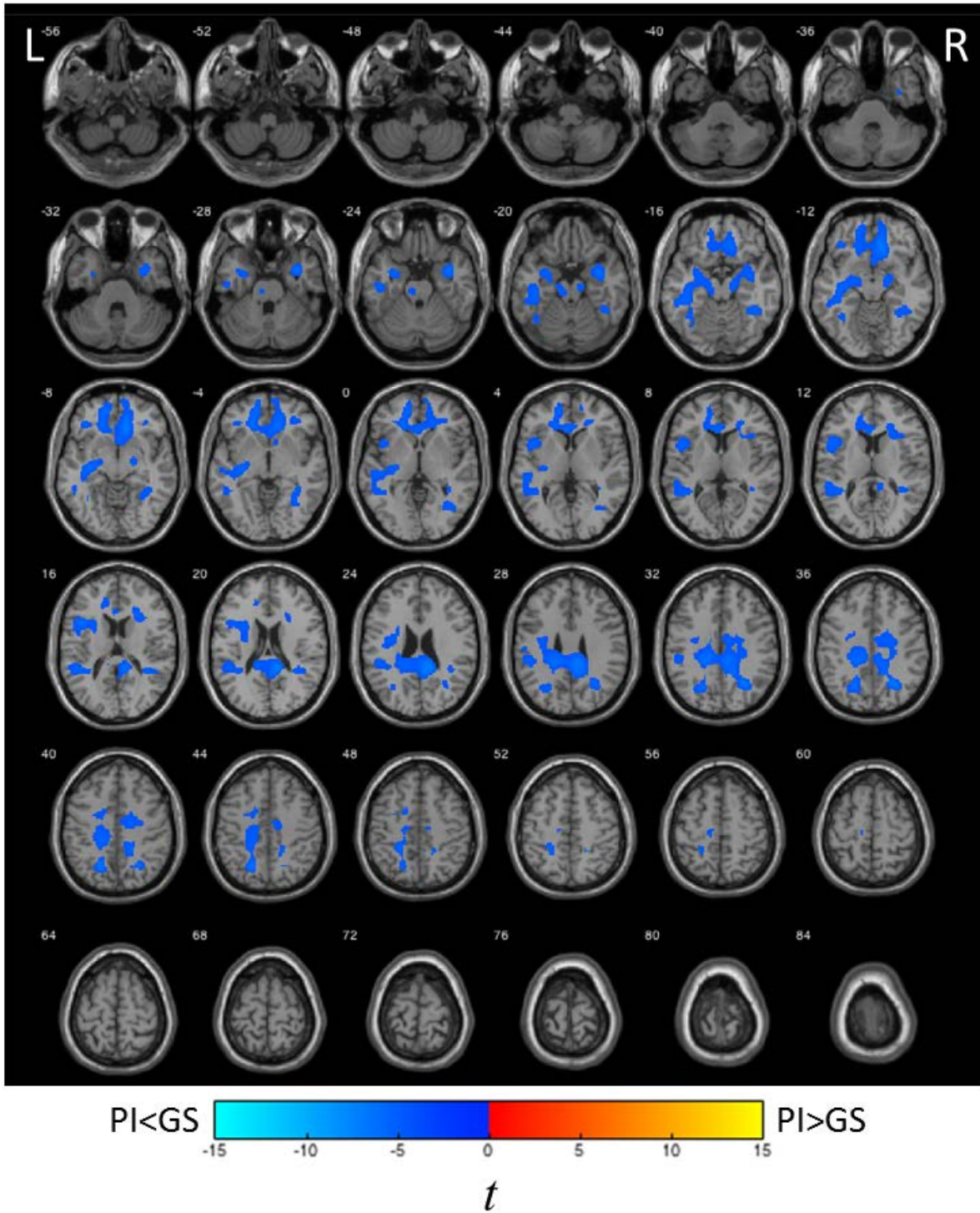
