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Research Report

Serum melatonin is an alternative index of Parkinson's disease severity

Ling Lin[a,b,1], Yuequn Du[b,1], Sutao Yuan[c], Jie Shen[d], Xiang Lin[e], Zhihong Zheng[a,b,*]

[a]Key Laboratory of Brain Aging and Neurodegenerative Diseases, Fujian Medical University, Fuzhou 350108, China
[b]Department of Biochemistry and Molecular Biology, Fujian Medical University, Fuzhou 350108, China
[c]Department of Neurosurgery, Fujian Provincial Hospital, #134 East Street, Fuzhou 350001, China
[d]Department of Geriatrics, Union Hospital of Fujian Medical University, #29 Xinquan Road, Fuzhou 350001, China
[e]Department of Neurology, Fujian Provincial Geriatrics Hospital, #147 Beihuan Road, Fuzhou 350003, China

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ABSTRACT

The protective potential of melatonin (MLT) in Parkinson's disease (PD) is the subject of considerable controversy. The purpose of the present study was to investigate serum MLT levels in unilateral 6-hydroxydopamine (6-OHDA) lesion rats and patients with PD. Blood samples were collected from rats at 10:00 am and from patients with PD and healthy subjects between 8:00 and 10:00 am. Serum MLT levels were measured using the enzyme-linked immunosorbent assay. Our results revealed that the morning serum MLT levels either in 6-OHDA-induced hemi-parkinsonian rats or patients with PD were significantly higher than that of control group. Our results also demonstrate that serum MLT levels are correlated with severity of PD according to H & Y scale.

1. Introduction

Insomnia and excessive daytime sleepiness are common non-motor symptoms of Parkinson's disease (PD) that can negatively affect the quality of life (Comella, 2007; Medeiros et al., 2007). Melatonin (MLT), which is secreted mainly from the pineal gland during the dark phase of the light/dark cycle, has been revealed to improve sleep in several conditions (Medeiros et al., 2007). Some previous reports have suggested that MLT might have neuroprotective effects in the amelioration of symptomatic features of PD (Pandi-Perumal et al., 2013; Schernhammer et al., 2006). Conflicting reports have raised impaired motor function after administration of MLT in animal models with experimental PD (Tapias et al., 2010; Willis, 2008). In addition, MLT was reported to be therapeutically ineffective in rats and patients (Medeiros et al., 2007; Willis and Armstrong, 1999). Unilateral intracerebral injection of 6-hydroxydopamine (6-OHDA) causes increased MLT levels in the lesioned and unlesioned striata of hemi-parkinsonian rats, particularly during the day in our previous and others'

Abbreviations: 6-OHDA, 6-hydroxydopamine; APO, apomorphine; H & Y, Hoehn and Yahr; MLT, melatonin; PD, Parkinson's disease; SEM, standard error of mean.

*Corresponding author at: Department of Biochemistry and Molecular Biology, No. 1, Xue Yuan Road, University Town, Fuzhou, Fujian Province 350108, China. Fax: +86 591 22862045.
E-mail address: zhzheng@mail.fjmu.edu.cn (Z. Zheng).
[1]These authors contributed equally to this work.

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study (Lin et al., 2013; Willis, 2008). Furthermore, higher levels of MLT were observed in patients with PD than in healthy controls (Catalá et al., 1997).

In light of the conflicting results and because the exact role of MLT in PD progression remains unclear, the first aim of this study was to measure serum MLT levels in 6-OHDA-induced hemi-parkinsonian rats, patients with PD and healthy subjects. The second aim was to analyse whether serum MLT levels were correlated with PD severity.

2. Results

2.1. Apomorphine (APO)-induced rotation in rats

The severity of dopamine depletion was evaluated by assessment of APO-induced rotational behaviour. An increase in rotational behaviour was observed at 2, 4, 6 and 9 weeks after 6-OHDA infusion compared with control and vehicle-treated rats, and there was a tendency for progressive increase in rotational frequency. As presented in Fig. 1, neither control nor vehicle-treated rats exhibited marked rotational response to APO, while 6-OHDA-lesioned rats responded with a significantly increased number of rotations towards the contralateral side ($p<0.001$). The rotations (in turns/20 min, $n=5$) were 191.4±12.98, 271.6±26.5, 306.4±38.96 and 336.6±16.04 at 2, 4, 6 and 9 weeks after 6-OHDA infusion, respectively.

