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Oxytocin dynamics in the body and brain regulated by the receptor for advanced glycation end-products, CD38, CD157 and nicotinamide riboside

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Abstract. Oxytocin in brain neurons is secreted somato-axono-dendritically and CD38-dependent fashion into the brain and released from the nerve terminals in the posterior pituitary into the circulation.Regarding possible candidates, we suspected the receptor for advanced glycation end-products (receptor for AGEs, RAGE) transports OT from the peripheral blood into the brain by RAGE in endothelial cells at the BBB.

Key words: oxytocin, brain, CD38, CD157.

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Oxytocin in brain neurons is secreted somato-axono-dendritically [1-3] and in CD38-dependent fashion into the brain and released from the nerve terminals in the posterior pituitary into the circulation [1,3]. Recently, however, based on the practical nasal administration of large doses of oxytocin to humans with and without social deficit-related psychiatric disorders, such as autism spectrum disorders and schizophrenia, oxytocin has been thought to cross the blood-brain barrier (BBB). However, there is little to no direct evidence for this transport process at the molecular level, such as transporters. Regarding possible candidates, we suspected the receptor for advanced glycation end-products (receptor for AGEs, RAGE) transports OT from the peripheral blood into the brain by RAGE in endothelial cells at the BBB [4-7].

NAD+ is one of the essential biomolecules, which participates in a large number of vital processes like ATP synthesis, redox homeostasis, and signal pathways. However, it is unclear whether elevating NAD+ levels have beneficial effects on brain function, especially on social memory and interaction. In our study we focused on the effect of NAD+ precursor supplementation on the behavior of a CD157KO mouse model for autism spectrum disorder, which displays anxiety, depression and social impairment from the side of oxytocin release pathways. CD157KO and C57BL6 mice were treated with an NAD+ precursor at the several doses/day in PBS solution or placebo in equal volume through gavage [8]. Social behaviors in the three-chamber or dark-light transition tests were improved after daily gavage for 12 days in CD157 knockout mice, but not in wild-type C57BL/6 mice. Identical effects were not observed by saline in both genotypes. Cerebrospinal fluid oxytocin levels and NAD+ levels were increased after gavage application in CD157 knockout mice, but of saline. Elevation of oxytocin level did not accompany by ADPR cyclase activity [8]. The results demonstrate for the first time that the NAD+

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