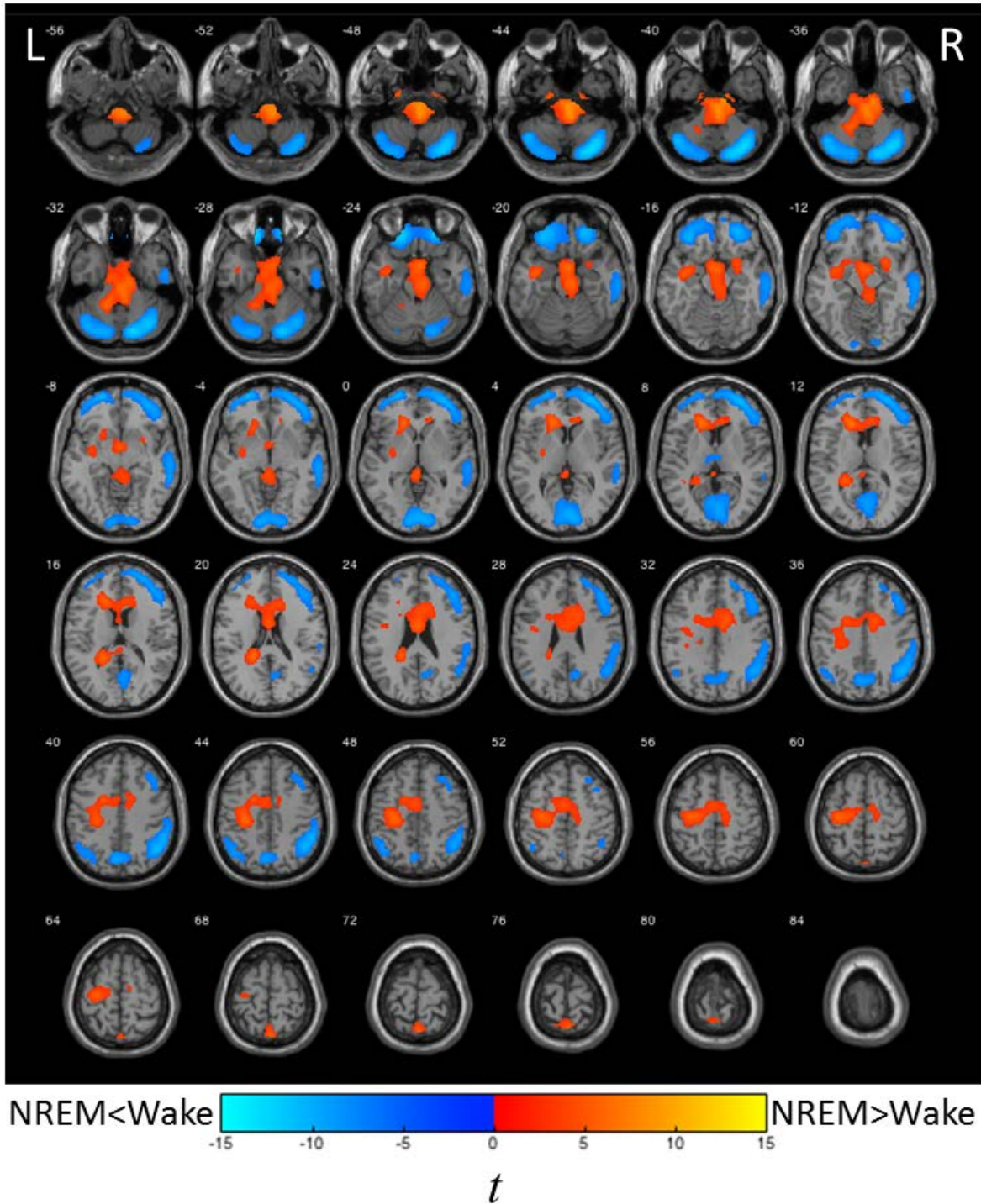


