

Newcastle
University

**Institute of
Neuroscience**

Are sleep and circadian rhythm
associated with cognitive function in
Bipolar Disorder?

Andrew Bradley

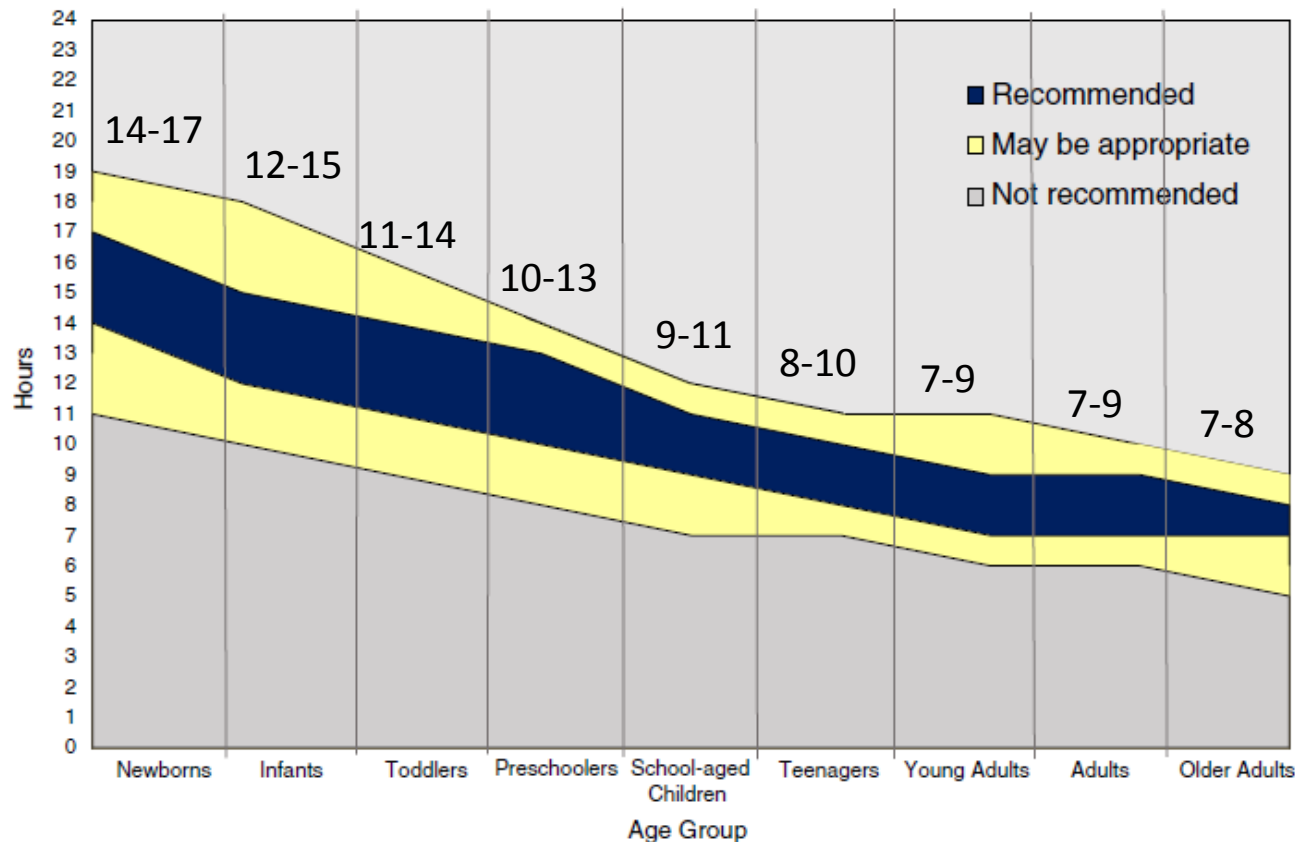
PhD Student Newcastle University
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Cognitive function in bipolar disorder

- Patients often complain of cognitive impairments (e.g. memory, concentration).
- Objectively measured moderate deficits in attention, working memory, verbal memory, processing speed and executive functions.
- Impairment present in euthymic patients and cannot be entirely explained by residual mood symptoms, IQ, age or drug treatment.

Sleep is important to preserve cognitive, physical and emotional health

Sleep duration recommendations across the life span



Sleep depth, quality and timing are also important.

Sleep and cognitive function

- Our own experiences of the effects of poor sleep.
- Primary sleep disorders e.g. insomnia, sleep apnoea and circadian rhythm disorders and shift working are associated with objectively measured deficits in cognitive function.

Fortier-Brochu E et al. *Sleep Med Rev* 2012;16:83-94

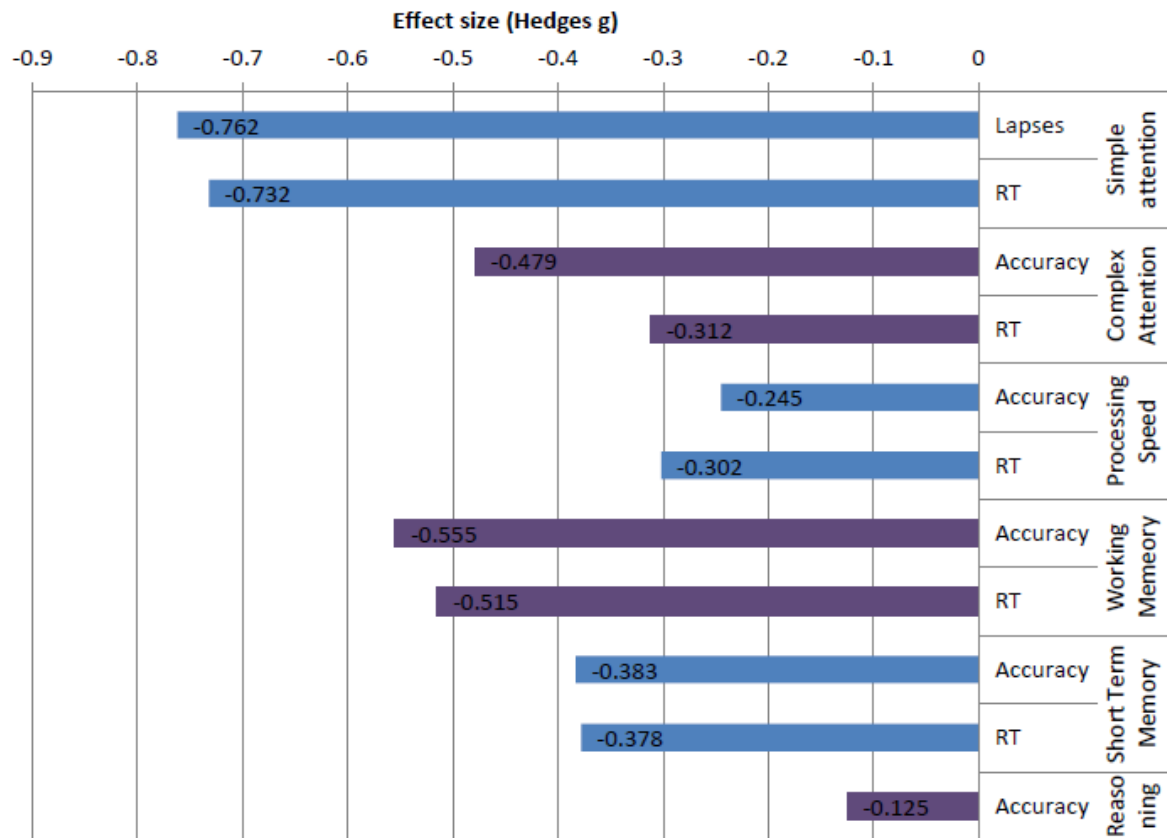
Beebe DW et al. *Sleep* 2003;26:298-307

Harrison Y & Horne JA. *J Exp Psychol Applied* 2000;6:236-49

Rouch I et al. *Ergonomics* 2005;48:1282-1293

Sleep deprivation and cognitive function

Effect sizes for impairment of cognitive function following short term SD (24-48 hours)



