Involvement of presynaptic mGluR receptors in regulating depolarisation-induced suppression of inhibition.

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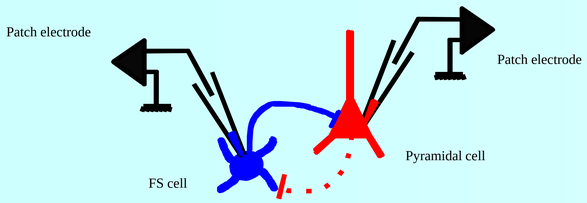
Introduction

Depolarisation-induced suppression of inhibition (DSI) is the reductionin $GABA_A$ receptor mediated inhibitory synaptic events in cells in response to depolarisation of their membranes.DSI requires the opening of the voltage dependant calcium channels in the postsynaptic cell and is thought to involve retrograde signaling acting on inhibitory interneurones presynaptically to reduce the release of GABA. It has been suggested that metabotropic glutamate receptors (mGluRs) are involved in regulating DSI with glutamate acting as the retrograde messenger. In the present study it was of interest to investigate whether pre and / or postsynaptic mGluR receptors are involved on regulating DSI.

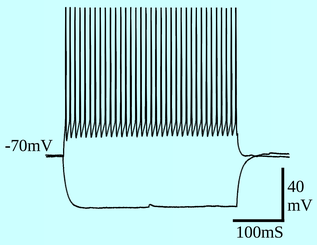
Method

Simultaneous somatic dual whole-cell recordings were made in current clamp in layer V of 17-22 day old rat motor cortex between elctrophysiologically identified interneurones and pyramidal cells. The cell types were selected using video-microscopy under near-infrared deferential interferencecontrast (DIC) illumination. Inhibitory postsynaptic potentials (IPSPs) were elicited by single, pairs or trains of presynaptic action potentials (APs) by injecting short (5-10 ms) pulses of depolarising current repeated at 0.2HZ.



Results

1. Presynaptic interneurones displayed FS behaviour.



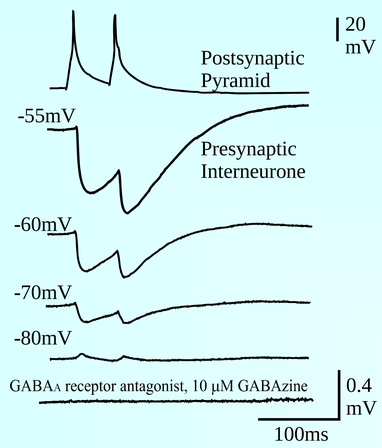
Fast spiking Interneurone

These FS cells dispalyed very fast action potentials and terminated with deep,fast spike after-hyper-polarisation. Trains of spikes showed little accommadation or adaptation.

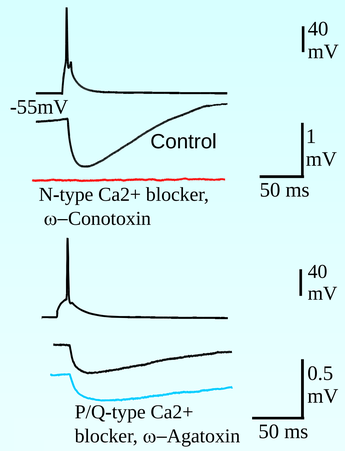
2. Synaptic connections between FS to pyramidal cells have the following characteristics:

* Mediated by $GABA_A$ receptors,shown in (A).
* Synaptic release of GABA involve N-type calcium channels (B).
* Always display DSI (C)

