Stimulatory Effects of Melatonin on Ependymal Epithelium of Choroid Plexuses in Golden Hamsters

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Summary

Ependymal epithelial cells from the choroid plexuses (CPs) separately of lateral (I + II), IIIrd and IVth ventricles of male Golden Hamsters were studied by electron microscopy and morphometry. The 16 hamsters were distributed between three injection groups: vehicle only, 25 μg and 2500 μg melatonin (M) by subcutaneous injection daily at L11 to L11.75 in a LD 14:10 daily photoperiod. After 28 consecutive daily injections, animals were killed and the CPs were dissected, fixed and prepared for electron microscopy. Thirteen measures of the CP ependymal cells were made, by planimetry, morphometry or direct counting or linear measurement on the EM prints. Effects of melatonin occurred only on the cells from the lateral ventricles. Here M at high dosage caused cell swelling (averaging 50% increase in area), and other cellular changes were graded in relation to M dosage. These were increase (to 26%) in mitochondrial area per cell, and increase (to 50%) in length of apical microvilli. Since in other work the latter form a major locus of ouabain-sensitive Na+, K+-ATPase, it is suggested that M may possibly have a stimulatory effect on transport and related CSF secretory activities by these cells.

Key words: Cerebrospinal fluid, choroid plexuses, ependymal epithelium, melatonin, microvilli, mitochondria, pineal, male Golden Hamsters.

Introduction

Melatonin (5-methoxy-N-acetyltryptamine) is increasingly shown to have effects on diverse aspects of function in the central
nervous system (Trentini et al., 1979; Mendelson et al., 1980; Datta and King, 1981). The mechanisms behind these effects, and their potential physiological and clinical significance are essentially unknown. Insofar as we have been able to determine, there is as yet no report of melatonin having an effect on either the tissues of the brain's choroid plexuses, or the amount or composition of the cerebrospinal fluid (CSF).

The choroid plexuses are generally held to have a dominant role in the elaboration of the CSF within the brain's system of ventricles (Sahar, 1972; Pollay, 1974). However, experimental evidence still suggests that they are not the only sites of production of CSF (Milhorat et al., 1971; Katzman and Pappius, 1973). Our interest in the possibility that the pineal gland and its best known product, melatonin, have physiologically important actions on choroid plexuses and CSF derives from an early experimental study. This showed that pinealectomized rats on a Na-deficient diet had a grater tendency to lowered brain K than either non-operated or sham-operated control animals in identical conditions (Quay, 1965). Both Na\(^+\) and K\(^+\) are actively transported from choroidal capillary blood to CSF, but Na\(^+\) is considered to be the main ion responsible for movement of water from blood to CSF. Basically, the relative constancy of the CSF's K\(^+\) concentration is thought to depend upon K-pumps located at blood-brain and blood-CSF "barriers" (Pollay, 1974). There is increasing evidence that neuroendocrine factors contribute to the regulation of the activities of the choroid plexuses. This remains true whether one views these structures as major and dynamic components of the blood-CSF "barrier", or as major sites for elaboration of CSF (Lindvall et al., 1978; Nathanson, 1980).

Melatonin occurs in CSF and follows 24-hour rhythmic changes there, at least in Rhesus Monkeys (Perlow et al., 1981). However, the enzyme responsible for the last step in melatonin's biosynthesis, hydroxyindole-\(O\)-methyltransferase (HIOMT), has not been detectable in mammalian choroid plexuses (Quay, 1966). Circulating melatonin and its cyclicity remain detectable long after pinealectomy according to some workers (Yu et al., 1981). Extrapineal sources of melatonin are known in several mammalian species (Ralph, 1980), including the Golden Hamster (Pévet et al., 1980), the species used in the present study.

This report presents ultrastructural and morphometric results that show for the first time that melatonin can have stimulatory actions \textit{in vivo} on the choroidal ependymal cells of a mammalian species.