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Rest-Activity Rhythm Disruption in Progressive Supranuclear Palsy

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Abstract

Objective/Background—The brainstem is among the first regions affected in Progressive Supranuclear Palsy (PSP) and is part of the sleep/circadian regulation network. In two small studies, blood pressure and core body temperature circadian patterns were disrupted in PSP, however it is unclear if circadian activity rhythms are also affected. Our objective was to perform circadian analyses of the rest-activity rhythms in PSP and determine the association with increasing disease severity.

Patients/Methods—Individuals with a clinical PSP diagnosis (n=17; 9 men) and healthy older adults (n=17; 9 men) were recruited for this study. Participants wore actigraphy wristbands and completed sleep diaries for up to 14 consecutive days. Data were analyzed to assess circadian activity strength (amplitude, mesor, f-ratio), phase (acrophase), and circadian stability (intradaily variability, interdaily stability, relative amplitude). Analyses controlled for sleep fragmentation, cognition and self-reported depression. The association between disease severity using the PSP rating scale and circadian activity rhythm disruption was assessed.

Results—Individuals with PSP had significantly smaller circadian activity mesor ($p \leq 0.001$), amplitude ($p \leq 0.001$), robustness (f-ratio, $p < 0.01$), relative amplitude ($p \leq 0.001$) and interdaily stability ($p \leq 0.01$), with increased intradaily variability ($p < 0.05$). CAR remained weaker in PSP after controlling for sleep fragmentation, and again when also controlling for cognitive impairment and depression. Weaker circadian activity (mesor, amplitude, f-ratio, and relative amplitude) was associated with increased disease severity.

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Conclusions—Circadian activity rhythms are disrupted in individuals with PSP as compared to controls, and worsen with disease severity. This is the first study to describe circadian activity rhythms in PSP.

Keywords

Progressive Supranuclear Palsy; actigraphy; sleep; circadian rhythms

1. Introduction

Progressive Supranuclear Palsy (PSP) is a neurodegenerative disease associated with progressive motor dysfunction, neuropsychiatric disturbance [1], and cognitive impairment. To date there have been a few quantitative sleep studies indicating sleep disruption on the night of testing. Specifically, using overnight polysomnography (PSG), individuals with PSP were found to take longer to fall asleep [2], spent less time asleep [3-5], and more time awake after initial sleep onset [5]. Summary measures found increased sleep fragmentation [5] and decreased sleep efficiency [3, 4]. Though these studies reported only a single night of recording, the type of sleep disruption reported, if chronically present, would likely disrupt circadian activity rhythms.

Both blood pressure and heart rate have cyclical circadian patterns with periodic drops in blood pressure during the night. In a study of blood pressure regulation and heart rate, 40% of individuals tested with PSP did not have the expected nocturnal drop in blood pressure, suggesting that the intrinsic circadian blood pressure patterns are disrupted in PSP [6]. In another study, core body temperature circadian rhythms were disrupted, with overall smaller circadian amplitude in PSP and a smaller drop in nocturnal temperatures [7]. Together, these two studies indicate circadian disruption in PSP.

To date, no studies have been done to measure circadian activity rhythms (CAR) in PSP or to test if disrupted rhythms were associated with disease severity. Based on 1) the type of sleep disruption measured using one to two nights of PSG, and 2) the circadian disruption in temperature and blood pressure, we predicted that CAR would be disrupted. The goal of this study was to perform circadian analyses of rest-activity rhythms using an at-home wrist actigraph to measure movement patterns across multiple days and nights; and to determine if disrupted circadian rest-activity rhythms are associated with PSP disease severity.

2. Methods

2.1. Sample

Participants were recruited through the University of California, San Francisco (UCSF) Memory and Aging Center's (MAC) longitudinal studies. As part of these longitudinal observation studies, all participants had undergone comprehensive evaluations including a neurological exam, neuropsychological assessment and an informant interview. Consensus diagnoses were made by a team of neurologists, nurses, neuropsychologists, and trained support staff at the MAC. Individuals who were enrolled in the Frontotemporal Dementia: Genes, Imaging and Emotions or 4 Repeat Tauopathy Neuroimaging Initiative studies with a

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diagnosis of possible or probable PSP diagnosis based on the Litvan criteria [8] were approached for this study. Based on previous research, though the initial report for the accuracy of these diagnostic criteria indicated a sensitivity of 83% and specificity of 100% [9], it has since been found that approximately 76% of those with a clinical diagnosis of PSP have PSP upon pathological examination [10]. Recruitment for this study was from July 2013 until January 2016. Twenty-one participants took part in the study, however only 17 individuals (9 men, 8 women; mean age: 71.5 ± 6.9 years) with a diagnosis of possible or probable PSP had data that passed the inclusion criteria (see actigraphy measures for details).

