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Intranasal oxytocin administration improves impaired social behavior in the POGZ-Q1038R mutant mice

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We previously showed that the autism spectrum disorder (ASD) patient-derived de novo mutation (Q1038R mutation) in the Pogo transposable element with zinc finger domain (POGZ) protein is associated with ASD-like social behavioral deficits in mice. Considering its amino acid sequences and putative domain structures, POGZ is suggested to be involved in transcriptional regulation; however its transcriptional targets in the brain are largely unknown. In order to identify genes transcriptionally regulated by POGZ, we knocked down the expression of POGZ using shRNA method in the mouse primary neurons and performed RNA-sequencing for these neurons. We observed that the expression level of the oxytocin receptor (OXTR) gene is low in POGZ knocked-down neurons compared with control neurons. Interestingly, we found that the expression level of the OXTR gene is also low in the POGZ-Q1038R mutant mice, suggesting that the Q1038R mutation downregulates the function of POGZ. To examine the causal relationship between the decreased expression of the OXTR gene and ASD-like social deficits in the POGZ-Q1038R mutant mice, we intranasally administered oxytocin to the mice 30 minutes before the social interaction test. We found that intranasal oxytocin treatment effectively ameliorates the impaired social interaction in the POGZ-Q1038R mutant mice. These results suggest that the impaired social interaction may be caused by the altered oxytocin system in the POGZ-Q1038R mutant mice and provide insights into the development of treatment strategies of ASD.