

Chronic social defeat is a well-known means of modeling depression- and anxiety-like phenotypes in mice. There has been little study of the effects of electroconvulsive stimulation (ECS) on mouse behavior after chronic social defeat. We applied a chronic social defeat stress to inbred C57BL/6J mice then assayed their behavior with social interaction test, social preference test, open field test, sucrose preference test, and forced swim test to evaluate the phenotype. We then exposed defeated and control mice to 10 days of either active (isoflurane 2%, current 50mA, 100 pulses/sec, 0.5msec pulse width, one second duration) or sham (same handling and electrode attachment) ECS stimulation and evaluated post-ECS behaviors (pre-ECS tests plus elevated zero maze, acoustic hyperarousal, tail flick, hot plate and the novel object recognition test) for changes in their behavioral phenotype. We investigated the distribution of microglia (Iba1) and astrocytes (GFAP) markers in the hippocampus and amygdala with immunofluorescence. After chronic social defeat, defeated mice displayed an anxiety-like phenotype ($p < 0.05$ for open field test corner time, center time, total distance, stereotypies, and vertical activity) a depression-like phenotype ($p < 0.05$ for sucrose preference, forced swim day 2) compared to controls. Post-ECS, we observed a robust ECS-effect on both control and defeated mice, although at this time point there were no behavioral differences between defeated and control mice that underwent sham ECS. Similarly, while there were no significant glial cell staining differences between defeated and control mice, there was a robust ECS effect on the amount ($p < 0.01$) and branching ($p < 0.01$) of GFAP staining in the dorsal and ventral hippocampus as well as the amygdala. These findings will drive further investigation into how these cellular changes regulate neurocircuitry changes in response to ECS.

Keywords:

808

SEPARABILITY OF LOGIC AND LANGUAGE: A TMS STUDY

J. Coetzee, M. Monti, M. Iacoboni, A. Wu, M. Johnson. *University of California, Los Angeles, USA*

The nature of the relationship between language and abstract thought has long been a contentious issue. One theory is that the hierarchical and combinatorial operations that subserve natural language also serve as the basis for similar operations in a diverse range of abstract human thought, such as mathematics, music cognition, and action sequencing. With regard to deductive reasoning, there are two dominant views about the relationship between it and language. According to the first, deductive reasoning is parasitic on language, in the sense that the structure-dependent operations which underlie deduction make use of the same neural machinery that underlies the structure dependent operations of language, with that common machinery being found in the inferior frontal gyrus, in an area traditionally referred to as Broca's area. According to the second, the structure dependent operations that underlie deductive reasoning, and the neural machinery that make them possible, are independent of the structure dependent operations of language. In this second view, the operations that support language occur primarily in Broca's area, while the operations that support deduction occur primarily in frontomedial (Brodmann area 8) and frontopolar (Brodmann area 10) cortices. We tested these two views using continuous theta burst stimulation (cTBS), a form of patterned transcranial magnetic stimulation (TMS) which has been shown to demonstrate relatively long lived inhibition of neural activity in a localized area. Using this approach, we were able to demonstrate that inhibition of Broca's area impairs accuracy on a linguistic task but not on a matched logic task. Additionally, we found that inhibition of frontomedial cortex (medial BA 8) produced a pattern opposite to that found in Broca's area. These results support the view the structure dependent operations which underlie deductive reasoning are not parasitic on those that support language, but are in fact ontologically distinct from them.