Healthy older adults were recruited from the UCSF Healthy Aging Cohort. Healthy older adult participants had no evidence of neurodegenerative disease, epilepsy, active neoplastic disease, or substance abuse. Further, they had a clinical dementia rating score (CDR) of 0, with no significant history of cognitive complaints and had normal cognitive testing. All healthy older adults had participated in the healthy aging study and were selected for this study based on gender and proximity in age to individuals within this study's PSP cohort. The demographics for the final healthy older adult control cohort for this study were: 9 males and 8 females, with a mean age of 72.9 ± 4.5 years. This study was approved by the UCSF Institutional Review Board (IRB). All participants gave informed consent prior to starting the study.

Among the measures assessed, participants were asked to wear an actigraph (see below for details) and complete a sleep journal for 10 days. Throughout the assessment period, participants were asked to maintain their usual medication use. Seven of the 17 PSP participants used dopaminergic medications and/or a monoamine oxidase inhibitor. Participants also used antidepressants, anxiolytics and sleep medications (Table 1).

2.2. Demographics: CDR, self-reported disease duration and PSP rating scale

Through the on-going co-enrolled studies and current study, measures of age, global cognition (Mini Mental State Exam, MMSE [11]), self-reported depression (30-item Geriatric Depression Scale, GDS [12]), and the clinical dementia rating scale (CDR [13]) were gathered. In individuals with PSP, both a subjective report of disease duration and the PSP rating scale (PSPRS [14]), a measure of disease severity were acquired. Scores for the PSPRS were available for 16 participants. The scale is 0-100, where the higher the PSPRS score, the more severe the disease symptoms. This measure was used to determine if there was an association between disease severity and worse (weaker or more disrupted) CAR.

2.3. Actigraphy measures

Participants were asked to wear a Micro SleepWatch (Ambulatory Monitoring Inc, Ardsley NY) actigraph wristband on their non-dominant arm (as long as there was no pronounced movement deficit greater than the dominant arm) for up to fourteen 24-hr periods. If a participant removed the watch for 4 hrs or more in any 24-hr period, that 24-hr period was removed from the analyses. A participant needed a minimum of 3 days/nights of high quality data after cleaning to be included. Data were cleaned in the Zero Crossing Mode (ZCM) using Action-W (version 2.7.3045, Ambulatory Monitoring Inc., Ardsley NY)

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software. The event markers and life detection markers were used to identify times when the watch was removed. Along with reported down times on the sleep journal, event markers were used as a guide to determine when the participant started trying to fall asleep, and when they got up in the morning. The down period was marked as the drop in activity measured closest to the event marker. In the absence of event markers, the drop in activity measured closest to the time indicated on the sleep journal as the time sleep was attempted was marked as the down period. A non-blinded rater scored the files utilizing the sleep journals. When it was unclear where to place a down period, a second rater was consulted. All files were checked twice to maintain scoring consistency across participants. Comparative control measures of interest were number of days analyzed and average amount of unscored (unusable) data declared within the 24 hr period.

Sleep measures were calculated using ZCM and processed using the Cole-Kripke with rescoring rules algorithm in Action-W. Latency to persistent sleep criterion was set at <1 min of wake in a 20-minute period. The descriptive and sleep actigraphy measures of interest were duration of the down period, duration of the up period, the amount of time spent asleep as a percent of the down period, the amount of time spent asleep as a percent of the up period, total time spent asleep across the entire 24 hr period and sleep fragmentation during the down period (a measure of how disrupted the sleep period was, measured using actigraphy). When calculating these measures, to not affect the overall reporting of the data, in addition to the removal of a 24hr period if 4 hrs of data were missing, an up period was not included if it deviated more than 200 mins from the remaining days. Further, during an up or down period, if the period contained more than 10% bad/unusable data, the period was not included.

