Abstract Information

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Title :	Melatonin modulates the diurnal variations in both cholinergic and dopaminergic release in the mouse striatum.

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Abstract : Background: Melatonin, an indolamine, is derived from the precursor tryptophan through a series of enzymatic steps. In a commonly used strain of C57BL/6J mice, the genes for these enzymes are truncated, resulting in a lack of circadian melatonin rhythmicity. By introducing these alleles, a C57BL/6J congenic line known as CBA/CaJ was created, with the ability to synthesize melatonin. It has been shown that extracellular striatal dopamine levels fluctuate during the day, as a result of changes in the cholinergic neurons' circadian rhythm activity, which itself would be controlled by melatonin?s rhythmicity. As diurnal changes in DA have been shown to alter synaptic connectivity and animal behaviour, understanding this modulation has consequences for diagnostics and treatment of neurodegenerative such as Parkinson?s disease and psychiatric disorders.

Methods: In this study, we examined the impact of melatonin on evoked DA release using fast-scan cyclic voltammetry in acute striatal slices from CBA/CaJ and C57BL/6J mice. Slices were prepared at two distinct points during the light/dark cycle, corresponding to the lowest and highest MLT levels.

Results: Our findings reveal that during the dark cycle, when MLT peaks, DA release decreases in CBA mice and not in C57BL6 mice. Furthermore, when physiological concentrations of exogenous MLT were applied to the slices, it inhibited DA release mainly in

CBA/CaJ mice. In contrast, C57BL/6J mice did not display a substantial response, likely due to their reduced sensitivity of receptors to melatonin.

Conclusion: Our results confirm that melatonin receptors? activation plays a vital role in modulating striatal DA release and establishing the dose- and time-dependent kinetics of release inhibition and recovery. Additionally, we showed that this regulation of DA rhythmicity by melatonin is mediated through the activity of cholinergic interneurons in the striatum.

Key words: dopamine, melatonin, circadian rhythms, fast-scan cyclic voltammetry, nicotinic acetylcholine receptor