USE OF ISONIAZID, AN INHIBITOR OF GLUTAMIC ACID DECARBOXYLASE, FOR THE IN VITRO ASSESSMENT OF THE ROLE OF GABAERGIC NEUROTRANSMISSION IN THE CONTROL OF THE CEREBELLAR CORTEX NEURONAL CIRCUITRY

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The cerebellar cortex plays a crucial role in the control of movement, motor coordination and certain cognitive functions. This neuronal circuit is composed of five different types of neurons that are wired together in a repetitive module. Four out of five of these neurons synthesize and release GABA, giving a primary role to this inhibitory neurotransmitter in controlling the excitability and the correct functioning of the cerebellar cortex. Isoniazid (INH), an inhibitor of glutamic acid decarboxylase (GAD), the enzyme responsible of the synthesis of GABA, was used to evaluate the importance of GABAergic transmission in different types of cerebellar cortical neurons. Parasagittal cerebellar slices were prepared from 30-45 day-old male rats and patch clamp recordings were performed in voltage and current clamp mode. Long term incubation (≥40 min) with INH (10 mM) significantly reduced the amplitude of evoked IPSCs recorded in Purkinje cells (PC) to 47 ± 5 % of the control value (n=6). No change in the probability of GABA release was observed during INH application using a paired pulse protocol. Cell attached recording from visualized PCs revealed that the same treatment induced a significant increase in firing frequency of 55 ± 23 % with respect to control (n=15). In granule neurons, incubation of at least 40 min with INH (10 mM) reduced both tonic and phasic GABAergic current. Our data support the notion that GABAergic transmission plays a major role in controlling the excitability of the cerebellar cortex, and suggest that INH is a suitable tool for studying the GABAergic transmission.