Circadian measures were calculated in Action4 (version 1.16, Ambulatory Monitoring Inc, Ardsley NY) using the Proportional Integration Mode (PIM) and processed with the cosinor waveform and averaged waveform method. To verify that CAR measures centered around 24 hrs were appropriate to use, the time of the maximum peak was calculated using the Maximum Entropy Spectral Analysis (MESA). An MESA value of 24 indicates an average 24 hr rhythm. Variables of interest were CAR amplitude (counts/min; peak to nadir difference), mesor (counts/min; mean activity), f-ratio (rhythm robustness; *f*), acrophase (time of peak activity), relative amplitude (ratio of average activity for the most active 10 hr period (M10) and least active 5 hr period (L5); (M10-L5)/(M10+L5)), intradaily variability (%) and interdaily stability (%). CAR amplitude, mesor, and f-ratio are measures of CAR strength. CAR intradaily variability (IV) and interdaily stability (IS) are measures to determine the CAR consistency. CAR relative amplitude provides an index of how different the active versus inactive periods are, with greater differences being closer to 1. CAR acrophase is a measure of the timing of phase changes, e.g. an overall delay or advancement of CAR.

2.4. Sleep journal

During each day of actigraphy recording, participants, with the help of caregivers as necessary, completed the standardized AASM sleep journal, recording time in bed, waking time and estimates of sleep onset latency.

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2.5. Statistics

No individual was an outlier (> 3 SD) across more than 1 key measure of interest, therefore all participants were included in the analyses.

Independent t-tests or non-parametric t-tests were done on demographic data, measures of disease severity, cognition, depression and sleep to determine if there were basic group differences. Measures which were not normally distributed were normalized to z scores. Independent t-tests were used when appropriate to determine if there were group differences on the key measures of interest.

To determine if medication use affected measures of CAR in PSP, non-parametric assessments were done dividing by medication use for each CAR measure of interest. Medication usage assessed was i) antidepressants, ii) cholinergics, iii) dopaminergics and iv) sleep aids. To reduce the chance of Type 1 error, a composite score for medication use was done by summing the medication sub-types.

To understand the relationship between age and sleep disruption with the CAR measures, we performed Pearson correlations. To separate the contribution of sleep disruption from CAR, ANCOVAs were used controlling for actigraphy-measured sleep fragmentation to assess CAR group differences. Intradaily variability was significantly correlated with age, therefore both age and sleep fragmentation were included in the ANCOVA. In a second model, to separate the contribution of cognition (MMSE) and self-reported depression (GDS), they were added as covariates in addition to sleep fragmentation (and age for intradaily variability). To evaluate if there was a relationship between PSP disease severity and measures of CAR, Pearson correlations were used.

3. Results

3.1. Demographics

As expected based on the selection of healthy older adult participants to best match the PSP participants for gender and age, there were no group differences in age (See Table 2). To ensure that there was no general bias in quantity or quality of data analyzed, we tested for group differences in the average number of unusable epochs within the 24 hr period and the final number of 24 hr periods included within the analyses. In both cases, there were no group differences. Therefore potential differences in CAR were not a result of fewer usable data points in either group.

To verify that both groups had similar mean periods of wrist activity, the MESA was assessed. Both groups had a maximum peak centered around 24 hrs. To understand sleep/wake patterns in the two groups, we measured the amount of sleep/rest calculated across the 24 hr period, in addition to the up and down periods. Though there was increased daytime sleep ($t=3.250$, $p\leq 0.1$) and decreased nighttime sleep ($t=2.995$, $p\leq 0.1$) in PSP, there were no differences in the amount of total sleep across the 24 hrs between the two groups ($t=1.309$, $p= 0.2$). As an overall measure of sleep disruption, we analyzed sleep fragmentation during the night. As expected, sleep was more fragmented in PSP than in controls ($t=3.358$, $p=0.001$).

