The Role of Mef2c Transcription Factor in the Development of Medium Spiny Neurons in the Mouse Striatum

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Introduction: we have shown the transcription factor myocyte enhancer factor (Mef2c) to be significantly upregulated in the striatum over a period encompassing peak generation of medium spiny neurons (MSNs). Here we present data that suggest a significant functional role of Mef2c in the maturation and survival of matrix MSNs in the mouse striatum. MSNs constitute more than 90 percent of neurons in the mouse striatum, and are the neurons predominantly degenerating in Huntington's disease.

Methods: Using the Gsx2-cre-loxp recombination system, the Mef2c gene was specifically deleted in the striatum to generate Gsx2-CreMef2c-/- mice. Proliferation assay using BrdU and Edu, motor behavioural testing, Golgi-cox based tracing of dendrites and dendritic spines development, RT qPCR, cell culture, TUNEL assay and stereological quantification of striatal volume and striatal cell counts for NeuN, and MSNs markers (Foxp1and Darpp-32) were all used in a developmental series between P2 to 12months.

Results: Mef2c expression in WT striatum peaks at postnatal day 0, a period critical for the maturation of matrix MSNs. Histological analysis revealed a significant reduction in the striatal volume. Also, total numbers of cells staining for NeuN, FoxP1 and Darpp-32, in Gsx2-Cre Mef2c-/- were reduced compared with wt mice. Furthermore, CKO mice exhibit significant motor function impairments and anatomical changes in dendrites development. A cell death assay revealed a mild, yet significant, increase in apoptotic cells at postnatal day 0.

Conclusions: Our results suggest that Mef2c has a significant role in the normal maturation and survival of MSNs, Further experiments are ongoing to explore the extent to which this is specific to matrix MSNs and the mechanisms underlying these findings.

Speaker Biography

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