

4th Global Congress on

SPINE AND SPINAL DISORDERS

September 05-06, 2018 Auckland, New Zealand

Protein synthesis inhibitors did not interfere with long-term depression induced either electrically in juvenile rats or chemically in middle-aged rats

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In testing the hypothesis that Long-Term Potentiation (LTP) maintenance depends on triggered protein synthesis, we found no effect of Protein Synthesis Inhibitors (PSIs) on LTP stabilization. Similarly, some studies reported a lack of effect of PSIs on Long-Term Depression (LTD). The lack of effect on LTD has been suggested to be resulting from the short time recordings. If this proposal were true, LTD might exhibit sensitivity to PSIs when the recording intervals were enough long. We firstly induced LTD by a standard protocol involving low frequency stimulation, which is suitable for eliciting NMDAR-LTD in CA1 area of hippocampal slices obtained from juvenile Sprague-Dawley rats. This LTD was persistent for intervals in range of 8-10 hours. Treating slices with Anisomycin, however, did not interfere with the magnitude and persistence of this form of LTD. The failure of anisomycin to block synaptic-LTD might be relied on the age of animal, the type of protein synthesis inhibitors and/or the inducing protocol. To verify whether those variables altogether were determinant, NMDA or DHPG was used to chemically elicit LTD recorded up to 10 hours on hippocampal slices obtained from middle-aged rats. In either form of LTD, cycloheximide did not interfere with LTD stabilization. Furthermore, DHPG application did show an increase in the global protein synthesis as assayed by radiolabeled methodology indicating that though triggered protein synthesis can occur but not necessarily required for LTD expression. The findings confirm that stabilized LTD in either juvenile, or middle-aged rats can be independent of triggered protein synthesis. Although the processes responsible for the independence of LTD stabilization on the triggered protein synthesis are not yet defined, these findings raise the possibility that de novo protein synthesis is not universally necessary.

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