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3.2. CAR measures

Overall we found CAR to be highly disrupted in PSP as compared to controls (Figure 1). Namely, CAR mesor (t=5.780, p≤ 0.001), amplitude (t=5.601, p≤ 0.001) and f-ratio (t=3.413, p≤ 0.01) were significantly smaller in PSP (Figure 2). Intradaily variability (t=2.824, p≤ 0.01) was increased and both relative amplitude (t=5.615, p≤ 0.001) and interdaily stability were decreased (t=2.250, p≤ 0.05) in PSP. There was no group difference in the phase of peak activity (t=0.041; 14:13:42 ±15 mins (Control), 14:14:38 ± 16 mins (PSP)).

To determine if medication use had an effect on CAR actigraphy measures, PSP participants were divided by medication usage. Overall, there were no differences in CAR measures based on medication use within the PSP cohort.

To determine factors that could be associated with disrupted CAR we assessed the association between i) age and ii) sleep fragmentation with individual CAR variables of interest across the 32 participants. Age was positively correlated with increased intradaily variability (r= 0.510, p<0.01). Increased sleep fragmentation was significantly correlated with smaller amplitude (r=-0.392, p<0.05), smaller relative amplitude (r= -0.737, p<0.001), worse interdaily stability (r= -0.377, p<0.05) and a trend for smaller f-ratio (r= -0.306, p<0.1). To determine the contribution of sleep fragmentation to the group differences observed in CAR, we performed ANCOVA controlling for sleep fragmentation. Overall we found that sleep fragmentation did not contribute to the differences in CAR. Specifically, PSP remained significantly worse on measures of CAR mesor ($F(1,31)=29.99$, p<0.001), amplitude ($F(1,31)=21.14$, p<0.001), f-ratio ($F(1,31)=7.46$, p<0.01), relative amplitude ($F(1,31)=14.71$, p=0.001) and intradaily variability ($F(1,31)=5.482$, p<0.05). Further, when accounting for age and sleep fragmentation, PSP was significantly associated with increased intradaily variability ($F(1,30)=12.797$, p=0.001).

To assess the contribution of global cognition (MMSE) and depression (GDS) to the group differences observed in CAR, we added both MMSE and GDS as covariates to our ANCOVA model. Measures of CAR strength, specifically mesor ($F(1,29)=5.256$, p<0.05), amplitude ($F(1,29)=5.173$, p<0.05) and f-ratio ($F(1,29)=4.471$, p<0.05) remained significantly different between the two groups. This indicated that CAR strength was reduced in PSP beyond that accounted by nighttime sleep fragmentation, cognitive impairment and depression.

To determine if there was an association between disease severity and CAR, we performed Pearson correlations between the PSPRS and CAR measures. PSPRS data were available for 15 of the 16 individuals with PSP. We found that increased disease severity (higher PSPRS) was associated with weaker CAR mesor (r= -0.661, p<0.01), amplitude (r= -0.720, p<0.01; see Figure 3), f-ratio (r= -0.50, p<0.05), and relative amplitude (r= -0.528, p<0.05). There was no significant association between disease severity and either interdaily stability (r= -0.365), intradaily variability (r= 0.276) or acrophase (r= 0.187).

A summary of our findings is shown Figure 4.

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4. Discussion

Overall we found that: i) CAR were weaker and more variable in PSP than healthy controls, ii) CAR phase is not altered in PSP as compared to healthy controls, and iii) weaker CAR were associated with increasing disease severity. Though our results were similar to prior circadian studies of core body temperature [7] and blood pressure [6], our findings were not limited to one measure, but were detectable on a number of rest-activity circadian-type measures. This is the first study in PSP to report on circadian analyses of rest-activity measures and extends our understanding of disrupted circadian rhythms in PSP beyond the expected decrease in circadian amplitude seen in other studies.

Our findings of abnormal CAR align with prior findings of disrupted sleep patterns on PSG [3-5]. Namely, the increased sleep fragmentation found in this study and described using PSG [3-5], suggests increased nighttime disturbance, thereby diminishing day-tonight differences in activity patterns. The relative amplitude was higher in controls than PSP, indicating that the difference between the 10 hours of maximum activity and 5 hours of least activity were more similar in PSP than controls, thus there is a flattening of the overall CAR waveform in PSP.

