FC02. Dementias and organic disorders

Chairs: W.S. Clark (USA), I. Bitter (H)

FC02.01

THE PATHOGENETIC ROLE OF DOPAMINE IN HIV-INDUCED CNS DISEASE

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Human immunodeficiency virus (HIV) infection is frequently associated with specific neurological symptoms. The neurological complications are characterized by cognitive impairement, behavioural abnormalities and motor disabilities that may mimic aspects of Parkinsonism. This syndrome presents predominantly as a subcortical dementia and HIV-positive cells and pathological changes in CNS are found primarily in dopamine-rich areas, the basal ganglia.

To study the role of the dopaminergic system in HIV infection we used the well-established simian immunodeficiency virus (SIV) infected rhesus monky model. This model is valuabe for the investigation of the pathogenesis of AIDS-related CNS disorders.

The study reports the involvement of the dopaminergic system in SIV infection, fascinating-novel results of dopaminergic substances in the development of SIV-induced CNS disease and reconsiders the current therapy.

FC02.02

EARLY AND DIFFERENTIAL DIAGNOSIS IN MILD COGNITIVE IMPAIRMENT, ALZHEIMER'S DISEASE AND DEPRESSION

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Introduction: To confirm the finding that P3b-amplitudes and P3a-latencies are affected in Alzheimer's disease (AD) and to evaluate the sensitivity of these P300 subcomponents for early diagnosis of AD and differential diagnosis between AD and depression.

Background: Due to recent advances in reliability as well as physiological validity of the P300 methodology, P300 parameters have become a promising tool for research in Alzheimer's disease (AD).

Methods: P300 was recorded within an oddball paradigm. Using an improved P300 method of dipole source analysis of P300, patients with Alzheimer's disease (AD; N = 26), Memory complainers (MC; N = 39), Mild cognitive impairment (MCI; N = 26); Major Depression MD; N = 11) and Healthy Controls (HC; N = 43) were analyzed. Cognitive testing was performed with the Consortium to Establish a Registry for Alzheimer's Disease (CERAD).

Results: Patients with AD showed smaller P3b-amplitudes and prolonged P3a-latencies compared to HC and patients with MD. Sensitivity was 88.5% to detect patients with AD in comparison to MD (specificity 72.7%). P3b-amplitudes were smaller in AD than MC or MCI, whereas P3a-latencies were prolonged for MC in comparison to HC.

Conclusion: P3b-amplitudes and P3a-latencies offer additional clinical information for the differentiation of AD from MD. Moreover, P300 might be interesting as a marker for patients with cognitive disturbances, who might convert to AD.

FC02.03

THYROID FUNCTION OF ELDERLY PATIENTS WITH MENTAL DISORDERS

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Introduction: Thyroid disorders are very frequent in old persons as well in the course of several mental disorders. It is important to detect eventual thyroid disorders to treat correctly the mental disorder. The main aim of this preliminary study is to analyse the thyroid function of a sample of elderly patients with mental disorders at the moment of admission at the Geriatric Psychiatry Day Hospital (DH), Lausanne, and compare it with their respective mental problem and nutritional status.

Material and Methods: Thyroid function (TSH, FT4, FT3) of 167 patients successively admitted at DH was studied (33 men, 134 women; mean age = 75.70 +/– 6.80). Some parameters such age, sex, cognitive status (MMS), intensity of depression (HDRS), nutritional status (MNA) were considered. Patients were divided in 4 groups according to their respective mental problem: A1, with cognitive impairment and depressive symptoms (n = 39); A2, without cognitive impairment but with depression (n = 69); B1, with dementia and without depressive symptoms (n = 18); B2 without cognitive impairment and without depressive symptoms (n = 41).

Results: Age was correlated to FT4 ($r = 0.37$, $p < 0.01$) and to the intensity of depression ($r = 0.20$, $p < 0.05$). TSH was only correlated to FT4 ($r = -0.30$, $p < 0.001$) and to the nutritional status ($r = 0.25$, $p < 0.02$). The group B2 had lower, but not significant, TSH, FT4 and FT3 plasmatic levels than other than other 3 groups.

Discussion et Conclusion: The absence of significant difference of thyroid function among the 4 groups could be explained by the difference size of the 4 groups but the lower plasmatic levels of thyroid hormones at the group with dementia is suggestive. More studies with better methodology are necessary to explore these results.

FC02.04

REDUCTION OF PSYCHOTIC SYMPTOMS IN PATIENTS WITH LEWY BODY-LIKE SYMPTOMS TREATED WITH OLANZAPINE

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Introduction: A post hoc analysis was performed on the results of a double-blind, 6-week study of nursing home patients (n = 206) with dementia to determine the efficacy and safety of olanzapine in reducing psychosis and behavioral disturbances.

Methods: The effects of 5, 10, and 15 mg/day olanzapine were assessed relative to placebo in patients who had possible Lewy body dementia (n = 29), determined by a nonzero score on the Simpson-Angus Scale and a nonzero score on the Hallucinations item of the NPI/NH. All data are reported as mean changes.

Results: Patients receiving 5 mg/day of olanzapine improved by 82.9% on the NPI/NH Delusions and Hallucinations combined score, compared to 17.4% for placebo (p = .015). On the Delusions item, olanzapine-treated patients improved by 77.8%, compared to 29.0% for placebo (p = .012). Olanzapine-treated patients showed 85.7% improvement in Occupational Disruptiveness related to the NPI/NH Delusions and Hallucinations items. Placebo-treated patients showed only 14.0% improvement (p = .002). Significant improvement (p = .042) was also found on the Mini-Mental State Exam for olanzapine-treated patients (2.4-point improvement),

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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

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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

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