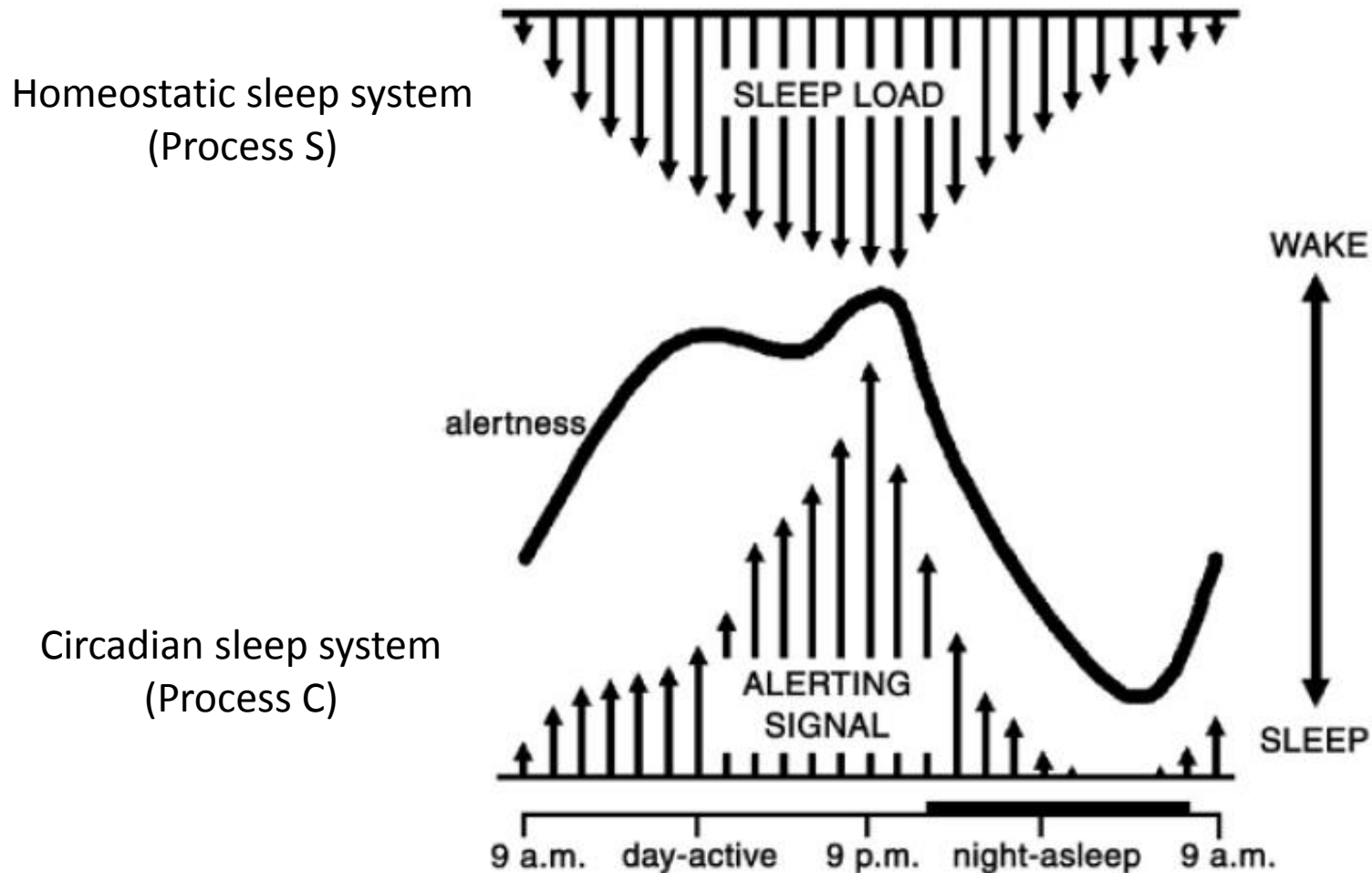
Largest effect on simple attention

Inter individual variability in the vulnerability to SD and SR

SD increases variability in performance

Simple attention is influenced by homeostatic and circadian sleep processes

The regulation of sleep and circadian rhythm



Sleep and circadian function in bipolar disorder



- Sleep disturbances
 - present throughout the illness
 - variable
 - Phase shifts in the timing of sleep- circadian rhythm disorder?
 - primary sleep disorders such as sleep apnoea may be more prevalent in people with bipolar disorder.

Measuring the Asociation between sleep and Cognitive function In Bipolar disorder