Using actigraphy, we found that the CAR disruption in PSP occurs beyond the contribution of sleep fragmentation, cognitive impairment or self-reported depression. The actigraph wristband measures movement activity. As PSP is a neurodegenerative disease that results in the progressive loss of movement, it is possible that the disrupted CAR observed is a result of decreased overall movement. This is particularly true for the CAR strength measures of mesor and amplitude. However, we also found a group difference with increased CAR intradaily variability and interdaily stability in PSP, indicating that the overall circadian activity pattern appears to be disrupted beyond movement-related impairments. Interestingly, the increased intradaily variability was not associated with disease severity, again indicating that increasingly limited movement due to the disease did not drive the disruption in circadian patterns. It is currently unclear what may be the underlying mechanism of these differences in circadian activity rhythms. Based on the limited studies assessing circadian rhythms in PSP [6, 7], there appears to be changes in autonomic rhythms, which are regulated by the hypothalamus. The central clock for circadian rhythms is also within the hypothalamus, so it is possible that the suprachiasmatic nucleus function is altered in PSP. Orexin, a hypothalamic neuropeptide that regulates sleep/wake regulation and thus impacts circadian rhythms, is decreased in PSP, with smaller levels occurring with disease progression [15]. Though the level of CSF orexin in PSP described in that study is not as severe as in narcolepsy where sleep regulation is profoundly affected, it is possible that the marginally depleted levels of orexin in PSP may offset the homeostatic balance of the sleep-wake balance to such an extent that CAR is somewhat disrupted. However, further research comparing CSF orexin and circadian measures in PSP is required to assess this and to identify the underlying mechanism of the altered CAR.

Typically in healthy aging, circadian patterns become weaker, with smaller amplitude, in addition to an advancing phase [16-19]. In general, with mild cognitive impairment, circadian patterns are weaker, with smaller CAR mesor and amplitudes, and a delay in

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activity phase [20-22]. There appear to be some subtle differences between neurodegenerative diseases. Specifically, in a study of Parkinson's disease compared to controls, CAR amplitude was decreased and continued to decline with increasing disease severity [23], while no other measures of CAR were noted to be affected. In a comparison of Alzheimer's disease (AD) and frontotemporal dementia (FTD) with controls [24], interdaily stability was lower in FTD and AD, intradaily variability and mesor were more affected in FTD than AD, while overall there were no differences between the three groups on amplitude. Another differentiating characteristic in the Harper et al study [24] was a difference in phase of peak activity, where AD was phase delayed, and FTD was phase advanced. The phase change that was observed in FTD, however was not seen in a more recent study [25]. Overall, in a comparison across study findings, there are differentiable features of CAR. In particular PSP and FTD appear to have the greatest disruption in CAR, though on different measures. Mechanistically, the sleep and arousal networks are likely affected through the brainstem's early involvement in PSP [26, 27].

Assessing CAR is a low burden measure for participants. Given that the clinical diagnostic accuracy has room for improvement, tools such as CAR assessment, may provide additional information, which in the future could provide useful insight to disease patterns and progression. Therefore, an important next step is to have a more extensive comparison between CAR in neurodegenerative diseases with a longitudinal component. Understanding how CAR is associated with individual diseases will enable its use as a specific marker of disease or inform underlying anatomical features.

The limitations in this study include a relatively small cohort size. Additional research is necessary to repeat this study in a larger sample. As this was an exploratory study, corrections for multiple comparisons were not applied. The measures reported here are analyzing correlates of sleep and wake in the form of rest and activity. To truly assess circadian activity rhythms, participants would need to be in a controlled environment to regulate exposure to external stimuli, which could affect the circadian clock. Further research is required to better understand our findings and the PSP-related physiological changes in circadian rhythms. It is possible that the nighttime periods were disrupted in the PSP cohort as a result of sleep disorders such as Periodic limb movements or REM sleep behavioral disorder (RBD), which the actigraph cannot discern from wake related movements. Only one study has described increased PLMs in PSP over the age of 70 [2]. Among the neurodegenerative disorders, RBD is typically associated with synucleinopathies and is less associated with PSP [28]. In previous research, REM sleep without atonia and RBD occurred in 5-40% of those with PSP [2, 4, 5]. Therefore, though the likelihood of sleep movement disorders are increased in PSP, it is unlikely that they are the sole reason for the disrupted CAR in this study. Among the participants included in this study, 8/17 had tremor observed during the neurological exam at the Memory and Aging Center, UCSF. The presence of postural or resting tremor could increase the reported activity in the PSP cohort. Also within the PSP cohort, CAR can be affected by the decreased daytime movement that occurs as a result of the movement disorder component of the disease. However, intradaily variability and interdaily stability would not be as susceptible to the effects of overall decreased movement as they are analyzing the stability of the patterns as opposed to the strength of the activity. Further, as disease severity progresses, movement disorder

