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Spotlight

Continuous monitoring of neonatal cortical activity: A major step forward

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Montazeri Moghadam et al.[1] report an automated algorithm to visually convert EEG recordings to real-time quantified interpretations of EEG in neonates. The resulting measure of the brain state of the newborn (BSN) bridges several gaps in neurocritical care monitoring.

Neurocritical care in neonates remains impeded by technical barriers and the expertise needed to interpret continuous EEG in real time, which is currently the only available functional method to monitor brain activity at the bedside. Large-scale implementation of a simple solution that is both available 24 h/day and user-friendly is still pending to better adjust treatment decisions and outcome predictions, not only for term infants with hypoxic-ischemic encephalopathy (HIE) but also for a large proportion of preterm infants at risk of brain damage and/or neurodevelopmental impairment. While major advances in structural brain imaging provide better individual prognosis,[2] precision medicine and assessment of innovative neuroprotective strategies require early biomarkers of brain function and recovery following perinatal insult. While we await future clinical developments of functional ultrasound brain imaging that can be done at the bedside,[3] EEG remains to date the best tool to reach these objectives.

Montazeri Moghadam et al.[1] construct a new measure of cortical function in the full-term newborn, the BSN, resulting from combining EEG background and sleep-state classifiers.

First, the authors train a deep-learning-based classifier for EEG background activity in brain-lesioned neonates. They guide their choice of background classes based on unsupervised learning methods analyzing class separation. Because EEG background is by default a global state in the brain activity (so at least in theory, equally recognizable from any EEG channel), the algorithm was trained using a single EEG channel at a time. Thereby, the resulting classifier is able to accurately generalize using recordings obtained with different EEG montages and can detect the presence of artefacted channels. This was confirmed as the authors found comparable performance of the classifier on their training dataset and on an external cohort validation dataset recorded with different electrode configurations.

Next, the authors combine the background EEG classification with an algorithm trained for quiet sleep detection to provide a sleep-state trend,[4] which is thought to reflect the integrity and maturity of the CNS in neonates.[5] This combination results in a novel continuous measure, the BSN, a trend value ranging visually from 0 to 100, updated every minute. The resulting time series can be displayed as a trend in the bedside monitors, with an indication of classifier uncertainty, for better information transparency (Figure 1). The trend reflects the progressive recovery of EEG activity continuity as a gradual increase in BSN, but also reveals emergence of fluctuation in brain states corresponding to sleep-wake cycles, hence containing the signatures of two major indicators of cerebral recovery and maturation.

Finally, they assess the clinical relevance of BSN by several proof-of-concept validation experiments correlating BSN values/trend with clinically relevant characteristics. These experiments confirmed that BSN can be used to accurately classify EEG background activity, to detect the onset of continuous EEG or sleep-wake cycling without any prior training of the user, and that its trajectory over the first 3 postnatal days is informative about clinical outcomes of infants with HIE.

By providing an easy-to-interpret, automated, and transparent measure at bedside, BSN addresses both the lack of available human expertise 24/7 as well as the need for standardized, objective interpretations of EEG signals. One of the major strengths of this automation is to provide robust assessment of the dynamic of EEG background and sleep state cyclicity recoveries, which are difficult to measure visually from the raw traces. This automation is all the more valuable as this dynamic is highly prognostic. Indeed, in absence of seizures, the recovery of normal or mildly altered EEG activity in the first 36–48 h following brain insult is highly predictive of a favorable outcome at 2 years of age.[6] Thus, BSN combined with other functional, structural, clinical, and biological prognostic indicators in multimodal prognostic models could contribute to improving neurodevelopmental outcome prediction at an individual level. Importantly, such objective measures would also hold significant promise in benchmarking clinical intervention trials, both in patient stratification and as an early functional outcome measure. The authors also want to facilitate further use of BSN by providing free access to a computational cloud where any researcher can upload their own deidentified amplitude EEG monitoring data and get the resulting BSN outputs (Figure 1). Such open access use of BSN and other

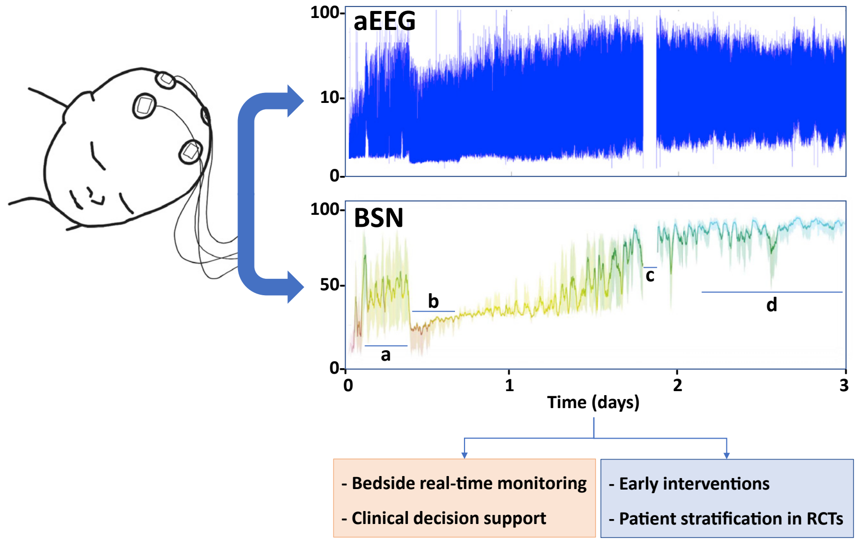

Figure 1. Automated bedside measure for monitoring neonatal cortical activity
A raw EEG signal recorded during 3 days in an infant recovering from perinatal asphyxia can be converted into either an amplitude-integrated EEG trace (aEEG) or Brain State of the Newborn (BSN). BSN, constructed from a novel EEG background classifier and a sleep-state classifier, improves accuracy of real-time assessment of brain functioning and provides several clinical and research opportunities. a, initial brain recovery; b, transient suppression; c, care procedure; d, emergence of an apparent sleep-wake cyclicity. RCT, randomized controlled trials.

algorithms is setting new perspectives to unlimited exploitation and validation of novel AI solutions in a scaled-up clinical research.

Further work in larger full-term populations, particularly those including neonates with seizures, is still needed to achieve standardization of BSN. However, the promising results demonstrating a good separation of BSN values between clinically relevant EEG background categories suggest that thorough benchmarking could provide clear boundary criteria for identifying brain states based on BSN ranges in full-term neonates. When it comes to preterm infants, who represent the majority of patients in the Neonatal Intensive Care Unit, the utility of BSN in its current form remains to be tested and, presumably, a different algorithm needs to be re-trained for that clinical purpose. Notably, monitoring of preterm infants is typically less focused on the background classes, while more emphasis is put on assessing, for instance, maturation of cortical activity (automated cot-side tracking of functional brain age),[7] or sleep-wake cycling.[5] Furthermore, in preterm infants, cortical activity assessment should also consider temporal and spatial characteristics of the age-related specific features that appear and disappear sequentially during development and maturation and that require specific processing of conventional EEG recordings, acquired with at least 11 channels.[8] At the other end, beyond neonatal care, older populations of patients could also benefit from a BSN-inspired bedside measure for the monitoring of recovery in Disorders of Consciousness following severe brain injury.[9]

Overall, BSN illustrates how bedside implementations of automated real-time EEG interpretations by artificial intelligence will potentially enable significant clinical benefits. Automatic EEG interpretation at bedside is not intended to replace specialized visual EEG assessment but to be combined to reveal all the richness of EEG signals, providing a holistic evaluation of brain function in neonates.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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