

## Session VI Discussion

Discussant: Walsh

Recorders: Medina/Wencil

Executive functions are a set of cognitive functions theorized to manage other cognitive processes. They include skills such as cognitive control, emotional regulation, initiating appropriate behaviors and inhibiting inappropriate ones. In fMRI studies, the lateral prefrontal cortex is consistently activated during traditional executive functioning tasks (e.g., the Wisconsin Card Sorting Task and the go, no-go task) and more recently during social decision-making tasks (e.g., the ultimatum game). Until recently, researchers have focused on the role of frontal cortex in executive functioning with a paucity of work modulating executive functioning or providing translational studies where executive functioning could be enhanced in persons with brain lesions. In this session, Dr. Alvaro Pascual-Leone presented a series of non-invasive brain stimulation experiments that not only continues to delineate the role of lateral frontal cortex (LFC) in executive functioning but also begins to address the enhancement of cognitive control and translates to human disorders.

Non-invasive brain stimulation has been successful in clarifying the role of LFC during cognitive control. During the Ultimatum Game, the player must decide whether to accept a portion of a pot of money that has been offered to her. If the player rejects the offer, neither participant receives any money; therefore self-interest is competing against belief in fairness. The dorso-lateral prefrontal cortex (DLPFC) has been implicated in this task; however it remains unknown whether DLPFC activity is involved with suppressing the fairness impulse or suppressing the selfish impulse. Studies in which transcranial magnetic stimulation (TMS) was used to activate or inhibit right DLPFC have been instructive in this regard: Inhibition of the right DLPFC led to increased acceptance of lower (“unfair”) offers, suggesting that it plays a role in suppressing the selfish impulse. Activating the rDLPFC led to release of the selfish impulse as seen by players modifying their response without altering their fairness judgment.

Non-invasive transcranial direct current stimulation (tDCS) has also been used to study the impact on cognitive control of modulating LFC activity in healthy individuals. Specifically, concurrent application of anodal (activation increasing) stimulation to rDLPFC and cathodal (activation decreasing) stimulation to IDLPFC led to increased selection of lower-risk but lower pay-off gambles on measures of risky behavior including the Risk Task and the Balloon Analog Risk Task (BART).

Given that non-invasive brain stimulation can enhance executive functioning and that many human neurological, psychological and behavioral disorders involve lack of control of self-motivated impulses relating to LFC failure, non-invasive brain stimulation seems poised for translational interventions. Indeed, transient reductions in cue-induced cravings for nicotine, alcohol, cocaine and food have been observed with DLPFC stimulation. Furthermore, neural stimulation not only reduced cravings it was shown to change behavior. Furthermore, neural stimulation to rDLPFC of relatives of obese individuals a) modulated that region’s activity and b) led to decreased risk-taking performance on the BART, decreased food ingestion and decreased amount of time fixating on food items.

Taken together, this series of studies suggests that rLFC exerts a repressive control on self-centered impulses. However, it is important to note that when targeting rDLPFC, non-invasive brain stimulation induces not only local changes but distant sites in the neural network are modulated as well. The imprecise anatomic specificity of stimulation was touched upon in the discussion in two ways. First, if as these studies suggest, the rDLPFC is responsible for suppressing self-centered impulses, when its activity is “wiped-out” why are the effect sizes so small (e.g., why only a 50% rate of acceptance during the Ultimatum Game?) Given the current state of transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (tMS) it is difficult to test the involvement of several brain regions that might be working in a complex network. Furthermore, one can not be certain of the degree of demobilization of the stimulated region. Secondly, the role of the left DLPFC remains unclear. It is plausible that the balance of left and right LFC activity is equal to or more important than the absolute rLFC activity level.

The second major theme that emerged during the discussion session related to generalizability of the behavioral change, across time and domain. Specifics regarding the number of sessions necessary to provide cumulative and sustained effect revealed that while one session is not sufficient, maybe ten sessions would be. Regarding domain, it seems that increasing executive functioning in one domain can impact other behaviors (decrease risk-taking behavior correlates with decreased food cravings, decreased caloric intake and increased exercise). However, it is

not known effects would generalize across behavioral domain (decreased caloric intake will correlate with decreased smoking) nor is there any evidence that it generalizes to affective response. Insofar as generalization does occur, the possibility of producing undesirable effects (e.g., depression) must be carefully studied.