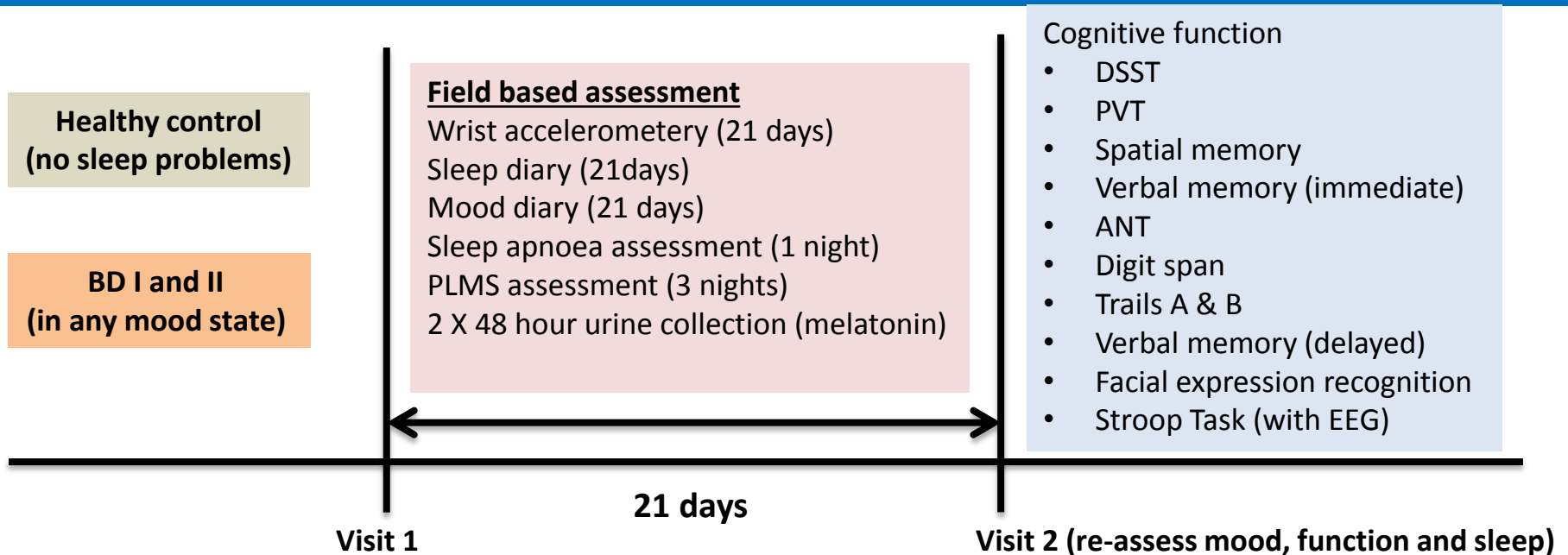
ASCRIBE - Study Aims

- To examine the relationship between sleep variables and cognitive function, quality of life and psychosocial function in people with BD.
 - To characterise sleeping patterns in BD patients and compare to healthy controls
 - Measure the prevalence of sleep apnoea in people with bipolar disorder
 - Measure core circadian function in people with bipolar disorder.

Hypothesis

- Performance on cognitive tasks will decline with increasingly abnormal sleep variables.
- Sleep variables will have a stronger relationship with cognitive function in bipolar patients than will mood symptoms.
- QoL and function will decline with increasingly abnormal sleep variables.

Study Design



Recruitment

- Healthy volunteer database
- MRC ABC BDII cohort
- Local Psychiatric Services
- Regional Sleep Service
- Local BD support group

Visit 1 assessments

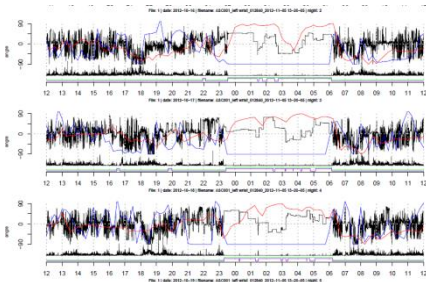
- **Demographics** – Age, Sex, BMI, employment, medication, smoking, alcohol, IQ
- **Diagnosis and Axis I co-morbidities** – Mini International Neuropsychiatric Interview
- **Mood** - Grid HAMD-17, BDI, YMRS, ASRM, STAI
- **Function** - Biological Rhythm Interview of Assessment in Neuropsychiatry (BRIAN), Function Assessment Short Test (FAST), QoL-BD
- **Sleep and circadian preference** - Pittsburgh Sleep Quality Index (PSQI) , Epworth Sleepiness Scale (ESS), Morningness/eveningness scale.

Accelerometry



GENEActiv accelerometer

- waterproof
- measures acceleration in three axes
- contains an inbuilt light meter.



- Visual actigram
- Sleep and movement related estimates.
 - Total sleep time, sleep onset latency, sleep efficiency
 - Total sustained inactivity and physical activity.
 - Relative amplitude between day and night activity.

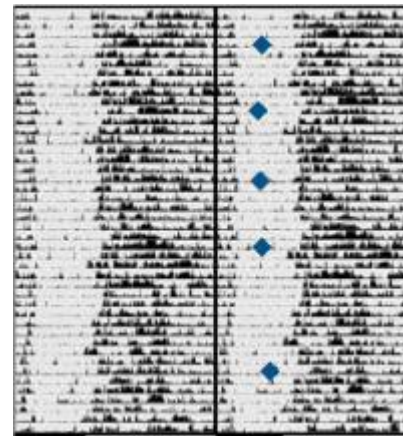
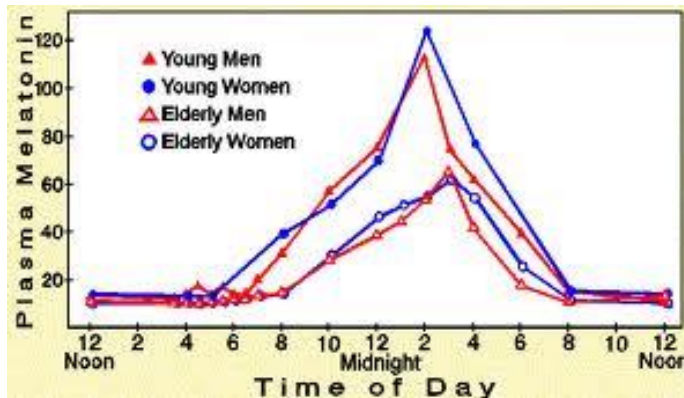


Sleep phenotypes can be described from these outputs.

- Short sleeper < 6 hours per night
- Long sleeper > 10 hours per night
- Circadian disturbances
 - Phase shift > 2hours
 - Irregular sleeper

