Sleep is an extremely sensitive biomarker of neurological conditions and is impaired in several neurodevelopmental disorders (NDD). Sleep disturbances are reported in 60% of patients carrying SYNGAP1 gene mutations, an haploinsufficiency associated with intellectual disability (ID), autism spectrum disorder (ASD) and epilepsy. We previously found an absence-seizure phenotype in the novel heterozygous Syngap+/- Gap rats model, showing spontaneous spike and wave discharges (SWDs) that were blocked by acute treatment with a standard anti-absence drug Ethosuximide (ETX). Here, we assessed sleep impairments in Syngap+/- Gap rats and tested a possible relation between altered sleep and the seizure phenotype.

Wireless EEG+EMG recordings were obtained during 6 consecutive days in 10 Syngap+/- Gap, WT, and saline day (black line). Black, grey and open squares indicate significant differences comparing BL vs. Saline day, and EXT vs. Saline, respectively. ETX treatment successfully blocked SWDs in Syngap+/- Gap rat model, showing spontaneous spike and wave discharges (SWDs) that were blocked by acute treatment with a standard anti-absence drug Ethosuximide (ETX). Here, we assessed sleep impairments in Syngap+/- Gap rats and tested a possible relation between altered sleep and the seizure phenotype.

Compared to control littermates, Syngap+/- Gap rats showed increased number of SWDs1 through the whole circadian cycle and a significant decrease of REM sleep across the day2, expressed in shorter bouts. Wake and non-REM sleep displayed less and longer bouts, without total time differences. ETX treatment successfully blocked SWDs in Syngap+/- Gap rats during the reported drug half-life time, but not during the subsequent dark phase3. Strikingly, REM sleep deficits in Syngap+/- Gap were reverted during ETX treatment day across the entire circadian cycle4, by increasing the number of REM sleep bouts. No effect was observed on Wake nor non-REM sleep, although the latter showed equivalent number and durations to WT controls during ETX treatment.

Our results suggest that seizure activity impairs sleep, possibly by disturbing the normal homeostatic flow of brain states, and ultimately affecting REM sleep expression. (Figure 1) These impairments may contribute to cognitive and social deficits in SYNGAP1 haploinsufficiency.

Abstract 11 Figure 1 EXT treatment blocks SWDs and reverts REM sleep impairment in Syngap+/- Gap rats. A) Circadian distribution of the number of SWDs displayed by Syngap+/- Gap rats during baseline (grey area), ETX treatment day (pink line) and saline treatment day (black line). B) Circadian distribution of minutes spent by hour on REM sleep showed by Syngap+/- Gap rats during baseline (grey area), EXT treatment day (pink line) and saline day (black line). Black, grey and open squares indicate significant differences comparing BL vs. ETX day, BL vs. Saline day, and ETX vs. Saline, respectively (2-tailed paired t-test, Holm-Bonferroni corrected).
Results Of 141 patients, there was a two-thirds male predominance, and half of the patients (56%) above 45 years of age and sleepy at baseline (Epworth Sleepiness Score >10, 48.9%). 114 patients (81%) were diagnosed with moderate or severe OSA. 54 patients (38.3%) achieved good adherence (≥70% of nights with ≥4 hours usage), with an average of 4.7 hours of PAP usage per night used. Patients receiving FTF PAP education had a comparable level of good adherence (38.03% versus 38.57%, p=0.915), and hours per nights used (4.76 versus 4.61 h/night, p=0.711) to remotely educated patients. More severe OSA, lower mask leak, and a nasal mask were associated with achieving good PAP adherence.

Discussion PAP adherence of newly diagnosed individuals with OSA during the COVID-19 pandemic was modest at 38.30%, and not significantly affected by remote PAP education delivery, but rather the effects of the COVID-19 pandemic.

THE EFFECT OF CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) ON KEY PLASMA METABOLITES IDENTIFYING OBSTRUCTIVE SLEEP APNEA HYPOPNEA SYNDROME (OSAHS)

We recently applied untargeted metabolomic profiling on the plasma obtained from consecutive attenders referred for conventional Level 3 home-sleep studies with excessive daytime somnolence, comparing 17 OSAHS patients (AHI≥15, Epworth Score 13.5±4.5) with 16 age, gender, and BMI matched sleepy subjects (sleepy snorers (SS)) with negative home polysomnography tests (AHI<15, Epworth Score 12.1 ±7.0). We reported 6 biologically plausible plasma metabolites that can differentiate OSAHS from SS of similar phenotype with an AUC of 0.982 (95% CI: 0.9-1.0) (figure 1), with these key metabolites being essential lipids involved in protein synthesis and the formation of antioxidative, antiglycat- ing, and free radical scavenging dipeptides. We now report early changes in these biomarkers following CPAP in those with OSAHS.

11 OSAHS patients with AHI≥15 (63.6% male, Age 54.4 ±6.9, BMI 34.2±4.0, AHI 47.6±25.6, Epworth 13.7±4.8) were commenced on standard auto-adjustment CPAP devices (Phillips DreamStation set at 4 to 18 cm H2O). Mean use of CPAP was 6.6±1.4 hours and average residual AHI was 6.9 ±6.0. Plasma was sampled pre and post treatment (42-70 days treatment), and metabolomically assessed using the Q Exactive Hybrid Quadrupole-Orbitrap mass spectrometry platform. 16 sleepy snorers with AHI<15 (75.0% male, Age 46.1 ±12.5, BMI 34.6±5.9, AHI 6.8±4.4, Epworth 12.1±7.0) were sampled at baseline only.

Our previously reported biomarkers associated with processes such as oxidative stress, inflammation, and dysregulation of energy homeostasis improve with short-term treatment with CPAP towards the level of sleepy snorers of similar age, phenotype, and no OSAHS (figure 2). We feel these metabolites have significant potential in the future care pathways of...