S-34-02

In vivo functional neuro-imaging provides new insights into the suicidal brain

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Objective: This review of neuro-imaging findings in attempted suicide patients, depressed non-suicidal patients, and healthy controls will show that, from a neuro-anatomical point of view, there is now increasing insight in the role of prefrontal-subcortical circuits in the development of suicidal behaviour through their involvement in the modulation of trait-dependent cognitive and/or emotional characteristics

Results: From a neurobiological point of view, the role of serotonin in particular is elucidated through receptor binding studies and through the study of correlations between receptor binding indices and psychopathological characteristics.

Conclusion: Taken together with the results of biological, neuropsychological and cognitive psychological challenge studies, these findings provide new insights in the suicidal brain.

S-34-03

Serotonergic genes influence suicidal behaviour

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Objective: The involvement of genetic risk factors and of interaction between genes and environment in suicidal behaviour is supported by family, twin, and adoption studies. Several lines of evidence indicate that disturbances of the central serotonin system are involved in the neurobiology of suicide, possibly by modulating a restraint function in which the ventromedial prefrontal cortex seems to play an important role. Accordingly, several molecular genetic studies of serotonin-related genes have been published. Promising results have been obtained with the serotonin transporter (5-HTT) gene. The 5-HTT plays a crucial role in maintaining presynaptic homeostasis in several ways. A recent meta-analysis provides significant evidence supporting the association between the S allele of a functional 5-HTT promoter polymorphism and suicidal behaviour, also with violent suicide. Interestingly, it has recently been shown that the 5-HTT gene interacts with life events to predict suicidality: the effect of life events on subjects reports of suicide behaviour was stronger among individuals carrying an S allele than among L/L homozygotes. The other widely studied gene is that coding for tryptophan hydroxylase (TPH). TPH is the rate-limiting enzyme in the synthesis of serotonin. Two different genes code for TPH: TPH1 and TPH2. Two meta-analyses of association studies between the TPH1 A218C polymorphism and suicidal behaviour in Caucasian populations clearly suggest an association between the A allele and suicidal behaviour. TPH2 gene has recently been associated with suicide but this result is not confirmed by recent studies. Studies of other serotonin-related genes are so far inconclusive.

S-34-04

Aggression-related genes in suicidal behavior: An intermediate phenotype strategy in the search for genetic susceptibility factors

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Risk of suicide-related behavior is supposed to be determined by a complex interplay of sociocultural factors, traumatic life experiences, psychiatric history, personality traits, and genetic vulnerability. This view is supported by adoption and family studies indicating that suicidal acts have a genetic contribution that is independent of the heritability of Axis I and II psychopathology. The heritability for serious suicide attempts was estimated to be 55%. Neurobiological studies have shown that serotonergic dysfunction is implicated in suicidal behaviors. These findings stimulated the investigation of variations in serotonergic genes in this context. We have initiated a large scale case control genetic association study which comprises of 250 suicide attempters and 600 healthy volunteers and investigated the role of a comprehensive set of serotonergic candidate genes in this behavior. We will present new data on a comprehensive set of serotonergic candidate genes. Since both, aggression related traits and serotonergic activity are partially heritable and correlate inversely, variations in genes of the serotonergic system might then, to some extent, account for variations in aggression-related behavior. Thus, we also investigated the relationship between serotonergic genes and anger, as a subtype of aggression-related behavior.

Monday, April 4, 2005

S-36. Symposium: German depression research network: Results from naturalistic and intervention studies

Chairperson(s): Hans-Jürgen Möller (München, Germany), Ulrich Hegerl (München, Germany)
16.15 - 17.45, Gasteig - Philharmonie

S-36-01

Diagnostic and treatment issues in primary care

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Objective: Under-diagnoses and under-treatment of depression has been recognized as a considerable problem at the primary care level. Only multifaceted interventions appear to be a promising strategy to reduce these deficits. Such an intervention has been implemented and evaluated within the "Nuremberg Alliance against Depression". Some of the elements of this intervention in Nuremberg will be presented.

Methods: Comparing several screening instruments for depression, the WHO-5 turned out to be the most promising tool at the primary care level and is recommended in the CME-activities with GPs. Two videos have been produced, which can bee handed out by the GPs to their patients in order to transmit information and a disease concept concerning depression. These activities are integrated in a professional public relation campaign, in a cooperation with community facilitators (teachers, priests, media, geriatric care givers) and in support of self help activities in Nuremberg.

Results: During the two-year-intervention a clear and significant reduction of suicidal acts has been observed in Nuremberg as compared to a one-year -baseline and a control region. Changes in prescription of antidepressants and other psychotropics are documented.

