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Altered brain perfusion patterns in wakefulness and slow-wave sleep in sleepwalkers

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Abstract

Study Objectives

The present study assessed brain perfusion patterns with single-photon emission computed tomography (SPECT) during sleepwalkers' post-sleep deprivation slow-wave sleep (SWS) and resting-state wakefulness.

Methods

Following a 24 hr period of sleep deprivation, 10 sleepwalkers and 10 sex- and age-matched controls were scanned with a high-resolution SPECT scanner. Participants were injected with ^{99m}Tc-ethylene cysteinate dimer after 2 min of stable SWS within their first sleep cycle as well as during resting-state wakefulness, both after a subsequent 24 hr period of sleep deprivation.

Results

When compared with controls' brain perfusion patterns during both SWS and resting-state wakefulness, sleepwalkers showed reduced regional cerebral perfusion in several bilateral frontal regions, including the superior frontal, middle frontal, and medial frontal gyri. Moreover, reduced regional cerebral perfusion was also found in sleepwalkers' left postcentral gyrus, insula, and superior temporal gyrus during SWS compared with controls. During resting-state wakefulness compared with controls, reduced cerebral perfusion was also found in parietal and temporal regions of sleepwalkers' left hemisphere, whereas the right parahippocampal gyrus showed increased regional cerebral perfusion.

Conclusions

Our results reveal patterns of reduced regional cerebral perfusion in sleepwalkers' frontal and parietal areas when compared with controls, regions previously associated with SWS generation and episode occurrence. Additionally, reduced perfusion in the dorsolateral prefrontal cortex and insula during recovery SWS is consistent with the clinical features of somnambulistic episodes, including impaired awareness and reduced pain perception. Altered regional cerebral perfusion patterns during sleepwalkers' resting-state wakefulness may be related to daytime functional anomalies in this population.

sleepwalking, somnambulism, parasomnias, slow-wave sleep, pathophysiology, single-photon emission computed tomography

Statement of Significance

Electroencephalographic-based studies have documented anomalies in the slow-wave sleep (SWS) of adult sleepwalkers, but systematic whole brain imaging had yet to be performed during patients' SWS. We used neuroimaging to investigate sleepwalkers' resting-state wakefulness and SWS after sleep deprivation. The results reveal that when compared with controls, sleepwalkers show reduced regional cerebral perfusion in several bilateral frontal, parietal, and temporal regions, with more pronounced decreases in the left hemisphere. These findings suggest the involvement of specific brain networks in patients suffering from sleepwalking. In addition, the results may help explain certain clinical features of the disorder, including patients' heightened sensitivity to sleep deprivation as well as altered consciousness and poor judgement during the episodes themselves.

Introduction

Sleepwalking (or somnambulism) is a non-rapid eye movement (NREM) parasomnia involving behaviors of varying complexity, usually initiated during slow-wave sleep (SWS) [1, 2]. Most behavioral episodes are characterized by misperception of, and relative unresponsiveness to, the environment, mental confusion, perceived threat or agitation, and variable degrees of retrograde amnesia [2].

Sleepwalking affects up to 4 per cent of adults [3] and represents a leading cause of sleep-related violence and self-injury [4, 5]. Although sleepwalking has been long conceptualized as a "disorder of arousal" [6] because of the autonomic and motor arousal which precipitates the patient towards incomplete wakefulness, this NREM parasomnia has also been conceptualized as a disorder of SWS [1] since the disorder is characterized by an inability to sustain stable, consolidated SWS. Specifically, sleepwalkers show anomalies in sleep intensity, as reflected by an unusual distribution of slow-wave activity across sleep cycles [7, 8], atypical patterns in the cyclic alternating pattern rate, a measure considered to be a physiologic marker of NREM sleep instability [9–11], and unusually elevated number of spontaneous awakenings and electroencephalographic (EEG) arousals out of SWS, even on nights without sleepwalking episodes [8, 12, 13].

