**Introduction:**

Autism spectrum disorders (ASD) are complex neurodevelopmental diseases whose diagnosis lies on the detection of impaired social skills together with restricted and repetitive behavior and interests (DSM-5). Although the etiology of ASD remains mostly unknown, impaired excitation/inhibition ratio appears as a common mechanistic feature. Bromide ion is known to reduce hyperexcitability, possibly by competing with chloride ions at channels and transporters and may thus have therapeutic potential in ASD. We evaluated the therapeutic potential of bromide ion in the Oprm1/− mouse model of ASD and the molecular mechanisms involved in bromide treatment, notably effects on GPCRs.

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**Chronic sodium bromide relieves autistic-like deficits in the Oprm1 model of autism and modulates the activity of serotonin and dopamine receptors in vitro**

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Chronic sodium bromide relieves behavioral deficits in Oprm1/− mice in a dose-dependent manner

Bromide impacts the expression of GABA<sub>A</sub> subunits involved in E/I balance, Arc involved in neuronal plasticity and Grm2, Htr7 (Cpu) and Grm4 (Nacc) involved in signalization

Bromide and chloride ion effects on 5-HT and dopamine receptor pharmacology

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**Chronic bromide treatment in Oprm1 knockout mice: behavioral deficits**

Behavioral deficits in Oprm1<sup>−/−</sup> mice:

Impact of chronic bromide treatment in behavioral deficits of Oprm1<sup>−/−</sup> mice, in the two core symptoms of TSA: Social abilities (upper panel) and stereotypes (bottom left panel); and on Anxiety (bottom right panel), a comorbid symptom. Statistics: All genotype x treatment effects. Except for 3 chamber test: three-way ANOVA followed by Newman–Keuls post hoc test. 3-chamber test: four-way ANOVA with one repeated measure: stimulus–mouse versus toy followed by Newman–Keuls post hoc test. *P<0.05; **P<0.01; ***P<0.001 vs. Oprm1<sup>+/−</sup> Saline. Data are presented as mean ± SEM

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**Bromide and chloride ion effects on 5-HT and dopamine receptor pharmacology**

**Conclusions:**

The beneficial effects of bromide administration in a genetic murine model of ASD and its impact on both gene expression and GPCR pharmacology predicts high translational potential in patients with autism, despite high heterogeneity in etiology and symptoms. The next step will be to test the effects of bromide on mGlur4 both in vitro, keeping in mind that Cl<sup>−</sup> is already known as a Positive Allosteric Modulator (PAM) of mGlur4, and in vivo, using a combination of subeffective doses of a mGlur4 PAM and bromide.