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symptoms would also progress, which is not necessarily observed in some of our CAR measures. Thus, our findings suggest again that the observed CAR disruption in this study extends beyond the movement disorder component of PSP and reflects changes in rest-activity patterns. A more extensive study is required to better understand how CAR is affected across multiple neurodegenerative diseases.

5. Conclusion

In this current study, CAR are disrupted in PSP, and are associated with disease severity. Further, our findings using actigraphy replicate and extend previous reports on disrupted circadian rhythms with blood pressure and heart rate. However, acquiring data using actigraphy is less burdensome on a participant and therefore may be a useful tool to further understand circadian differences in PSP as compared to other cohorts.

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Highlights

- Rest activity rhythms are less stable in Progressive Supranuclear Palsy (PSP)
- The weaker rhythms in PSP are independent of cognitive impairment and depression
- Rest activity rhythms are weaker in PSP, and worsen with disease progression

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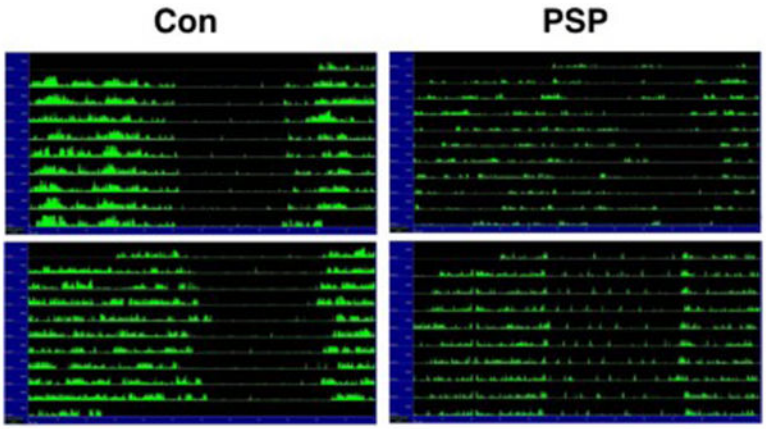

Figure 1.

Sample Actigraphy Plots.

Sample activity plots were made using Action4 software (Ambulatory Monitoring Inc.), with activity (green) plotted on a scale of 100,000 counts/minute (y-axis) for each line of 24hr recordings, centered at midnight for 2 healthy controls (left) and 2 PSP (right).

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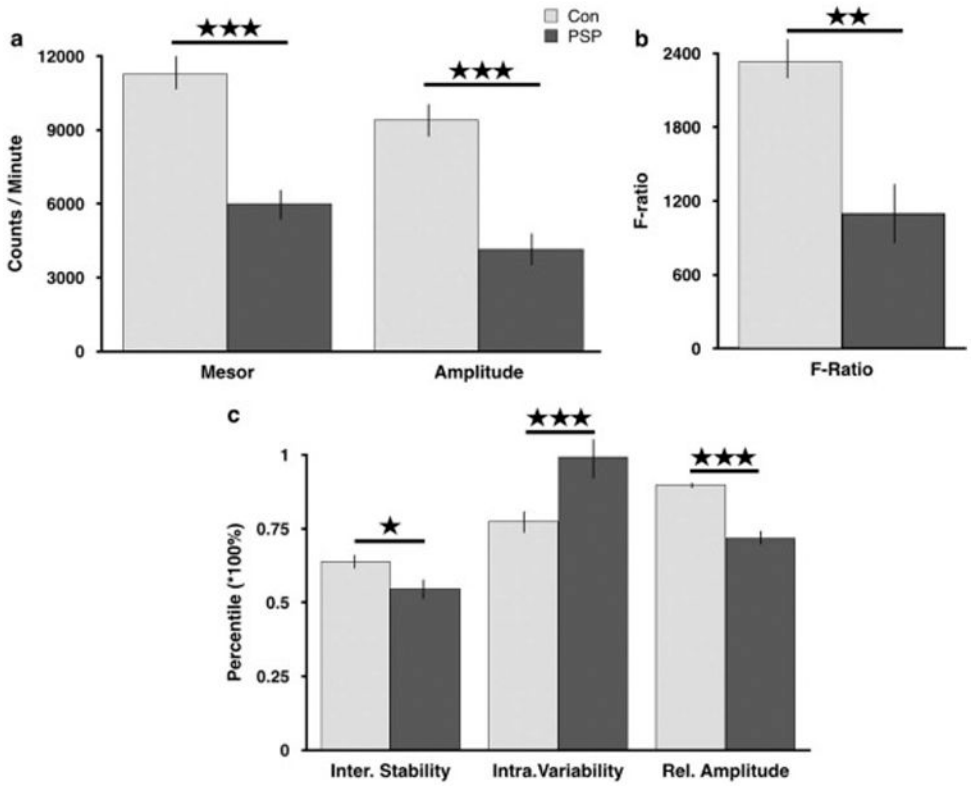