**Figure S1**—Regions of the brain showing a group (PI vs. GS) by state (wake vs. NREM sleep) interaction for relative regional cerebral metabolic rate for glucose (Figure 1 and Table 3) mapped onto a high-resolution MRI. The right hemisphere of the brain is indicated with R. The color bar represents  $F$  values.



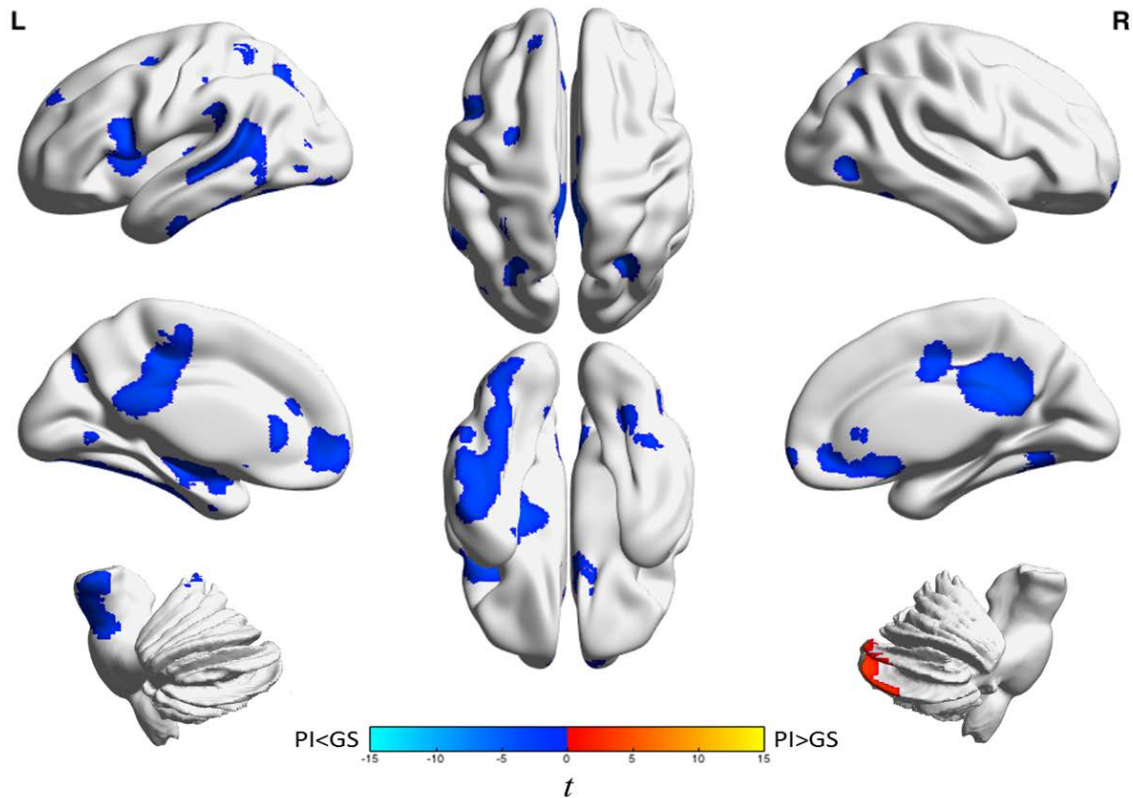
**Figure S2**—Results of the group (PI-GS), independent of sleep-wake state, analysis (Figure 2 and Table 4) for relative regional cerebral metabolic rate for glucose ( $rCMR_{glc}$ ) mapped onto a

high-resolution MRI. The left and right hemispheres of the brain are indicated with L and R, respectively. The color bar represents  $t$  values; blue indicates regions where PI had lower relative  $rCMR_{glc}$  than GS across wake and NREM sleep.



