Multi-modal brain dynamics of fast motor skill learning

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ABSTRACT

Introduction: Neuroimaging can help characterize changes in surgeons' brains as they learn laparoscopic skill (Modi et al., 2017a). In this study we sought to elucidate the ability of noninvasive functional neuroimaging to describe those changes and supplement the insights from techniques such as blood tests and subjective questionnaires that have been used traditionally as a measure of stress. Bimanual motor skill acquisition is known to induce sustained changes in grey matter thickness and myelination which, in turn, affect neuronal synchronization detectable by electroencephalography (EEG) (Halsband and Lange, 2006; Wu et al., 2014). Early stages of acquisition is characterized by fast improvements in accuracy and speed, accompanied by distinct functional changes in cortex (Dayan and Cohen, 2011). Thus, we investigated the interrelations among EEG metrics and NASA-TLX scores as well as protein expression (determined by blood sample) in early motor skill acquisition. Results from novices performing training tasks in laparoscopic box-simulators indicate that the frequency of local and inter-area cortical synchronization is associated with changes in the NASA-TLX scores and cortisol and brain derived neurotropic factor (BDNF) concentrations.

Methods: Data sets from a study (Zakeri et al., 2020b) with 31 participants were used including brain electrical activity collected with a wireless system (TMSi Mobita) with 19 gel-based electrodes, following the international 10–20 system of electrode placement at a sample rate of 2000 Hz. Concurrent prefrontal fNIRS data were also collected, however not used in this report. For each subject, the experimental session (using box-trainers by Inovus Medical Systems) started by performing a secondary task for two minutes, which was considered as a baseline. For the rest of the experiment, participants performed primary (laparoscopy) and secondary tasks (pedal response to randomly timed auditory stimuli) simultaneously. The primary tasks included two Fundamentals of Laparoscopic Surgery tasks, Ring Transfer and Threading, in alternating sequence (T1 and T2) followed by repetition of the first task (T1R). Fingertip blood samples and NASA-TLX scores were collected 4 times including baseline and immediately after completion of each task to assess the individual variation between participants, the length and type of the tasks. The experimental procedure is illustrated in **Figure 1A** and **B**. EEG were pre-processed in order to reject artifacts and minimize nonbrain components of the signals using an ICA-based method (Zakeri et al., 2020b). Then, the relative frequency band-power (FBP) and the phase-locking value (PLV) were calculated (Omurtag et al., 2017). The FBP at each electrode site quantified the extent of frequency dependent local synchronization of neuronal populations while for each pair of sites the PLV indicated the degree of inter-area synchronization. Serum cortisol concentration and BDNF concentration were determined from the blood samples.

Results: **Figure 1C** shows the topographic distribution of local synchronization measured by subject-averaged FBP. Rows in this subplot correspond to frequency bands and the columns are the experimental episodes labelled at the top. Results indicate the prominent task-evoked increases in the midline theta and decreases in the posterior alpha power. In **Figure 1D** the long-distance phase synchronization (PLV) is displayed as a function of the frequency (x-axis) for selected pairs of sensors during resting (blue curve) and task performance (red). For each subplot, the labels of the sensor pairs are shown at the top and the topographic location of the corresponding connection are schematically illustrated in the inset. Frequency

bands where the rest-task difference was statistically significant (False discovery-corrected Wilcoxon sign-rank test) are indicated by an asterisk. The top row of sub-plots in Figure 1D shows that during task performance there was a relative decrease in the connectivity in the alpha-band associated with the default-mode network. The bottom row of sub-plots suggests that there was a task-evoked increase in the intra- and inter-hemispheric motor cortex connectivity in the beta and higher frequency ranges associated with information processing. **Figure 1E** depicts the associations between the local cortical synchronization and the NASA-TLX (top panel) and cortisol (middle) and BDNF (bottom) concentrations. The boxplots indicate the distribution of the values of the Pearson correlation between the FBP and the workload measure as well as the blood concentration of the proteins. The FBP value for each subject was averaged over all electrodes. The results show that low frequency synchronization had a positive correlation with cortisol (or BDNF) while higher frequencies had negative correlations. However in the low-beta range (12-16 Hz), FBP was positively correlated with NASA-TLX or cortisol while it was negatively correlated with BDNF.

