Schizophrenia: brain morphology and treatment aspects

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Since the first findings of enlarged ventricles in computer tomography studies and with the development of MRI-based segmentation, brain morphology findings in schizophrenia point to abnormal structural findings in several brain regions involved in neuronal circuits [1]. One of the often cited environmental risk factors in schizophrenia is cannabis abuse. In an invited review, Malchow et al. [2], however, found inconclusive results with respect to alterations in brain morphology. They assume that chronic cannabis abuse may induce structural changes, whereas in first-episode and high-risk patients, studies need replication. In subjects at high risk and patients with schizophrenia, the gyrification index as a measure of cortico-cortical connection differed from healthy controls in the frontal and parietal cortex [3]. This may be based on the neurodevelopmental abnormalities, since the gyrification pattern is determined during the perinatal period. Accordingly, in a recent post-mortem study, a reduced gyrification index has been observed in the parietal cortex in schizophrenia [4] showing no differences between monozygotic twins compared to dizygotic twin pairs which points to the influence of different intrauterine and postnatal factors [5].

Postmortem studies with a resolution on the cellular and even molecular level with, for example, focus on synaptic structural elements [6] may contribute to elucidate the pathophysiology of schizophrenia. Williams et al. [7] investigated neuronal cell density and found decreased pyramidal layer thickness resulting in decreased frontal lobe thickness in schizophrenia patients. They additionally

report decreased astrocyte density in the subgenual cingulate cortex and callosal genu for their sample [8], which extends neurobiological hypotheses on the dysfunction of astrocytes in maintaining synaptic stability.

Investigations in healthy subjects are indispensable to elucidate risk factors influencing brain volumes and for exclusion of confounding factors such as other disease-related and treatment effects. Beside environmental factors, schizophrenia risk genes may contribute to altered brain structures. Trost et al. [9] found a dysbindin-1 gene variant to be associated with hippocampal and prefrontal gray matter volumes. On the molecular level, another risk gene such as brain-derived neurotrophic factor (BDNF) val66-met polymorphism has been shown to affect the glutamate system [10]. Moreover, D-amino acid oxidase activator gene (DAOA) variation has been found to affect homovanillic acid levels in cerebrospinal fluid [11]. Unraveling neurobiological effects of such risk factors may contribute to develop a more personalized medicine in psychiatry [12].

Even effects of traditional neuroleptic treatment strategies may be influenced by genetic factors. Giegling et al. [13] found that three haplotype blocks, one among ankyrin repeat and kinase domain containing 1 (ANKK1) and two among dopamine receptor D2 (DRD2) genes, were associated with better clinical improvement in schizophrenia patients. These often are heavy smokers attempting to treat negative and cognitive symptoms themselves. In a clinical trial investigating effects of transdermal nicotine patch, Chen et al. [14], however, found no correlation with replacement doses and only a low smoking cessation rate. They recommend more effective smoking cessation programs for this group of hospitalized patients.

Due to restricted therapeutic effects of current treatment strategies in severe psychiatric disorders, the editorial

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board of EAPCN decided publishing a series of invited reviews on novel therapeutic approaches in the schizophrenia-affective spectrum, starting in spring 2013. Interested authors are invited to submit proposals (abstracts) to the editor for invited reviews, Prof. Hans-Jürgen Möller.

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