Figure 2.

Circadian activity rhythms in PSP as compared to controls.

As compared to controls (light grey), PSP (dark grey) had **a**) significantly smaller mesor and amplitude, **b**) smaller F-ratio and **c**) larger intradaily variability but no difference in interdaily stability. Data are shown as Mean ± SEM. *p<0.05

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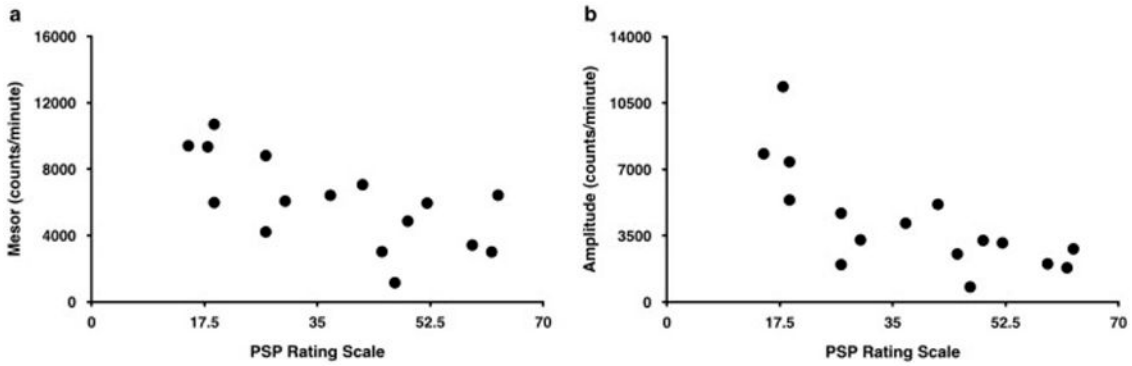

Figure 3.

The association between PSP disease severity and CAR measures of mesor and amplitude. Both CAR **a**) mesor (r= -0.661, p<0.01) and **b**) amplitude (r= -0.720, p<0.01) are negatively associated with the PSP rating scale, where the greater disease severity was associated with smaller mesor and amplitude.

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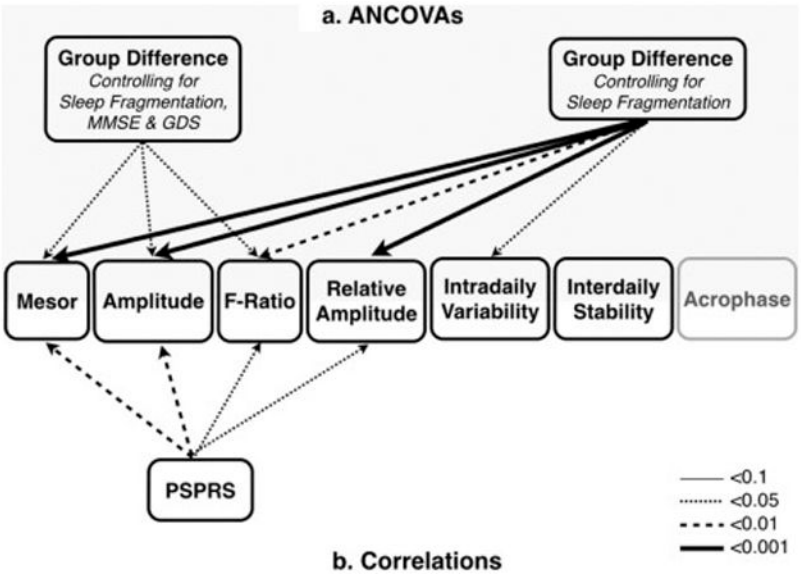

Figure 4.