Keywords: TMS, TBS, cognition, brain

811

HIGH TEMPORAL RESOLUTION DYNAMIC NETWORK STUDIES OF SCHIZOPHRENIA BRAINS BY 3-D TMS-EEG TECHNIQUES

D. Gupta¹, X. Du², E. Hong², F. Choa¹. ¹ *University of Maryland Baltimore County, USA*; ² *University of Maryland School of Medicine, USA*

Synchronization of neural activity and cortical connectivity is heavily explored with electroencephalography (EEG) in combination with transcranial magnetic stimulation (TMS) for non-invasive study of causal brain networks' dynamic. By using the sLORETA algorithm, a well-established technique for source localization, we studied three-dimensional signal propagation inside brains, 68 cortical regions, from EEG response to a single TMS subthreshold (80%) pulse targeted at the left motor cortex of 6 schizophrenia patients and 6 healthy controls. The dynamic connectivity was studied by computing time-evolved spatial coherence, for 2278 pairs of cortical regions, with sliding window technique of 200ms window size and 20ms shift, a much higher temporal resolution than that of fMRI. On monitoring both unstable and stable networks, we identified and report the following stable connections: Across all subjects, superior frontal gyrus was highly coherent with the lingual gyrus, middle temporal gyrus and cortical regions near the calcarine sulcus in the right hemisphere. Similarly, insula was coherent with caudal anterior cingulate gyrus and post-central gyrus was coherent with caudal middle frontal gyrus among other coherent pairs. In left hemisphere, inferior parietal lobe and inferior temporal lobes were coherent with each other as well as with precentral gyrus. Furthermore, fusiform gyrus was consistently very coherent with lateral occipital cortex and medial orbitofrontal cortex in left hemisphere and with lingual gyrus in right hemisphere. On comparison, we found that the temporal coherent dynamics of cortical region pairs involving fusiform gyrus in the left hemisphere and the pairs involving superior frontal region in the right hemisphere of controls were significantly different from that of patients (p -value < 0.05). To conclude, we uncovered stable neural networks through connectivity dynamics at temporal resolution higher than any other existing neuroimaging modality along reporting patterns that differ between controls and schizophrenia patients.

Keywords: EEG, TMS, source localization, neural network connectivity

812

INDIVIDUAL ALPHA FREQUENCY PROXIMITY TO STIMULATION FREQUENCY IS ASSOCIATED WITH CLINICAL OUTCOME DURING 10 HZ REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (RTMS) TREATMENT OF MAJOR DEPRESSIVE DISORDER (MDD)

L. Carpenter^{1,2}, E. Tirrell¹, P. Gobin¹, B. Kavanaugh¹, J. Corlier³, A. Wilson³. ¹ *Butler Hospital, USA*; ² *Brown University, USA*; ³ *UCLA, USA*

10 Hz rTMS is a common form of treatment for Major Depressive Disorder (MDD). 10 Hz is the center frequency of the alpha band, however the peak frequency of alpha oscillations varies across individuals. While individual alpha frequency (IAF) has been tested as a potential biomarker for treatment outcome, the proximity of the stimulation frequency to the IAF and its association with response to 10 Hz rTMS treatment has not been yet investigated.

We examined the relationship among IAF, rTMS stimulation frequency, and treatment outcome in 136 patients. Outcome was percent change in Inventory of Depressive Symptomatology – Self Rated (IDS-SR) from pretreatment baseline to treatment 30. All patients initially received 10 Hz rTMS stimulation administered to left dorsolateral prefrontal cortex (DLPFC). 68 subjects received only 10 Hz stimulation at left DLPFC for the majority of treatment, while 68 subjects received primarily another form of stimulation (5 Hz at left DLPFC, 1 Hz at right DLPFC, or sequential bilateral stimulation). The absolute value of the numerical difference between IAF and 10 Hz stimulation frequency ($|IAF - 10 \text{ Hz}|$) was examined in relation to outcome for the overall sample as well as separate stimulation groups.

Numerical difference of IAF was significantly correlated with percentage change in IDS-SR for patients who received 10 Hz stimulation ($P < 0.01$). Responders were 30% more likely than non-responders to have $|IAF - 10 \text{ Hz}| \leq 1 \text{ Hz}$. There was no relationship between IAF and treatment outcome for other stimulation frequencies.

We found the relationship between the IAF and the stimulation frequency to be an important factor in clinical outcome of rTMS treatment of MDD. Intrinsic rhythms and networks are likely to be entrained more efficiently