Introduction: Sleep and wakefulness are no more considered mutually exclusive states. In the last decades, several findings pointed out the local and use-dependent nature of sleep features, demonstrating that electrophysiological patterns of both sleep and wakefulness can co-occur simultaneously, in different cortical areas. By definition, Sleep Onset (SO) is an instable state of transition between wakefulness and sleep, and its spatiotemporal dynamics have been exhaustively described in healthy adulthood. The human sleep electroencephalographic (EEG) topography is characterized by strong age-related changes. However, the specific local EEG features of SO during preadolescence and healthy aging have been not extensively described.
Materials and Methods: We aimed to investigate regional and temporal electrophysiological patterns of SO in a group of 23 preadolescents (9-14 years, Exp. 1) and in a group of 36 older participants (59-81 years, Exp 2). Specifically, the pre- vs- post-SO changes in the topography of the 1 Hz bins' EEG power and the time course of the EEG frequency bands during the wake-sleep transition were assessed in both experimental groups. Furthermore, we compared delta activity and delta/beta ratio during the SO between these two groups (Exp. 1: preadolescent, Exp. 2: elderly) and a group of 40 healthy young adults (18-29 years).
Results: In Exp. 1 preadolescents exhibited: a) a generalized post-SO increase in the low frequencies (0.5-6 Hz), especially in the lowest bins (0.5-2 Hz) with a central predominance; b) activity in the 12-13 and 14-15 Hz increased over frontal or central areas, respectively; c) the slowest bins in the beta band showed a slight central increase post-SO. Compared to young adults, delta/beta ratio in preadolescents was higher in posterior areas in both pre- and post-SO and lower in frontal areas in the post-SO. This finding was paralleled by higher delta power in posterior (pre-SO) and centro-posterior areas (post-SO) and lower delta activity in frontal areas (post-SO) in preadolescents.
Exp. 2 showed that elderly had: a) a generalized post-SO power increase in the slowest frequencies; b) a specific pattern of post-SO changes of the alpha frequency; c) a slight post-SO increase of the sigma activity, whereas its highest bins exhibited a frontotemporal decrease. Older adults showed a global decline of the delta power and delta/beta ratio in both pre- and post-SO intervals compared to young adults.
Conclusions: In preadolescents the predominance of the delta activity in more posterior areas compared to young adults and the observation of a not completely mature spindles should be ascribed to development-related maturational processes, pointing to higher homeostatic need from the more mature areas, rather than to different SO dynamics. The reduced delta activity and delta/beta ratio observed in elderly likely depict lightened homeostatic pressure at SO. Taken together, findings parallel the SO process in adults, with a notable difference concerning homeostatic process. In fact, most differences point to crucial developmental changes in homeostatic regulation that play a role in determining age-related wake-sleep transition features.
Acknowledgements: Dr Ludovica Annarumma is funded by grants from the Italian Ministry of Health, grant number RF-2018-12365682.

THE IMPACT OF OBSTRUCTIVE SLEEP APNEA AND ITS TREATMENT IN CELLULAR AND MOLECULAR AGING

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Introduction: Obstructive Sleep Apnea (OSA) is one of the most common sleep disorders worldwide. There is sizable evidence showing the association of OSA with aging by inducing cellular and molecular aging mechanisms (*Gaspar, et al. 2017, 2021*). Understanding OSA putative negative effect on aging progression might contribute to understand new strategies to develop new OSA diagnosis and treatment but also to counteract aging.
Aim: To investigate whether OSA patients show peripheral aging-related cellular and molecular impairments and the impact of OSA treatment.
Materials and Methods: Twenty-six adult male patients (56±10 years) diagnosed with severe OSA were monitored from the moment of diagnosis with polysomnography (PSG), and up to 4 months and 24 months of treatment with continuous pressure positive mask (CPAP) and 13 men of the same age group (49±8 years). Several hallmarks of cellular and molecular aging were evaluated in Peripheral Blood Mononuclear Cells (PBMC). This study was approved by the ethical committee of the Faculty of Medicine of the University of Coimbra and by Coimbra Hospital and University Centre, Portugal.
Results: OSA patients' blood samples show increased mRNA levels of genomic instability players, in comparison with 24 months of treatment ($p<0.05$). In addition, telomeres of OSA patients showed to be shorter in comparison to healthy controls ($p<0.01$), an alteration that accentuates with the treatment (t_{4M}: $p<0.01$; t_{24M}: $p<0.001$). Regarding proteostasis impairments, mRNA levels of autophagy receptors in OSA patients are upregulated in relation to age-matched controls ($p<0.01$).
Conclusions: These results suggest that OSA might induce impairments in hallmarks of aging and CPAP treatment might partially re-stablish some alterations. Hence, OSA early diagnosis and specific treatment may constitute a new strategy to delay ageing.
Acknowledgements: This work was financed by the European Regional Development Fund (ERDF), through the Centro 2020 Regional Operational Programme, under the project CENTRO-01-0145-FEDER-000012 (HealthyAging 2020); through Operational Programme for Competitiveness and Internationalisation (COMPETE 2020) and Portuguese national funds via Fundação para a Ciência e a Tecnologia (FCT), under the projects POCI-01-0145-FEDER-029002 (noOSAnoAGEING, PTDC/MEC-MCI/29002/2017), UIDB/04539/2020 and UIDP/04539/2020; and by the European Social Fund through POCH - Human Capital Operational Programme and Portuguese national funds via FCT under PD/BD/135497/2018, 2020.04499.BD and 2021.05334.BD.
The authors have no conflicts of interest to declare.