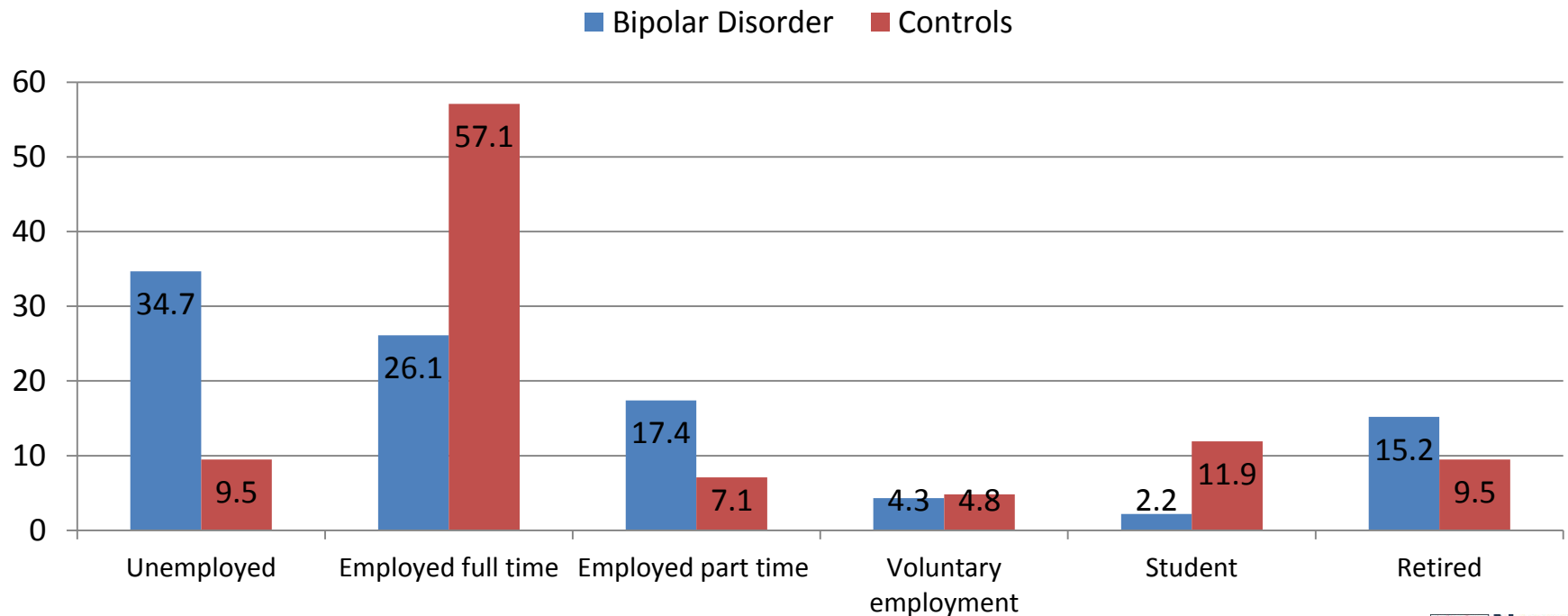
Core circadian rhythm

- The onset of the melatonin secretion rhythm is considered an accurate measure of circadian timing.
- 2 X 48 hour urine samples collected 14 days apart to measure levels of 6-sulphatoxymelatonin (aMT6S) – a metabolite of melatonin.
- Core circadian rhythm timing can be overlaid onto sleep onset timing and the relationship examined.

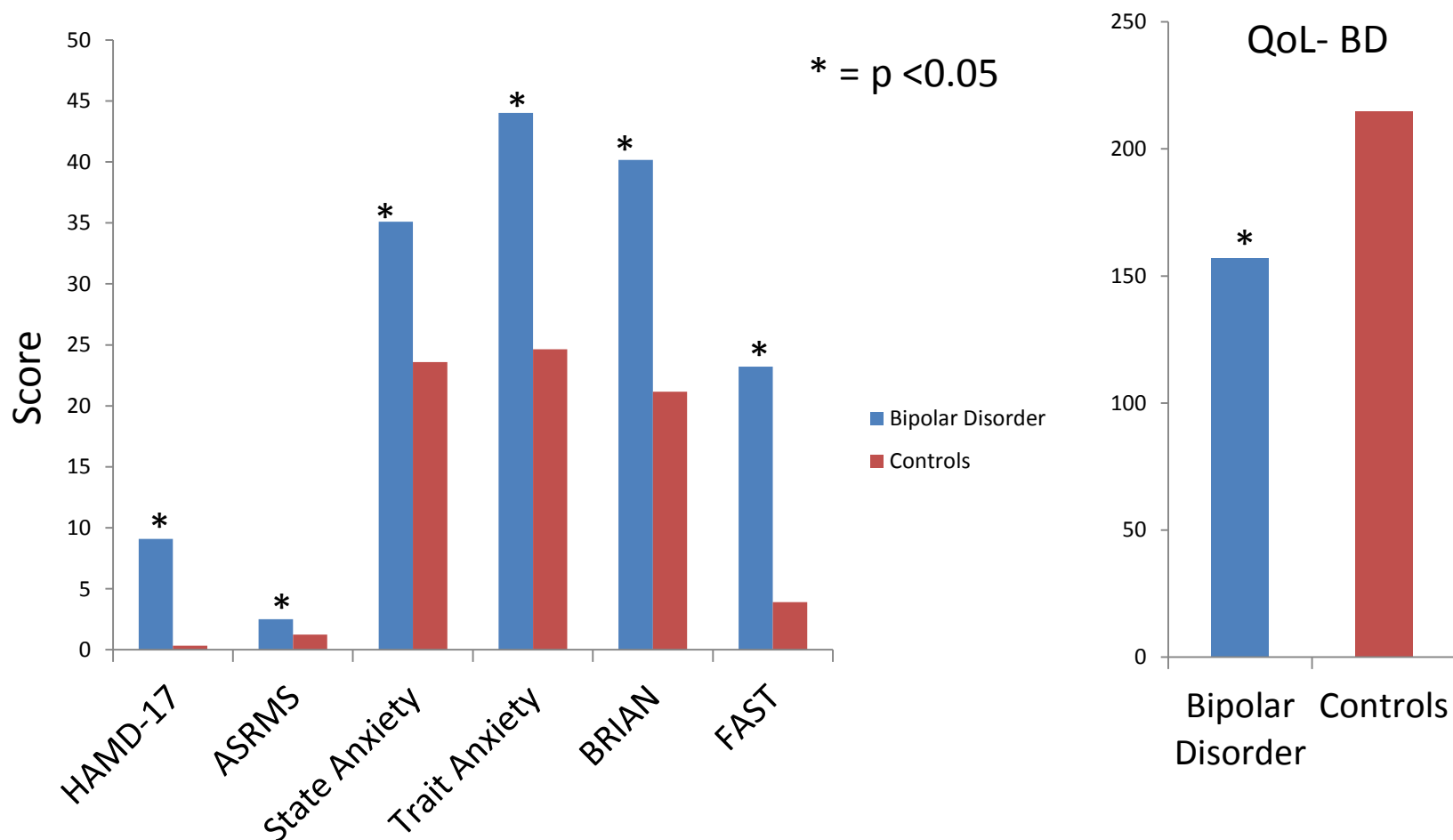


Participants

	Bipolar Disorder (n=46)	Controls (n=42)
Male	15 (33%)	13 (31%)
Female	31 (67%)	29 (69%)



