Assessing EEG biomarkers of consciousness using Angelman syndrome

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Abstract: 1.7

Angelman syndrome (AS) is a rare genetic disorder in which patients present with intellectual disability, epilepsy, and an awake-state electroencephalogram (EEG) phenotype that strongly resembles EEG recordings from typical individuals in states of reduced consciousness (e.g., sleep or anesthesia). The AS EEG phenotype is characterized by hypersynchronous delta (1-4 Hz) activity and is present even in the absence of seizures [Sidorov et al 2017; Frohlich et al 2019]. Nonetheless, individuals with AS clearly demonstrate purposeful behavior and, by implication, consciousness. To elucidate this paradoxical EEG phenotype, we investigated whether EEG biomarkers of consciousness are modulated by sleep in AS.

We analyzed EEG power and signal complexity in 35 children with AS ages 1 to 10 years with awake and asleep spontaneous EEG. We derived EEG power using a Morlet wavelet transform and two complexity measures: modified multiscale entropy (mMSE) [Costa et al, 2002; Xie et al, 2008] and generalized multiscale Lempel-Ziv complexity (gMLZ) [Yeh and Shi, 2018]. The former captures the balance between order and disorder whereas the latter captures the incompressibility of the signal. Both measures examine complexity across 20 timescales. We accounted for multiple comparisons using cluster randomization statistics to identify clusters in channel-frequency (power) and channel-timescale (complexity) space that show large changes with sleep.

EEG power was decreased in wakefulness relative to sleep in two spatially broad clusters (p = 0.0005 each) encompassing slow-frequency oscillations (< 21 Hz). EEG complexity was increased in wakefulness relative to sleep (mMSE, 16 timescales, p = 0.0007; gMLZ, 20 timescales, p < 10^-4). Our results validate EEG biomarkers of consciousness under conditions of abnormal cortical dynamics in AS. Furthermore, the cluster with the largest channel-timescale extent was found using gMLZ, suggesting that Lempel-Ziv based complexity measures may yield the greatest promise for detecting consciousness under unusual physiological circumstances.