Cortical excitability dynamics during fear processing

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Little is known about the modulation of cortical excitability in the prefrontal cortex during fear processing in humans. Here, we aimed to transiently modulate and test the cortical excitability during fear processing using transcranial magnetic stimulation (TMS) and brain oscillations in theta and alpha frequency bands with electroencephalography (EEG). We conducted two separate experiments (no-TMS and TMS). In the no-TMS experiment, EEG recordings were performed during the instructed fear paradigm in which a visual cue (CS+) was paired with an aversive unconditioned stimulus (electric shock), while the other visual cue was unpaired (CS-). In the TMS experiment, in addition the TMS was applied on the right dorsomedial prefrontal cortex (dmPFC). The participants also underwent structural MRI (magnetic resonance imaging) scanning and were assigned pseudo-randomly to both experiments, such that age and gender were matched. The cortical excitability was evaluated by time-frequency analysis and functional connectivity with weighted phase lag index (WPLI). We further linked the excitability patterns with markers of stress coping capability. After visual cue onset, we found increased theta power in the frontal lobe and decreased alpha power in the occipital lobe during CS+ relative to CS- trials. TMS of dmPFC increased theta power in the frontal lobe and reduced alpha power in the occipital lobe during CS+. The TMS pulse increased the information flow from the sensorimotor region to the prefrontal and occipital regions in the theta and alpha bands respectively during CS+ compared to CS-. Pre-stimulation frontal theta power (0.75-1 s) predicted the magnitude of frontal theta power changes after stimulation (1-1.25 s). Finally, the increased frontal theta power during CS+ compared to CS- was positively correlated with stress coping behavior. Our results show that TMS over dmPFC transiently modulated the regional cortical excitability and the fronto-occipital information flows during fear processing, while the pre-stimulation frontal theta power determined the strength of achieved effects. The frontal theta power may serve as a biomarker for fear processing and stress-coping responses in individuals and could be clinically tested in mental disorders.