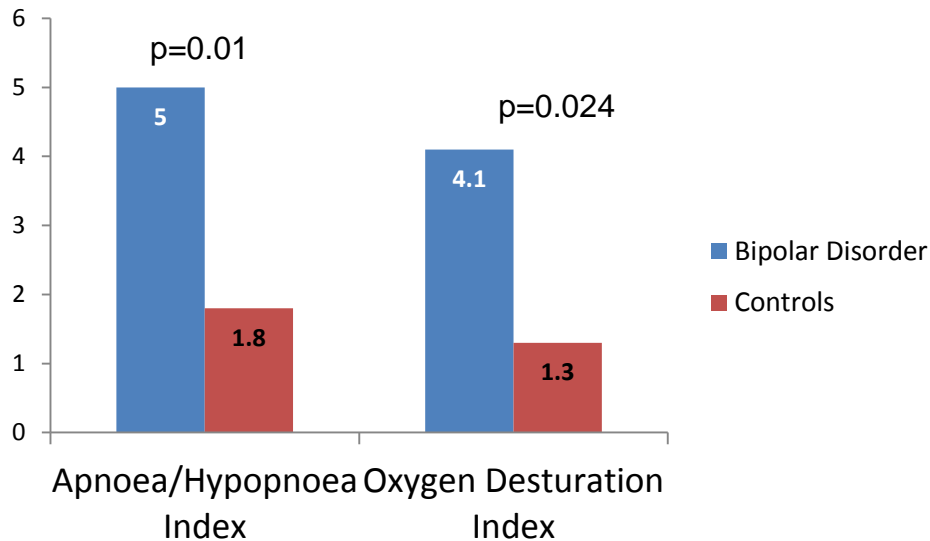
Mood, function and QoL



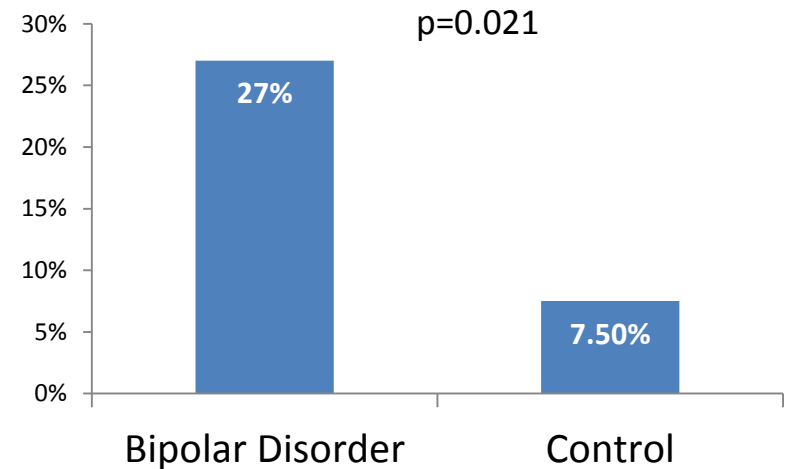
HAM-17 = 17 item Hamilton depression rating scale, ASRMS = Altman Self Rating Mania Scale, BRIAN = Biological Rhythm Interview of Assessment in Neuropsychiatry, FAST = Functioning Assessment Short Test.