Sleep deprivation, known to result in a rebound of SWS during recovery sleep, increases the frequency and complexity of sleepwalking episodes in predisposed patients, while having no such effect in normal controls [14–16]. However, the differential effect of sleep deprivation on sleepwalkers is not limited to the clinical manifestation of the episodes themselves. In fact, sleep deprivation also enhances SWS abnormalities associated with sleepwalking, resulting in a more consolidated SWS in normal sleepers, but an even more fragmented SWS in sleepwalkers [1, 16].

Brain imaging techniques have helped clarify the functional neuroanatomy of normal human sleep [17], as well as the pathophysiology of several sleep disorders, such as obstructive sleep apnea [18]. Studies investigating normal SWS with brain imaging techniques report global reduction of brain metabolism when compared with wakefulness [19]. Regionally, this reduction is even more pronounced in the brainstem, thalamus, basal ganglia, and basal forebrain, at a subcortical level, and in the prefrontal cortex, anterior cingulate cortex, and precuneus, at a cortical level [17, 20].

With regards to sleepwalking, one single-photon emission computed tomography (SPECT) study of perfusion patterns during a somnambulistic episode revealed a coexistence of activation in the posterior cingulate cortex and the anterior cerebellum with reduced brain perfusion in frontoparietal associative cortices [21]. More recently, a SPECT imaging study of resting-state wakefulness in sleepwalkers and controls after normal sleep and following a night of total sleep deprivation revealed specific brain imaging patterns in sleepwalkers, including a bilateral reduction of cerebral perfusion in the inferior temporal gyri that was not observed after a night of regular sleep [22]. Thus, in addition to facilitating the occurrence of somnambulistic episodes, sleep deprivation can uncover patterns of neural dysfunction that characterizes sleepwalkers during wakefulness.

Systematic whole brain imaging, however, has yet to be performed during sleepwalkers' SWS. We thus used high-resolution SPECT with ^{99m}Tc-ethylene cysteinate dimer (ECD) to assess regional cerebral perfusion during post-sleep deprivation wakefulness as well as recovery SWS in sleepwalkers compared with a control group of matched good sleepers. Given that sleepwalking is associated with SWS anomalies, we hypothesized that sleepwalkers would show distinct perfusion patterns during recovery SWS when compared with controls in regions such as frontal, parietal, and cingulate cortices. Moreover, given that sleepwalking is conceptualized as a disorder of arousal and that brain perfusion anomalies were previously documented during wakefulness in this population, we hypothesized that distinct brain perfusion patterns during resting state wakefulness would be found in sleepwalkers compared with paired controls following sleep deprivation.

Materials and Methods

Participants and sleep recording

Participants were 10 adult sleepwalkers (3 men, 7 women, mean age: 28 ± 6.9 years) either referred to the Sleep Disorders Clinic of the Hôpital du Sacré-Coeur de Montréal by a physician (n = 8) or recruited through local advertisements (n = 2). Sleepwalkers were between 18 and 45 years old and had a history of chronic (>3 years) and frequent (>1 episode per month) sleepwalking that was not of a drug-induced, traumatic, or neurological origin. All received a final diagnosis of sleepwalking according to the International Classification of Sleep Disorders [2]. Ten healthy participants without sleep complaints and matched for age and gender were recruited as controls. Sleepwalkers and controls underwent a full screening night of polysomnographic recording (PSG; 32-channel Grass polygraph) that included a 19 electrode montage, an electrooculogram, an electromyogram at the chin and the anterior tibialis muscle, nasal and oral cannulas, a transcutaneous oximetry apposed on a finger, and thoracic and abdominal strain gauges. This screening night served as a habituation night for all participants and allowed detection of any sleep disorders in control participants or concomitant sleep disorders in sleepwalkers. Exclusion criteria for all participants were as follows: (1) the presence of neurological or psychiatric condition(s); (2) sleep disorders (other than sleepwalking for the experimental group); (3) a history of head injury; (4) a history of epilepsy; (5) the use of medications altering vigilance or sleep (e.g. antidepressants, psychostimulants, and hypnotics); or (6) self-reported claustrophobia or fear of needles and/or injections. The protocol was approved by the Research Ethics Committee of the Hôpital du Sacré-Coeur de Montréal, and written informed consent obtained from each participant.

