

compared to placebo (0.1-point worsening). Changes in EPS were not statistically or clinically significantly different for patients treated with olanzapine.

Conclusion: Compared to placebo, 5 mg/day of olanzapine significantly improved psychotic symptoms and behavioral disturbances in patients with possible DLB. Additional well-controlled studies are needed to confirm these results.

FC02.05

ASSOCIATION OF A CATHEPSIN D GENE POLYMORPHISM WITH ALZHEIMER'S DISEASE

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The proteolytic cleavage of amyloid precursor protein (APP) by the beta- and gamma-secretases resulting in the formation of beta amyloid peptide (betaA4) is a crucial step in the pathogenesis of Alzheimer's disease (AD). Overexpression or enhanced activity of beta- and gamma secretases may result in increased amounts of betaA4 and therefore be causative of AD. Cathepsin D (catD) is an intracellular acid protease with in-vitro beta- and gamma-secretase-like features. A C to T (ala to val) transition at position 224 of the card gene (exon 2) was associated with increased pro-catD secretion and altered intracellular maturation of the enzyme. We tested the hypothesis that this polymorphism is associated with an increased risk for AD in two independent case/control samples. The cathepsin D T allele was over-represented in demented patients compared to non-demented controls ($p = 0.001$), the corresponding odds ratio being 3.0. Our data suggest that the catD T allele poses an increased risk for AD which is independent of the individual's age. At least for some forms of AD, card might be a putative target of therapeutic strategies aimed to block secretase activity.

FC02.06

OBSESSIVE-COMPULSIVE DISORDER AND HUNTINGTON'S DISEASE IN A LARGE ITALIAN PEDIGREE

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Background: Huntington's Disease (HD) is a progressive neurological condition with onset usually in midlife. It is due to a trinucleotide repeat expansion localized on the short arm of chromosome 4, and is clinically characterized by chorea and dementia. The initial and most severe degeneration occurs in the basal ganglia. We have previously described a nuclear HD family with three cases of Obsessive-Compulsive Disorder (OCD) and two of Pathological Gambling (PG). It was noteworthy that all subjects with OCD and related disorders carried the HD mutation.

Study Design: We are presently investigating a large pedigree from a psychiatric, neurological, and genetic viewpoint. All members studied suffer from HD or are at 50% risk for it. They are related to the individuals described in our previous study.

Results: To date, 25 subjects have been examined. Among these, 7 exhibited a full OCD (28%). There was a significant difference with the 1% prevalence rate of OCD reported in the general population ($p = 0.00004$). No cases of OCD have been identified in our control population so far ($n = 29$). Three probands with HD had a previous history of OCD. This strengthens the hypothesis that there may be a genetic effect in the pathogenesis of OCD in this family.

Conclusions: These preliminary results show a significantly heightened risk for OCD in members of this HD family. It can be

hypothesized that OCD may be caused by an initial impairment of the basal ganglia and related circuits before onset of the full choreic picture. It is alternatively possible that there may be a genetic linkage between the HD gene and one of the genes predisposing to OCD. Verification of both these hypotheses will require the investigation of an extension of this sample and analysis of the lid mutation, which we are presently carrying out.

DE01. Is the borderline personality disorder a fiction and irrelevant for treatment?

Chair: J.Guimon (CH)

DE01.01

BORDERLINE PERSONALITY DISORDER IS A FICTION & IRRELEVANT FOR TREATMENT

M.H. Stone. *USA*

Borderline Personality Disorder is one of about 200 disorders listed as psychiatric conditions in DSM-IV. It enjoys the dubious distinction of being the only one in this long list whose label conveys no meaning whatsoever as to the nature of the entity supposedly being described. Unlike "anorexia" (which immediately signifies "no appetite") or "paranoid personality" (which immediately signifies "pathological suspiciousness"), *borderline* gives no hint of what sort of condition lay behind the diagnostic label.

A personality disorder should be defined, obviously, by terms that relate purely to the area of personality – that is, by genuine personality *traits*. Thus "schizoid" personality is (properly) defined by the traits of aloofness, emotional coldness, indifference to praise or criticism, etc. But *borderline* is defined almost entirely by symptoms – that by rights should relegate the condition to a place in DSM's Axis-One, which is for symptom conditions. Self-cutting, identity disturbance, stormy relationships and mood lability, for example, are all symptoms, not traits.

Because of the polythetic nature of the definition in DSM – any 5 of the 9 items can suffice to support the diagnosis – there are 256 ways of being "borderline." This makes for a bewildering heterogeneity, allowing for so many different kinds of conditions to fit themselves under the broad umbrella of "BPD" as to render the diagnosis rather meaningless. This heterogeneity also robs the label of any real clues as to what kind of treatment might be appropriate, given the wide array of different clinical pictures that satisfy BPD's all-too broad and confusing.

