning it to a baseline state. The theory states that flumazenil effects depend on the anxiety level: When anxiety is high, flumazenil reduces it; when anxiety is low, flumazenil increases it. Our study tested these assumptions.

**Methods:** 23 female spider phobics were diagnosed as having simple phobia according to the criteria of DSM-III-R. They were about to receive exposure therapy and were given either an infusion of 2 mg flumazenil in 0.9% saline solution at a rate of 0.2 mg per minute or saline solution 0.9% alone under randomized double-blind conditions. Immediately after the infusion patients were asked to rate their pre-infusion state anxiety and their maximum state anxiety (if increased) or minimum state anxiety (if decreased) during the infusion on a scale from 0 to 10.

**Results:** Mean anxiety ratings were not significantly changed by the infusion in either group. While retrospective ratings of state anxiety before the infusion and ratings of anxiety experienced during the infusion were positively correlated for placebo subjects ( $r = 0.68$ ,  $p < 0.02$ ), they were negatively correlated in the flumazenil group ( $r = -0.73$ ,  $p < 0.02$ ): phobics with high ratings of pre-infusion state anxiety showed low ratings of anxiety while receiving flumazenil and vice versa.

**Conclusion:** The findings of our study support the theory suggested by File and Hitchcott.

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#### DECREASED PERIPHERAL-TYPE BENZODIAZEPINE RECEPTOR IN POSTTRAUMATIC STRESS DISORDER

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Peripheral-type benzodiazepine receptors (PBR) have been located in various peripheral organs and in non-neural tissue in the brain. PBR is involved in steroidogenesis and is sensitive to stress and hormonal changes. In a previous study we demonstrated that PBR is decreased in patients with generalized anxiety disorder (GAD) but not in obsessive-compulsive patients (OCD). In the present study we assessed [<sup>3</sup>H] PK 11195 binding characteristics in posttraumatic stress disorder (PTSD). Eighteen PTSD patients and 7% age- and sex-matched controls participated in the study. All subjects underwent a psychiatric interview using the Structured Clinical Interview for DSM-III-R-Patient Version. Symptom severity was assessed using: DSM-III-R Scale for PTSD, Impact of Event Scale, Beck Depression Inventory, State-Trait Anxiety Inventory. All psychological measures were significantly higher in PTSD patients when compared to control subjects ( $p < 0.001$ ). Decreased platelet PBR density ( $-62\%$ ;  $p < 0.001$ ) was observed in the PTSD patients when compared to controls. The results in the present study are in accordance with the finding in GAD patients, but differ from those obtained in OCD patients. It is possible that the reduction in PBR density is an adaptive response in order to avoid chronic hypercortisolemia secondary to stress.