Posters

P.4.001 The effects of sleep disruption on central pain modulation: A polysomnographic study in healthy volunteers

L. Harrison[1]*, C. Durant[1], S. Wilson[2], J. Brooks[3], M.R. Munafo[4]. [1]*University of Bristol, Social Medicine, Bristol, United Kingdom;* [2]*Imperial College London, Neuropsychopharmacology, London, United Kingdom;* [3]*University of Bristol, CRIC Bristol, Bristol, United Kingdom;* [4]*University of Bristol, Experimental Psychology, Bristol, United Kingdom*

Purpose of study: Sleep and pain share a complex, reciprocal relationship: pain can disrupt sleep and, conversely, poor sleep can produce hyperalgesic effects. Hyperalgesia due to sleep-disturbance may be related to impaired endogenous pain control (i.e., descending pain facilitatory or inhibitory processes). Previous studies have found sleep to be associated with impaired endogenous pain-inhibitory function both in healthy volunteers and chronic pain patients [1,2]. This experimental within-subjects study sought to explore the effects of non-stage specific sleep disruption on endogenous pain networks in healthy volunteers.

Methods: Healthy volunteers took part in a single blind, randomised, cross-over study, in which they experienced one night sleep disturbance and one normal night sleep. For the sleep-disturbed condition, non-stage specific sleep disruption was implemented using a loud auditory stimulus played every 30 minutes after sleep onset. Live polysomnography was used to ensure that the participants awoke after each stimulus. The following morning, participants underwent quantitative sensory testing within an hour of waking. Pain inhibition was tested using the Diffuse Noxious Inhibitory Control (DNIC) paradigm [3]. In this paradigm, thermal heat stimuli were delivered to the left volar forearm as the phasic pain stimulus using a contact thermode (Pathway/CHEPS, Medoc) A cold pressor test acted as the conditioning stimulus, requiring each participant to immerse their contra-lateral hand (right) into a water bath maintained at 2–4ºC. A DNIC index was calculated as the average percentage change in thermal pain ratings (NRS 0–10) during the cold pressor task within the testing session (i.e., [(mean thermal pain rating during the cold pressor task)/(mean thermal pain rating prior to cold pressor)] × 100). One-way analysis of variance (ANOVA) tests were used to establish whether there were group differences in subjective pain ratings.

Results: Participants (n = 20; 10 females) had an average age of 23.16 years (SD = 3.07, range 20–33). Following a normal night sleep, average thermal pain ratings were 6.11 (SD = 1.96) compared to 6.85 (SD = 1.69) in the disturbed condition but no clear difference was observed between the groups ($F[1,19] = 2.99$, $p = 0.10$). There was weak evidence to suggest the normal (8.75; SD = 1.68) and disturbed conditions differed (8.93; SD = 1.37) on average cold pressor test ratings ($F[1,19] = 3.692$, $p = 0.07$). However, the DNIC index was found to be higher after sleep disturbance (59.58 vs. 79.04; $F[1,19] = 22.16$, $p < 0.001$). Associations between objective measures of sleep, pain sensitivity and central pain modulation were also explored.

Conclusions: Our findings indicate that sleep disturbance can impair pain modulation, specifically endogenous descending pain inhibitory systems. Impairments in the descending pain inhibitory circuits can have significant consequences for dealing with the immediate sensation and threat of pain. Such impairments and in particular, abolished DNIC effects, have been found in a number of chronic pain conditions. Developing a better understanding of the hyperalgesic effects of sleep disturbance on central pain systems could be critical in improving interventions for chronic pain patients.

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P.4.002 Successful antidepressant chronotherapeutics enhance fronto-limbic neural responses and connectivity in bipolar depression

B. Vai[1]*, S. Poletti[1], I. Bollettini[1], E. Smeraldi[1], C. Colombo[1], F. Benedetti[1]. [1]*IRCCS Ospedale San Raffaele, Department of Clinical Neurosciences, Milan, Italy*

Introduction: The identification of predictors of antidepressant response in bipolar depression may provide new potential enhancements in treatment selection.