Procedures and brain perfusion recording

All participants were evaluated with two SPECT ^{99m}Tc-ECD scans: the first consisted of an injection during morning wakefulness following 24 hr of sleep deprivation, whereas the second condition (at least 1 week apart from the first) involved an injection during recovery SWS in the morning following 24 hr of sleep deprivation. SPECT scans were performed with a high-resolution SPECT scanner yielding a 2 mm full width at half maximum resolution (FWHM; NeuroFocus, NeuroPhysics, Shirley, MA). During each session, participants were monitored and observed throughout the night to ensure that they remained awake and did not consume caffeine. Following the 24 hr sleep deprivation protocol, a technician performed each SPECT imaging test with the injection of a prepared dose of 750 MBq of ^{99m}Tc-ECD followed by a saline flush of 30 cc.

In the resting-state wakefulness condition, the injection was performed while the participant was lying awake, relaxed, and with eyes open, in the preparation room next to the scanner. After a standardized delay, participants were scanned for a static 20 min acquisition according to the manufacturer's prescribed procedure. In the recovery SWS condition, the injection was performed after 2 min of stable SWS (stage N3), as determined by live EEG recordings. Participants in this condition went to sleep after a night of total sleep deprivation, and the injection was performed using a polyvinyl chloride tube linking the preinstalled catheter and solution to the monitoring room. This ensured that participants would not be awakened by the experimental procedures. After the injection, participants were awakened and brought to the scanning room, where the 20 min acquisition procedure was performed. For both conditions, the delay between the injection and image acquisition was set for optimal image quality (mean delay of 45 min). After image acquisition, participants were brought back to the sleep laboratory so that they could return to sleep.

Statistical analyses

Demographic data and sleep characteristics were analyzed using SPSS (SPSS Statistics for Windows, Version 17.0). Statistical differences between the two groups (sleepwalkers and controls) for sleep characteristics and demographic data were assessed using Student's t-tests. PSG variables such as microarousal index, apnea–hypopnea index, periodic limb legs movement arousal index, and sleep stages were scored according to standardized criteria [23]. The apnea–hypopnea index represents the number of respiratory events per hour of sleep. The periodic limb movement arousal index represents the number of limb movements per hour of sleep.

After standard reconstruction (filtered back projection, subtraction of 50 per cent of the Compton window from the peak window) and attenuation correction (noniterative Chang algorithm), data were imported in Statistical Parametric Mapping 12 (SPM12) implemented in Matlab R2015a (version 8.5). Standard preprocessing was applied: images were coregistered and spatially normalized to a standard SPECT template included in SPM12 and then smoothed with a 14 mm FWHM filter. Global normalization was performed using ANCOVA scaling based on each participants' mean voxel value and a grey matter mask applied. Differences in brain perfusion data between sleepwalkers and controls were assessed using two-sample t-tests separately for both conditions (wakefulness and SWS). Significance was set at $p < 0.005$ at the voxel level (height threshold) uncorrected for multiple comparisons combined with >100 contiguous statistically significant voxels by cluster (extent threshold). Although these parameters are better suited to exploratory observations than statistically significant contrasts, they were chosen based on recent evidence showing that SPM thresholding based on liberal p-values and restrictive cluster sizes leads to results more closely linked to clinical data [24]. Results were overlaid on a single participant magnetic resonance imaging scan to localize brain perfusion changes.

Results

Demographic and PSG data from the screening night are summarized in Table 1. Sleepwalkers and controls were comparable on all variables but two: when compared with controls, sleepwalkers had a smaller proportion of SWS and more SWS-wake transitions.

Table 1.