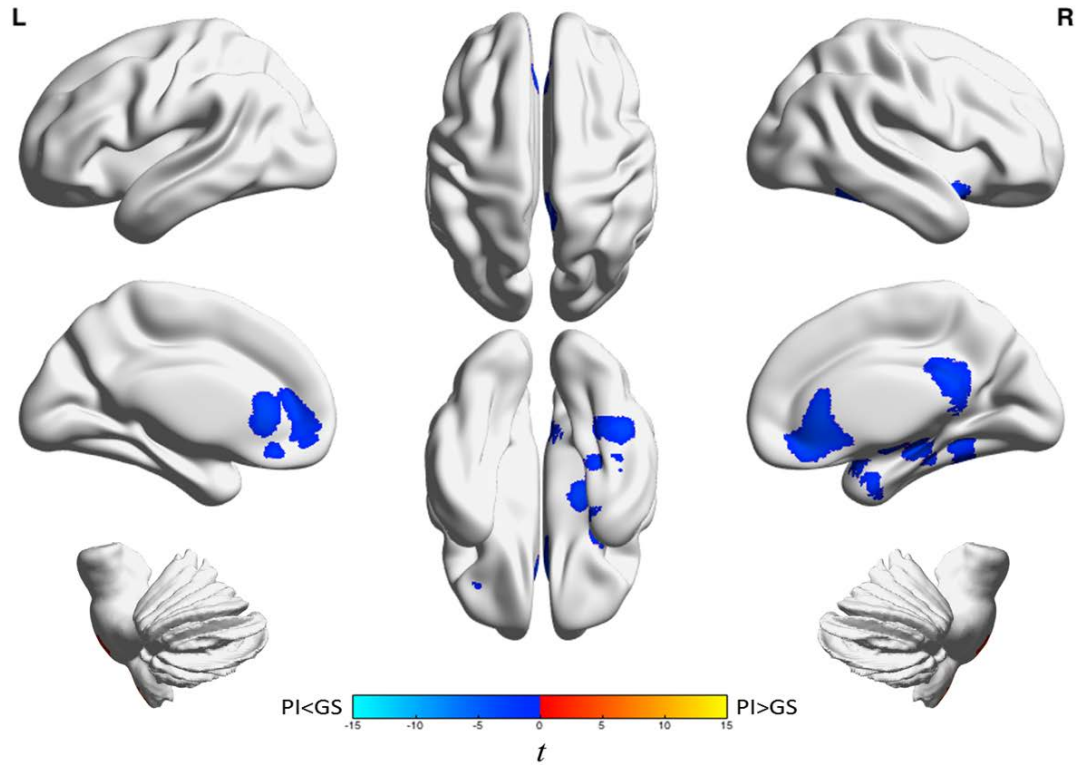
**Figure S3**—Results of the state (NREM sleep-wake), independent of group, analysis (Figure 3 and Table 5) for relative regional cerebral metabolic rate for glucose ( $rCMR_{glc}$ ) mapped onto a

high-resolution MRI. The left and right hemispheres of the brain are indicated with L and R, respectively. The color bar represents  $t$  values; blue indicates regions where  $rCMR_{glc}$  was relatively lower during NREM sleep than wake, and orange indicates regions where it was relatively higher during NREM sleep than wake.



**Figure S4—Group Differences in Relative Glucose Metabolism during Wake.** We assessed relative regional cerebral metabolic rate for glucose ( $rCMR_{glc}$ ) in a sample of 44 patients with primary insomnia (PI) and 40 good sleeper controls (GS) during morning wakefulness. PI had lower relative  $rCMR_{glc}$  in 4 clusters spanning the neocortex and brainstem. PI also had higher relative  $rCMR_{glc}$  than GS in the right cerebellum. All clusters were significant at  $P_{3DC\_corrected} < 0.05$ . A full list of brain regions involving these clusters is presented in Table S1. The color bar represents  $t$  values; blue indicates regions where PI had lower relative  $rCMR_{glc}$  than GS and orange indicates regions where PI had higher relative  $rCMR_{glc}$  than GS during wakefulness.