THE LINK BETWEEN SLEEP AND GAIT AMONG COMMUNITY DWELLING ADULTS

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Introduction: Alarming recent findings indicate that older adults with poor sleep quality have as much as a 4.5-fold higher risk of falls. The potential comorbidity between reduced sleep quality and balance problems has led to growing interest in the study of the relationships between them. Gait and sleep are two basic, modifiable functions that decline throughout the aging process and are associated with deterioration in health and functional outcomes. Although seemingly distinct, both functions share common cognitive, psychological and physiological mechanisms; however, the associations between sleep and gait among community adults with no sleep or balance complaints are poorly understood. The present study aims to explore the associations between sleep indices and gait performance among community dwelling adults.
Materials and Methods: This cross-sectional investigation is based on the "Kibbutzim" longitudinal study. One hundred and three community-dwelling adults (mean age 64±13 years), with no sleep or gait complaints participated. Sleep was evaluated objectively by 7-days of actigraphy (ActiGraph, LLC) and by self-report. Measures included bedtime (BT), sleep duration (SD), sleep efficiency (SE), and wake after sleep onset (WASO). Gait parameters (speed, variability) were measured using the Dual-Task Paradigm, in which gait is assessed twice during a one-minute walk by a mobility lab (APDM Wearable Technologies, Inc.), once with (dual task – DT) and once without (single task – ST) an added cognitive load.
Results: Based on actigraphy, increasing age was significantly associated with earlier BT ($p=0.007$), lower SE ($p=0.1$) and increased WASO ($p=0.1$). Consistent with the literature, sex differences were found for objective (actigraphy, $p=0.002$) and subjective ($p<0.001$) SD, with women sleeping significantly longer than men. No sex differences were found for BT, SE or WASO. A significant main effect was found for SD on gait speed. When comparing gait speed by actigraphy-based SD tertiles (short / intermediate / long), gait speed was significantly slower under the DT condition in long

compared to short and intermediate sleep duration (p=0.018). No associations were found for stride length. These findings are consistent with studies demonstrating negative health outcomes for long vs. short and intermediate sleepers.
Conclusions: This study demonstrates early pre-clinical manifestations of comorbidity between sleep and gait, both of which significantly affect daily functioning in older adults. The Dual-Task Paradigm is a sensitive tool that can easily be used for early diagnosis of comorbid gait-sleep deterioration. Such investigations may pave the way to a better understanding of the mechanisms underlying their comorbidity and lay the groundwork for interventions.
Acknowledgements: Basic Research

