**The protective role of melatonin in an organotypic model of Spinal Cord Injury secondary damage.**

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Spinal cord injury (SCI) is characterized to be a two-step process composed by the primary lesion consisting of the initial trauma and the secondary damage, characterized by multiple processes including inflammation, oxidative stress and cell death that lead to a significant expansion of the original damage and to an increase of the functional deficit. Among the aforementioned processes, the oxidative stress plays a significant role in pathophysiology of SCI. In this study, we evaluated the role of the melatonin, the major secretory product of the pineal gland recognized as a potent antioxidant and immunomodulator indoleamin, on the oxidative stress, the tissue vitality and the neuritic plasticity deriving from the gray matter in an experimental model of organotypic cultures consisting of Sprague Dawley rat spinal cord slice treated with hydrogen peroxide (H2O2). In five experimental groups, A) Control Group (CTR) – Organotypic spinal cord slice culture (350μm); B) Stressed Group (H2O2) – Organotypic spinal cord slice culture (350μm) exposed to H2O2 (50 μM); C) Control Group with a melatonin treatment (10-5M) of 24 hours (CTR+MEL) – Organotypic spinal cord slice culture (350μm) treated with melatonin for 24 hours; D) Treatment Group (H2O2+MEL-POST) – Organotypic spinal cord slice culture (350μm) exposed to H2O2 (50 μM) and treated after 24 hours with melatonin (10-5M) for 24 hours; E) Treatment Group (H2O2+MEL-PRE) – Organotypic spinal cord slice culture (350μm) pre-treated with melatonin (10-5M) for 24 hours (50 μM) and exposed to H2O2 for other 24 hours, it was investigated the slice cellular death by propidium iodide (PI) assay, the slice vitality by MTT assay, the superoxide dismutase (SOD) and total thiols (SH) levels for the contrast to the oxidative stress, the neuronal (NeuN) and the synaptophysin (Syp) immunopositivity. Melatonin significantly decreases the number of dead cells, increases slice vitality, mainly in slices treated before H2O2 exposition. It enhances SOD immunopositivity, contrasts total thiols decrease, attenuates Syp reduction and increases NeuN immunopositivity. Overall, these findings suggest that melatonin may exert a potentially beneficial effect upon the progression of SCI secondary damage, protecting the tissue from a further degeneration.