Several authors suggested that abnormalities within fronto-limbic structures might provide a neurobiological basis for the pathophysiology and maintenance of the bipolar disorder [1,2]. Neuroimaging studies confirmed alterations within this network in BD and consistently reported a reduced functional and effective connectivity. Depression recovery has been consistently associated with activity of fronto-limbic structures including the ACC, medial prefrontal cortex, DLPFC, Amy and insula, with higher baseline metabolic rates in ACC and Amy as correlates of antidepressant response. The chronotherapeutic combination of repeated total sleep deprivation and light therapy (TSD+LT) can acutely reverse depressive symptoms in approximately 60% of bipolar patients, also involving the life-threatening suicidal symptoms. Due of its rapidity and its multi-target mechanism of action, chronotherapeutics has been proposed and confirmed as a model for antidepressant treatment to investigate biomarkers of clinical recovery [3].

Despite the proposed role of cortico-limbic circuitries in BD, no study evaluated the hypothesis that changes of cortico-limbic connectivity and of neural responses in emotional processing could parallel antidepressant response in bipolar depression. By combining conventional fMRI with a technique that allows to investigate the connectivity in terms of causal relationships between regions (Dynamic Causal Modeling, DCM), we investigated the effect of TSD and LT treatment on neural responses to negative facial expressions in a homogeneous sample of bipolar depressed patients.

Method: We used fMRI with Dynamic Causal Modeling (DCM) to study the effect of chronotherapeutics on neural responses to emotional faces and effective connectivity in healthy controls (HC, $n = 35$) and bipolar depressed patients either responder (RBD, $n = 26$), or non responder (nRBD, $n = 11$) to 3 consecutive TSD+LT. Twenty-four DCM models, exploring model space between anterior cingulate cortex (ACC), dorsolatelar prefrontal cortex (DLPFC), Amygdala, fusiform gyrus, and visual cortex were constructed. Bayesian Model Averaging provided DCM parameters, subsequently entered into statistical analyses.

Results: After treatment, patients significantly increased their neural responses in DLPFC, ACC and insula to emotional stimuli, but nRBD had lower baseline and endpoint neural responses than RBD ($pFWE < 0.05$). DCM showed that only RBD patients had a significant increased intrinsic connectivity from DLPFC to ACC ($t = 2.74$; $p = 0.011$), and reduced the modulatory effect of the task on the connection Amy–DLPFC ($t = 2.2$; $p = 0.037$).

Conclusion: Our study revealed that the clinical antidepressant response to chronotherapeutics is associated with an increase of neural responses and effective connectivity within prefrontal cortico-limbic networks during the implicit regulation of affective states. A rebalancing of neurotransmitters and a recover of the homeostasis between neural systems may underlie these changes. Furthermore, the functional activity seems to differentiate RBD from nRBD at the baseline, thus suggesting that fMRI might provide biomarkers which could help to appropriately select treatment, and predict and monitor its efficacy in BD.

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P.4.003 Timing matters: vulnerability and resilience to acute trauma vary according to the circadian phase at which exposure occurs

S. Cohen[1]*, E. Vainer[2], M.A. Matar[2], N. Kozlovsky[2], Z. Kaplan[2], J. Zohar[3], A. Mathé[4], H. Cohen[2]. *[1]Ben Gurion University of the Negev, Psychology, Beer-Sheva, Israel; [2]Mental Health Center Ministry of Health Anxiety and Stress Research Unit Ben-Gurion University of the Negev, Faculty of Health Sciences, Beer-Sheva, Israel; [3]Ministry of Health The Chaim Sheba Medical Center Ramat-Gan Israel Sackler Medical School Tel-Aviv University Israel, Division of Psychiatry, Tel-Aviv, Israel; [4]Karolinska Institutet – Clinical Neuroscience Karolinska University Hospital Huddinge SE-141 86, Stockholm, Sweden*

The hypothalamic–pituitary–adrenal (HPA) axis displays a characteristic circadian pattern of corticosterone release, with higher levels at the onset of the active phase and lower levels at the onset of the inactive phase. Since corticosterone levels modify the response to stress and influence the susceptibility to and/or severity of stress-related sequelae [1], we examined the effects of an acute psychological trauma applied at different circadian phases on behavioral stress responses.

Rats were exposed to predator scent stress (PSS) either at the onset of the inactive phase [at lights-on ($ZT = 0$)], or at the onset of the active phase [lights-off ($ZT = 12$)]. Anxiety-like behaviors were assessed seven days after