Autonomic Dysfunction in PD During Sleep

A recent work by Sauvageot et al. on heart rate variability (HRV) in idiopathic PD during nocturnal sleep showed no difference between patients and healthy controls with regard to sleep-stage characteristics. However, the ratio of low frequency and high frequency (LF/HF) of HRV was significantly smaller in PD patients during rapid eye movement (REM) and nonrapid eye movement (NREM) sleep. We did a similar study on patients with full-blown PD, under levodopa medication and high frequency (HF) of HRV was significantly related to sleep-stage characteristics. However, the ratio of low frequency (LF) and HF ratio should be considered equivalent carriers of information regarding sympathovagal balance.

1-dopa-treated PD patients (N = 8; 6 males, 2 females; age, 60.1 ± 8.9 SD; PD duration, 1–5 years; UPDRS total score, 34.4 ± 15.8 SD; HYR stage, 2.1 ± 0.7 SD) and healthy controls (N = 11; 9 males, 2 females; age, 60 ± 8.8 SD) were taken from a pool of subjects participating in the SIESTA project. An electrocardiogram was registered during the course of nighttime polysomnography. Sleep-stage scoring was done according to Rechtschaffen and Kales. For the detection of QRS events, subsequent calculation of LF/HF ratio, as well as analysis of the sleep hypnogram, we used the BioSig-toolbox software.

Patients with PD did not show a significant time course of their LF/HF ratio during progression of polysomnography registration (Friedman’s analysis of variance [ANOVA], χ² = 3.057, df = 5, P = 0.731). In contrast, controls varied significantly, with high values of LF/HF ratio during wake and REM and a relatively steady decline from stage 1 to stage 4 (Friedman-ANOVA, χ² = 17.063, df = 5, P = 0.002). Controls surpassed PD patients throughout the experiment. During wake, sleep stage 2, and REM, the difference was significant (Mann-Whitney U tests) (Table 1). These results hint at a significant impairment of autonomic regulation during sleep in PD patients. Our patients presented very little variation during sleep. Their LF/HF ratio did not show any signs of increasing sympathetic activity during REM. In addition, the ratio was significantly lower during wake, when compared to controls, and even showed a slight increase to stage 1 and 2 of NREM sleep.

The possibility exists that 1-dopa may have affected HRV. However, a clear effect has not been shown yet.1 Thus, autonomous dysfunctions may rather result from the disease itself than from treatment. The impaired sympathetic activity we have found may have been caused by loss of action in orexinergic neurons. These neurons play a regulatory role in the physiological sleep cycle and can alter autonomic activity as well. In PD, they are not spared from degeneration,4 which may explain the lack of increase of LF/HF ratio during REM. Finally, patients with PD can show decreased cardiac iodine-123 metaiodobenzylguanidine uptake,5 a diagnostic marker for myocardial sympathetic neuron activity, which could have also contributed to the sympathovagal dysbalance we had observed during sleep.

In our study, PD affected sympathovagal balance both in nREM and REM sleep. This may indicate the impairment of one or both branches of the autonomous nervous system. Further investigations are needed to clearly isolate all different contributors, which would enable a much wider view on the pathophysiological processes behind this disease.

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References

Table 1. Comparison of Mean LF/HF Ratio Between PD Patients and Healthy Controls During Sleep

<table>
<thead>
<tr>
<th></th>
<th>PD Patients (N = 8)</th>
<th>Healthy Controls (N = 11)</th>
<th>P Value</th>
<th>Mann-Whitney U Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>W</td>
<td>0.983 ± 0.177</td>
<td>3.017 ± 0.546</td>
<td>0.001</td>
<td>7</td>
</tr>
<tr>
<td>Stage 1</td>
<td>1.318 ± 0.535</td>
<td>2.685 ± 0.633</td>
<td>0.105</td>
<td>24</td>
</tr>
<tr>
<td>Stage 2</td>
<td>1.320 ± 0.483</td>
<td>2.327 ± 0.329</td>
<td>0.043</td>
<td>19</td>
</tr>
<tr>
<td>Stage 3</td>
<td>1.058 ± 0.304</td>
<td>1.289 ± 0.273</td>
<td>0.105</td>
<td>24</td>
</tr>
<tr>
<td>Stage 4</td>
<td>0.921 ± 0.204</td>
<td>1.509 ± 0.323</td>
<td>0.006</td>
<td>12</td>
</tr>
<tr>
<td>REM</td>
<td>1.087 ± 0.228</td>
<td>3.556 ± 0.766</td>
<td>0.002</td>
<td>8</td>
</tr>
</tbody>
</table>

Mann-Whitney-U tests. Means ± standard error of the mean are given. Significant differences: P values in bold.

Abbreviations: W, wake.