groups, only KYN correlated with SERT in the midbrain in HC (ρ = -0.544, p = 0.001). A further analysis showed that, at TBI > 0.06, midbrain SERT correlated with TRP (ρ = -0.900, p = 0.037), KYN (ρ = -0.900, p = 0.037), and TBI (ρ = 0.900, p = 0.037) in HC. However, this could not be replicated in MDD.

Conclusion: Our results are the first to demonstrate complicated interactions between TRP metabolism and SERT in different brain regions. The significance of the association between TRP metabolism and SERT in HC, in particular at different levels of TBI, is warrant for further study.

PS193 MicroRNAs as biomarkers for treatment-resistant depression
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Abstract
There is an unmet need to improve the diagnosis of treatment-resistant depression (TRD). Current diagnostic metrics fail to accurately identify patients who will not respond to first-line and subsequent therapeutic strategies. However, there is increasing evidence to support the concept of biomarkers as a means to improve diagnostic precision and refine treatment options for TRD. MicroRNAs are small nucleotide sequences that regulate gene expression and accumulating evidence has linked their presence in the periphery to the pathophysiology of depression. Thus, we hypothesized that microRNAs could serve as biomarkers for TRD. We further proposed that baseline microRNA expression could predict remission with ketamine infusions (KET) or electroconvulsive therapy (ECT).

To test these hypotheses, we studied the peripheral microRNA expression profiles of healthy controls (n=17) and patients (n=30) with TRD who received treatment with infusions of KET ([0.5mg/kg IV over 40min] or ECT (average of 8.9 sessions per patient). Remission following treatments was defined as at least a 50% reduction in the Hamilton Depression Rating Scale scores. RNA was isolated from blood samples collected at baseline and after treatments. To determine differences in microRNA expression, microarray (Exiqon) and qPCR analyses were performed on samples.

The baseline expression of let-7b was significantly reduced by 40% in TRD patients. Bioinformatic analysis revealed that let-7b regulates the expression of 25 genes in the PI3k-Akt-mTOR signaling pathway which has previously been reported to be dysfunctional in depression. KET and ECT both had positive effects in attenuating depression symptomatology and 72% of patients achieved remission. However, we found no microRNAs altered by treatment and remission could not be predicted from baseline microRNA expression profiles.

Our data suggests that let-7b is a putative peripheral trait-biomarker for TRD. Experiments are on-going to study the functional effects of let-7b and how they relate to the pathophysiology of depression.

PS194 Discovery of serum protein biomarkers in drug-free patients with major depressive disorder
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Abstract
Objective: Major depressive disorder (MDD) is a systemic and multifactorial disorder involving complex interactions between genetic predisposition and disturbances of various molecular pathways. Its underlying molecular pathophysiology remains unclear, and no valid and objective diagnostic tools for the condition are available.

Methods: We performed large-scale proteomic profiling to identify novel peripheral biomarkers implicated in the pathophysiology of MDD in 25 drug-free female MDD patients and 25 healthy controls. First, quantitative serum proteome profiles were obtained and analyzed by liquid chromatography-tandem mass spectrometry using serum samples from 10 MDD patients and 10 healthy controls. Next, candidate biomarker sets, including differentially expressed proteins from the profiling experiment and those identified in the literature, were verified using multiple-reaction monitoring in 25 patients and 25 healthy controls. The final panel of potential biomarkers was selected using multiparametric statistical analysis.

Results: We identified a serum biomarker panel consisting of six proteins: apolipoprotein D, apolipoprotein B, vitamin D3-binding protein, ceruloplasmin, hornerin, and profilin 1, which could be used to distinguish MDD patients from controls with 68% diagnostic accuracy. Our results suggest that modulation of the immune and inflammatory systems and lipid metabolism are involved in the pathophysiology of MDD.

Conclusions: Our findings of functional proteomic changes in the peripheral blood of patients with MDD further clarify the molecular biological pathway underlying depression. Further studies using larger, independent cohorts are needed to verify the role of these candidate biomarkers for the diagnosis of MDD.

Key words: Major depressive disorder, proteomics, immune system, inflammation, lipid metabolism.

PS195 Reduced cerebrospinal fluid ethanolamine concentration in major depressive disorder
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Abstract
Amino acids play key roles in the function of the central nervous system, and their alterations are implicated in psychiatric disorders. In the search for a biomarker for major depressive disorder (MDD), we used high-performance liquid chromatography to measure amino acids and related molecules in the cerebrospinal fluid (CSF) of 52 patients...
with MDD (42 depressed and 10 remitted; DSM-IV) and 54 matched controls. Significant differences were found in four amino acid concentrations between the depressed patients and controls. After Bonferroni correction, only ethanalamine (EA) levels remained significantly reduced in depressed patients (nominal $P=0.000011$). A substantial proportion of the depressed patients (40.5%) showed abnormally low CSF EA levels ($<12.1$ μM) ($P=0.000033$; OR=11.6, 95% CI: 3.1–43.2). When patients with low EA and those with high EA levels were compared, the former had higher scores for overall depression severity ($P=0.0033$) and ‘Somatic Anxiety’ symptoms ($P=0.00026$). In unmedicated subjects, CSF EA levels showed a significant positive correlation with levels of homovanillic acid ($P=0.0030$) and 5-hydroxyindoleacetic acid ($P=0.019$). To our knowledge, this is the first study showing that patients with MDD have significantly lower CSF EA concentrations compared with control subjects. CSF EA could be a state-dependent biomarker for a subtype of MDD. Further replication studies are currently under way.

