Acute, chronic and conditioned effects of intranasal oxytocin in the mu opioid receptor knockout mouse model of autism: social context matters

Fani Pantouli[1], Camille Pujol[1], Cécile Derieux[1], Mathieu Fonteneau[2], Lucie P. Pellissier[1], Claire Marsol[3], Julie Karpenko[4], Dominique Bonnet[5], Marcel Hibert[3], Alexis Bailey[6], Julie Le Merrer[2], and Jerome A.J. Becker[2]

[1]Physiologie de la Reproduction et des Comportements
[2]UMR 1253 Imaging and Brain
[3]Laboratoire d'Innovation Thérapeutique, UMR7200 CNRS/Université de Strasbourg, Labex MEDALIS, Faculté de Pharmacie
[4]Laboratoire d'Innovation Thérapeutique
[5]Laboratoire d'Innovation Therapeutique
[6]University of London Saint Georgeś

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Abstract

Background and Purpose Autism Spectrum Disorders (ASD) are neurodevelopmental disorders whose diagnosis relies on deficient social interaction and communication together with repetitive behaviours. Multiple studies have highlighted the potential of oxytocin (OT) to ameliorate behavioural abnormalities in animal models and subjects with ASD. Clinical trials, however, yielded disappointing results. Our study aimed at challenging hypotheses accounting for such negative results by assessing the behavioural effects of different regimens of OT administration in the Oprm1 null mouse model of ASD. Experimental Approach We assessed the effects of intranasal OT injected once at different doses and time points following administration, or chronically, on ASD-related behaviours in Oprm1+/+ and Oprm1-/- mice. We then tested whether pairing intranasal OT injection with social experience would influence its outcome on ASD-like core symptoms, and measured gene expression in several regions of the reward/social circuit. Key Results Acute intranasal OT improved social behaviour in Oprm1-/- mice at a moderate dose (0.3 IU) shortly after administration (5 min). Effects on non-social behaviours were limited. Chronic OT at this dose maintained beneficial effects in Oprm1 null mice but was deleterious in wild-type mice. Finally, improvements in the social behaviour of Oprm1-/- mice were greater and longer lasting when OT was administered in a social context, while the expression of OT and vasopressin receptor genes, as well as marker genes of striatal projection neurons, was suppressed. Conclusions and implications Our results highlight the importance of considering dosage and social context when evaluating the effects of OT treatment in ASD.

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