Sleep Apnoea

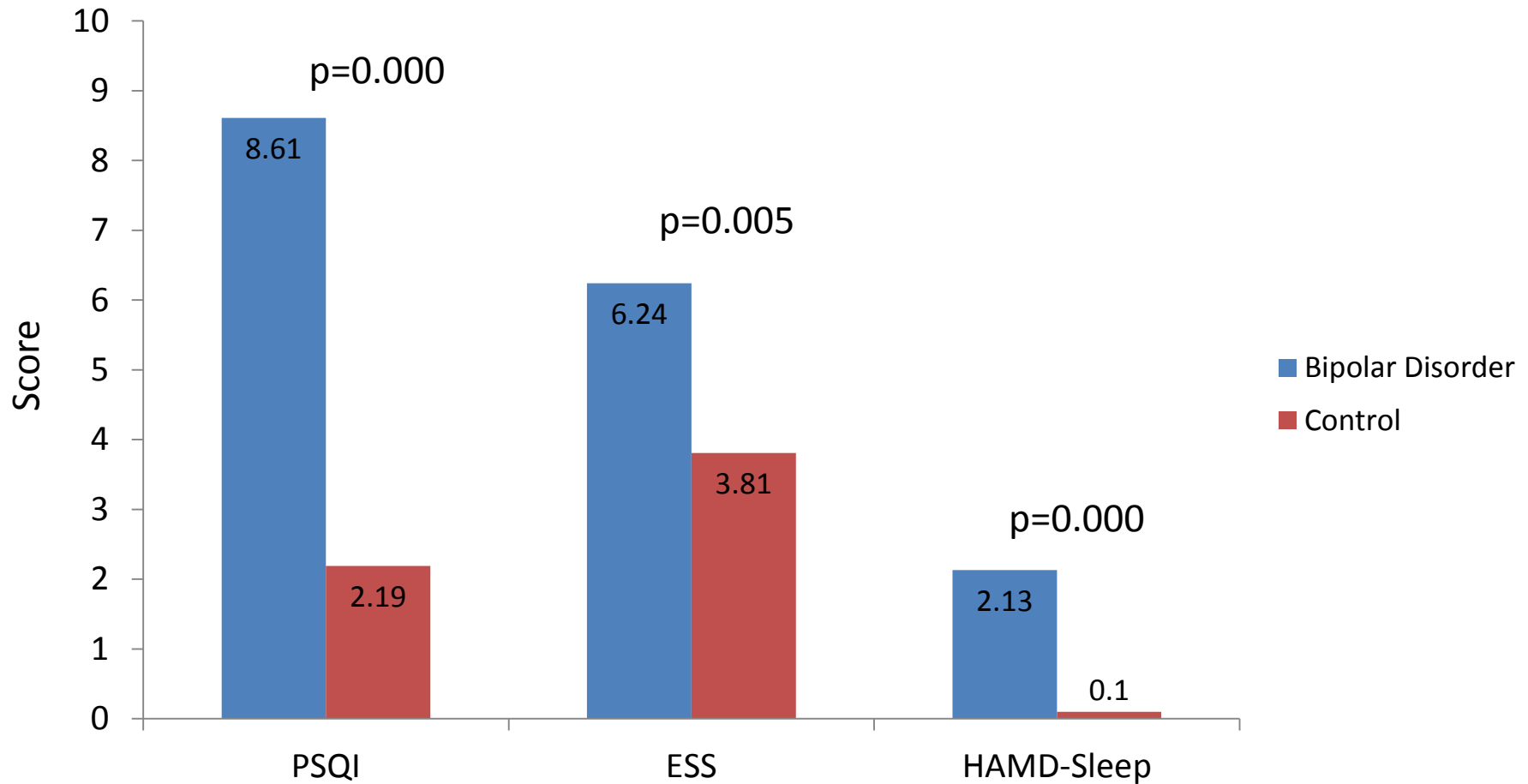
Mean score on AHI and ODI



Percentage of participants with AHI > 5



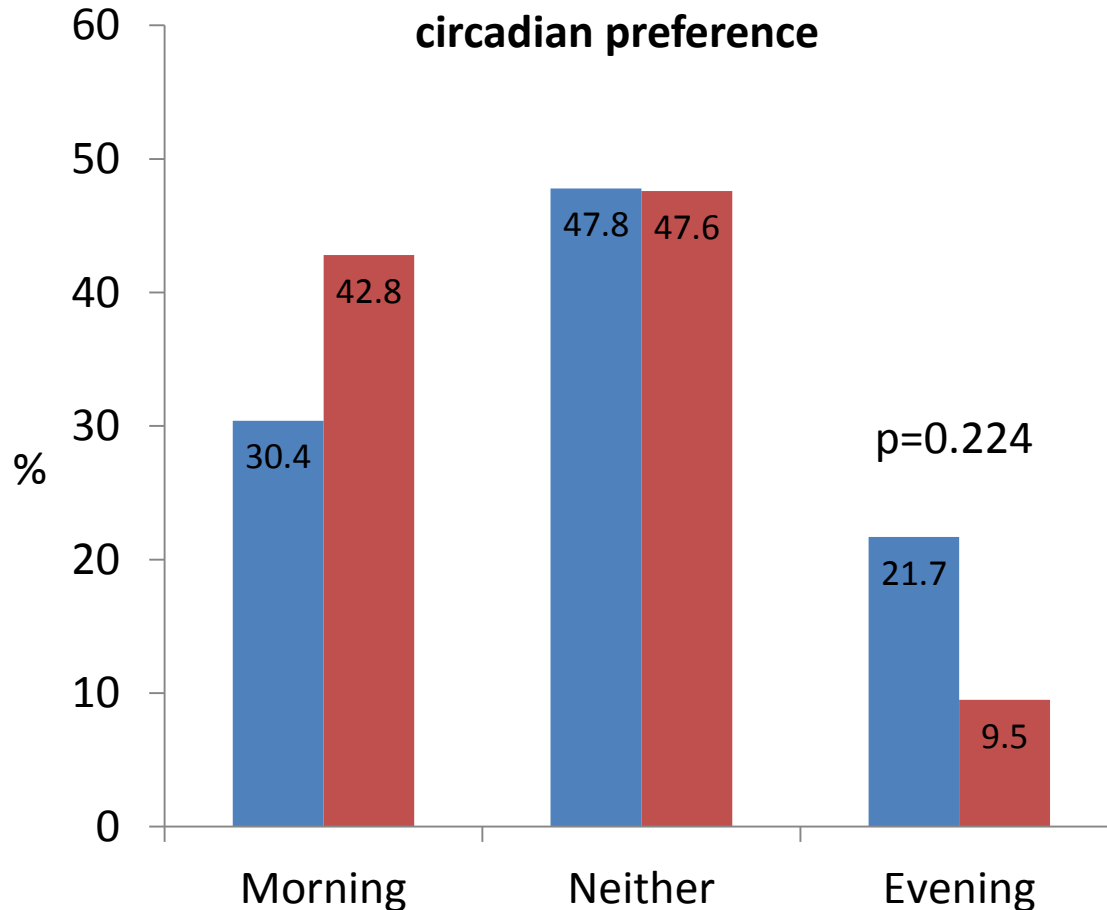
Baseline sleep measures



PSQI = Pittsburgh Sleep Quality Index, ESS = Epworth Sleepiness Scale, HAMD-Sleep = sleep items on Hamilton Depression Rating Scale

Circadian Preference

Percentage of participants with circadian preference



Morningness/evening total score

Bipolar Disorder 19.35

Control 21.79 $p=0.041$

■ Bipolar Disorder

■ Control

Sleep phenotypes

Nocturnal sleep period

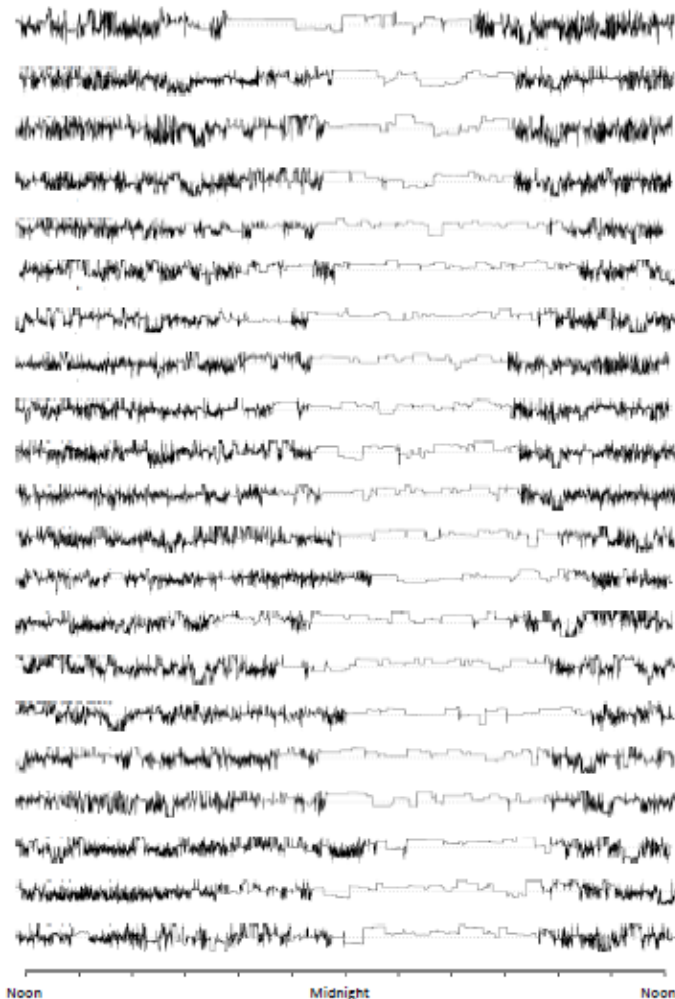
	Normal Sleep >6hrs <10hrs	Short (<6hrs)	Long (>10hrs)	Irregular
Control (n=42)				
Bipolar (n=46)				

Irregular sleepers may also be normal, short or long in terms of hours of nocturnal sleep

