

## Poster Presentations

**P001 COMMUNICATION FROM THE CEREBELLUM TO THE NEOCORTEX DURING SLEEP SPINDLES**

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**Introduction** Surprisingly little is known about neural activity in the sleeping cerebellum.<sup>5–17</sup> Using long-term wireless recordings, we have made routine recordings of local field potentials (LFPs) and action potentials for the entirety of natural sleep in non-human primates.

**Methods** We were able to record simultaneously from the primary motor cortex (M1), the thalamus and the cerebellum using both rigid multi-contact linear electrode arrays and flexible microwires.<sup>11–12</sup> Recording for the entirety of the natural sleep was achieved using a custom-made wearable device.

**Results** We find that the M1 and cerebellum communicate with each other during sleep,<sup>13–14</sup> with cerebellum-to-M1 signals passing via the thalamus. We find that both M1 and cerebellar neuronal firings are broadly synchronous and phase-locked to the sleep cycle.<sup>7</sup> Additionally, both spikes and LFPs in M1 and cerebellum also show coherence at slow (<1Hz), delta (1-4Hz) and alpha (7–15Hz) frequencies.<sup>8–15–16</sup> We also see phase-locking between the spikes of M1 and the LFPs of the cerebellum (and vice versa) at these same frequencies. Using Granger causality analysis on the LFPs we were able to observe directed connectivity from motor cortex to the cerebellum in deep sleep. This suggested a neocortical origin of slow oscillations. By contrast, sleep spindles (in the alpha frequency range) in light sleep revealed a causal influence from the cerebellum to motor cortex, going via the thalamus.

**Discussion** Our results shed new light on the mechanisms of sleep spindle generation<sup>9</sup> and show that the cerebellum is an active participant of sleep. We postulate that the cerebello-thalamo-neocortical pathways is implicated in sleep-dependent consolidation of procedural learning.<sup>1–4–6–18–20</sup>

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**P002 USING ANTHROPOMETRIC MEASUREMENTS TO DETERMINE THE IDEAL MATTRESS FIRMNESS**

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**Introduction** There is limited evidence to suggest that a 'one-size fits all' mattress provides the appropriate support in individuals with diverse body shapes, a greater understanding of how different mattresses affect the human body is required. By having a more objective approach to choosing a mattress, individuals may improve quality of sleep.

**Materials** A ten-camera infrared movement analysis system recorded Upper-Mid Thoracic, Mid-Lower Thoracic, Lower Thoracic–Upper Lumbar, Upper-Lower Lumbar and Lower Lumbar–Pelvic areas of the spine in side lying. Deviations away from a neutral position were assessed under different conditions. Three aesthetically identical mattresses were tested, internally each mattress contained a different firmness of spring unit (soft, medium, firm). In addition, height, weight, shoulder width and hip circumference measurements were taken to determine differences in body types.

**Results** Spinal alignment was assessed on sixty healthy participants and no significant differences were seen between the different mattress configurations. However further analysis showed significant differences in spinal alignment between the different mattress conditions within different body shape subgroups. Subgroups were defined using body weight, height, BMI, shoulder width and hip circumference. Those with a higher body weight had a more neutral spinal alignment when on a firmer mattress, whereas those with a lower body weight were better suited to a softer mattress. Shorter people were better aligned on a softer mattress, and a medium mattress kept the spine in a more neutral position amongst taller individuals.

**Discussion** This study suggests that a ‘one-size fits all’ approach to mattresses may not be appropriate and contrasting body types need different levels of support to improve overall spinal alignment. The use of simple anthropometric measurements could make the selection of the most appropriate mattress easier for the public.

P003

### RANDOMISED, PLACEBO-CONTROLLED STUDY OF SOLRIAMFETOL FOR EXCESSIVE DAYTIME SLEEPINESS IN NARCOLEPSY TYPES 1/2

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**Introduction** Solriamfetol (formerly JZP-110), a dopamine and norepinephrine reuptake inhibitor, has been approved in the United States to improve wakefulness in adults with excessive daytime sleepiness (EDS) associated with narcolepsy (75–150 mg) or obstructive sleep apnoea (OSA) (37.5–150 mg). A Marketing Authorisation Application for these indications is under review with the European Medicines Agency. This phase 3 study assessed safety and efficacy of solriamfetol in participants with narcolepsy types 1 and 2 (NT1/2).<sup>1</sup>

**Methods** In this 12-week, double-blind, randomised, placebo-controlled study, participants with or without cataplexy were randomised to solriamfetol 75 mg, 150 mg, 300 mg, or placebo. Eligibility criteria: NT1/2 diagnosis; mean sleep latency <25 minutes on Maintenance of Wakefulness Test (MWT); Epworth Sleepiness Scale (ESS) score ≥10. Exclusion criteria: medications that could affect EDS or cataplexy; night-time or variable shift work; other conditions causing EDS.

