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A study of individual behaviour in age-related decline in the pineal secretion of melatonin: possible implications in the prevention of age-related human diseases

Abstract

The pineal gland has appeared to exert a fundamental role in the modulation of most biological functions in relation to the universal rhythms through the release of several in dole hormones, the most investigated of them is melatonin (MLT), which is mainly released during the night with a following light/dark rhythm in MLT secretion. The circadian rhythm of MLT tends progressively to disappear with age, and old people have been proven to have no MLT nocturnal increase, with a following loss of MLT rhythm. However, the behaviour of MLT secretion with age has not been adequately investigated up to now. The present study was carried out to investigate the profile of MLT secretion in a group of healthy adults and aged people. The study included 50 healthy volunteers, divided into adult and aged groups of 25 subjects for group. To evaluate MLT serum levels, venous blood samples were collected at the four main times of the photoperiod. A normal MLT night increase occurred in all adult subjects and in 16/25 (64%) aged subjects, and MLT nocturnal mean levels were significantly higher in the young group than in the aged group. In contrast to previous results by other authors, this preliminary study shows the possible persistence of a normal MLT light/dark rhythm also in some healthy aged subjects. If longitudinal studies will demonstrate that the presence of a normal light/dark MLT rhythm in aged subjects is associated with a lower incidence of age-related diseases, including cancer and cardiovascular diseases, the measurement of MLT rhythm could constitute a new important screening for the aged population.

Keywords: aging, melatonin, pineal gland, diseases, healthy, treatment, melatonin

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Introduction

According to the recent advances in the psychoneuroendocrinoimmune (PNEI) regulation of the human biology,[1] the old age has appeared to be a reversible phenomenon by acting on the same mechanisms responsible for age-related progressive decline in the biological functions.[2] At present, it is known that the old age is mainly characterized by a progressive decline in the regulation of the biological rhythms, an enhanced free-radical production and a progressive increase in fibrosis processes involving the different organs of the human body, mainly the vascular system.[3] Several hypotheses have been proposed to explain age-related processes, including a reduced telomere length, and free radical-induced DNA damage. Moreover, it has to be remarked that one of the most important regulator of the biological life is represented by the immune system, since it has been demonstrated that it is involved not only in host defences, but also in the control of several biological functions, including the endocrine secretions and the cardiovascular function.[4] Therefore, the progressive decline in the immune functionless, mainly in its capacity of balance between stimulatory and immunosuppressive events, could play an essential role in aging processes.[5] In addition, since the pineal gland plays an essential role in the regulation of the biological rhythms and free-radical production,[6] age-related processes would mainly depend on the functionless of the pineal gland, whose most investigated hormone is the in dole hormone melatonin (MLT).[7] MLT secretion has been proven to be characterized by a well defined light/dark circadian rhythm, with low levels during the light phase of the day and highest concentrations during the night period of the day.[8]

Moreover, the pineal endocrine function has appeared to progressively decline with age, with a following disappearance of the light/dark rhythm in MLT daily secretion.[9] In animals, the progressive decline in the nocturnal production o MLT has been proven to be associated with an enhanced frequency of both tumors and cardiovascular diseases.[10] However, despite the well documented role of pineal MLT production in influencing the status of health of the human body, no study has been carried out to investigate the influence of age-related decline in MLT secretion on the incidence of the human diseases, which is justified by the fact that preliminary results have suggested a different individual behaviour in age-related pineal deficiency.[11] The present study was carried out to investigate MLT light/dark circadian rhythm in a group of young and aged healthy volunteers.

Materials and methods

The study included 50 healthy subjects, who were investigated during the same period of the year and were subdivided into two different groups, consisting of 25 subjects for group with 65-year younger or older people (median age 39 years, range 26-58, and 73 years, range 68-85). The criteria of exclusion were, as follows: no

cardiovascular, renal, hepatic and neuropsychiatric disturbance and no treatment with psychoactive drugs, beta-blockers and alpha-2 agonists for at least 1 week prior to study, because of their potential influence on melatonin secretion. The experimental protocol was explained to the subjects, and their consent was spontaneously obtained. To evaluate MLT light/dark rhythm, venous blood samples were collected at the four main phases of the photoperiod, corresponding to 8am, 12am, 6pm and 1am. The night sample was collected after at least 3 hours of exposure to a complete darkness. Serum levels of MLT were measured by the RIA method using commercially available kits. According to the data observed in our laboratory (95% confidence limits), MLT nocturnal concentrations were considered to be within the normal range when they were at least three times greater than those found during the phase of the maximum light, corresponding to 12am. Data were reported by mean+/-SE, and statistically evaluated by the chi-square test, the Student's t test and the analysis of variance, as appropriate. Healthy subjects were subdivided in two groups according to their age on the basis of age-related decline in the pineal function.

