

## Symposium: Subtypes of schizophrenia

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### Characterization of different subtypes of schizophrenia: Premorbid functioning, neurophysiological differences, functional outcomes

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**Introduction** Although not included in current diagnostic systems, deficit versus non-deficit and resistant versus non-resistant schizophrenia subtypes look more promising than traditional schizophrenia subtypes in terms of stability across time, clinical utility and interest for research.

**Aims** To critically analyze evidence supporting the validity of two schizophrenia subtypes: Deficit Schizophrenia (DS) and Treatment Resistant Schizophrenia (TRS).

**Methods** Empirical data supporting the validity of DS and TRS subtypes will be critically reviewed.

**Results** DS, in comparison with non-deficit schizophrenia, is characterized by poorer premorbid functioning, more insidious onset, lower prevalence of dysphoria, hostility, suicidal ideation, depressive symptoms and substance abuse, different neurobiological abnormalities, and poorer response to treatment. The diagnosis of DS shows high reliability and stability across time. However, research based on this approach has proven difficult, especially in first-episode schizophrenia, and findings have not been as homogeneous as expected.

TRS patients, as compared to non-TRS ones, show persisting psychotic symptoms, greater severity of negative symptoms, more severe cognitive dysfunctions, poorer premorbid functioning, longer duration of untreated psychosis, more frequent co-morbidity with personality disorders, earlier illness onset and poorer social functioning.

**Conclusions** Future research should consider a) refining diagnostic criteria for DS and identifying valid DS endophenotypes; b) dissecting TRS based on psychopathological characteristics (e.g. presence of primary and persistent negative symptoms or persistently severe positive symptoms), and underlying neurobiological mechanisms (e.g. dopamine synthesis capacity and glutamatergic transmission).

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### Genetics and neurophysiological characterization of first episode and deficit schizophrenia

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The deficit subtype of schizophrenia (DS) is hypothesized to constitute a pathophysiologically distinct subgroup of schizophrenia patients suffering from enduring, idiopathic negative symptoms. The aim of the present study was to assess a relationship between the deficit/non-deficit dichotomy and various markers. We tested a hypothesis that stem cells and factors that modulate their trafficking may be biological markers of acute psychosis.

**Methods** The DS was identified using the SDS. The MMP-9, BDNF, and COMT gene polymorphisms were genotyped. DNA methylation of the human endogenous retrovirus type K (HERV-K) sequences was determined. Smell identification test was performed using the Sniffin' Sticks test. For the assessment of executive function we used the Wisconsin Card Sorting Test, the Trail Making Test, Verbal Fluency Test Phonemic, Stroop Color Word Test and Go/No Go task.

**Results and Discussion** There was no association between the examined functional gene polymorphisms, methylation levels and DS. Similarly, there was no relationship between overall odor identification abilities and the deficit/non-deficit dichotomy. The results tended to indicate specific problems in the identification of few odors in DS. DS, compared with the non-deficit group, obtained lower scores in the WCST and TMT and exhibited greater interference within concept formation and non-verbal cognitive flexibility. Furthermore, in patients with the first schizophrenia-like episode, the number of circulating Lin (-)/CD45 (-)/CD34 (+) very small embryonic like stem cells (VSELs) and the S1P plasma level were the best predictors of risk and are proposed as novel markers for the first "schizophrenic" episode of psychosis.

**Disclosure of interest** The authors declare that they have no competing interest.

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### From identification of neurofunctional systems to individualization of treatment for schizophrenic disorders

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Schizophrenia is a severe brain disorder characterized by positive, negative, affective and cognitive symptoms and can be viewed as a disorder of impaired neural plasticity. Schizophrenia leads to long-term disability in a substantial proportion of the sufferers and it still connected with an unfavorable outcome. Therefore, it is inevitable to find and apply interventions to reduce the risk of psychosis and/or prevent a further chronification of the illness. There are two major obstacles translational schizophrenia research has to face: One is the introduction of easy to measure and reliable biomarkers; the second are add-on treatments to improve the residual symptoms of this illness. To reach the first goal, subgroups must be identified utilizing biomarkers in order to induce specifically targeted treatments. For the long-term prognosis and outcome it is necessary for biomarkers to constitute easy measurable clinical routine parameters. Studies will be summarized using clinical (GAF, PANSS, CGI) and imaging data in order to accurately predict the outcome in the first week, for 4 and for 52 weeks. This will help to subdivide these groups into a good, an intermediate and a fair outcome group. Future clinical studies will benefit enormously if it was possible to focus on the intermediate group, where recovery could be reached by targeted treatment as most of those subjects are showing partial recovery or remission.

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