Statistical differences between sleepwalkers and controls on demographic data and screening night sleep characteristics

	Sleepwalkers (*N* = 10) *mean (SD)*	**Controls (*N* = 10) *mean (SD)***	***P***
Gender	7 women; 3 men	7 women; 3 men	1
Age (y)	28.2 (6.9)	28.2 (7)	1
Sleep latency (min)	14.05 (10)	19.3 (16)	0.4
Total sleep time (min)	451 (29.7)	421 (72.4)	0.2
Sleep efficiency (%)	94.13 (3.6)	91.25 (13.7)	0.5
N1 stage (%)	10.28 (4.4)	7.70 (4.1)	0.2
N2 stage (%)	55.44 (6.5)	54.30 (8)	0.7
N3 stage (%)	15.44 (3.9)	19.37 (4.4)	p<0.05
REM stage (%)	18.84 (5.4)	18.65 (5.7)	0.9
Micro-arousals (event/hour)	7.67 (3.6)	7.11 (2.4)	0.7
N3-wake transition (nb)	3.3 (1.9)	1.1 (1)	p<0.01
AHI (event/hour)	1.5 (1.5)	0.79 (0.5)	0.2
PLMA (event/hour)	0.57 (0.8)	0.70 (0.9)	0.7

N = sample size; *SD* = standard deviation; REM = rapid eye movement; AHI = apnea–hypopnea index; PLMA = periodic limb movement arousal index.

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Group comparisons of SPECT data revealed differences in the brain perfusion patterns during recovery SWS as well as during post-sleep deprivation resting-state wakefulness. When compared with the SWS of controls, sleepwalkers' SWS showed decreased perfusion in several brain regions, most notably in frontal areas (Table 2 and Figure 1). Reduced brain perfusion was found in clusters that include bilateral superior frontal gyri, middle frontal gyri, and medial frontal gyri. Most of these regions correspond to the dorsolateral prefrontal cortex (DLPFC). In the left hemisphere, additional clusters of reduced brain perfusion were located in the postcentral gyrus (parietal cortex), the insula, and the superior temporal gyrus (temporal cortex). No area showed increased perfusion in sleepwalkers during SWS.

Table 2.

Reduced regional cerebral perfusion in sleepwalkers' versus controls' SWS

Region	Cluster size (*K*)	*x*	*y*	*z*	T-value	*P*
Frontal cortex						
L **s**uperior frontal gyrus	439	−22	30	42	5.05	0.000
L **m**iddle frontal gyrus		−20	30	34	4.27	0.000
	125	−42	6	46	3.53	0.001
		−38	8	48	3.47	0.001
	266	−36	48	24	5.46	0.000
R **s**uperior frontal gyrus	616	34	14	54	4.64	0.000
		24	36	38	3.60	0.001
		24	26	48	3.20	0.003
R **m**iddle frontal gyrus		30	46	26	4.52	0.000
R **m**edial frontal gyrus	119	2	−10	52	3.41	0.002
	104	2	8	68	3.34	0.002
R precentral gyrus	135	42	−16	46	4.52	0.000
Parietal cortex						
L **p**ostcentral gyrus	182	−46	−22	52	5.12	0.000
Insular cortex						
L **i**nsula	170	−44	12	−4	4.38	0.000
Temporal cortex						
L **s**uperior temporal gyrus	116	−58	−2	0	3.87	0.001

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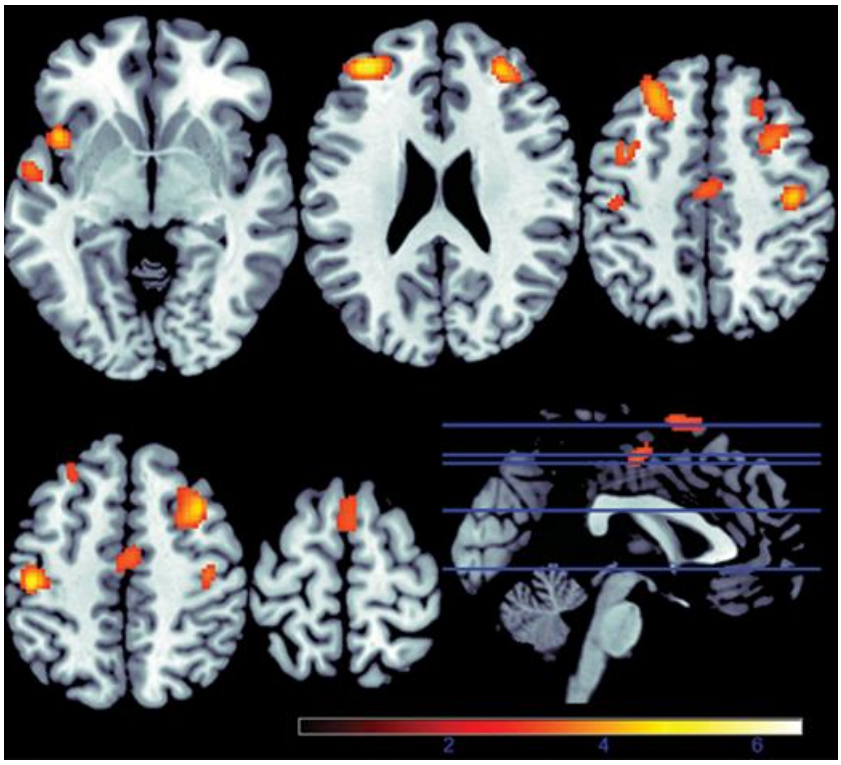
Figure 1.



