

Immediate early genes expression in the cerebellar cortex correlates with LTP and LTD induction

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The consolidation of changes following activity-dependent neural plasticity are believed to involve specific patterns of gene expression. In the hippocampus, immediate early genes are thought to contribute to long-term synaptic plasticity (LTP and LTD); this phenomenon may occur also in the cerebellum, in which the transcription factors c-Fos and P-CREB have been identified. The cerebellum granular layer (GL) can manifest both LTP and LTD following a Theta Burst Stimulus (TBS) delivered to the mossy fibers. We have employed VSD imaging in rat cerebellar slices (P18-24) in order to map the spatial distribution of LTP and LTD in the cerebellum GL. Fluorescence changes were correlated to LTP or LTD in two different post-TBS time ranges (15 and 120 min). Slices were then fixed and processed for immunohistochemistry in order to identify levels of c-Fos and P-CREB expression. The induction of long-term plasticity increased the average level of P-CREB both at 15 min ($+39\pm 4.9$, $p < 0.01\%$) and 120 min ($+24\pm 7.2$, $p < 0.05\%$) after TBS. The level of c-Fos was unaltered at 15 min, while it significantly increased at 120 min ($+37\pm 8.9$, $p < 0.05\%$). By spatially correlating long-term synaptic plasticity with the corresponding variation of P-CREB and c-Fos, we observed that regions showing LTP well correlated ($p < 0.05$) with positive variations of P-CREB and c-Fos. Conversely, areas showing LTD correlated exclusively ($p < 0.05$) with negative variations of P-CREB. Slices were also evaluated by in situ hybridization and a similar analysis was performed. The levels of fos and CREB mRNA expression and their spatial correlation with the sign of long-term synaptic plasticity corresponded with the immunohistochemical results. As a further test, VSD recordings showed that the induction of granular layer LTP and LTD could be prevented by applying 50 mM D-APV, a selective NMDA receptor blocker. Moreover, in situ hybridization and immunohistochemistry analysis evidenced that in these conditions both mRNA and protein expression levels of c-fos and CREB were unchanged, confirming the involvement of these two transcription factors in cerebellar granular layer plasticity.

Keywords: Cerebellar cortex granular layer, immediate early genes, long-term synaptic plasticity.