Applications of multimodal neuroimaging and pharmacogenetics to develop oxytocin as a novel therapeutic for autism spectrum core symptoms

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Autism spectrum disorders, a highly prevalent neurodevelopmental disorder, currently have no established treatment for its core symptoms. The disorders are characterized by two core symptoms including deficits in social communication and interaction, and repetitive and restricted behavior. Accumulated evidence with a number of previous neuroimaging studies has suggested dysfunctions in various brain regions such as medial prefrontal and insular cortices and their networks underlying pathophysiology of autism spectrum disorders. Although such evidence has promoted our understanding of brain pathophysiology of autism spectrum disorders, difficulties associated with autism spectrum disorders in daily life situations seems not to be reduced by such neurobiological evidence. In this context, some recent studies have tried to apply neuroimaging as a tool to assess effects of novel therapeutics on clinical symptoms. In the symposium, my talk will focus on our studies testing oxytocin as a potential therapeutic for deficits in social communication and interaction in individuals with autism spectrum disorders. We have reported oxytocin-induced improvements of autistic behaviors and core symptom and their neural bases such as basically disrupted brain functions. Furthermore, we showed associations between individual differences in response to oxytocin and genotypes in oxytocin-related genes. Based on these findings, a new concept of an endophenotype-associated surrogate endpoint (EASE) was proposed. The findings suggest that, to examine effect of a novel therapeutic molecule on a target phenotype of a genotype associated with the molecule, state-dependent aspect of an endophenotype can be used as a surrogate endpoint. Ongoing studies are further conducting to examine several unresolved issues such as 1) bio-markers predicting individual differences in therapeutic effects in advance, and 2) potential genetic and molecular mechanisms of oxytocin's effects on autism spectrum behaviors. In my talk, integration of previous findings and introductions of ongoing studies will be presented to promote productive interactions with audiences from various research fields.