ハンチントン病モデルマウスにおけるナトリウムチャネルβ4 サブユニットの発現抑制

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Dysregulation of β4 gene transcription in the striatum of Huntington Disease transgenic mice

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Sodium channel β4 (β4) is a recently identified auxiliary subunit of the voltage gated-sodium channels. We found that β4 is significantly downregulated in the striatum of Huntington Disease (HD) model mice and patients. *In situ* hybridization with β4 probe, followed by immunohistochemistry using anti preproenkephalin (PPE) or anti preprotachykinin A (PPTA) indicated that β4 mRNA is expressed in two groups of striatal neurons projecting to globus pallidus (GP)(marker protein: PPE) and substantia nigra (SN)(marker: PPTA). TaqMan RT-PCR analysis indicated that both β4 and PPE mRNAs are preferentially decreased in striatum at a presymptomatic stage of HD mice, while PPTA mRNA and its peptide are unaltered even at the symptomatic stage. These results indicate that there is a difference in downregulation of mRNA and its product among striatal projection neuron proteins and suggest that loss of β4 in the striatum of HD transgenic mice is due to dysregulation of β4 gene transcription.