an end-to-end fashion to avoid manual feature extraction. This allows for short prediction times and allows the model to learn more complex relations as the size of the training data increases. The model output is a temporal sequence of arousal probabilities, which are then used to generate discrete arousal events in a post-processing step. Furthermore, the output probabilities are calibrated to correct for the poor calibration of modern neural networks.
The model was trained and tested on over 1800 and 900 manually scored PSG and SAS sleep studies, respectively. The PSG data came from a population of patients referred to a sleep clinic by a medical doctor, but the SAS data from various research datasets.
Results: The ResTNet-Arousals model was validated on two previously unseen datasets. The first included traditional PSG sleep studies (N = 160, epochs = 119,774) and the other SAS sleep studies (N = 88, epochs = 70,349). On PSG data, the ResTNet-Arousal model achieved a positive percentage agreement (PPA) 68.82% (95%CI 63.87 - 69.67%) and a negative percentage agreement (NPA) 90.06% (95%CI 88.57 - 91.41%). The model had similar results when validated on data from SAS sleep studies, with a PPA of 68.10% (95%CI 65.52 - 70.64%), and an NPA of 94.48% (95%CI 93.33 - 95.46%).
Conclusions: The ResTNet-Arousal model shows good performance both for PSG and SAS sleep studies. Furthermore, a systematic comparison of manually scored arousals from different sleep clinics and the model predictions showed a systematic difference between the sleep clinics in the propensity to score arousal events; a manifestation of the low inter scorer agreement when scoring arousals.

SAMELISANT (SUVN-G3031), A HISTAMINE H3 RECEPTOR INVERSE AGONIST IN ANIMAL MODELS OF SLEEP DISORDERS

V. Benade [1], R. Abraham [1], R.C. Palacharla [1], S. Petlu [1], V.R. Mekala [1], S.K. Pandey [1], R.K. Badange [1], K. Bojja [1], V. Reballi [1], P.K. Achanta [1], P. Choudakari [1], R. Nirogi [1]. [1] *Suven Life Sciences Ltd, Hyderabad, India*

Introduction: Samelisant (SUVN-G3031) is a potent and selective H3 receptor (H3R) inverse agonist with hKi of 8.7 nM. It is selective against 70 other targets which includes GPCRs, ion channels, transporters, enzymes, peptides, steroids, second messengers, growth factors and prostaglandins. Samelisant exhibited desired pharmacokinetic properties and favorable brain penetration in preclinical species. Samelisant blocked R-α-methylhistamine induced dipsogenia in rats and increased *tele*-methylhistamine levels in brain and cerebrospinal fluid as well, which confirm its binding towards H3R.
Samelisant is currently being evaluated in a Phase-2 proof-of-concept study as monotherapy for the treatment of excessive daytime sleepiness (EDS) in patients with narcolepsy with and without cataplexy (ClinicalTrials.gov Identifier: NCT04072380). In the current research work, samelisant was evaluated for neurotransmitter modulation and sleep wake profile in orexin knockout mice, a reliable animal model for narcolepsy.
Materials and Methods: In brain microdialysis, samelisant was evaluated for its effects on modulation of neurotransmitters like dopamine, histamine and norepinephrine in prefrontal cortex. In male orexin knockout mice, electroencephalography (EEG), electromyography and activity were monitored using telemetric device. Effects of Samelisant on sleep/ wake were evaluated during active period of animals. Animals were allowed recovery period of 3 weeks after surgery.
Results: Samelisant significantly increased histamine, dopamine and norepinephrine levels in the prefrontal cortex. Samelisant did not change dopamine levels in the striatal and accumbal brain regions. These results suggest that samelisant may not have propensity to induce abuse liability. Samelisant produced significant increase in wakefulness with concomitant decrease in non-rapid eye movement sleep in orexin knockout mice. It also significantly decreased number of cataplectic episodes in orexin knockout mice.
Conclusions: The results from non-clinical studies presented here provide a strong evidence for the potential utility of samelisant for the treatment of EDS and cataplexy in patients with narcolepsy.
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SELECTIVE THERMAL STIMULATION TO MANIPULATE THE CIRCADIAN COMPONENT OF SLEEP REGULATION

