Effect of the inhibition of ROCK signaling on the Hippocampal Metaplasticity

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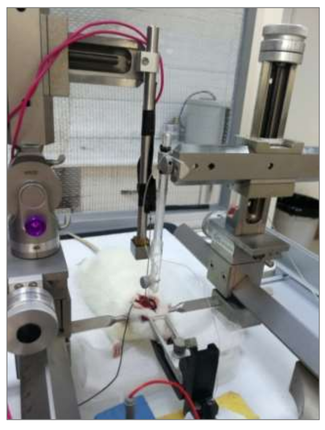
OBJECTIVE

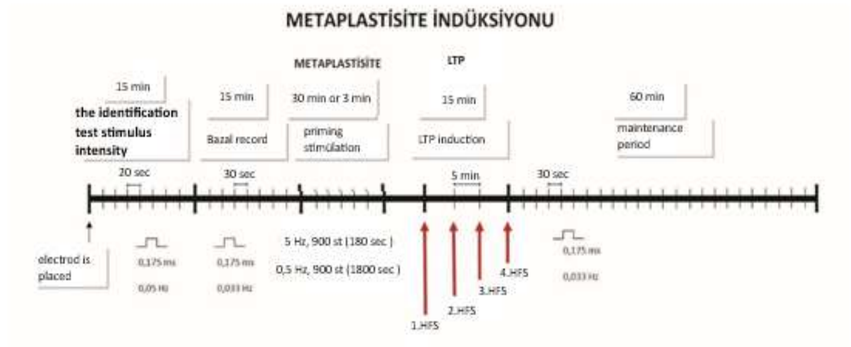
Rho/Rho-kinase (ROCK), has an important role in the develpment of synaptic plasticity in presynaptic and postsynaptic hippocampal neurons. It has been reported in the literatüre that ROCK protein levels increase in cognitive disorders such as Alzheimer's. In our study, changes in synaptic plasticity were investigated by infusing the ROCK inhibitör fasudil into healthy rat hippocampuses.

METHOD

Control (C, n=8) and Fasudil (F, n=8) groups were composed of Wistar-Albino male rats. The anesthetized animal skull was fixed to the stereotaxic system and stimulated with electrode inserting to the perforating path. Serum physiological or Fasudil were infused into the dentate gyrus. Metaplasticity was induced by delivering high frequency stimulation (HFS) 5-min after low-frequency stimulation. Population spike amplitude (PS) and excitatory postsynaptic potential slope (EPSP) evaluated.

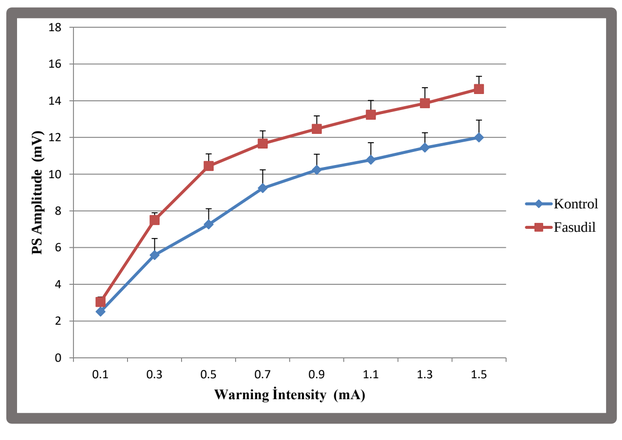


EXPERIMENT PROTOCOL SCHEMA

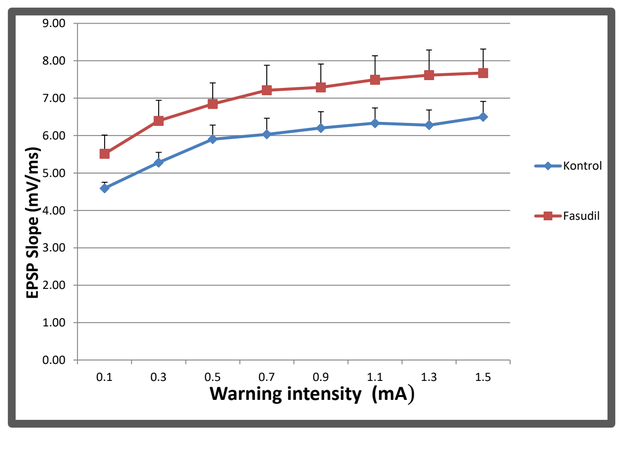


RESULTS

I/O in evaluation, PS amplitude and EPSP slope increased in both groups, this increased (group effect: p>0.05; interaction effect: p>0.05) was not significant.

