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The synaptic protein phosphatase 1 targeting protein, spinophilin, mediates striatal neuroadaptations underlying motor function

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The striatum is part of the striatal-thalamic-cortical-striatal loop and is one brain region that integrates signals to regulate myriad behaviors, including motor learning, locomotor sensitization to drugs of abuse, and repetitive motor outputs observed in obsessive-compulsive spectrum disorders. We have found that global loss of the post synaptic density-enriched protein phosphatase 1 (PP1) targeting protein, spinophilin, mediates multiple striatal-associated behaviors, including rotarod motor learning and psychostimulant-induced locomotor sensitization. Moreover, using recently characterized cell type-specific spinophilin knockout mice, we have observed that loss of spinophilin in specific striatal neurons, direct or indirect pathway medium spiny neurons, attenuates pathological grooming associated with excessive metabotropic glutamate receptor 5 (mGluR5) function. Interestingly, it has previously been suggested that spinophilin is highly locally translated; however, our preliminary data suggest that this local translation may be different in different brain regions. Therefore, these data position spinophilin specifically in the striatum, as a critical regulator of striatal neuroadaptations; however, how spinophilin mediates striatal neuroadaptations is unclear. Herein, we discuss mechanisms by which spinophilin regulates striatal neuroadaptations underlying motor output changes associated with striatal pathophysiology, including locomotor responses to psychostimulant drugs of abuse and dopamine receptor agonism.

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