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Reduced regional cerebral perfusion during recovery SWS in sleepwalkers compared with controls. The color scale indicates the range of T-values for this contrast.

During resting-state wakefulness following sleep deprivation, decreased perfusion was also found primarily in frontal areas in sleepwalkers (Table 3 and Figure 2). Bilaterally, reduced brain perfusion was found in the middle frontal gyri and superior frontal gyri. In addition, decreased perfusion was observed in the medial frontal gyrus of the right hemisphere and in many frontal (precentral gyrus, orbital gyrus), parietal (inferior parietal lobule, supramarginal gyrus, superior temporal gyrus, postcentral gyrus, and superior parietal lobule), and temporal regions (middle and inferior temporal gyri) of the left hemisphere.

Table 3.

Regional cerebral perfusion decreases and increases in sleepwalkers' versus controls' resting-state wakefulness

Region	Cluster size (*K*)	*x*	*y*	*z*	T-value	*P*
Reduced cerebral perfusion Frontal cortex						
L precentral gyrus	527	−40	−8	44	6.35	0.000
L middle frontal gyrus		−38	8	50	2.95	0.004
	146	−40	50	16	3.54	0.001
		−40	50	6	3.14	0.003
	544	−42	30	32	6.01	0.000
		−40	36	26	3.54	0.001
		−42	32	26	3.44	0.002
L superior frontal gyrus		−20	26	46	4.18	0.000
R orbital gyrus	319	24	40	−16	4.97	0.000
		18	26	−32	3.60	0.001

Region	Cluster size (*K*)	*x*	*y*	*z*	*T* value	*P*
R medial frontal gyrus		8	38	−18	2.93	0.005
	287	2	−2	62	4.17	0.000
		−14	−8	64	3.43	0.002
R middle frontal gyrus	142	38	38	26	3.73	0.001
		36	36	32	3.55	0.001
		34	36	28	3.54	0.001
		30	50	22	3.41	0.002
		38	48	22	2.99	0.004
	347	38	2	54	4.57	0.000
		44	12	48	3.33	0.002
R superior frontal gyrus		22	12	52	3.81	0.001
Parietal cortex						
L inferior parietal lobule	939	−58	−34	36	4.19	0.000
		−54	−24	30	4.11	0.000
L supramarginal gyrus		−52	−48	30	3.87	0.001
		−54	−26	22	3.75	0.001
		−56	−44	24	3.65	0.001
L superior temporal gyrus		−50	−26	−2	3.30	0.002
L postcentral gyrus		−54	−18	26	3.14	0.003
		−50	−24	24	3.09	0.003
L superior parietal lobule	329	−30	−68	44	4.21	0.000
		−30	−58	50	3.76	0.001
		−18	−60	42	3.12	0.003
Temporal cortex						
L middle temporal gyrus		−58	−44	6	4.34	0.000
	152	−48	−64	0	3.42	0.002
		−56	−52	−14	3.09	0.003
		−40	−66	14	3.04	0.004
L inferior temporal gyrus		−52	−44	−24	3.04	0.004
Increased cerebral perfusion						
Limbic region						
R parahippocampal gyrus	142	6	−46	10	4.62	0.000