**Figure S5—Group Differences in Relative Glucose Metabolism during NREM Sleep.** We assessed relative regional cerebral metabolic rate for glucose ( $rCMR_{glc}$ ) in a sample of 44 patients with primary insomnia (PI) and 40 good sleeper controls (GS) during NREM sleep. Patients with PI had lower relative  $rCMR_{glc}$  in three clusters centered on the anterior cingulate, right medial temporal lobe, and right precuneus/posterior cingulate,  $P_{3DC\_corrected} < 0.05$  for all clusters. A full list of brain regions involving these clusters is presented in Table S1. The color bar represents  $t$  values; blue indicates regions where PI had lower relative  $rCMR_{glc}$  than GS during NREM sleep.

**Table S1—Group (GS vs. PI) differences in relative glucose metabolism during wake and NREM sleep.**

<b>Analysis</b>	<b>Brain region</b>	<b><i>k</i><sup>A</sup></b>	<b><i>t</i>-statistic (max)<sup>B</sup></b>	<b><i>x</i></b>	<b><i>y</i></b>	<b><i>z</i></b>
Wake	Left frontal cortex and anterior cingulate gyrus	1439	-4.0	-18	38	-4
	Left inferior frontal gyrus and left insula	947	-44	-44	14	14
	Right medial frontal gyrus, anterior cingulate, frontal-orbital gyrus, superior frontal gyrus, and caudate	1128	-4.7	14	28	-10
NREM	Temporal lobe, parietal lobe, precuneus, middle and posterior cingulate gyri, frontal lobe, occipital lobe, left hippocampus, putamen, insula, left brainstem, and left amygdala	11925	-5.4	26	-60	-36
	Right cerebellum	729	3.8	16	-88	-32
	Anterior cingulate, medial frontal gyrus, orbitofrontal cortex, inferior frontal gyrus, and right caudate	2335	-4.6	14	30	-10
	Right posterior cingulate, bilateral precuneus, and	1100	-5.3	12	-40	20



middle cingulum

Right fusiform gyrus, parahippocampus, superior            2076            -5.1            38            2            -24

