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 fir 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

https://doi.org/10.1016/S0924-9338(00)93988-9 Published online by Cambridge University Press