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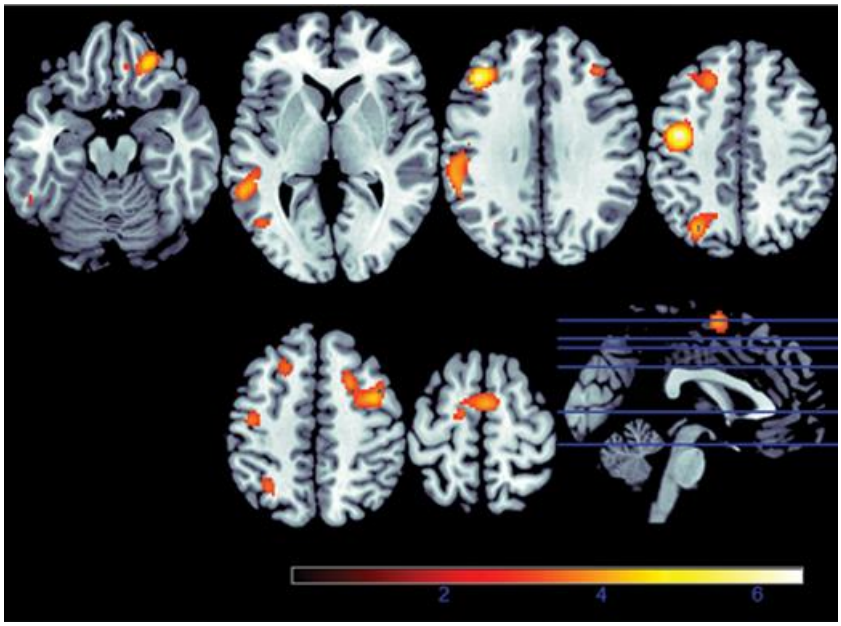
Figure 2.



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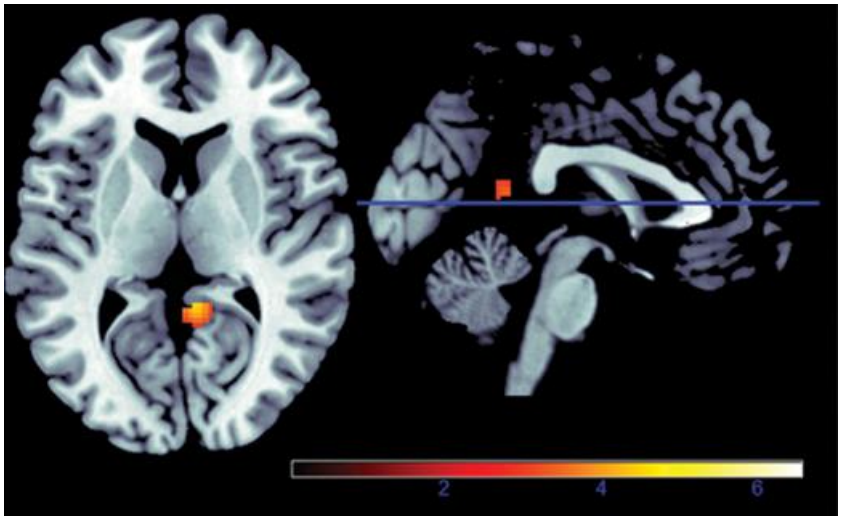
Reduced regional cerebral perfusion during resting-state wakefulness following sleep deprivation in sleepwalkers compared with controls. The color scale indicates the range of T-values for this contrast.

Finally, when compared with results from controls, sleepwalkers' resting-state wakefulness following sleep deprivation showed increased perfusion in the right parahippocampal gyrus (Table 3 and Figure 3).

Figure 3.



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Increased regional cerebral perfusion during resting-state wakefulness following sleep deprivation in sleepwalkers compared with controls. The color scale indicates the range of T-values for this contrast.

