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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

of stressful life events on severity. The biological phenotype responsible for these effects remains to be elucidated

### FC01.05

DAT binding and psychopathological features in depressed patients

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**Introduction:** Many evidences stress the implication of dopamine systems in the pathophysiology of depression. Currently, few and uncertain results are available on pre-synaptic dopaminergic dysfunction during depression. Our aim was to assess dopamine transporter (DAT) density in Major Depressive Disorder (MDD) with marked psychomotor retardation or anhedonia using 123I-FP-CIT SPET.

**Methods:** 15 drug-free patients (F/M=8/7, mean age=44.6 SD=12.6 years) with MDD according to DSM-IV-R criteria, were enrolled for:

1. Psychometric assessment (of depression, anxiety, anhedonia and psychomotor impairment using Hamilton Depression Rating Scale, Hamilton Anxiety Rating Scale, Snaith-Hamilton Pleasure Scale and Depression Retardation Rating Scale);
2. DAT measurement with 123I-FP-CIT SPET.

14 healthy subjects, comparable for gender and age, formed the control group.

**Results:** Patients had moderate-to-severe depression. They showed a significant decrease in DAT density in whole striatum bilaterally compared to controls. Furthermore, mean 123I-FP-CIT uptake ratios were significantly lower in caudate and putamen bilaterally. Patients were then divided into two subgroups: 7 had a relevant psychomotor retardation without anhedonia; 8 had severe anhedonia without retardation. The psychomotor retardation group showed significantly lower 123I-FP-CIT uptake ratios in left putamen compared to the anhedonic group. An inverse correlation between DAT density in left putamen and retardation scores were observed.

**Conclusion:** Present results confirm a decrease of DAT binding in MDD. Low DAT availability could represent a compensatory mechanism following dopamine reduction. Moreover, DAT reduction seems to be related more to retardation than anhedonic features, in agreement with previous PET imaging findings.

### FC01.06

Long-term monitoring of HRV and activity with a new acquisition system: Preliminary data from a pilot study with depressive inpatients

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**Background:** Variations of circadian activity profiles and sleep patterns are altered in various neuropsychiatric disorders. In this context, changes in heart rate (HR), -variability (HRV) and related parameters have been reported, too. However, data situation is presently heterogeneous and nonstandardized. As long-term evaluation may provide more valuable information, applicability and data

usability of a new data acquisition system was tested in patients with major depression.

**Methods:** The course of a depressive episode in inpatients was assessed by standard psychometric instruments. ECG and motor activity were recorded continuously with a new wearable sensor system (EP04106001.3) consisting of a textile with three electrodes for 1-lead ECG recordings, and an electronic module (2D-accelerometer, microcontroller, memory, rechargeable batteries, Bluetooth unit) to be attached to the waistband of standard underpants.

**Results:** ECG signal quality highly depended on physical activity, but sufficient data quality was obtained during sleep. From the accelerometer signal, time in bed and movement time were identifiable. Preliminary data of patients (n=15) versus healthy controls (n=9) showed a reduction of HRV in several time domain parameters, high frequency (HF) power, and daytime activity (24h/day, mean 8 weeks).

**Conclusion:** This first pilot study demonstrates alterations of physiological parameters potentially relevant for depression, with continuous monitoring of inpatient treatment period. Facing long-term monitoring the device proved to be robust and safe and might provide a psychobiological profile of the clinical course of depression, useful for evaluation of disorder and therapy.

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### FC01.07

Medical comorbidities in patients with recurrent depressive disorder

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**Objective:** The course and outcome of depression could be influenced by several clinical characteristics, medical comorbidity being one of them. Our main purpose was to identify the medical comorbidities in depressive clinical population and to compare them with the figures encountered in other diagnostic categories.

**Material and method:** We performed a retrospective study on 248 subjects (studied sample) admitted in our Clinic during 2001 – 2004 with a diagnosis of Recurrent depressive disorder, accordingly with ICD-10. There were collected several demographic and clinical data. Also, it was done two comparable control samples, one with persistent delusional disorder (N=60) and the other with Bipolar disorder (N=44). All data were statistically analyzed.

**Results:** In our studied sample, we found a highly statistical significant difference regarding cardiovascular diseases ( $p < 0.001$ ), digestive ( $p < 0.001$ ) and musculoskeletal disease ( $p < 0.001$ ), depending on the time elapsed from the onset of depression. Interestingly, only the digestive diseases were not correlated with the age. Also, comparatively with control samples there was a statistical significant difference regarding cardiovascular diseases (the figures were influenced by age and gender in sense that male aged subjects were more affected). The endocrine diseases were more prevalent in Bipolar sample while in Persistent delusional sample we found more nephrological and urological diseases.

**Conclusion:** We consider that depressive population is more vulnerable to develop medical comorbidities. In consequence, the clinicians must pay more attention on physical health status in depressive patients and to take into account it in therapeutically management of these patients.