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Topic: S545 - The mild encephalitis hypothesis of severe psychiatric disorders - epidemiology, findings, definitions, therapy aspects

The mild encephalitis hypothesis updated

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Schizophrenia seems to be a heterogeneous disorder.

A ‘late hit’ and gene-environment interaction are required to explain major findings about schizophrenia, both aspects being consistent with the ME hypothesis. Schizophrenia risk genes stay rather constant within populations despite a resulting low number of progeny, suggesting advantages associated with risk genes, e.g., an improved immune response, which may act protectively within changing environments.

Low level neuroinflammation (LLNI) may be involved.

According to the mild encephalitis (ME) hypothesis, LLNI represents the core pathogenetic mechanism in a schizophrenia subgroup, possibly triggered by infections, autoimmunity, toxicity, or trauma, supported by the results of the first scale epidemiological studies in psychiatry. Specific schizophrenic symptoms may arise with instances of LLNI when certain brain functional systems are involved. The transition to disease may relate to LLNI processes emerging and varying over time. Criteria for subgrouping neurodevelopmental, genetic, ME, and other types of schizophrenias are proposed.

We found in 70 % of therapy resistant cases some CSF pathology (intrathecal immune response, blood CSF barrier dysfunction, neopterin increase).

CSF abnormalities and CSF signalling by LLNI could represent a common pathogenetic link for the distributed brain dysfunction, dysconnectivity, and brain structural abnormalities observed, which may extend into peripheral tissues via the CSF outflow pathway along brain nerves and peripheral nerves, and may explain the topology of may abnormalities found, like olfactory dysfunction, dysautonomy, and pathology even in peripheral tissues, i.e., the muscle lesions found in 50 % of cases.

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