Discussion

This study aimed to investigate brain perfusion patterns in sleepwalkers during resting-state wakefulness and SWS, both following 24 hr of sleep deprivation. When compared with controls' SWS and resting-state wakefulness, sleepwalkers showed reduced brain perfusion in several bilateral frontal regions, including the superior frontal, middle frontal, and medial frontal gyri. Most of these regions form part of the DLPFC. Sleepwalkers' SWS was also characterized by reduced brain perfusion in the left postcentral gyrus, insula, and superior temporal gyrus. During resting-state wakefulness, reduced brain perfusion was additionally found in parietal and temporal regions of sleepwalkers' left hemisphere. Finally, resting-state

wakefulness was associated with increased brain perfusion in sleepwalkers' right parahippocampal gyrus.

Normal SWS has been found to be associated with a global reduction of cerebral blood flow (CBF) [17], with particularly pronounced reductions over frontal and parietal regions [25, 26]. Thus, the observation of patterns of reduced brain perfusion in many frontal and parietal regions in sleepwalkers' recovery SWS compared with controls' recovery SWS suggests that sleepwalkers exhibit CBF patterns that are qualitatively consistent with normal SWS patterns. EEG slow waves, a key component of NREM sleep, have also been shown to be associated with brain activity in frontal and parietal cortices, including in the middle frontal gyri [27, 28]. The finding of reduced brain perfusion in sleepwalkers' left hemispheres is also in line with results showing that slow waves recruit left frontal regions and insula during sleep more than their right homologs [28]. Our results thus indicate that although sleepwalkers' patterns of brain perfusion during recovery SWS are consistent with those underlying normal SWS, they likely represent an intensification of the patterns observed in healthy participants.

Frontal and parietal brain perfusion patterns during sleepwalkers' SWS are consistent with conditions facilitating episodes

Reduced brain perfusion in frontal and parietal regions during sleepwalkers' SWS, especially in prefrontal region such as the DLPFC, is also in line with cerebral processes underlying actual somnambulistic episodes. Indeed, these regions show decreased perfusion during sleepwalkers' recovery SWS, in the present study, as well as during an actual episode of sleepwalking [21]. Several authors have suggested that key components of SWS persist in frontal and parietal cortices during actual somnambulistic episodes and that the awakening of the motor and cingulate cortices during behavioral episodes is in apparent conflict with the simultaneous persistent sleep state of associative cortical areas [1, 21, 29, 30]. This simultaneous interplay between states of sleep and wakefulness has led to a conceptualization of sleepwalking as a dissociative state between motor arousal and persisting sleep in executive regions of higher functions. The present finding that recovery SWS, known to facilitate the occurrence of somnambulistic episodes in predisposed patients [15, 16], is also characterized by decreased brain perfusion in frontal regions, suggests that SWS-related patterns of activation observed in sleepwalkers may persist into, and may then facilitate, actual behavioral episodes.

With regards to this hypothesis, it should be noted that the coexistence of sleep and wake-like processes has been well documented in healthy participants, at sleep onset as well as during NREM sleep [31–36]. The localized coexistence of sleep and wake-like EEG activity observed in sleepwalkers may thus reflect a deregulation of an intrinsic property of the brain that can culminate in somnambulism in predisposed individuals and reflect regional differences in arousal thresholds [1, 37].

Reduced brain perfusion patterns in prefrontal and insular regions during SWS may be related to sleepwalking manifestations

The finding of reduced perfusion in several associative brain regions may also shed light on phenomenological features of somnambulistic episodes themselves (e.g. misperception of external stimuli, poor judgement, and altered self-perception). First, reduction of brain perfusion in the DLPFC is associated with the reduction of executive functions and conscious awareness during SWS [38]. A delay in achieving waking levels of activation in that area is associated with a gradual, not immediate, recovery of cognitive functions [39].

The insula, found in the present study to have reduced perfusion during sleepwalkers' SWS, is also implicated in self-consciousness and, more precisely, in interoception, or the sensitivity toward stimuli arising from within one's body. Interoception is involved in awareness, subjectivity, sense of self, and behaviors [40, 41], all of which are manifestly impaired during somnambulistic episodes. Furthermore, the insula is also implicated in pain perception [42], and sleepwalkers have been reported to frequently have a greatly diminished or even absent perception of pain during episodes [43]. Thus, the brain perfusion patterns observed in prefrontal and parietal regions, as well as in the left insula during sleepwalkers' recovery SWS, may be related to the clinical characteristics of sleepwalking episodes.

