High-throughput antibody-based profiling of serum in schizophrenia and bipolar disorder patients: an integrative genomics-proteomics pilot study

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Abstract

The identification of biological markers in the peripheral blood for the prediction of the individual clinical outcome in major psychiatric disorders remains an unmet clinical need. Studies based on serum protein profiles aiming to create predictive models for these disorders have provided inconclusive results so far. The aim of this pilot study was to perform a high-throughput antibody-based serum protein profiling taking advantage of the biosamples available in the German KFO241/PsyCourse cohort. Using this method, the expression of a selected panel of ~100 proteins was determined in the serum samples of 113 schizophrenia (SCZ) and 125 bipolar disorder (BD) patients. Overall, assays had a good performance according to the low technical variation in replicates and the low background noise of the technique. Exploratory analyses showed that the levels of all these circulating proteins cannot differentiate between SCZ and BD samples. Single- and multi-protein analyses detected significant differences in the serum levels of several proteins among the fifteen proteins with differences in the serum levels, the most interesting findings according to previous literature were NRG1, BACE1 or complement factor C4B (Figure 2).

Results

Technical performance and quality control (QC) of the antibody-based assay

Methodology, the assay performed properly on the basis of two QC parameters: fifteen technical replicates were included in the array with the goal to ascertain the technical variation of each of the antibody-based assays. In a vast majority of the assays the replicates displayed a small variation among them. A second QC parameter was based on the use of bare beads in order to quantify the background noise of the technique. In all assays the technical variation in replicates and the background intensity was kept to a low level, not overlapping the signal of the assays using the antibodies (data not shown).

Multivariate analyses

Multi-variant profiles based on the whole panel of quantified proteins did not significantly differentiate between both diagnoses (SCZ, BD). Both K-means clustering (data not shown) and principal components analysis (Figure 1) showed such a lack of discriminative power.

Discussion

Taken together, the remarkable performance of the bead array technology insures the accurate and reliable quantification of the selected proteins in serum and major technical artifacts are not expected to interfere with the analyses. The observed differences in protein levels between diagnoses warrant replication in independent samples controlling the effect of other important confounders like medication.

GRANTS

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References


Comes et al. (2011). Protein and multiple immunoassay methods for brain tumor detection is oversee review. Under review.


Table 1. Serum analytes quantified in this study

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Figure 1. Results of principal component analyses based on the serum proteomic profile. X-axis: first principal component (PC1); Y-axis: second principal component (PC2). Red: BD patients. Blue: SCZ patients.