Definition: Long-term follow up study of BPD shows that patients given this diagnosis vary in their outcome all the way from suicide to becoming CEO's of large corporations, successful professionals, creative artists, and the like. Some BPD patients are essentially untreatable, others require massive efforts to stave off suicide and restore some measure of function; others are actually good candidates for psychoanalysis. The label, in other words, gives little direction as to what type of treatment would be indicated, or what the outcome might prove to be.

The term "borderline" has its origin in the 19th century effort to deal with conditions that were neither altogether psychotic nor healthy enough to be called neurotic: there were "in between" conditions; i.e., "borderline." To be sure, there are such patients. But we now recognize that there are so many different varieties, that to call them "borderline" (and then to append the term "personality disorder" in addition) only confuses the picture. Those patients

who are at once anger-prone, suicidal, unreasonable, manipulative, and moody (and these make up an important sub-set of BPD patients) do exist, and deserve a separate, and meaningful, label that (a) characterizes them adequately by its very term, and (b) is homogeneous with respect to optimal treatment.

DE01.02
POINTS CONCERNING THE UTILITY OF B.P.D.'s
RELEVANCY FOR TREATMENT

H. Sass. *Clinic of Psychiatry and Psychotherapy, Technical University of Aachen, Germany*

There is a 110-year-old tradition in psychiatry, identifying certain clinical states as "in between" mild (Neurotic) & severe (Psychotic) levels of pathology.

BPD represents, as a long tradition in psychiatry & psychoanalysis, a clinical syndrome containing elements of marked personality aberration of the "Dramatic" type, and elements of symptom-disturbance, involving mostly mood instability.

Granted that the term "borderline" conveys no clue as to what kind of personality aberrations the term signifies, it has been difficult to find better alternatives: to change the name to "impulsive" personality disorder overlooks the striking degree of self-destructiveness BPD patients exhibit; the same is true if one renamed it "unstable" personality.

The constellation of characteristics that make up the BPD definition – chiefly, impulsivity, inordinate anger, self-destructive acts, marked moodiness – has been noted and described in many countries around the world. It has been shown to have construct validity.

There appears to be a close relationship between childhood trans-generational incest and the development of BPD in young women – in a manner not seen to nearly the same degree in the other DSM-personality disorders. There are other etiological routes to BPD, but this type of childhood trauma is important and helps explain the preponderance of women in most samples of BPD.

Clinically, BPD patients tend to exhibit "splitting" – envisioning themselves and other people as "all good" or "all bad" or else as alternating between these polarities.

This sets the tone for the course psychotherapy must take – in helping the BPD patient integrate these dichotomized perceptions.

There is also a set of pharmacological interventions that are useful in many patients with BPD – that are fairly specific to the condition, and seldom as useful with the other personality disorders (e.g., the SSRI's & the MAOI's).

Certain neurophysiological findings are beginning to emerge that are found with some regularity in BPD patients, but seldom in the other personality disorders.

**PD01. AEP Board of Education: Panel
discussion on the future of education in
Europe**

Chairs: M. Musalek (A), N. Sartorius (CH)

No abstracts received.

**S11. The dysconnectivity hypothesis of
schizophrenia**

Chairs: K. Vogeley (D), P. Falkai (D)

S11.01
FROM EARLY MISCONNECTIONS TO ADULT
MISCONCEPTIONS

R.M. Murray

No abstract was available at the time of printing.

S11.02
TRANSCALLOSAL MISCONNECTIVITY: THE
CONSEQUENCE OF ANOMALOUS LATERALIZATION

T.J. Crow

No abstract was available at the time of printing.

S11.03
THE DISCONNECTION HYPOTHESIS: THEORETICAL
UNDERPINNINGS

K.J. Friston. *Wellcome Senior Fellow in Clinical Science, Wellcome Department of Cognitive Neurology, Institute of Neurology, UCL, London, UK*

This talk reviews the disconnection hypothesis of schizophrenia and Presents a mechanistic account of how dysfunctional integration among neuronal systems might arise. This neurobiological account is based on the central role played by neuronal plasticity in shaping the connections and the ensuing dynamics that underlie brain function. The particular hypothesis put forward here is that the pathophysiology of schizophrenia is expressed at the level of modulation of associative changes in synaptic efficacy; specifically the modulation of plasticity in those brain systems responsible for emotional learning and memory, in the post-natal period. This modulation is mediated by ascending neurotransmitter systems that; (i) have been implicated in schizophrenia and (ii) are known to be involved in consolidating synaptic connections during learning. The proposed pathophysiology would translate, in functional terms, into a disruption of the reinforcement of adaptive behaviour that is consistent with the disintegrative aspects of schizophrenic neuropsychology.

S11.04
USING FUNCTIONAL NEUROIMAGING TO EXPLORE
CONNECTIVITY AND DYSCONNECTIVITY IN
SCHIZOPHRENIA

P. Fletcher

No abstract was available at the time of printing.