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Dopamine D3 receptor modulates tissue type plasminogen activator (tPA) activity in mouse brain

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Growing amount of evidence points to the dopamine D3 receptor (D3R) as an important mediator in the broad array of events that regulate memory function, perhaps through the modulation of molecular pathways involved in neurotrophic factor activation. Tissue type plasminogen activator (tPA) is a proteolytic enzyme that cleaves the precursor of brain derived neurotrophic factor (proBDNF) into the biologically active form of mature BDNF. However, whether D3Rs modulate tPA activity on BDNF in brain has not been ascertained yet. Here in the present study, using D3R knock-out (D3-/-) mice, we demonstrate that receptor inactivation is associated with increased tPA expression both in prefrontal cortex and, to a greater extent, in the hippocampus, two regions associated with memory processes. The heightened tPA levels observed in D3-/- mice inversely correlated with proBDNF protein expression, whereas they positively correlated with both BDNF mRNA and mature BDNF protein levels. In conclusion, our finding strongly suggest that D3Rs might modulate tPA-mediated post-transcriptional processing of BDNF in brain regions critical to memory function.

Keywords: BDNF, dopamine D3 receptor, tissue plasminogen activator, BDNF.