**Results** 236 participants received ≥1 dose of solriamfetol (67.2% female; 80.2% white). Baseline MWT mean sleep latency: 7.5 minutes; baseline ESS score: 17.2. Solriamfetol significantly increased MWT sleep latency at week 12 (P<0.0001 for 300 mg and 150 mg); least squares (LS) mean change: 12.3 minutes for 300 mg, 9.8 for 150 mg, 4.7 for 75 mg, and 2.1 for placebo. Solriamfetol significantly decreased ESS scores at week 12 (P<0.0001 150 mg and 300 mg; P<0.05 75 mg). LS mean change in ESS: -6.4 for 300 mg, -5.4 for 150 mg, -3.8 for 75 mg, and -1.6 for placebo. Most common treatment-emergent adverse events (TEAEs; ≥5%): headache, nausea, decreased appetite, nasopharyngitis, dry mouth, and anxiety. Discontinuations due to TEAEs were more frequent in solriamfetol 150 mg and 300 mg groups.

**Discussion** Solriamfetol improved wakefulness and reduced EDS in participants with NT1/2. Most AEs were mild to moderate.

**Support** Jazz Pharmaceuticals.

### REFERENCE

1. Thorpy MJ, et al. *Ann Neurol* 2019;**85**(3):359–370.

P004

### SOLRIAMFETOL FOR EXCESSIVE DAYTIME SLEEPINESS IN OBSTRUCTIVE SLEEP APNOEA: A RANDOMISED CONTROLLED TRIAL

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**Introduction** Obstructive sleep apnoea (OSA) is often associated with persistent excessive daytime sleepiness (EDS) despite sleep apnoea therapy. There are currently no approved treatments in the European Union for the treatment of EDS in this population. Solriamfetol (formerly JZP-110), a dopamine and norepinephrine reuptake inhibitor, has been approved in the United States to improve wakefulness in adults with EDS associated with narcolepsy (75–150 mg) or OSA (37.5–150 mg). A Marketing Authorisation Application for these indications is under review with the European Medicines Agency. This study evaluated the efficacy and safety of solriamfetol for treatment of EDS in participants with OSA with current or prior sleep apnoea treatment.<sup>1</sup>

**Methods** In this double-blind, placebo-controlled, parallel-group phase 3 trial, participants with OSA and associated EDS were randomly assigned to solriamfetol 37.5 mg, 75 mg, 150 mg, or 300 mg or placebo for 12 weeks.

**Results** Of 476 randomised participants, 459 were included in the prespecified efficacy analyses. Co-primary endpoints (Maintenance of Wakefulness Test sleep latency, Epworth Sleepiness Scale score) were met at all solriamfetol doses (P<0.05), with dose-dependent effects observed at week 1 and maintained over the study duration. All doses except 37.5 mg resulted in significantly higher percentages of participants reporting improvement on Patient Global Impression of Change (key secondary endpoint; P<0.05). Adverse events (AEs) were reported in 47.9% of placebo- and 67.9% of solriamfetol-treated participants; 5 participants experienced serious AEs (2 [1.7%] placebo, 3 [0.8%] solriamfetol); none were deemed related to study drug. The most common AEs with solriamfetol were headache (10.1%), nausea (7.9%), decreased appetite (7.6%), anxiety (7.0%), and nasopharyngitis (5.1%).

**Discussion** Solriamfetol significantly improved wakefulness and reduced sleepiness in participants with OSA and EDS. Most AEs were mild or moderate.

**Support** Jazz Pharmaceuticals.

### REFERENCE

1. Schweitzer PK, et al. *Am J Respir Crit Care Med* 2019;**199**(11):1421–1431.