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Background: To examine prospectively the natural course of major depressive disorder (MDD) and to test the effects of personality disorders (PDs) on remission and relapse over six- year follow-up.

Methods: Subjects were 302 patients (196 women, 106 men) with current MDD at baseline enrollment in the Collaborative Longitudinal Personality Disorders Study (CLPS), a NIMH-funded multi-site study (Yale, Brown, Columbia, Harvard). MDD and psychiatric disorders were assessed with the Structured Clinical Interview for DSM-IV and PDs with the DIPD-IV. The course of MDD was assessed with the Longitudinal Interval Follow-up Evaluation and the course of PDs with the Follow-Along version of the DIPD-IV at 6- and 12-months and then yearly for 6 years. Good inter-rater and test-retest reliabilities were established.

Results: Lifetable survival analyses revealed an overall 24-month remission rate of 74% for MDD that differed little by gender but was significantly lower among patients with PDs (range 52% to 81%) than without PDs (89%). Cox proportional hazards regression analyses revealed that MDD patients with co-existing PDs had significantly longer time to remission than did MDD patients without any PD even when controlling for other negative prognostic predictors (psychiatric co-morbidity, dysthymia, gender, ethnicity, early-onset and recurrent MDD, and treatment). Among patients who achieved remission from MDD, the probability of relapse was significantly greater and time to relapse was significantly shorter in patients with PD than without PD.

Conclusions: PDs are a robust predictor of slowed remission and accelerated relapse in MDD.

FC01.02

Long-term outcome of depressive pseudodementia in the elderly

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Background: The term depressive pseudodementia has proved to be a popular clinical concept. Little is known about the long-term outcome of this syndrome.

Aims: To compare depressed elderly patients with reversible cognitive impairment and cognitively intact depressed elderly patients.

Methods: All patients suffering from moderate or severe depression admitted to St Margaret's Hospital, UK as inpatients or day hospital outpatients between January 1, 1997 and December 31, 1999 (n=182) were screened for entry into the study. Eligible patients were divided into those presenting with pseudodementia and those who were cognitively intact and followed up for 5 to 7 years.

Results: Seventy one percent point four percent of those suffering from pseudodementia had converted into dementia at follow up compared to only 18.2% in the cognitively intact group. The relative risk was 3.929 (95% CI: 1.985 to 7.775) and the 'number needed to harm' 1.88.

Conclusions: Reversible cognitive impairment in late-life moderate to severe depression appears to be a strong predictor of dementia. Patients with pseudodementia should probably have a full dementia screening, comprehensive cognitive testing and ongoing monitoring of their cognitive function.

FC01.03

Depression and HPA-axis dysregulation: A large cohort study

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There is a central belief that depression is associated with hyperactivity of the HPA-axis, resulting in higher cortisol levels. However, results are inconsistent. Our research aim was to determine whether there is an association between depression and cortisol levels in a large cohort, taking into account the use of psycho-active medication. Data are from 447 adults of the ongoing Netherlands Study of Depression and Anxiety. Participants were divided into 3 groups; 243 controls, 134 persons with major depressive disorder (MDD) without psycho-active medication and 100 with MDD with psycho-active medication. MDD was diagnosed using the CIDI interview and cortisol levels were measured in 7 saliva samples, covering a cortisol awakening response, basal evening level and a dexamethasone-suppression test. The 3 groups showed no significant differences in their cortisol awakening response. The mean value for the area under the curve with respect to the increase was 2.3 nmol/l*h for controls, 2.7 nmol/l*h for MDD without medication and 2.0 nmol/l*h for MDD with medication (p=0.77). In addition, basal evening levels and the ratio of morning cortisol before and after taking dexamethasone did not differ between groups. The findings did not change after adjustment for sociodemographics and health indicators. First results of this large cohort study indicate that depression is not associated with altered cortisol levels or difference in suppression after dexamethasone ingestion. Further analyses should explore the association between anxiety or trauma with cortisol values and whether there are certain subgroups of depressed patients with HPA-axis alterations.

FC01.04

A triallelic serotonin transporter gene, life events and depression

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Background: The short allele of the serotonin transporter gene 5' promoter region polymorphism (5-HTTLPR) is reported by A. Caspi and others to be associated with susceptibility to depression and suicidality in response to stressful life events. We examined the relationship of a triallelic 5-HTTLPR polymorphism to stressful life events (SLE) and severity of major depression and suicidality.

Method: Mood disorder subjects (N=191) and healthy volunteers (N=125), all Caucasians of European origin, were genotyped for the triallelic 5-HTTLPR polymorphism, two low expressing alleles (LG, S) and a higher expressing LA allele. All subjects underwent structured clinical interviews for DSM IV diagnoses, ratings of psychopathology, stressful life events, developmental history and suicidal behavior. Cerebrospinal fluid (CSF) 5-HIAA was assayed in a subsample.

Results: Lower expressing alleles independently predicted greater depression severity and predicted greater severity of major depression with moderate-severe life events compared with the LA allele. No associations with suicidal behavior and CSF 5-HIAA were found.

Conclusions: Low expression transporter alleles explain 31% of the variance in major depression severity and increase the impact

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