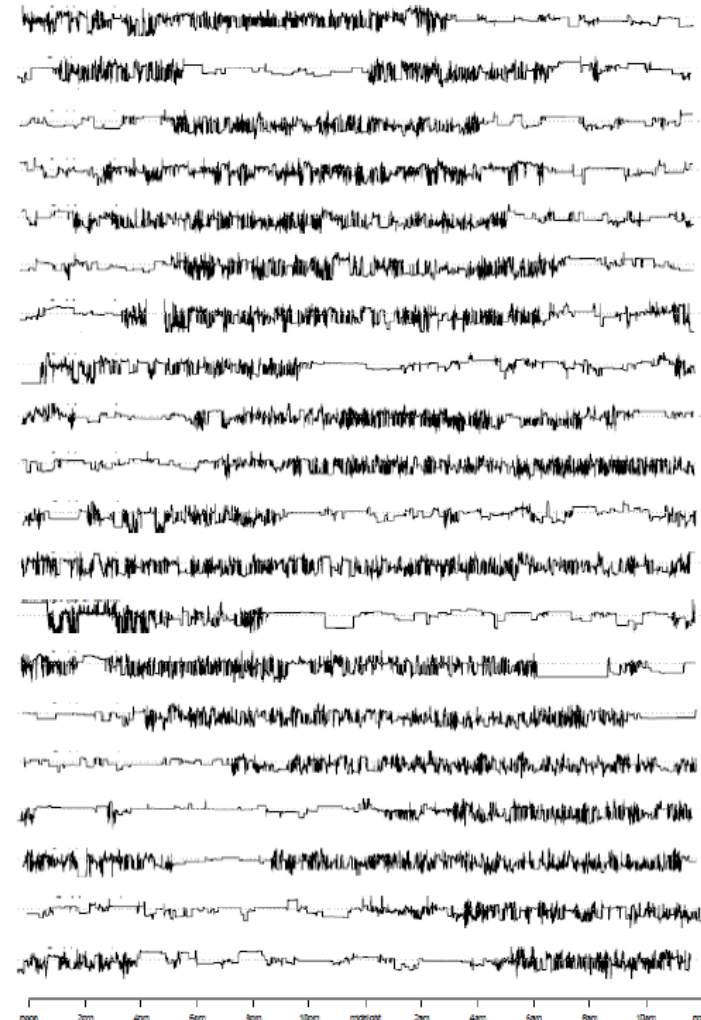
Normal Sleeper

Irregular sleeper

Mean nocturnal sleep time 7 hours

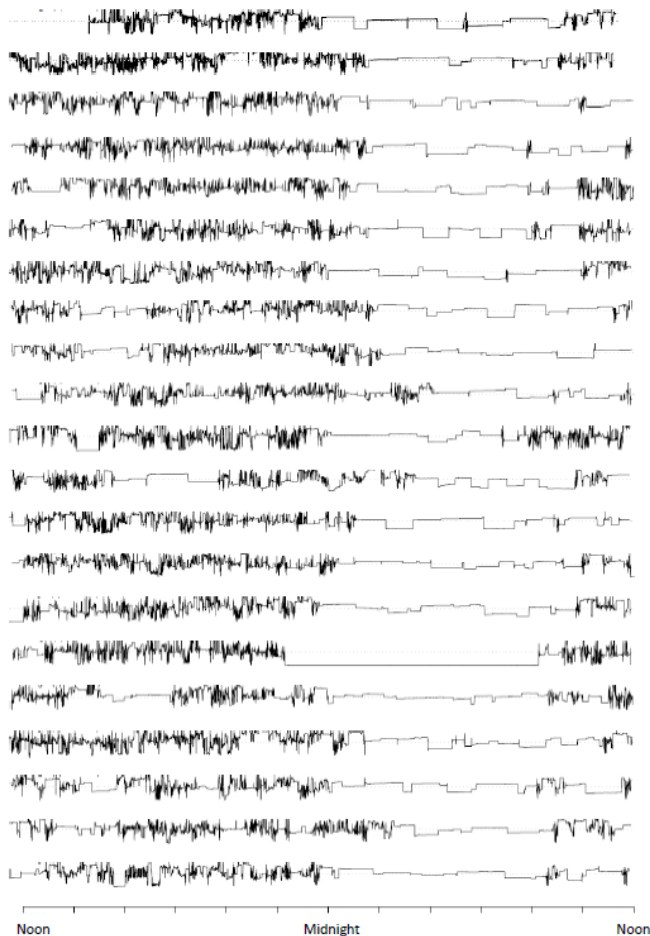


Mean nocturnal sleep time 6.1 hours



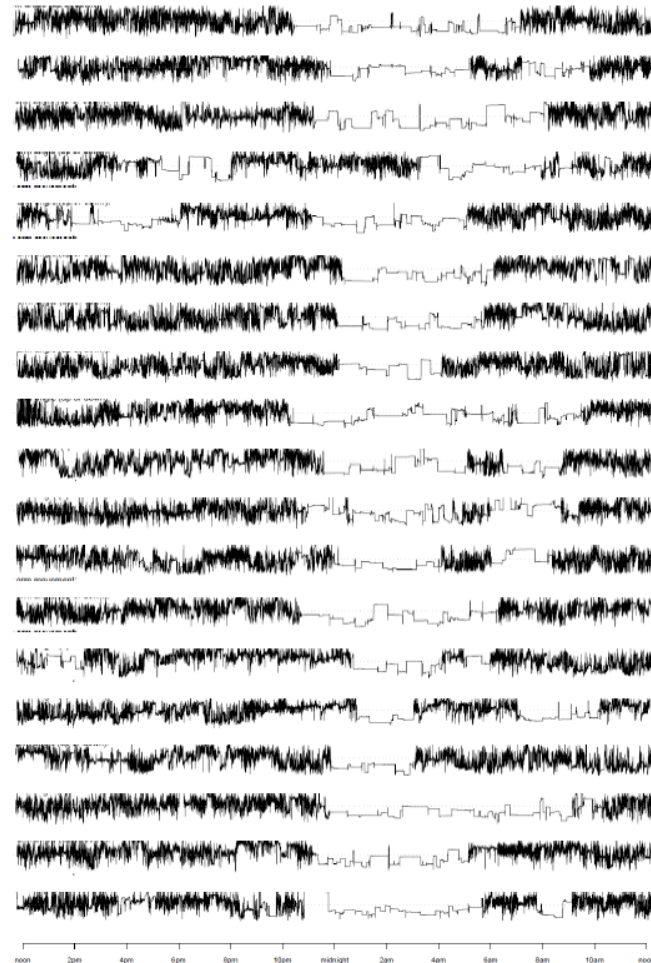
Long Sleeper

Mean nocturnal sleep 10.1 hours



Short Sleeper

Mean nocturnal sleep 5.6 hours



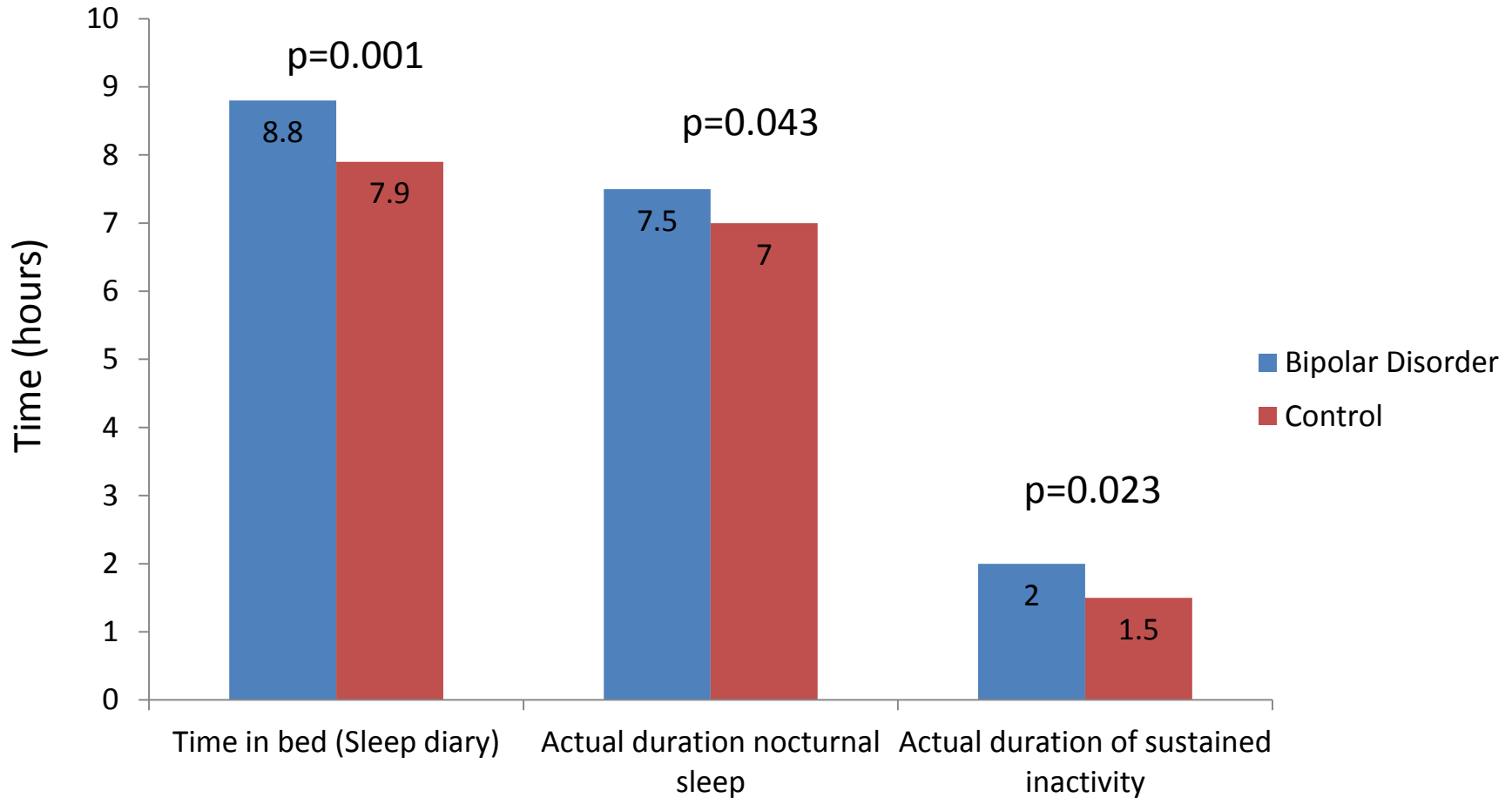
Sleep phenotypes

Nocturnal sleep period

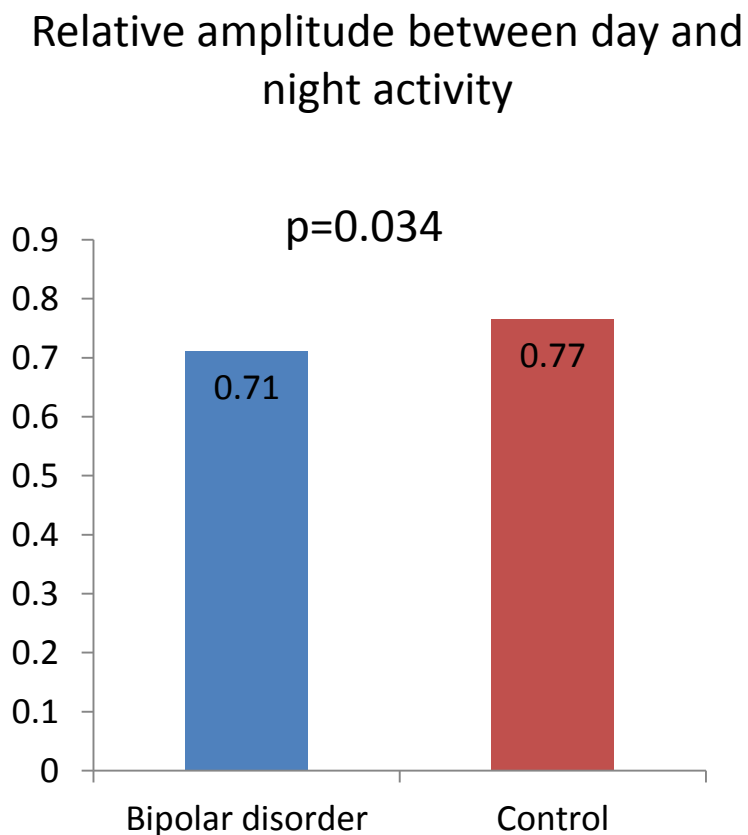
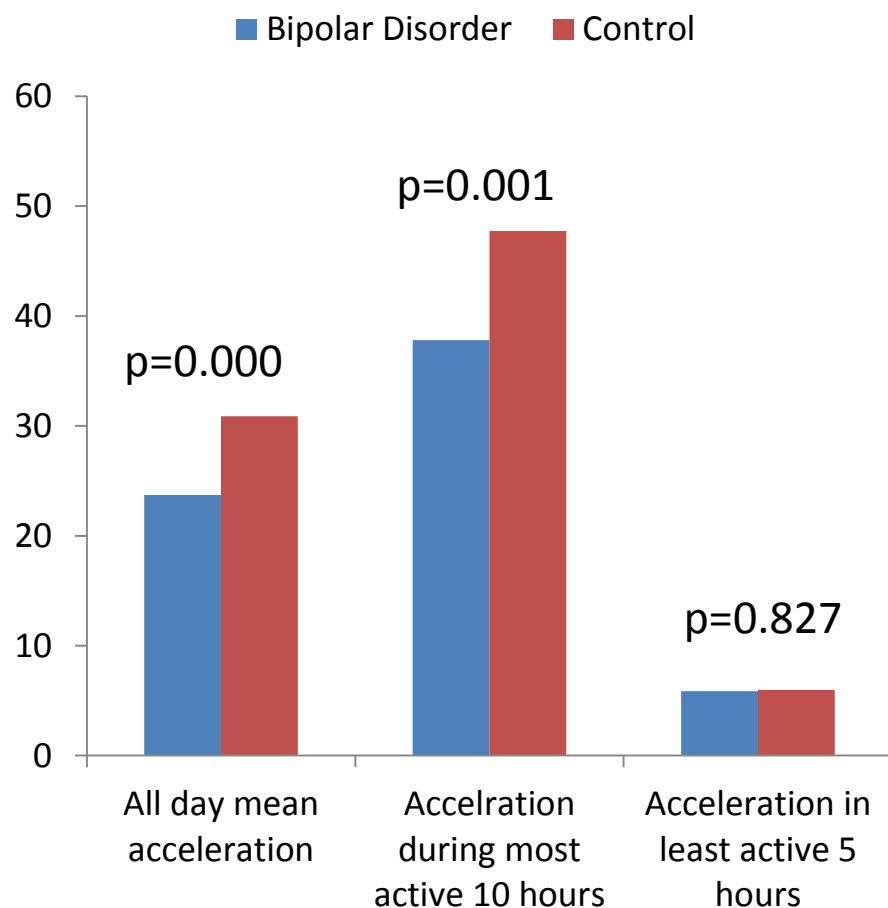
	Normal Sleep >6hrs <10hrs	Short (<6hrs)	Long (>10hrs)	Irregular
Control (n=42)	39	3	0	2
Bipolar (n=46)	40	4	2	8

Irregular sleepers may also be normal, short or long in terms of hours of nocturnal sleep

Accelerometer measured sleep



Accelerometer recorded movement



Association between sleep and cognitive function

Next Steps

- Compare groups on cognitive function
 - significant deficits in simple attention already identified.
- Examine data for associations between sleep and cognitive function.
 - Total sleep time
 - Sleep phenotypes
 - Circadian disorders
- Examine data for associations with physical activity
 - BMI
 - Mood
 - Function
 - QoL

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Thank you for listening