The neuroprotective role of melatonin in stroke

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Stroke is a leading cause of adult death and disability worldwide. Around 80% of all stroke cases are classed as ischemic stroke, which affects both gray and white matter brain regions. During ischemia, reactive oxygen species are generated and initiate multiple damaging processes such as lipid peroxidation, mitochondrial dysfunction, blood–brain barrier damage and brain edema. Melatonin is a neurohormone secreted from the pineal gland and has a wide-ranging regulatory and neuroprotective role. It has been reported that melatonin level is disturbed in some neurological conditions such as stroke, Alzheimer's disease and Parkinson's disease, which indicates its involvement in the pathophysiology of these diseases. Its properties qualify it to be a promising potential therapeutic neuroprotective agent, with no side effects, for some neurological disorders. Melatonin is considered one of the most potent agents playing an important protective role in all stages of ischaemic injury. It has an anti-excitotoxic, antioxidant, and an anti-inflammatory effect. Melatonin helps in maintaining Ca2+ homeostasis and preventing BBB (Blood Brain Barrier) leakage and brain oedema which in turn improves stroke outcomes. Our studies have extended to study the effect of melatonin in astrocyte brain section during OGD (Oxygen Glucose Deprivation) ischaemia model. Using live cell imaging of transgenic mice, the viability of astrocytes in the corpus callosum of adult brain sections was monitored during a standard 60 minutes period of modeled ischemia (oxygen-glucose deprivation). Addition of melatonin significantly reduced the level of astrocyte death during oxygen-glucose deprivation. This protective effect was blocked by luzindole, a nonselective melatonin receptor antagonist, or propionamidotetralin, a selective melatonin receptor 2 antagonist. Following known scoring categories for glial injury, ultrastructural morphology showed the protective effect of melatonin against acute ischaemic injury in the white matter glial cells.

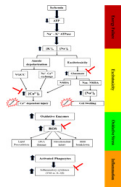

Figure 1: Ischaemia pathophysiology at four stages: energy failure, excitotoxicity, oxidative stress and inflammation. ( ) represents the site of melatonin action.

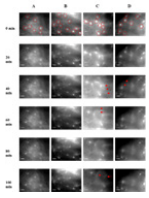

Figure 2: Live GFP imaging of corpus callosum astrocytes.

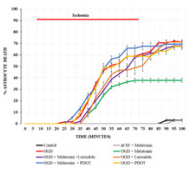

Figure 3: Incidence of astrocyte lysis under various conditions plotted at 5-minute intervals (minimum of four brain sections per condition)

Conclusion: Melatonin is a promising neuroprotective agent during white matter ischemia

Biography

Badrah Alghamdi has her expertise in the molecular basis of white matter ischemia. She is now working as an Assistant Professor at King Abdulaziz University

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