Results

Mean levels of MLT observed during the photoperiod in the two groups of healthy subjects are illustrated in Figure 1. In the young group, night mean values of MLT were significantly higher than those observed during the daily period of the day (P<0.001). MLT mean values were higher during the night than during the day also in the aged group, without, however, statistically significant differences. Moreover, night mean MLT levels observed in the young group were significantly higher than those found in the aged group (P<0.001). A normal increase in the nocturnal production of MLT was seen in the overall subjects of the young group. On the contrary, a normal nocturnal increase in MLT levels, with values at least three times greater than those found during the light period, occurred in only 16/25 (64%) subjects of the aged group. The difference was statistically significant (P<0.01). The different behaviour in the subjects of the aged group is also illustrated in Figure 1. Subjects with normal nocturnal increase in MLT levels showed statistically significantly higher night mean levels of MLT than those with no nocturnal MLT rise (P<0.05), whereas no significant differences were found during the light phase of the day.

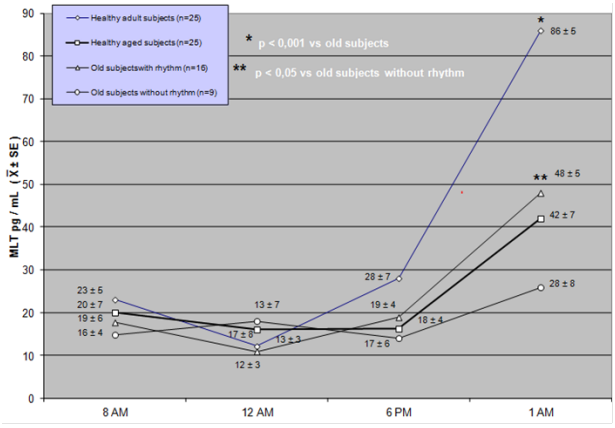

Figure 1 MLT light/dark rhythm in healthy adult and old subjects.

Discussion

This preliminary study, carried out in an acceptable number of healthy subjects according to the common routinely laboratory analyses, would seem to suggest the existence of a different individual behaviour in age-related decline in the pineal nocturnal production of its main hormone, MLT, since aged subjects may be characterized by a normal or an absent circadian light/dark rhythm in MLT pineal secretion. Then, in contrast to the results previously reported by other authors,[9] this study would show that the progressive disappearance of MLT light/dark rhythm is not an absolute and constant condition of the old healthy subjects. In addition, because of the pineal importance and involvement in age-related processes and diseases, according to the experimental results observed in animals, subjects characterized by a progressive disappearance of the pineal circadian rhythm would be exposed to a higher risk of age-related pathologies, including cardiovascular disorders and neoplasms.[10] Therefore, a mass screening carried out to measure MLT production in 65-year older subjects could allow to identify people with an early age-related decline in the pineal function, who could be at higher risk of undergoing age-related diseases. Unfortunately, the evaluation of the pineal function by collecting blood samples during the main phases of the light/dark circadian rhythm cannot be clinically proposed as a routinely investigation. However, the endocrine pineal function may be also investigated by measuring the daily urinary production of the main metabolite of MLT, the sulphatoxy-melatonin (6-MTS).[12] Therefore, the measurement of 6-MTS urinary production during the day would constitute in a future a new simple inexpensive screening test to identify people at higher risk of age-related human pathologies. However, further longitudinal studies will be required to establish which relation may exist in healthy subjects between age-related decline in the pineal function and frequency of age-related human diseases in the healthy population. A greater number of aged subjects will be required to establish which may be the pineal function in the elderly population, as well to identity the period during which the pineal function starts to decline in the healthy population in relation to the life style.

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None.

Conflict of interest

Author declares there is no conflict of interest.

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