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Conclusion: Although the cooperation with GPs was only one element in the Nuremberg alliance against depression, there are good reasons to assume, that these activities have contributed to the prevention of suicidality.

S-36-02

Results of the algorithm study in acute depression

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Objective: The Berlin Algorithm Project is a multi-step project which aims at evaluating the effectiveness, acceptance and efficiency of systematic algorithms for the treatment of inpatients with major depressive disorders. The first open prospective observational phase of the project showed moderate acceptance but good clinical effectiveness of a standardized stepwise drug treatment regimen (SSTR) for patients hospitalized for depression. The second project phase was a prospective randomized controlled clinical trial which demonstrated a significant overall superiority in terms of effectiveness of a SSTR compared to standard treatment as usual (STU).

Methods: The present third and final phase of the project which is realized within the German Research Network on Depression compares three different SSTRs with a computerized clinical database and expert system (CDES) and with STU in a five-arm, prospective, longitudinal, parallel-group, multicenter approach. Seven academic and three non-academic psychiatric hospitals are participating in this trial. Enrollment of patients started in 2004 and will be closing in mid 2005. Study design and preliminary results will be presented.

Results: As of November 2004, 432 patients with a unipolar depressive disorder were enrolled. An interim analysis of available data of the third phase shows that significantly more patients achieve remission with SSTR therapy which includes a trial of lithium augmentation after a trial of antidepressive monotherapy has failed.

Conclusion: Medication algorithms for the treatment of acute major depression are ideal instruments to optimize both treatment implementation and the appropriateness of treatment strategies.

S-36-03

Lithium treatment as prevention strategy

W. Felber. *Karl-Gustav-Carus-Universität, Dresden, Germany*

S-36-04

Short- and long-term outcome of hospitalised unipolar depressive patients

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Unipolar depression is the most prevalent and under different aspects the most relevant affective disorder. It therefore seems necessary to learn more about results of short-term treatment and long-term outcome under naturalistic conditions. In the context of the German research network depression/suicidality a 3-year follow-up study was performed on patients being treated in hospital for an acute depressive episode. Due to the network structure several university hospitals and non-academic hospitals participated in this study, thus guaranteeing a reasonable representativeness of the results. At the moment data from about 690 patients are available for the preliminary analysis. First results of this study demonstrate that even in such a sample of depressive inpatients, a high proportion of which were transferred to hospital due to treatment resistance under outpatient conditions, the treatment result is generally satisfying. However, with an average of 60 days the mean duration of inpatient treatment is quite long, which underlines that these patients are difficult to treat and mostly need several sequences of treatment with different drugs and also intensive co-medication strategies and sometimes ECT. Under these conditions response can be achieved in approximately 75% of patients. 53% are even remitters, which seems to be quite a good result. On the other hand, even after such long hospital treatment and using drug treatment strategies of all kinds, at discharge from hospital about 25% of patients do not reach the response criterion of 50% reduction of the Hamilton Depression Scale from admission. The most important point is that the stage of response at discharge from hospital after index admission is closely associated with the severity of depression at 1-year follow-up. This underlines the need to force remission or response as far as possible using all kinds of treatment strategies. But even then it might be necessary to accept that a certain subgroup of depressive patients have a more or less chronic course, which has also been demonstrated by other follow-up studies, such as the huge North American one.

S-36-05

Follow up imaging in major depression: New insight in the neurobiology of affective disorders?

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Although the hippocampus has been found to be smaller in patients with depression, prospective longitudinal in vivo studies are necessary to investigate whether depression can result in a further diminution of hippocampal volumes or whether a smaller hippocampal volume predisposes an individual to the development of depression. Method: Thirty patients with DSM-IV major depressive disorder as well as 30 healthy control subjects matched for age, gender, and handedness were examined at admission to the hospital and 1 year later using a documentation of the medical history and high-resolution magnetic resonance imaging (MRI) for the presence of depression and to determine changes in hippocampal as well as amygdala volumes. Patients were enrolled from March 2000 to August 2002.

Results: No significant hippocampal and amygdala volume changes were observed in patients or controls between baseline and 1-year follow-up investigations. However, the subgroup of patients who were nonremitted at the time of the follow-up investigation showed significantly reduced left and right hippocampal volumes at both baseline and the 1-year follow-up compared with remitted patients. Moreover, the right hippocampal volumes of nonremitted patients were significantly smaller compared with matched healthy controls.

Conclusion: These results do not support the hypothesis that hippocampal volumes diminish during the 1-year follow-up period. However, smaller hippocampal volumes may be related to a poor clinical outcome after 1 year.

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