Sleepwalkers' reduced brain perfusion in frontal and parietal regions is also observed during resting-state wakefulness

Our finding of reduced perfusion over specific brain areas was not limited to SWS, but also characterized sleepwalkers' resting-state wakefulness, with reductions being observed in frontal and parietal regions. Similar findings were reported by Dang-Vu and colleagues [22], who concluded that sleep deprivation reveals brain perfusion anomalies in sleepwalkers' resting-state wakefulness. Our results largely reproduce this observation, even though the reported regions do not extend to the previously identified bilateral inferior temporal gyri. Moreover, several findings point to excessive daytime sleepiness as an intrinsic characteristic of sleepwalkers [44–46], and one recent study found daytime cognitive impairment in sleepwalkers in the form of disrupted inhibitory control following sleep deprivation [47]. Considering the implication of frontal regions in cognitive and inhibitory

functions [48, 49], our results of reduced perfusion in these regions in sleepwalkers suggest that these daytime anomalies may be based specifically on alterations in the function of those areas.

Sleepwalkers' resting-state wakefulness and SWS show reduced perfusion in regions affected by sleep deprivation

Finally, the finding of reduced perfusion in several brain regions during sleepwalkers' SWS as well as during resting-state wakefulness is consistent with the literature on the effects of sleep deprivation on brain activity and reinforces the idea that sleepwalkers are particularly sensitive to its effects. Sleep deprivation is known to preferentially affect frontal regions, as evidenced by a more pronounced rebound in δ and θ spectral power during recovery SWS [50, 51]. Prefrontal regions are also known to be particularly vulnerable to the effect of sleep deprivation [38]. Sleep deprivation also produces a lateralized response, with greater increases in slow waves in the left hemisphere [52, 53]. These observations are consistent with our results of reduced perfusion in frontal regions, particularly in the left hemisphere, suggesting that although amplified, sleepwalkers' perfusion patterns in response to sleep deprivation are qualitatively congruent with findings in normal sleepers.

The resting-state wakefulness cerebral perfusion patterns observed in our sample of sleepwalkers also support an increased vulnerability to sleep deprivation. In normal sleepers, resting-state wakefulness is associated with activation in prefrontal and parietal regions [54]. More precisely, these regions include the posterior cingulate, precuneus, inferior parietal cortices, left dorsolateral/ventrolateral prefrontal cortex, and medial frontal regions [17, 55]. Following sleep deprivation, most of these regions show decreased cerebral perfusion [56, 57]. These reductions, however, are even more pronounced in several regions corresponding to those showing reduced regional CBF (rCBF) in sleepwalkers when compared with controls: prefrontal regions, inferior and superior parietal lobules, and middle and inferior temporal gyri [57]. The finding that post-sleep deprivation perfusion patterns in sleepwalkers are similar to, yet more pronounced, those observed in healthy controls provides further evidence of this population's heightened sensitivity to the effects of sleep deprivation.

One limitation of this work is the absence of imaging data during nonrecovery SWS as well as resting-state wakefulness following a normal night of sleep. As this was the first brain imaging study of SWS in a group of sleepwalkers, the choice to focus on post-sleep deprivation data was guided by clinical and empirical observations highlighting sleepwalkers' atypical response to sleep deprivation and by the fact that only a limited number of scans could be ethically performed on each participant given the use of radioactive tracers. That being said, it would of interest for future neuroimaging studies to investigate normal SWS and resting-state wakefulness in chronic sleepwalkers as well as to combine functional neuroimaging studies of somnambulism with cognitive and behavioral assessments to further characterize the potential impact of these abnormal brain responses on sleepwalkers' daytime functioning. Such data could help clarify how specific brain activity patterns, as revealed in the present study, may be implicated in the pathophysiology of somnambulism as well as of other NREM sleep parasomnias.

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