Summary of the CAR in PSP results.

CAR measures are outlined in black (significant group difference on *t*-tests) or grey (no significance). A) The upper half of the figure represents ANCOVA analyses controlling for either sleep fragmentation, or for sleep fragmentation, global cognition (MMSE) and self-reported depression (GDS), while B) the lower half of the figure indicates correlational analyses with disease severity measured by the PSP rating scale (PSPRS). The weight and style of each line indicates the p-value of the association. When sleep fragmentation was controlled for, CAR remained significantly worse in PSP. Similarly, when global cognition, depression and sleep fragmentation were controlled for group differences persisted between CAR mesor, amplitude and f-ratio. CAR mesor, amplitude, f-ratio and relative amplitude were negatively associated with PSP disease severity.

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Table 1

Medication Use.

The name and dose of medications used under each medication sub-type listed is presented in the table. The number of individuals within each cohort to use the medications listed are shown. A dash indicates no one in the group used that medication at the time of the study.

	Dose	Control	PSP
Dopaminergic / Monoamine Oxidase Inhibitor			
Carbidopa/Levodopa	25-100mg	-	7
Carbidopa/Levodopa - CR	50-200mg	-	1
Amantadine	100mg	-	1
Rasagiline	1mg	-	1
Cholinesterase			
Rivastigmine	9.5mg	-	1
Donepezil	10mg	-	1
SSRI			
Escitalopram	10mg	1	-
Fluoxetine	40mg	-	1
Citalopram	20mg	-	2
Benzodiazepine			
Diazepam	5mg	-	1
Clonazepam	0.5mg	-	1
Other antidepressant			
Amitriptyline	25mg	1	-
Mirtazapine	30mg	-	2
Quetiapine	50mg	-	1
Hypnotic or Sleep Disorder Related			
Zolpidem	5mg	-	1
Melatonin		-	1
Trazadone	150mg	-	1
Gabapentin	300mg		

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Table 2

Days/Nights represents the number of days/nights that reached criteria and were included in the data analyses. Data are shown as Mean ± SEM. Self-reported disease duration is shown as the percent of those who report possible symptoms starting within the past 5 years. PSPRS is reported as the range of scores within the cohort.

	Con	PSP	t
Gender	9 male; 8 female	9 male; 8 female	NA
Age (years)	72.94 ± 1.1	71.53 ± 1.7	0.707
MMSE	29.18 ± 0.29	23.47 ± 1.0	4.521*
GDS	1.65 ± 0.4	12.41 ± 1.6	4.674*
CDR Sum of Boxes	0	3.74 ± 0.7	4.723*
Self-reported Disease Duration ≤ 5 years	NA	70.6%	
PSPRS	NA	38.19 ± 4.1	
Days/Nights (count)	8.45 ± 0.1	7.20 ± 0.4	1.688
Number of Unusable Epochs Per 24 hr Period	31.77 ± 6.2	44.57 ± 12.2	0.413
MESA Maximum Peak (hrs)	24.03 ± 0.1	24.21 ± 0.1	1.087
Up Period Duration (epochs)	962.03 ± 10.3	916.20 ± 21.6	1.671
Percent Sleep During Up Period	5.36 ± 0.9	16.85 ± 3.4	3.324*
Down Period Duration (epochs)	472.04 ± 9.6	535.8 ± 20.5	2.359*
Percent Sleep During Down Period	92.53 ± 1.0	77.37 ± 5.0	3.186*
Sleep Duration Across 24 hr Period	490.53 ± 12.3	559.21 ± 51.0	1.361
Down Period Sleep Fragmentation	1.66 ± 0.2	4.40 ± 0.8	3.358*

*$p<0.05$