Abstract

Objective: Early antidepressant response predicts later treatment outcome in patients with major depressive disorder (MDD) [1]. MDD is characterized by changes to the behavioral and neuronal correlates of emotion processing [2]. Functional magnetic resonance imaging (fMRI) studies have demonstrated that neuronal activity related to emotion processing allows for prediction of antidepressant response after 6–8 weeks [3, 4]. We aimed to investigate if emotion processing related fMRI activity predicts early response to antidepressant psychopharmacologic treatment.

Methods: 23 MDD patients (16 female, mean age±SD=32.61 ± 9.44 years) were investigated once with fMRI (EPI-sequence, TE/TR=23/1400ms, matrix size 128x128 voxel, FOV 192x192 mm, 78 slices of 1mm with 0.25 mm gap, Siemens Magnetom 7T scanner), during which they performed a block-design emotion discrimination task (EDT). Standard preprocessing was carried out using SPM12. First level analysis comprised the contrast EDT vs. the control condition (object discrimination task, ODT). Following baseline fMRI, patients received Escitalopram in a flexible dose schema and were assessed with the Hamilton Depression Rating Scale (HAM-D) after 2 and 4 weeks of treatment. Correlation analyses were performed using SPM12.

Results: Deactivation of the posterior cingulate cortex at baseline correlated with change in HAM-D scores from baseline to 2-weeks after treatment start (p < 0.05 cluster level FWE-corrected). This correlation remained significant when correcting for baseline symptom severity, age, and sex (p < 0.05 cluster level FWE-corrected). Baseline EDT vs. ODT activity did not correlate with HAM-D change after four weeks of Escitalopram treatment.

Conclusion: As an emotion-processing task, the EDT represents a promising target for fMRI response prediction studies, considering the integral nature of affective and emotional dysregulation to MDD. The lack of correlation between baseline fMRI activity and HAM-D reduction by 4 weeks suggests that neuronal processes related to early response may differ from those associated with more long-term outcome.

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PS192

A study of tryptophan, kynurenine and serotonin transporter in first-episode, drug-naïve patients with major depressive disorder

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Abstract

Objective: Balance between serotonin (5-HT) and kynurenine (KYN) pathway of the tryptophan (TRP) metabolism is associated with the pathophysiology of major depressive disorder (MDD). 5-HT functioning is modulated by the serotonin transporter (SERT), which terminates neurotransmitter action. The aim of this study was to examine the association between TRP metabolism and SERT availability in first-episode drug-naïve MDD patients.

Methods: Thirty-three MDD patients and 33 age- and sex-matched healthy controls (HC) were recruited. SEKT availability was measured using the radiotracer 3‘H-ADAM with single photon emission computed tomography in the midbrain, thalamus, caudate and putamen. Serum TRP and KYN concentrations were measured using enzyme-linked immunosorbent assay. Tryptophan breakdown index (TBI) was calculated from the KYN/TRP ratio. Mann-Whitney U Test and Spearman’s rank correlation were performed for statistical tests.

Results: There was a borderline significance between MDD and HC in TRP (71.01 ± 33.11 vs. 52.29 ± 21.25, p=0.058) but lack of difference in KYN (1.30 ± 0.42 vs. 1.34 ± 0.33, p=0.438). TBI was lower in MDD than HC (0.02 ± 0.01 vs. 0.03 ± 0.02, p=0.021). No differences in SERT availability between MDD and HC in all regions (midbrain: 2.81 ± 0.64 vs. 2.84 ± 0.55, p=0.990; thalamus: 1.06 ± 0.48 vs. 1.07 ± 0.48, p=0.903; caudate: 0.74 ± 0.33 vs. 0.80 ± 0.24, p=0.705; putamen: 1.02 ± 0.45 vs. 1.17 ± 0.29, p=0.254). When correlating TRP, KYN, and TBI with SERT in four brain regions in both
groups, only KYN correlated with SERT in the midbrain in HC ($p=0.544$, $p=0.001$). A further analysis showed that, at TBI $>0.06$, midbrain SERT correlated with TRP ($p=0.900$, $p=0.037$), KYN ($p=0.900$, $p=0.037$), and TBI ($p=0.900$, $p=0.037$) 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 hypothesised 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.

**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

**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...