Abstract of Doctoral Dissertation

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Title of Doctoral Dissertation

Inter- and intra-species differences in muscarinic acetylcholine receptor expression in the neural pathways for learned vocalization in songbirds

（鳴禽類歌神経回路において種内個体差・種間差発現を示すムスカリン性アセチルコリン受容体の研究）

Acetylcholine receptors (AChRs) abound in the central nervous system. Muscarinic AChRs (mAChRs), a functional subclass of AChRs, mediate neuronal responses via intracellular signal transduction. They also play roles in sensorimotor co-ordination and motor skill learning, such as song learning by enhancing cortical plasticity. Songbirds, such as the zebra finch, acquire their songs, a complex sequence of vocal patterns, through sensorimotor coordination during a critical learning period. However, the functions of AChRs in the neural circuits for vocal learning during song learning remain largely unexplored. I investigated the precise expression patterns of chrms in the major brain subdivisions, during the critical period of vocal learning, among songbird species, in early-deafened zebra finches. Further, I examined the effects of overexpressing chrm2 on crystallized adult song in the zebra finch. I found that chrm1 is not expressed in the songbirds whereas there is unique expression of mAChRs subclass (chrm2–5) in the song systems for vocal learning and production in the zebra finch. The expression of excitatory subunits (chrm3 and chrm5) was downregulated in the song nuclei compared with the surrounding regions. In contrast, inhibitory mAChRs (chrm2 and chrm4) were upregulated in the premotor song nucleus HVC relative to the surrounding caudal nidopallium. Chrm4 showed developmentally different expression level in HVC during the critical period of song learning. Compared with chrm4, individual differences in chrm2 expression level in HVC emerged during the early stage of the critical period. These individual differences in chrm2 expression persisted despite testosterone administration or auditory deprivation, which altered the timing of song sing stabilization in the zebra finch. Instead, the variability in chrm2 expression level in HVC correlated with parental genetics. In addition, chrm2 expression level in HVC showed species differences and individual variability among songbird species. In early-deafened zebra finches, chrm2 expression level correlated positively and negatively with the motif and repetition indices of song, respectively. In zebra finches at the subsong stage, chrm2 expression level correlated with the coefficient of variation in syllable entropy variance of songs. In adult zebra finches, over-expressing CHRM2 protein had no clear effects on crystallized learned song. These results suggest that mAChRs may contribute to the development of individual and species differences in learned song patterns by modulating the excitability of HVC neurons.