Pharmacological activation of PPAR-alpha reduces repetitive behavior in a mouse model of autism spectrum disorders

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The autism spectrum disorders (ASD) are a heterogeneous group of neurodevelopmental conditions defined by behavioral abnormalities characterized of impairments in communication and social interactions accompanied by restrictive and repetitive behaviors (American Psychiatric Association, 1994). The inbred BTBR T+tf/J (BTBR) mouse strain has been recently used as animal model of core behavioral deficits in autism compared to typical strains.
Recent studies have demonstrated that a lot of neurological diseases and behavioral abnormatilities appear to be associated with systemic metabolic abnormalities. In particular among several comorbidities in ASD, dysbiosis of the gut microbiota, a higher prevalence of inflammatory bowel disease and gastrointestinal symptoms are common in ASD patients (Kohane IS et al., 2012). Moreover, the peroxisome proliferator activated receptor alpha (PPAR-alpha) is very well characterized for its contribution to the regulation of lipid homeostasis, obesity, inflammation and its utility as a target for the treatment of metabolic diseases as dyslipidemia (Staels and Fruchart, 2005).
The aim of the study is to investigate the possible therapeutic application of PPAR-alpha agonists to alleviate behavioral symptoms in BTBR mice.
Consistent with a growing interest in the ubiquitous presence of metabolic abnormalities in neurological disorders, we have found that BTBR mice exhibit an alterated intestinal permeability and a significant deficit in intestinal barrier integrity.
In addition, the similar behavioral phenotype between ASD mouse model BTBR mice and PPAR-alpha null mice, suggest a possible role of these agonists to alleviate behavioral impairments (D'Agostino et al., 2015).
BTBR mice were treated with synthetic and endogenous PPAR-alpha agonists at different doses (10-30mg/Kg) for 10 days and subsequently scored for spontaneous marble burying, self-grooming and social behaviors. In order to rule out that the positive effects of PPAR-alpha agonists reducing repetitive behavior in BTBR mice could not be due to an effect on general activity or increased anxiety, no motor impairment or anxiety profile were found during the open field and elevated plus maze tests.
Our preliminary results suggest that PPAR-alpha activation significantly improves multiple autistic behaviors in the BTBR mouse model. Further studies are needed to better elucidate the potential role of PPAR-alpha agonists to alleviate behavioral impairments given that these agonists are currently used in clinical practice.

References:

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