**PS196**

Alterations of the cortisol and dehydroepiandrosterone in perinatal depression

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**Abstract**

**Objectives:** The purpose of this study is to investigate the alterations of the hypothalamic-pituitary-adrenal axis hormones, especially salivary cortisol and dehydroepiandrosterone (DHEA) in perinatal depression.

**Methods:** 44 patients with depression and 217 normal subjects in perinatal period were included in this study. Edinburgh Postnatal Depression Scale (EPDS) and Beck Depression Inventory II (BDI-II) were performed. The subjects below 10 points of EPDS score or below 13 points of BDI-II score were classified to normal subjects. Among the subjects more than 11 points of EPDS score or more than 14 points of BDI-II score were diagnosed depression by DSM-IV TR by psychiatrists. All subjects were to collect their saliva in each 4 collecting tubes, immediately upon awakening (IA), 30 minutes after awakening (30A), 60 minutes after awakening (60A) and before bedtime (BB).

**Results:** The number of subjects in antenatal period were 103, and in antenatal depression (AD) patients were 21, antenatal normal (AN) subjects were 82. The number of subjects in postnatal period were 114, and postnatal depression (PD) patients were 23, postnatal normal (PN) subjects were 91. Salivary cortisol levels in subjects with AD collected IA, 30A and 60A were lower than with AN subjects significantly except BB. Salivary cortisol levels in subjects with PD collected 60A only were lower than with PN subjects significantly. Salivary DHEA levels in subjects with both AD and PD were lower than with normal subjects significantly. Also cortisol/DHEA ratio (F/D ratio) in subjects with both AD and PD were much higher than with normal subjects significantly.

**Conclusions:** These results suggest that the blunted response was shown in AD, and the characteristics between AD and PD are different. Also the differences of salivary DHEA levels and F/D ratio between subjects with PD and normal subjects are suggested the one of the key points of difference among both groups.

**PS197**

Low level of perineuronal nets in the medial prefrontal cortex predicts vulnerability to stress

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**Abstract**

Perineuronal nets (PNNs) are extracellular matrix structures enwrapping parvalbumin-positive γ-aminobutyric acid (GABA)ergic interneurons which are crucial for modulating anxiety and depressive-like behaviors. Perineuronal nets have recently been implicated in experience-dependent neuroplastic changes in central nervous system, but it is poorly understood that whether PNNs modulates the neural maladaptation after repeated exposure to stress. We found that adolescent rats with vulnerability to chronic unpredictable mild stress (CUMS) showed decreased level of PNNs, tenascin-R and aggrecan in the medial prefrontal cortex (mPFC). Degradation of PNNs in mPFC produced vulnerability to stress in adult rats. Elevating PNNs in the mPFC through environment enrichment prevented CUMS-induced depressive and anxiety-like behavior. Fluoxetine reversed the stress vulnerability in adolescent rats and increased PNNs levels. Lower level of PNNs rendered GABAergic neurons susceptible to CUMS, manifesting as decreases in expression of glutamic acid decarboxylase 67 (GAD 67) and frequency and amplitude of inhibitory postsynaptic current (IPSC) after CUMS. The organization of PNNs coincided with the developmental switch in stress vulnerability to resilience. These findings indicate a role of PNNs in mPFC in predicting and modulating vulnerability to stress-induced depressive-like behavior, and the effect may be produced though regulating GABAergic functions.

**Keywords:** perineuronal nets; stress vulnerability; GABAergic neuron

**PS198**

Pathological analysis of refractory depression using fetal alcohol and adolescent corticosterone double stress model

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**Abstract**

The clinical strategy for treatment-resistant depression which includes overlap between bipolar disorder remains inadequate. Establishment of a diagnostic method and understanding of the detailed pathogenesis of those patients are urgently needed. In this study, we performed comparative analysis of depressive-like behaviors and variations of depression-related molecules in the brain and peripheral blood between controls and refractory depression model animals established by the combined stress of fetal period alcohol and adolescent chronic corticosterone (CORT) treatment. With a part of this model animal, we have also administered antidepressants (SSSRIs) for the purpose of investigation of possible treatment method and molecular pathogenesis in refractory type of depression. Focusing on the report of region specific BDNF activity in the pathogenesis of