

SUMATRIPTAN IN THE RETINAL SPREADING DEPRESSION (Abstract)\*. **THESIS. RIO DE JANEIRO, 1997.**

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The mechanisms of Leão Spreading Depression (SD), a neurophysiological phenomenon described more than 50 years ago, remain obscure.

The objective of the present study was to analyze the effects of sumatriptan and related compounds on SD in isolated chick retina.

The influence of serotonin agonists (sumatriptan and piperazine) and an antagonist (methiothepin) upon the SD propagation velocity was registered and analyzed *in vitro*. Some neuropeptides (CGRP, CGRP(8-37), VIP and Endotelin-3) were also tested.

Forty chicks (134.6±24.1 g; range 46-500 g) were enucleated immediately after decapitation and the eyes sectioned in the equator. The vitreous humor was removed and the posterior eyecup immersed in buffer solution (NaCl: 120; KCl: 4; CaCl<sub>2</sub>: 1; MgSO<sub>4</sub>: 1; NaHCO<sub>3</sub>: 30; NaH<sub>2</sub>PO<sub>4</sub>: 1; glucose: 20. Values in mM) aerated with 95% O<sub>2</sub>-5% CO<sub>2</sub> to maintain pH between 7.8-8.0, as in previous experiments. Eyecup fragments (4 x 10 mm) were cut into strips, the nervous tissue layer isolated from other ocular structures, and mounted on strips of filter paper (retinal vitreous layer facing upwards). The preparations were placed in 0.2 ml plexiglass chambers and superfused with 3 ml 30°C buffer solution by an infusion pump (1.5 ml/min). Two 1 µm o.d. glass microelectrodes containing 150 mM NaCl were inserted perpendicularly 4 mm apart in the inner plexiform layer of the retina. The microelectrodes were connected to a dual channel electrometer (World Precision Instruments, Inc) and a Grass polygraph.

A 100 µm tungsten rod was used to induce RSD mechanically, the propagation being contrary to the flux of superfusion. Propagation was observed visually under an optical microscope and the typical negative voltage variation of the Leão wave was recorded.

The velocity of the RSD propagation was calculated from the time required by the waves to spread from the first to the second microelectrode. The preparations were equilibrated in order to obtain two successive RSDs with the same velocity (RSD<sub>1</sub>). The drug is added, three new RSDs were elicited, and the corresponding velocities recorded (V<sub>1</sub>, V<sub>2</sub> and V<sub>3</sub>). The preparations were then washed and a final RSD (RSD<sub>f</sub>) obtained. All RSDs were induced during 10 minutes intervals.

The effect on retinal SD produced by subcutaneous (SC) sumatriptan *in vivo* was also verified.

Sumatriptan and piperazine block retinal SD in a concentration-dependent way. Methiothepin does not modify the spread velocity neither antagonizes the sumatriptan-induced velocity reduction. At tested concentrations, neuropeptides have no effect on retinal SD *in vitro*. SD was normal in samples removed from animals following SC injections of sumatriptan in up to 1000 times the therapeutical doses.

The present results may contribute to a better understanding of the mechanisms involved in the pathophysiology and treatment of migraine.

**KEY WORDS: migraine, retinal spreading depression, sumatriptan, piperazine, methiothepin.**

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