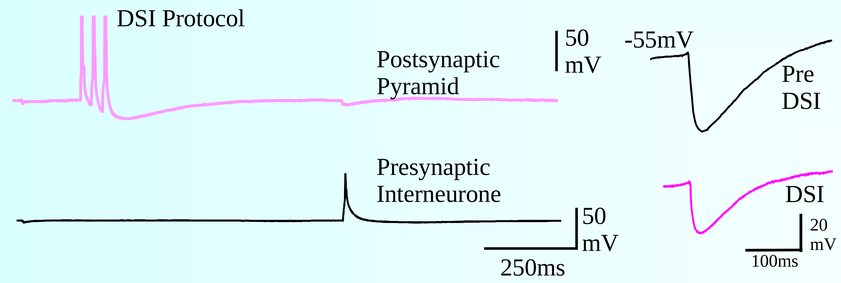
A. I/V of FS to Pyramid Connections



B. Synaptic release mediated by N-Type calcium channels

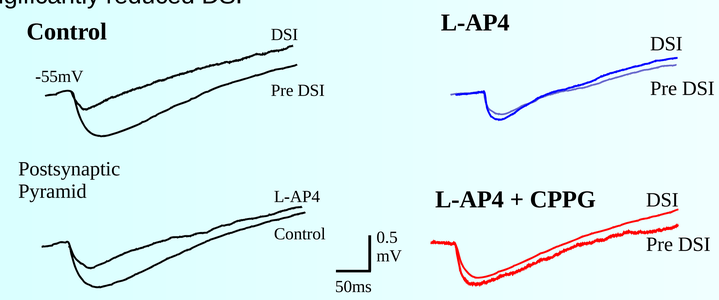


C. FS to Pyramid connections display DSI



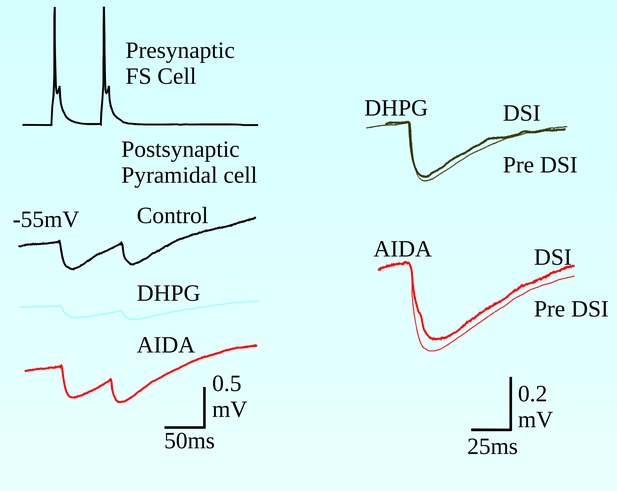
3. Group III mGluRs modulates DSI.

* Group III mGluR agonist L-AP4 decreased unitary IPSPs and occluded DSI
* mGluR III antagonist CPPG blocked L-AP4-induced IPSC supression and sigificantly reduced DSI

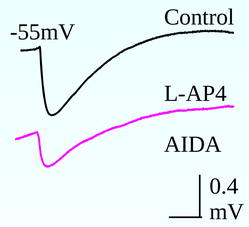


4. Group I mGluRs regulate DSI.

Group I agonist DHPG mimicked DSI by suppressing unitary IPSPs. Group I antagonist AIDA blocked the effects of DHPG and prevented DSI



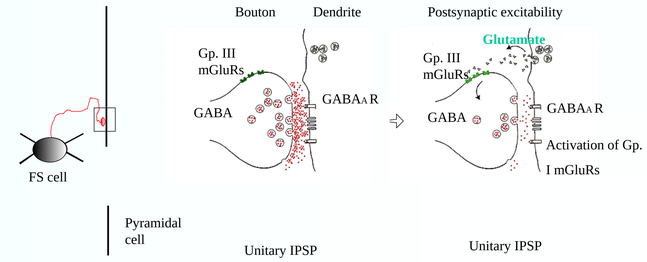
5. Group I and III mGluRs co-operate to control DSI.



The group III agonist L-AP4 suppressed unitary IPSPs which was prevented by group I antagonist AIDA.

6. Summary

The data presented here suggests that glutamate is probably released as an retrograde messanger from pyramidal cells via the activation of postsynaptic group I mGluRs which mediate DSI by reducing GABA release from presynaptic interneurones via the activation of presynaptic group III mGluRs.



Acknowledgements

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