Discussion and Conclusions: Our results suggest that higher alpha band power (known to be related to greater expertise) is associated in novices with not only lower subjective load (**Figure 1E** top panel) but also with mechanisms of arousal and focus (suggested by higher cortisol) and plasticity (higher BDNF) (**Figure 1E** middle and bottom). It emerges in the same figure, on the other hand, that greater low-beta band power (12-16 Hz), implies greater subjective load and cortisol, but lower BDNF. An examination of the particular areas leading to this result (not shown) suggested that motor related and parietal low-beta power were particularly negatively correlated with the level of BDNF. Cortisol and BDNF are both implicated in multiple aspects of stress and brain plasticity important for skill acquisition (Arora et al., 2010; Crewther et al., 2016). Beta synchronization in particular is known to be associated with preparation and execution of voluntary movements and, in simpler movement tasks, has been shown to correlate negatively with the exploratory adjustments and with the uncertainty associated with movement choices (Tan et al., 2016). How these are influenced with BDNF levels in the laparoscopic training context remains to be clarified. We believe that quantitative understanding (Zakeri et al., 2020a) of these interrelationships and their underlying mechanisms can provide useful tools for training of surgeons (Modi et al., 2017b; Sarker et al., 2013), leading to improvements in patient health and safety.

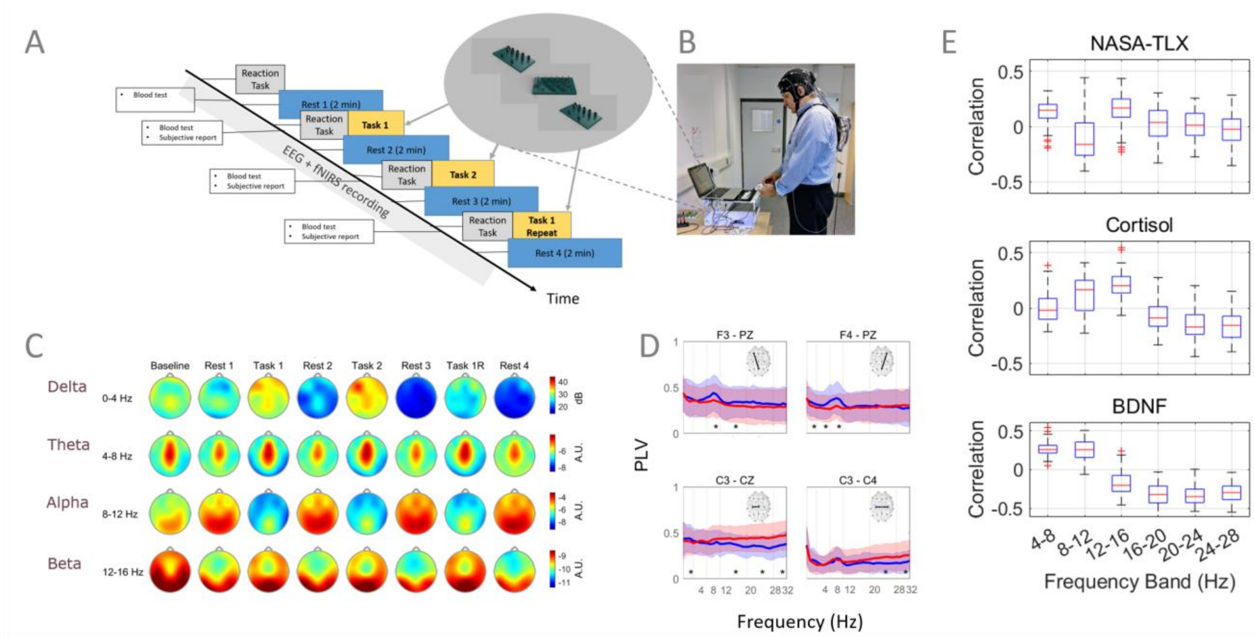

Figure 1. Study design and results. **A**, Experimental procedure. **B**, Photograph of subject during task. **C**, Topographic distribution of Frequency Band-Power averaged over all subjects. **D**, Inter-area synchronization measured by Phase

Locking Value for Task performance (red curve) and Resting state (blue). **E**, The Pearson correlation between local synchronization (channel averaged FBP) and the average NASA-TLX score and cortisol and BDNF concentrations.

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