ALTERED SLEEP BEHAVIOR IN A GENETIC MOUSE MODEL OF ALZHEIMER'S DISEASE FOLLOWING ANESTHETIC EXPOSURE

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Introduction: Due to demographic changes, the number of senior patients undergoing surgery and suffering from Alzheimer's disease (AD) is expected to expand. It has been hypothesized that anesthetics may deteriorate or even trigger the development of AD. Upon administration of anesthetics, AD patients may experience sleep disturbances, exacerbated initial postoperative emergence delirium or even postoperative delirium (POD), which may concomitantly lead to worsening of cognitive impairments. Recent research suggests that certain volatile anesthetics such as sevoflurane may not only cause short-term cognitive dysfunction but may even exacerbate AD-related long-term cognitive decline. Concurrently, accumulating evidence indicates a linkage of sleep disorders with AD not only as a symptom, but also as a potential facilitator of the disease. With this study, we aimed to examine face validity and constructive validity of the AD ArcAβ mouse model by inspecting whether anesthetic exposure has an altered detriment on sleep architecture. Additionally, we investigated potential predictive EEG-biomarkers deriving from the basal sleep/wake behavior for estimating the extent of anesthetic detriment following its exposure.
Materials and methods: We used 14 ArcAβ mice (7 transgenic with AD pathology and 7 wildtype) with an age of 8-11 months. Chronic electroencephalogram (EEG) and electromyogram (EMG) recordings were performed to assess sleep/wake behavior. Following baseline recordings, experimental administration of sevoflurane was performed (0.2%vol every 2 min up to 3%vol max.) until EEG burst suppression was achieved (10s inter-burst interval). Sevoflurane concentration was then reverted to 0%vol in 0.2%vol steps, followed by another set of EEG/EMG recordings.
Results: Age-independent baseline EEG recordings showed significant differences in spectral features, most importantly decreased delta power in transgenic mice during NREMS compared to wildtype littermates with a relative increase in remaining power spectra. Administration of experimental anesthesia in wildtype mice, regardless of age, did not result in any profound alterations in sleep architecture. On the other hand, transgenic mice showed increased transitions from NREMS to wakefulness, accompanied by a decrease in delta power during NREMS compared to wildtype littermates, independent of the age group.
Conclusions: Our results, supporting face validity and constructive validity, suggest that anesthetic administration results in an age-independent disruption of sleep-wake behavior in ArcAβ mice. Further, wildtype mice appeared to regain basal sleep/wake behavior, whereas transgenic mice showed a reduction in sleep quality and an alteration of sleep architecture after anesthesia. Spectral EEG-biomarkers, as found in our study, could potentially play a role in predicting cognitive decline after anesthesia. Our future experiments will focus on impaired sleep quality in ArcAβ mice after anesthetic exposure as a potential trigger for cognitive impairments due to anesthetics.

AN EEG STUDY ON SLEEP HOMEOSTASIS IN A SONGBIRD SPECIES, THE EUROPEAN STARLING (*STURNUS VULGARIS*): REM SLEEP, WHY BOTHER?

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Introduction: Sleep is considered to be of crucial importance for optimal performance and health. However, most of what we know about sleep is based on a handful of mammalian species under laboratory conditions. Perhaps much can be learned from comparative studies in other species. Birds are interesting in that respect because they exhibit two sleep states that are similar to mammalian rapid eye movement (REM) and non-REM (NREM) sleep. We therefore did a series of electro-encephalogram (EEG) studies in European starlings (Sturnus vulgaris) for a detailed assessment of sleep architecture and sleep homeostasis under laboratory and semi-natural conditions.
Materials and Methods: We implanted 12 European starlings with epidural EEG electrodes and applied miniature dataloggers to record their sleep-wake behavior. In the first experiment under controlled indoor conditions, we measured baseline sleep and sleep homeostatic responses to 4 and 8-hour sleep deprivations. In the second experiment, we measured sleep under seminatural outdoor conditions across the seasons.
Results: The birds showed a homeostatic NREM sleep response reflected in elevated EEG spectral power across a broad frequency range and increased daytime napping. Starlings had hardly any REM sleep (1.6% of total sleep time) and no REM sleep rebound after sleep deprivation.
Under seminatural outdoor conditions, the birds showed extreme variation in the amount of NREM sleep across the seasons with 5 hours more sleep in winter than in summer (12.5 h and 7.5 h respectively, $p < 0.001$). The daily sleep variation was best explained by photoperiod ($p < 0.001$) and was also negatively affected by moonlight ($p < 0.001$). During long photoperiod, starlings showed an increased sleep pressure that was reflected in the slope of the decay of EEG spectral power during the nights ($p = 0.008$), resulting in an increase in daytime naps. Also, under seminatural conditions starlings only displayed negligible amounts of REM sleep.
Conclusions: This study confirms homeostatic regulation of NREM sleep in songbirds. Yet, it also demonstrates high flexibility and strong photoperiodic regulation of NREM sleep under natural conditions. Finally, this study does not support an important role for REM sleep.
Acknowledgements:
This study was supported by an Adaptive Life Program scholarship from the Groningen Institute for Evolutionary Life Sciences and an Ubbo Emmius scholarship provided by the Faculty of Science and Engineering at the University of Groningen. N.C.R. was supported by the Max Planck Society.

A NEW METHOD FOR PRECISE OSCILLATORY PHASE TARGETING AFFECTS SLOW WAVES AND SLEEP SPINDLES ON THE SHORT AND LONGER TERM

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Introduction: Several studies have shown manipulation of slow oscillations and sigma power through sensory stimulation during sleep. Most of the evidence, however, regards effects immediately following stimulation rather than longer-term effects. Moreover, effects on doscrete spindles have as yet not been assessed. Here we use a modeling-based approach to predict upcoming oscillatory activity in the EEG and phase-lock subtle acoustic stimuli to the start of the SO positive deflection.
Materials and Methods: Here we use a modeling-based approach to predict upcoming oscillatory activity in the EEG and precisely phase-lock subtle acoustic stimuli to the start of the SO positive deflection. We assess effects the effects of stimulation on discrete slow oscillations and spindles on the short (seconds) and longer () term. We relate our findings to