

### **63. Lasting wake/sleep disturbances in traumatic brain**

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#### Background:

Traumatic brain injury (TBI) is relatively widespread among young adults following driving and work-and sports-related accidents. Mood depression, fatigue, sleepiness, concentration difficulties, generalized anxiety, and vegetative or somatic symptoms arise within the first year post-TBI. Depression and other post-concussion symptoms can persist for months to years post-TBI, and may eventually become a permanent symptomatology that causes significant and costly disability. Serious alterations in neuroendocrine as well neurobehavioral processes (e.g., sleep phases, circadian rhythms) are common in animal experimental preclinical models, and in human clinical studies of patients with TBI, however, whether they are sustained in the long-term is not known. Our hypothesis is to further characterize the alterations in behavioral and neuroendocrine (i.e., disruptions in hypothalamic-pituitary-adrenal (HPA) axis regulation) regulation that we have observed in our rat model of TBI to human TBI subjects.

Methods: Subjects underwent continuous assessment of activity over 11 consecutive days (Friday to Monday) by means of the Actiwatch device (Respironics-Mini Mitter, Bend, OR, USA). This device is an ambulatory, non-invasive, water-proof, FDA-approved, and well tolerated instrument to measure wake-sleep periods. Circadian activity has been tested by the presence of sinusoidally varying diurnal trends in the profile. Eleven patients with TBI and 4, uninjured, age-matched controls were recruited from Centre for Neuro Skills. There were 4 females and 11 males who participated in the study. Age ranged from 28-65 years of age. Cosine rhythmometry analysis of circadian activity, Midline Estimating Statistic of Rhythm (MESOR), amplitudes, and acrophases were analyzed. Since standard work days are about 8.00 AM to 5.00 PM, we set up 8.00 AM as our daily activity starting point.

#### Results:

TBI subjects showed reduced activity and more episodes of inactivity (naps) during the daytime according to the severity of injury. Regardless of severity of injury, TBI subjects showed more daytime naps than normal controls. Moreover, TBI subjects showed an activity pattern like they have a tendency to live on longer-than-24-hour days.

#### Conclusions:

Following our previous research on a rat model that TBI causes long-term dysregulation of the neuroendocrine stress response, our findings in human subjects demonstrate that TBI produces long-lasting dysregulation in activity daily rhythm, thus bringing evidence that TBI has an effect amidst central substrates for allostasis and circadian rhythmicity.