Indirect Dopaminergic Fiber Modulation of Purkinje Cells through Bergmann Glial Cells in Rett Syndrome Mice

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Rett Syndrome (RTT) is an autism spectrum disorder categorized by stereotypic hand movements, dyspraxic gait, and dystonia. Dysfunction in the cerebellum may be responsible for these abnormalities, due to RTT commonly involving motor coordination issues. Since dopamine receptors are highly involved in movement, we hypothesize that dysfunctional dopaminergic signaling is responsible for the lack of motor coordination in RTT. Our lab has investigated dopamine receptor 1 (D1), and have learned that it is mainly distributed on Bergmann Glial Cells (BGCs) as opposed to the cerebellum's only neuronal input: Purkinje Cells (PCs). Our goal is to investigate the location of the major dopaminergic inputs to the cerebellum: either the substantia nigra pars compacta (SNc) and/or the locus coeruleus (LC), as well as their role in modulated PCs through BGCs. Through immunohistochemistry in brain sections, we determined that the dopaminergic fibers from the cerebellum partially originate from the SNc. By performing single-molecule fluorescence in situ hybridization (smFISH), we learned that D1 receptors are located in BGs as opposed to PCs (which indicated that PCs are indirectly modulated). Future studies involve removal of D1 receptors in the cerebellum of RTT mice, specifically removal of D1 in BGCs, to study the effects on behavior and motor function.