2.2. Serum MLT concentrations in rats and correlation with APO-induced turning behaviour

Serum MLT levels in control and vehicle rats at 2, 4, 6 and 9 weeks post lesion exhibited no significant differences. As presented in Fig. 2, the mean concentrations of serum MLT at 2, 4, 6 and 9 weeks post lesion in blood samples collected from the tail vein at 10:00 am were 50.4±0.66, 51.2±0.91, 50.08±0.22 and 51.2±1.11 pg/ml in vehicle; 49.79±0.83, 50.45±0.23, 50.19±0.46 and 50.45±0.23 pg/ml in control and 51.28±0.46, 52.72±0.75, 53.76±0.96 and 61.52±1.02 pg/ml in PD rats, respectively. Serum MLT levels in PD rats were significantly increased compared with those in vehicles 2 weeks post lesion, which increased 1.75% at 2 weeks, 2.97% at 4 weeks, 7.35% at 3 weeks and 20.16% at 9 weeks post lesion.

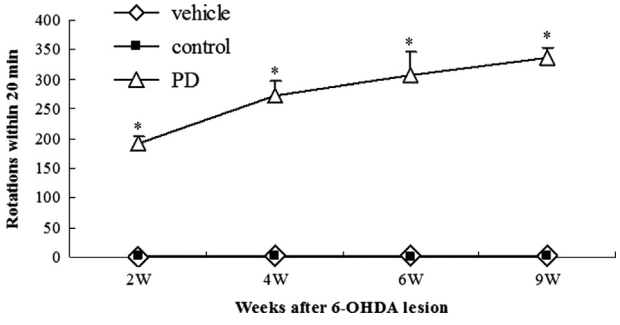

Fig. 1 – Apomorphine (APO)-induced rotational behaviour in rats. 6-OHDA infusion into the right medial forebrain bundle revealed rotation toward the contralateral side at 2, 4, 6 and 9 weeks post lesion. Values are presented as mean±SEM. *$p<0.001$ vs. the control and vehicle groups ($n=5$).

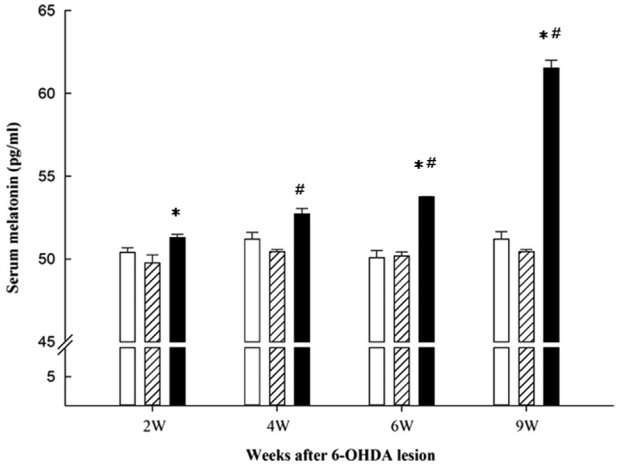

Fig. 2 – Changes in serum melatonin (MLT) in rats at 2, 4, 6 and 9 weeks post 6-OHDA lesion. Serum MLT concentrations were measured by ELISA using blood samples collected from the tail vein at 10:00 am. Values are presented as mean±SEM. *$p<0.05$, #$p<0.01$, *#$p<0.001$ vs. the vehicle and the control groups ($n=5$).

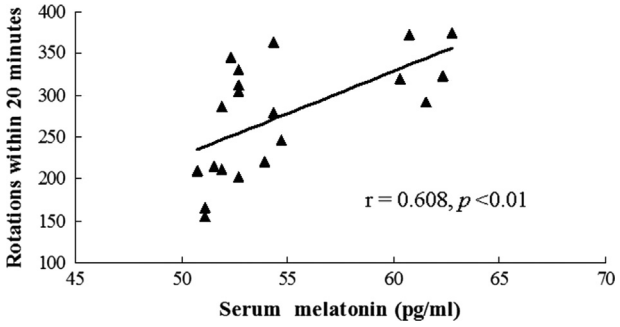

Fig. 3 – Correlation between apomorphine (APO)-induced turning behaviour and serum melatonin (MLT). Positive correlation between APO-induced turning behaviour and serum MLT concentration in PD rats at 10:00 am. Pearson's correlation coefficient is indicated ($n=20$).

There was a significant positive correlation between morning serum MLT levels and APO-induced turning behaviour (Fig. 3). Pearson's correlation coefficient for rotational frequency and MLT levels was 0.608 at the 0.01 level (two-tailed).

2.3. Serum MLT concentrations in patients with PD and control subjects

The PD patient group comprised 44 males and 12 females, and the healthy subject group comprised 13 males and 9 females.

There were no significant differences on the basis of gender and age in serum MLT levels in patients with PD ($p>0.05$) (Fig. 4). Both male (87.31±5.59 pg/ml, $n=44$) and female (103.07±18.52 pg/ml, $n=12$) patients with PD exhibited significantly higher levels of morning serum MLT compared with healthy subjects (52.63±3.27 pg/ml for males and 46.22±1.72 pg/ml for females) ($p<0.05$). No significant gender difference was observed in control subjects.