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An Automated Method for Determining Awareness and Predicting Recovery after Brain Injury, Using Event-Related Potentials

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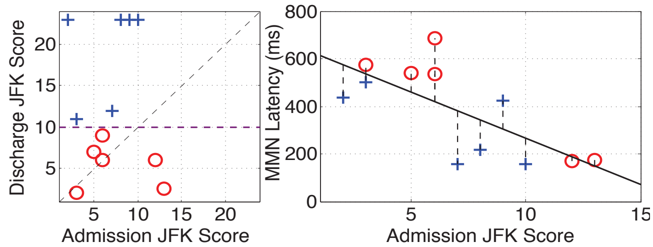
Introduction: There is mounting evidence that event-related potentials (ERPs) are useful predictors of recovery from disorders of consciousness following brain injury. So far, these approaches have typically used the amplitude of certain ERP components, such as the mismatch negativity (MMN) that typically appears fronto-centrally at 150–250 ms following an oddball stimulus. However, the latency of ERP components can also be expected to change as a function of awareness level. This leads to a problem in identifying ERP components of interest, since in damaged, atypical brains they no longer correspond to known textbook patterns. This problem is compounded by the reduced signal-to-noise ratio of EEG following brain injury. One approach to this problem is to identify ERP components by expert examination—however, the results are then affected by the subjectivity of this process. Alternatively, amplitude can be computed at fixed textbook latencies—but this leads to noisy estimation, and/or applicability only to the subset of subjects that exhibit standard latencies (leading to a high rate of rejection of subjects from the analysis). In the current study, we address these problems by: (a) using a subspace decomposition method to enhance signal-to-noise ratio in estimating the source of interest; (b) developing this into a fully-automated processing pipeline for identifying ERP components despite latency differences; and (c) using the latency itself as a diagnostic and predictive feature.

Method and Materials: **Subjects:** 13 participants ≥16 years old, with traumatic brain injury admitted to the Neurorecovery Program at Helen Hayes Hospital (West Haverstraw, NY, USA), 30-60 days post-injury. JFK Coma Recovery Scale score was measured at admission and discharge. **Protocol:** 32-channel referential EEG was recorded (0-3 days of admission), while the subject passively listened to an oddball tone sequence (80% standards, 16% duration deviants, and 4% rare deviants). Standard stimuli were 1000-Hz tones of 100-msec duration delivered at 80 dB SPL. Duration-deviant stimuli were similar except that their duration could be 50 or 150 msec. Rare deviant stimuli were English spoken words at 80 dB SPL. The paradigm was 15 min long, with a total of 2025 stimuli, partitioned into 15 one-min runs. **Analysis:** EEG data were pre-processed by applying a notch filter, a common average spatial filter, and a bandpass filter of 0.5-8 Hz. Trials containing artifacts were eliminated automatically by statistical detection of outliers. Spatially constrained ICA (ScICA) was then applied to the epochs following standard and deviant stimuli, using a soft fronto-central spatial constraint to estimate a single source that had the classic MMN topography. This single source was projected back into the signal space to retrieve the correct signal polarity, and a signed coefficient of determination (signed r^2) was computed between standard and deviant trials. The final measure was the latency of the first negative peak of the difference wave in the interval 100-700 msec whose r^2 exceeded the 5%-significance threshold (one of the 13 subjects was removed as no significant peak was found).



Results: The left figure shows JFK score at admission and discharge. We define "recovery" as a discharge JFK score >10 with a 5-point or more improvement on the JFK score (blue crosses). Admission JFK score alone did not predict recovery ($r = -0.03$, $p = 0.9$, $r^2 = 0.002$). We found that the ERP latency was significantly correlated with the admission JFK score ($r = -0.71$, $p = 0.009$), showing the diagnostic value of the ERP (right figure). For prognosis, we aimed to obtain a predictor that was independent of admission JFK score: therefore, we were interested in whether an individual had a long or short ERP latency *relative to the latency that the clinical score would lead us to expect*. In the future, we envisage that expected latencies would be obtained from a large normative database; for now, we interpolate them from the current data set itself. Hence, we use the *residuals* of ERP latency in the regression against admission JFK score (vertical dashed lines in right figure). We found that the residuals were significantly correlated with recovery ($r = -0.65$, $r^2 = 0.41$, $p = 0.02$). ***Significance:*** These initial results support the feasibility of using ERP latencies as a biomarker for assessing awareness and predicting recovery after brain injury. They also demonstrate an advanced signal-processing pipeline based on ScICA to objectively reduce data dimension, enhance the signal-to-noise ratio, and extract informative ERPs in a fully automated way from atypical, noisy EEG. With further development, this approach might provide a useful new diagnostic and prognostic tool for evaluating patients in a minimally conscious or apparently unresponsive state. This new tool might aid in formulating individual treatment and disposition plans, including selection of patients who could use brain-computer interface (BCI) communication systems to aid in their functional recovery.