levels, suggesting that this association might be especially apparent when no other confounding risk factors such as inflammation are present.
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0420

FIBRE-SPECIFIC WHITE MATTER NEURODEGENERATION IS ASSOCIATED WITH LONG SLEEP DURATION AFTER STROKE

Gottlieb, E. W. Egorova, N. Khlif, M. S. Khan, W. Werden, E. Pase, M. P. Howard, M. Brodtmann, A.
University of Melbourne, Florey Institute of Neuroscience, Melbourne, AUSTRALIA.

Introduction: Long sleep duration in aging populations has recently been proposed as a key modifiable risk factor and sequela of stroke. It is unclear whether the pathogenesis of post-stroke sleep-wake dysfunction is due to focal infarction to regional sleep-wake hubs in the brain, or to accelerated whole-brain neurodegeneration. We utilise a novel technique known as whole-brain fixel-based analyses (FBA) to characterize the first fibre-specific white-matter markers of long sleep duration after stroke.
Methods: We included 98 radiologically-confirmed ischemic stroke participants (67 male; mean age = 68) and 40 age-matched controls with no history of neurodegenerative disease imaged 3-months post-stroke. Sleep-wake was measured for one week using BodyMedia's SenseWear armband. Diffusion-weighted MRI (DWI) were acquired using echoplanar imaging and preprocessed using MRtrix3. FBA were employed to identify tracts with altered white-matter fibre-density and fibre-bundle cross-section (FDC) in the long sleep duration (>8 hr, n=20) and normal sleep duration groups (between >6 hr and <8 hr, n=59) compared to controls. Statistical comparisons of FDC between groups were performed at each FDC fixel by a general linear model controlling for age, sex, and intracranial volume.
Results: Stroke participants with long sleep duration exhibited significant FDC reductions of up to 40% within the cortico-ponto-cerebellar tract when compared to healthy controls (family-wise-error-corrected p=<0.05). Bilateral pontine degeneration was observed at the decussation of the superior cerebellar peduncles. Stroke participants with normal sleep duration exhibited diffuse whole-brain degeneration most apparent along the corpus collosum and cingulum; however, the distribution was less extensive relative to long sleepers (i.e., no cortico-cerebellar projections) and percentage effect reductions did not exceed 20%.
Conclusion: Long sleep duration after stroke is associated with cortico-ponto-cerebellar degeneration when compared to controls or stroke-participants with normal sleep duration. Excessively long sleep may contribute to post-stroke neurodegeneration beyond the effects of direct infarction and may be a modifiable pharmacological target for abating brain volume loss after stroke.
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0421

DECREASED ACTIGRAPHIC DAYTIME ACTIVITY IS ASSOCIATED WITH LOWER MEMORY PERFORMANCE IN COGNITIVELY-UNIMPAIRED INDIVIDUALS WITH AUTOSOMAL DOMINANT ALZHEIMER'S DISEASE

Pardilla-Delgado, E.[1] Ramirez Gomez, L.[1] Baena, A. Y.[2] Montes, M. I.[3] Bocanegra, Y.[2] Martinez, J. E.[1] Lopera, F.[2] Quiroz, Y. T.[1]
[1]Massachusetts General Hospital, Boston, MA, [2]Grupo de Neurociencias de Antioquia, Universidad de Antioquia, Medellin, COLOMBIA, [3]Universidad de Antioquia, Medellin, COLOMBIA.

Introduction: Alzheimer's disease (AD) impacts brain regions that control circadian regulation systems such as wakefulness and daytime physical activity. Recent evidence shows that AD pathology is damaging for wake-promoting neurons. Whether early changes in wakefulness and daytime activity occur during asymptomatic stages of familial AD (fAD) remains unknown. In this study, we aimed to investigate whether daytime activity differs between cognitively-unimpaired carriers of early-onset fAD and age-matched non-carrier family members. Further, we examined the associations between daytime activity and memory performance.
Methods: A total of 25 members of the large Colombian kindred with the Presenilin1 (*PSEN1*) E280A mutation were included in the study (9 mutation carriers and 16 non-carriers, mean age=38.2). *PSEN1* mutation carriers develop dementia before the age of 50. All subjects underwent wrist actigraphy for 7-14 days to measure daytime activity (average activity per minute and per epoch), and completed the CERAD Word List Learning and the Free and Cued Selective Reminding Test (FCSRT).
Results: Compared to non-carriers, mutation carriers had less average daytime activity (Mann-Whitney U Test p=.04). Higher average daytime activity was associated with better memory recall in both the CERAD word list delayed recall (r=.47, p=.05) and the FCRST delayed total recall (r=.53, p=.02). No associations with age were observed.
Conclusion: Our results suggest that cognitively-unimpaired mutation carriers have reduced daytime activity, years before the onset of dementia. Reduced daytime activity in carriers is also associated with lower memory performance. Our preliminary findings add to the growing evidence that circadian dysfunction is present in early AD, and may play an important role in subsequent memory impairment. Future research with large samples is needed to further examine sleep and circadian dysfunction in asymptomatic individuals at genetic risk for AD.
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0422

APOCALYPSE TAU: THE RELATIONSHIP BETWEEN INFLAMMAGING AND LOCAL SLEEP DISRUPTION IN OLDER ADULTS IS MEDIATED BY TAU BURDEN

Dave, A.[1] Sprecher, K. E.[2] Lui, K. K.[1] Chappel-Farley, M. G.[3] Chen, I. Y.[1] Blennow, K.[4] Zetterberg, H.[4] Riedner, B. A.[2] Bendlin, B. B.[5] Mander, B. A.[1] Benca, R. M.[1]
[1]Department of Psychiatry and Human Behavior, University of California, Irvine, CA, [2]University of Wisconsin School of Medicine and Public Health, Department of Psychiatry, Madison, WI, [3]Department of Neurobiology and Behavior, University of California, Irvine, CA, [4]Department of Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology, the Sahlgrenska Academy at the University of Gothenburg, Mölndal, SWEDEN, [5]University of Wisconsin School of Medicine and Public Health, Department of Medicine, Madison, WI.