Genes of neurotrophic factors and responsiveness to antidepressive psychopharmacotherapy in patients with depressive disorders

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ment based on the prior identification of objective individual characteristics.

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P.516 Large-scale serum biomarker profiling in patients with bipolar disorder

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Bipolar disorder is a psychiatric disorder with recurrent mood episodes that causes a huge disease burden and high societal costs [1]. Available medication can prevent new episodes but not all patients get well and stratified treatment options remain unavailable. The molecular understanding of the disease is poor which hinders the development of new treatments or optimization of current medication. One way to meet these needs is to identify peripheral markers that can be used in clinical practice to improve diagnosis and to stratify patients [2]. Peripheral markers are easy to implement in a clinical setting and previous work has identified e.g. altered concentrations of inflammatory proteins in patients with bipolar disorder [3]. Further, recent years' technological development has provided multiplex platforms that enables output of high throughput data in small sample volumes [4,5]. The aim of this study was to identify serum markers that can be used in personalized psychiatric care of bipolar disorder patients.

We utilized an explorative approach to analyze serum samples from two independent cohorts of bipolar disorder patients and healthy controls. Patients were recruited from the St. Göran bipolar project, enrolling patients from two Swedish bipolar units in Stockholm and Gothenburg respectively. Blood was sampled in a euthymic phase of the disorder. Protein concentrations in serum were analyzed using the Olink Proseek Multiplex Oncology I panel, Proseek Multiplex Inflammation I panel, and Proseek Multiplex Cardiovascular I panel and quantified by real-time PCR using the Fluidigm BioMark HD real-time PCR platform at the Clinical biomarker facility at SciLifeLab Sweden and at Olink Biosciences. Linear regression models with age, gender, study population, and BMI as covariates were used to compare protein concentrations between patient and control groups.

A total of 202 unique markers were measured in serum and 171 markers were detectable in more than 80% of all samples. Of the 171 markers, a total of 62 serum proteins were significantly ($q<0.05$) associated with bipolar disorder in a combined analysis of the two cohorts. When the two cohorts were analyzed separately, 27 of the original 62 proteins were significantly ($p<0.05$) altered in the same direction in both cohorts. In post-hoc analyses we further explored association with life style factors, clinical parameters, and medications. Interestingly, lithium treatment was associated with changes in 10 of the 27 proteins linked to a bipolar disorder diagnosis in both cohorts.

The present study demonstrates that the recently developed Olink Proseek Multiplex panels can be used to identify novel blood markers for bipolar disorder. Further work is needed to reveal underlying biological pathways with relevance for the pathophysiology or treatment of bipolar disorder. A significant portion of the identified markers were linked to lithium treatment which may point to novel pathways with relevance for the mechanism of action of lithium.

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P.517 Genes of neurotrophic factors and responsiveness to antidepressive psychopharmacotherapy in patients with depressive disorders

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Major depressive disorder (MDD) is a clinically and biologically heterogeneous disorder with a heavy personal and socio-economic burden [1]. The neurotrophic theory of the development of depression most fully explains the morphological changes that occur in the brain of patients [2,3]. Among the various neurotrophic factors brain-derived neurotrophic factor (BDNF) and prolactin play an important role in pathogenesis of depression [4]. Objective of the study was to investigate the association of genes polymorphisms of BDNF and prolactin with responsiveness to therapy in patients with MDD.

Methods The study group included 185 MDD patients (F32,F33,ICD-10) and 134 healthy persons. Severity of depressive symptoms on the baseline and on the 14th and 28th day of therapy was assessed using Hamilton Depression Scale (HDRS-17) and Clinical Global Impression – Severity scale (CGI-S). Antidepressive therapy response on the 14th and 28th day of therapy was evaluated using Clinical Global Impression – Improvement scale (CGI-I). Genotyping was carried out on polymorphic variants of BDNF genes (rs6265, rs7124442, rs11030104) and PRL gene (rs1341239). The SPSS software was used for statistical analysis. The Hardy-Weinberg equilibrium (HWE) of genotypic frequencies was tested by the chi-square test.

Results The study found no deviation of genotype frequencies from HWE ($p > 0.05$), except for the SNP rs11030104 in the group of patients ($\chi^2 = 37.540$; $p = 0.001$). Important differences in frequency of genotypes and alleles of SNPs rs11030104 of BDNF and rs1341239 of PRL genes between patients and healthy persons at entry have been found. The final multivariate binary logistic regression analysis shows that the A/A genotype of SNP rs11030104 has a more than 6 times higher risk of developing depression than G/G or G/A genotype ($p = 0.009$). Allele G of SNP rs1341239 gene was more common in patients (63%) compared to control (59%) ($p < 0.001$).

We studied the association between the scores on the HDRS-17, CGI-S and CGI-I scales and gene polymorphisms. A statistically significant reduction in scores on all scales during therapy was observed ($p < 0.01$). A decreased scores on the HDRS-17 is associated with G/G genotype of SNP rs6265 ($p = 0.049$), C/C genotype of SNP rs7124442 ($p = 0.009$) and A/A genotype of SNP rs11030104 ($p = 0.07$), patients with these genotypes are characterized by mild depressive disorder on the 14th day of therapy. We showed a relationship between the carriage of the C allele of SNP rs7124442 ($p = 0.014$) and the G/G genotype of SNP rs6265 ($p = 0.078$) and a reduced CGI-S score indicating a good response to therapy in this patients. There was a correlation between the presence of the T allele of SNP rs1341239 and the absence of remission according to the CGI-S scale ($p = 0.004$) and the worst response to antidepressant therapy.

Conclusions Our results suggest that SNPs rs11030104 of BDNF gene and rs1341239 of PRL gene are associated with higher risk of developing depression, SNPs rs6265 and rs7124442 of BDNF gene are probably related to the clinical characteristics of the disorder and the response to pharmacotherapy.

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P.518 Personality disorder comorbidity and rehospitalization rates in bipolar disorder: A cohort study

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Introduction: Bipolar disorder (BD) is a chronic mental illness characterized by recurrent manic and depressive episodes that typically begin in early adulthood and affects 1% to 4% of the general population. Extensive research has been dedicated to elucidate the factors that affect the frequency of manic and depressive episodes recurrences which is a major determinant of the level of function and quality of life of BD patients. Personality disorder (PD) comorbidity is highly prevalent in BD patients, and the presence of comorbid PD among BD patients has been associated with a more severe illness course. Even though the clinical impression that PDs worsens outcome of BD is generally supported by the literature, only a paucity of studies, based on unselected real world BD patients, contemporary pharmacological interventions and uptodate PD classification, have examined the relationship between PD comorbidiy and BD