ALTERATIONS IN THE CIRCADIAN REST-ACTIVITY RHYTHM IN AGING AND ALZHEIMER’S DISEASE

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ABSTRACT

Due to degenerative changes in the hypothalamic clock (the suprachiasmatic nucleus) and the visual system, circadian rhythms deteriorate in aging and Alzheimer’s disease. Rat studies suggest that increased environmental light intensity might effectively counteract such disturbances.

Alterations in circadian rhythms in aging and Alzheimer’s disease

Circadian rhythms are regarded to be crucial for optimal functioning of an individual. The suprachiasmatic nucleus, considered to be the endogenous circadian clock in the mammalian brain, shows morphological changes with aging, which become even more pronounced in Alzheimer’s disease (AD). In order to study possible functional consequences of this deterioration, circadian rhythms are investigated in relation to aging and Alzheimer’s disease in both humans and rats. The human part being predominantly descriptive, the rat more experimental.

Human studies

Although the practical possibilities for studying circadian rhythms in human subjects, and especially in AD patients, have been rather limited to date, the recent development of a small ambulatory rest-activity monitor (Mirmiran et al., 1988) has enabled us to study the alterations in the circadian rest-activity rhythm with aging and in AD in detail (Witting et al., 1990).

Young (n=6) and old (n=13) volunteers showed no differences in their rest-activity rhythm in any of the variables studied. Comparison of old controls vs. AD patients (n=12) revealed that (i) rest-activity rhythm was markedly disturbed in many of the AD patients and tended to be correlated with the severity of the dementia, (ii) disturbances were more pronounced in subjects using sedating drugs, (iii) disturbances in the latter group did not result from medication since no differences were found in the rest-activity patterns before and after administration of sedating drugs, (iv) negative findings reported in the literature concerning circadian disturbances in AD may well have resulted from selection criteria that
excluded the group of patients with the most severely affected rest-activity rhythm, and (v) rest-activity monitors offer a practical and fruitful approach in studying circadian rhythms in human.

**Rat studies**

Several studies have reported alterations in the period of free-running rhythms (FR) during aging. However, as the level of activity directly influences the FR period, and old rats are always less active than young ones, the reported findings need re-examination. By comparing the temperature, drinking and sleep/wake rhythms instead of wheel running in young (3-5 months) and old (30-32 months) Brown-Norway rats, we found no differences either in the total amount of active wakefulness, or in period of FR during aging. There was also no indication of internal desynchronization among the various rhythms.

Under light-dark (LD) conditions old rats have been reported to show a reduced amplitude of various circadian rhythms. As perception of light may directly influence the level of activity we have studied the effect of 5 different light intensities (ranging from 445 to 3.5 lux) during the light phase of the LD cycle in young and old rats. Reducing the light intensity had a significant negative effect on the amplitude of the sleep/wake rhythms in both age groups. Furthermore, a reduced amplitude in old as compared with young rats was seen at all light intensities. The amplitudes of old rats under the highest light intensity were comparable to those of young rats under the lowest light intensity. We conclude that amplitude reductions of circadian rhythms during aging can be compensated for by increasing the environmental light intensity.

**REFERENCES**
