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MEETING ABSTRACT

A17.2
Impact of brain lipid composition on reward processing and mesolimbic dopamine transmission: a role in schizophrenia endophenotypes?
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Various though very distinct psychiatric disorders, such as schizophrenia, obsessive–compulsive disorder or attention-deficit hyperactivity disorder are associated with a dysfunction of the reward system linked to an alteration of dopamine transmission. Furthermore, these pathologies are also accompanied by changes in brain lipid composition and in particular by a decrease in the content of docosahexaenoic acid (DHA), the main n-3 polyunsaturated fatty acid (PUFA) in the brain. However, despite that n-3 PUFA supplementation seems to improve or prevent some psychiatric symptoms, the implication of brain lipid composition in the etiology of psychiatric endophenotypes has been overlooked.

Using operant conditioning tasks in mice, we show that developmental n-3 PUFA deficiency leads to avolition and anhedonia in adulthood with no change in locomotion. Moreover, n-3 PUFA-deficient animals display blunted response to amphetamine in motivational tasks. These behavioral deficits are accompanied by altered dopamine D2 receptor-dependent transmission, selectively in the ventral striatum. More precisely, D2 receptor-dependent signaling in the ventral striatum is blunted in n-3 PUFA-deficient animals, despite an increase in receptor expression, suggesting that the upregulation of D2 receptor is a compensatory mechanism to impaired signaling. Accordingly, downregulation of D2 receptor by shRNA expression in adulthood does not rescue—and even worsens—behavioral deficits. Interestingly, both the behavioral and neurobiological alterations induced by n-3 PUFA deficiency recapitulate some endophenotypes of schizophrenia. Indeed, avolition and anhedonia are two main negative symptoms of schizophrenia, and an increase in D2 receptor expression in the striatum—which seem to participate to those symptoms—has been consistently described in schizophrenic patients. Therefore, it is tempting to propose that the decreased n-3 PUFA in schizophrenia could directly participate to some symptoms. The genetic and/or environmental factors responsible for such alteration in lipid metabolism should therefore be more profoundly explored.

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