S. Haghayegh [1,2,3], S. Khoshnevis [3], M.H. Smolensky [4,3], R.C. Hermida [5,3], R.J. Castriotta [6], E. Schernhammer [1,2,7,8], K.R. Diller [3]. [1] *Harvard Medical School, Boston, United States;* [2] *Brigham and Women's Hospital, Boston, United States;* [3] *The University of Texas at Austin, Austin, United States;* [4] *The University of Texas Health Science Center, Houston, United States;* [5] *University of Vigo, Vigo, Spain;* [6] *University of Southern California, Los Angeles, United States;* [7] *Harvard TH Chan School of Public Health, Boston, United States;* [8] *Medical University of Vienna, Vienna, Austria*

Introduction: Borbély's two-process model of sleep regulation entails circadian rhythm Process C and homeostatic sleep pressure Process S. We developed a novel thermal sleep system composed of selective thermal stimulation (STS), i.e., mild heating (39°C) of the skin over the cervical spine to manipulate blood flow to the dense network of arteriovenous anastomoses (AVAs) of the glabrous skin, e.g., hands and feet, plus a dual-temperature zone mattress with a warmer (33°C) peripheral zone to improve vasodilation of AVAs on the hands and feet and a cooler central (27°C) zone to enhance heat transfer by conduction from the central body core to the environment. We hypothesized this novel thermal sleep system, which increases heat transfer by redistributing blood flow from the body core to the glabrous skin, increases the distal-proximal-gradient temperature (DPG) and reduces core body temperature (CBT), elements of Process C, resulting in shortened sleep onset latency (SOL) and improved sleep quality.
Materials and Methods: After acclimating to the study environment and conditions through an afternoon nap, 11 healthy normal sleeper males, 23.6±3.9 [mean±SD] years of age, were randomly subjected to two non-consecutive nocturnal sleep sessions -a treatment night with the thermal sleep system activated and a control night with it deactivated. Participants were challenged to go to bed (lights-out) two hours earlier than usual. Data collection commenced 45 min before lights-out to establish baseline values of the study variables. On the treatment night, the dual-temperature zone mattress was activated during the entire sleep period, while the STS pillow was activated only during the first 30 min.
Results: There was no significant difference between the control and treatment nights in the baseline values of glabrous skin blood flow (GSBF), DPG, and CBT. During the first 30 min after lights-out on the treatment night, when both the STS pillow and dual-temperature zone mattress were activated, GSBF (Δ=49.77±19.13 PU, P=0.013, Cohen's d=0.85) and DPG (Δ=2.05±0.62°C, P=0.005, Cohen's d=1.10) were significantly higher and CBT (Δ=-0.15±0.07°C, P=0.029, Cohen's d=0.58) was significantly reduced compared to the control night. Moreover, the SOL was significantly shorter (Δ=-48.6±23.4 min, P=0.032, Cohen's d=0.83), and participants rated their subjective sleep quality statistically significantly better (P<0.001) on the treatment night than on the control night.
Conclusions: This proof-of-concept study supports the proposed hypotheses that the dual-temperature zone mattress, which maintains high blood flow in the glabrous skin (via the warm peripheral zone) and increases conductive heat transfer from the body core to the environment (via the cooler central zone), in combination with STS resulting in increased GSBF and DPG and decreased CBT, with beneficial effects being shortening of the SOL through re-enforcement of Process C plus improvement of sleep quality that is consistent with diminution of the sleep pressure of Process S.
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SLEEP AND SHOUTS: THE INTRINSICALLY AVERSIVE NATURE OF ROUGH SOUNDS IS PRESERVED DURING NREM SLEEP

G. Legendre [1], M. Moyne [2], J. Dominguez-Borras [3], V. Sterpenich [1], D. Grandjean [4,5], S. Schwartz [1,4], L. Arnal [6]. [1] *University of Geneva, Department of Basic Neuroscience, Geneva, Switzerland;* [2] *EPFL, Geneva, Switzerland;* [3] *University of Barcelona, Department of Clinical Psychology and Psychobiology, Barcelona, Spain;* [4] *University of Geneva, Swiss Center*