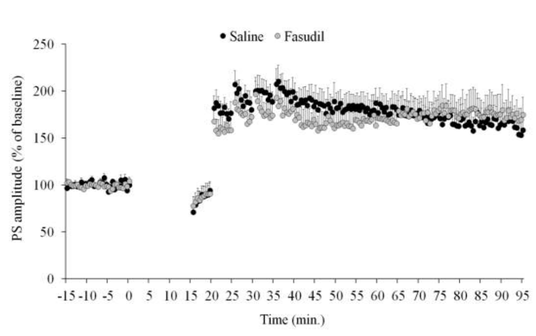


PS amplitude values measured against 8 different stimulation intensities ranging from 0,1 mA – 1,5 mA from dentate gyrus neurons in the control and fasudil groups ; before MP

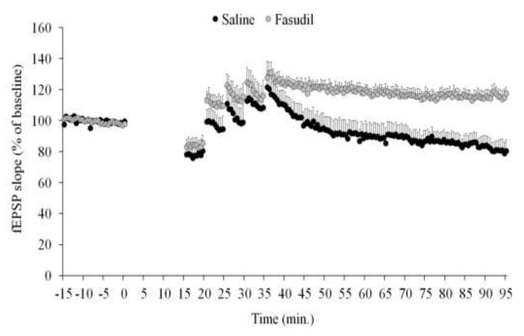


EPSP slope values measured against 8 different stimulation intensities ranging from 0,1 mA – 1,5 mA from dentate gyrus neurons in the control and fasudil groups ; before MP

Fasudil infusion eliminated EPSP slope inhibition both in post-tetanic (F=%126,86±5,27, K=%115,29±8,87, $p<0.05$) and maintenance periods (F=%117,40±4,58, K= %80,81±6,76; $\boldsymbol{p} < 0.05$). This change reached statistically significant levels.
There was no significant difference in PS amplitudes between groups at post-tetanic period (F=%180.93±18.34, C=%201.19±14.09 $\boldsymbol{p}>0.05$), while fasudil infusion resulted in the increased PS amplitude at the maintenance period (F=%173.13±16.30 C=%162.78±12.79, $\boldsymbol{p}>0.05$).



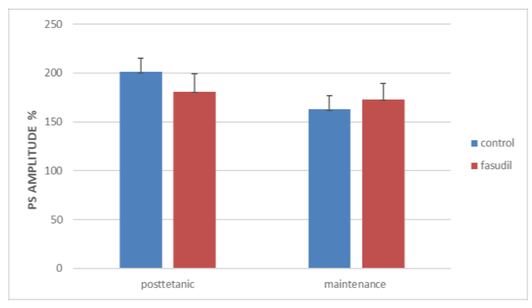
PS AMLİTUDE
1;Induction period 2: maintenance period

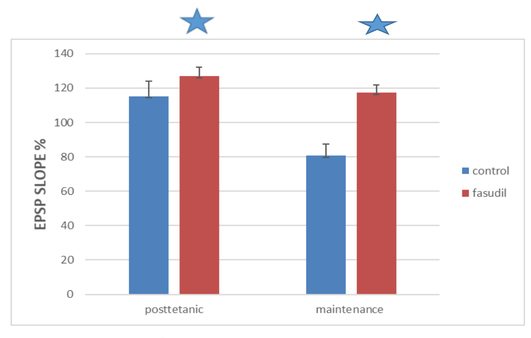


EPSP SLOPE
1:Induction period 2: maintenance period

DISCUSSION

In our study, neuronal suppression was removed in the fasudil experimental group in the MP experiments and an increase in synaptic plasticity response was observed. While the ROCK signaling pathway affects the regulation of synaptic function ıt is among the literature data that ROCK inhibition increases synapse formation and neuronal plasticity. This situation emphasizes the complex and sensitive role of Rho in synapses during the activation of neurons.





Based on the current results, it is know that the Rho/ROCK signaling pathway has an effect on the underlying cellular mechanisms of learning and memory. Therefore the molecular links of the ROCK signal cascade with other forms plasticity and neurodegeneration patterns deserve further study.

CONCLUSİON

Our study demonstrated the importance of the ROCK pathway in the dentate gyrus synaptic plasticity functions. There are not electrophysiological studies in the literatüre investigating the effect of ROCK on plasticity function with in-vivo hippocampal infusion. Therefore our work is orginal. Moleculer connections of neurodegenerative diseases and ROCK require more detailed investigation.

RESOURCES

1. **Olofsson B.** Rho guanine dissociation inhibitors: pivotal moleculse in cellular signalling. Cell Signal, 1999; 11(8):545-554.
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