and inferior temporal gyri, hippocampus, and

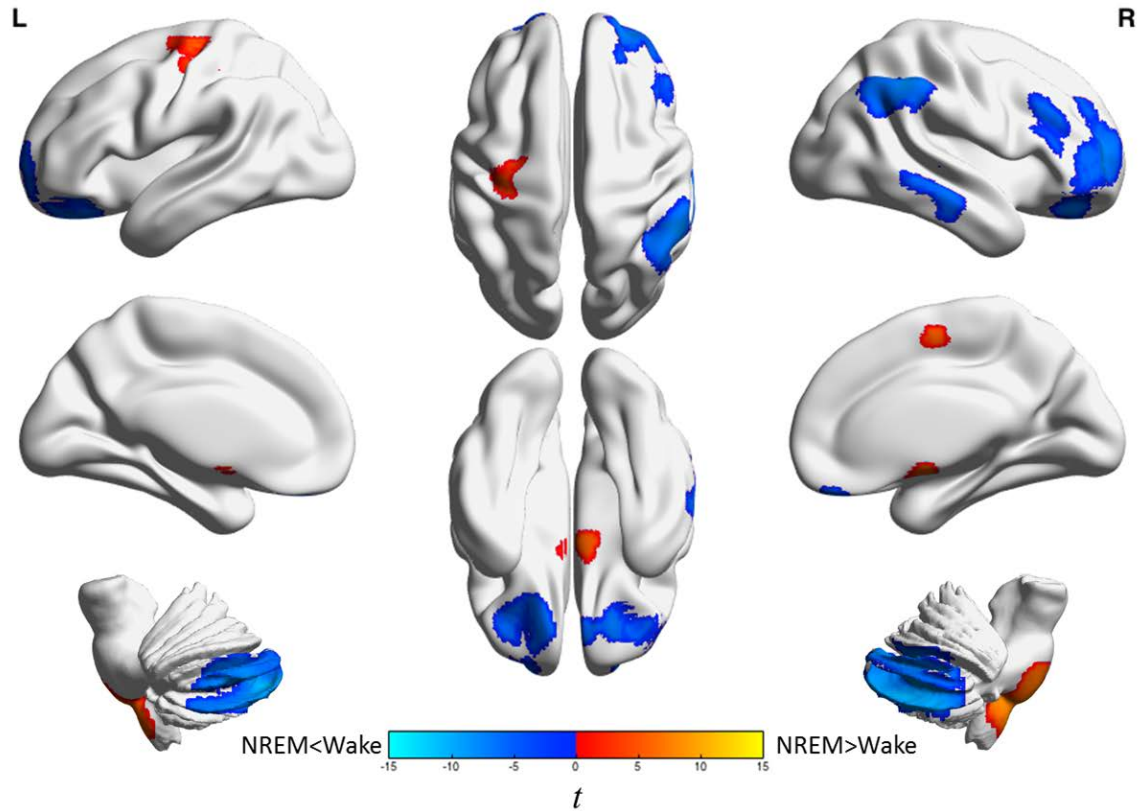
amygdala

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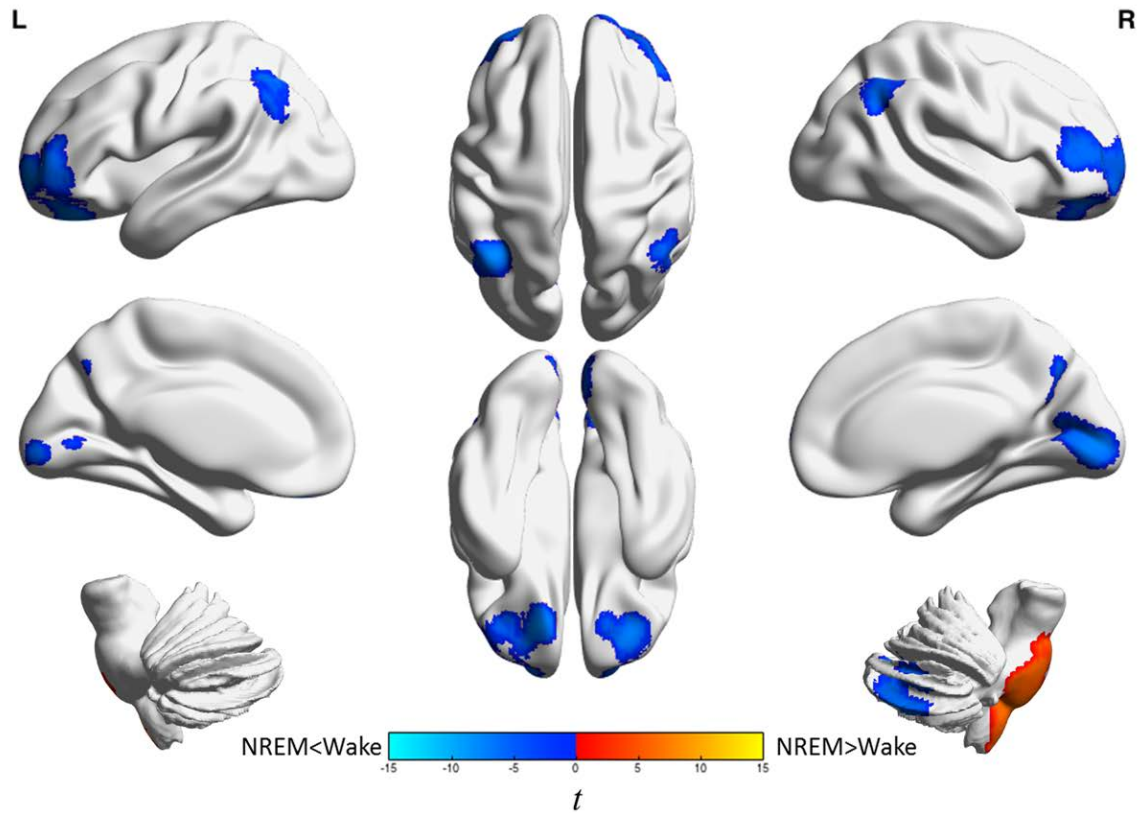
Note. <sup>A</sup>Cluster sizes ( $k$ ) greater than 670 voxels for wake and 708 voxels for NREM sleep were significant at height threshold

$p_{uncorrected} > 0.005$  and cluster threshold  $P_{3DC\_corrected} < 0.05$ . <sup>B</sup>Negative  $t$ -statistics indicate regions where PI had lower relative  $rCMR_{glc}$

than GS; positive  $t$ -statistics indicate regions where PI had higher relative  $rCMR_{glc}$  than GS.



**Figure S6—Sleep-Wake Differences in Relative Glucose Metabolism in Patients with Primary Insomnia.** We compared relative regional cerebral metabolic rate for glucose ( $rCMR_{glc}$ ) during NREM sleep to that during wake in a sample of 44 patients with primary insomnia. The color bar represents  $t$  values; blue indicates regions where  $rCMR_{glc}$  was relatively lower during NREM sleep than wake, and orange indicates regions where  $rCMR_{glc}$  was relatively higher during NREM sleep than during wake. All clusters were significant at  $P_{FWE\_corrected} < 0.05$ . A full list of regions associated with these significant clusters is presented in Table S2.



**Figure S7—Sleep-Wake Differences in Relative Glucose Metabolism in Good Sleepers.** We compared relative regional cerebral metabolic rate for glucose ( $rCMR_{glc}$ ) during NREM sleep to that during wake in a sample of 40 good sleeper controls. The color bar represents  $t$  values; blue indicates regions where  $rCMR_{glc}$  was relatively lower during NREM sleep than wake, and orange indicates regions where  $rCMR_{glc}$  was relatively higher during NREM sleep than during wake. All clusters were significant at  $P_{FWE\_corrected} < 0.05$ . A full list of regions associated with these significant clusters is presented in Table S2.

**Table S2—Sleep-wake differences in relative regional cerebral metabolic rate for glucose (rCMRglc) in patients with primary insomnia (PI) and good sleeper controls (GS).**

Analysis	Brain region	$k^A$	$t$ -statistic			
			(max) <sup>B</sup>	$x$	$y$	$z$
PI	Left orbitofrontal cortex and anterior aspects of the left superior, middle, and inferior frontal gyri	61	-8.9	-28	36	-22
	Right frontal cortex	13	-7.8	34	54	0
		17				
	Left medial frontal gyrus and left supplemental motor area	24	7.1	0	-4	52
		3				
	Left precentral and postcentral gyri	12	8.9	-30	-20	46
		73				
	Right inferior parietal lobe	90	-8.4	54	-44	42
		8				
	Right middle temporal gyrus	34	-6.6	64	-24	-10
		7				
	Left putamen	40	7.1	-32	-8	-2
		1				
Subgenual area and hypothalamus	61	7.1	4	2	-18	
	4					
Brainstem	14	10.2	4	-32	-44	
	98					

	Left cerebellum	20	-11.0	-16	-82	-40
		08				
	Right cerebellum	27	-10.7	30	-74	-42
		49				
GS	Left frontal cortex	97	-8.4	-16	-38	-28
		8				
	Right frontal cortex	91	-7.4	28	46	-14
		0				
	Left inferior parietal lobule	45	-8.3	-40	-56	48
		3				
	Right inferior parietal lobule	23	-6.8	46	-58	40
		2				
	Bilateral cuneus, precuneus, calcarine, lingual gyrus, and posterior cingulate	13	-7.6	10	-90	4
		14				
	Brainstem	18	8.0	8	-16	-46
		79				
	Right cerebellum	78	-7.1	16	-78	-32
		2				

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Note. <sup>A</sup>Cluster sizes ( $k$ ) greater than 200 voxels were significant at height threshold  $P_{\text{FWE\_corrected}}$

$< 0.05$ . <sup>B</sup>Negative  $t$ -statistics indicate regions where  $\text{rCMR}_{\text{glc}}$  was relatively lower during NREM sleep than wake; positive  $t$ -statistics indicate regions where  $\text{rCMR}_{\text{glc}}$  was relatively higher during NREM sleep than during wake.