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Interaction of the Left Dorsolateral Prefrontal Cortex (l-DLPFC) and Right Orbitofrontal Cortex (OFC) in Hot and Cold Executive Functions: Evidence from Transcranial Direct Current Stimulation (tDCS)

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Abstract—An organizing principle which has recently emerged proposes that executive functions (EF) can be divided into cognitive (cold) and affective/reward-related (hot) processes related to the dorsolateral prefrontal cortex (DLPFC) and orbitofrontal cortex (OFC) respectively. A controversial question is whether cold and hot EF are functionally and structurally independent or not. This study investigated how the left DLPFC (l-DLPFC) and right OFC (r-OFC) interact in hot and cold EF using transcranial direct current stimulation (tDCS). Twenty-four healthy male subjects received anodal, cathodal and sham tDCS (20 min, 1.5 mA) over the l-DLPFC (F3) and r-OFC (Fp2) with a 72-h interval between each stimulation condition. After five minutes of stimulation, participants underwent a series of cold and hot EF tasks including the Go/No-Go and Tower of Hanoi (TOH) as measures of cold EF and the BART and temporal discounting tasks as measures of hot EF. Inhibitory control mostly benefited from anodal l-DLPFC/cathodal r-OFC tDCS. Planning and problem solving were more prominently affected by anodal l-DLPFC/cathodal r-OFC stimulation, although the reversed electrode position with the anode positioned over the r-OFC also affected some aspects of task performance. Risk-taking behavior and risky decision-making decreased under both anodal l-DLPFC/cathodal r-OFC and anodal r-OFC/cathodal l-DLPFC tDCS. Cold EF rely on DLPFC activation while hot EF rely on both, DLPFC and OFC activation. Results suggest that EF are placed on continuum with lateral and mesial prefrontal areas contributing to cold and hot aspects respectively.

Key words: cold executive functions, hot executive functions, dorsolateral prefrontal cortex, orbitofrontal cortex, transcranial direct current stimulation.

INTRODUCTION

Executive functions of the brain

Executive functions (EF) of the brain are defined as high-level, complex processes by which individuals optimize their performance in a situation that requires the operation of a number of cognitive processes (Baddeley, 1986) based on goals (Miller and Cohen, 2001). Executive functioning, or what is sometimes referred to as *cognitive control* (Gazzaniga et al., 2014), allows us to use our perceptions, knowledge, and goals to bias the selection of action and thoughts for purposeful goal-directed behavior and decision making. Moreover, it allows us to plan, predict consequences of our plans and evaluate them. Cerebral areas involved in EF can be seen as central hubs which modulate other brain regions to perform and coordinate goal-oriented activity (Goldberg, 2002). Thus, these areas have a meta-cognitive, supervisory, or controlling function that is not restricted to specific cognitive processes (Ward, 2015).

A number of models have been proposed to explain the organization of EF. While the multiple-demand network model (Duncan, 2010) assumes that a group of brain regions in the prefrontal cortex (PFC) is involved in and activated by a wide range of EF tasks, others propose a specific organization of the EF consisting of a hierarchy that runs from the premotor cortex (posteriorly) to the frontal poles (anteriorly) (Koechlin and Summerfield, 2007; Badre and D'Esposito, 2009). All models of EF share some common characteristics. For

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example, the biasing influence of EF (Miller and Cohen, 2001), distinction between automatic and controlled processing in EF (Gilbert and Burgess, 2012), and a flexible nature of EF processing in order to cope with novel situations (Shallice, 2002) are suggested by most models of EF. A key distinction between these models is the extent to which they assume that EF can be decomposed into several modular-like processes or constructed as a more unitary concept.

The least controversial organizing principle of EF is the distinction between the control of affective or reward-related (i.e. ''hot") versus purely cognitive (i.e. ''cold") stimuli (Ward, 2015) which has emerged only recently in the theoretical and empirical literature (Peterson and Welsh, 2014). *Hot* EF are goal-directed and future-oriented cognitive processes elicited in contexts that engender emotion, motivation, and a tension between immediate gratification and long-term rewards (Zelazo et al., 2005). Examples of hot EF include affective decision-making or delay of gratification (Poland et al., 2016). In contrast, *cold* EF are defined as goal-directed and future-oriented skills that are purely cognitive. Their corresponding cognitive processes do not involve much emotional arousal and are relatively ''mechanistic" or ''logically" based (Chan et al., 2008), such as inhibition, planning, and working memory (Poland et al., 2016). Hot and cold EF can also be distinguished regarding corresponding cortical regions in the brain. Hot EF primarily involve the orbitofrontal cortex (OFC) or ventromedial PFC (VMPFC) activity (Gazzaniga et al., 2014), whereas cold EF involve the lateral PFC including the dorsolateral PFC (DLPFC). This reflects the anatomical connectivity of lateral and orbital regions of the PFC involved in affective/rewarding versus cognitive/motor processes (Elliott et al., 2000; Öngür and Price, 2000).

The PFC is the main brain region primarily concerned with EF or cognitive control (Miller and Cohen, 2001) and is subdivided into the dorsolateral (i.e., DLPFC), medial (anterior cingulate), and orbitofrontal/VMPFC regions (Otero and Barker, 2014). While these regions are highly interconnected, it has been suggested that the dorsolateral regions are involved more closely in cognitive/metacognitive EF while the orbital and medial regions are involved in emotional/motivational EF (Otero and Barker, 2014). This implies that different EF domains are served by functionally and structurally different brain regions, however, it should be noted that a wide range of brain regions appears to be involved in EF, which can vary depending on the specific task employed (Chung et al., 2014). As such, there might be gradually overlapping contributions of different prefrontal areas in the performance of a specific task (Otero and Barker, 2014).

Role of DLPFC and OFC in hot and cold EF

Although PFC regions interact structurally and functionally, distinct regions of the PFC subserve discrete executive and cognitive functions (Van Snellenberg and Wager, 2009). Historically, the construct of EF, particularly regarding ''cool" EF, originates from studying patients with frontal lobe damage (Welsh et al., 2006). Current models of cool EF emphasize three independent components including working memory, inhibition, and shifting identified by Miyake et al. (2000) which are measures of core cognitive processes (Peterson and Welsh, 2014) and are strictly interrelated (Nejati et al., 2017b). Other cold EF include problem-solving and planning (Otero and Barker, 2014). These components together allow conscious and goal-directed thought and behavior (Prencipe et al., 2011). Clinical and experimental findings have led to a consensus that the DLPFC mediates these core cognitive functions (Duncan and Owen, 2000; Miller and Cohen, 2001). The DLPFC is part of the central-executive network (CEN) that plays a role in effortful cognitive control like cold EF (Turner and Spreng, 2015). Furthermore, left and right DLPFC are interhemispherically strongly connected, resulting in an interhemispheric balance, which is functionally disturbed in disorders accompanied by executive dysfunctions, such as major depression (Grimm et al., 2008; Salehinejad et al., 2017a) or attention-deficit hyperactivity disorder (Nejati et al., 2017a). Such a lateralized role of the DLPFC has been shown in executive control functions such as stroop performance too (Vanderhasselt et al., 2009). Studies showed enhanced cold EF by modulating cortical activity in the DLPFC in both normal (Brunoni and Vanderhasselt, 2014; Salehinejad et al., 2017b) and abnormal individuals (Wolkenstein and Plewnia, 2013; Rostami et al., 2017; Salehinejad et al., 2017a).

Emotional/motivational EF on the other hand are primarily mediated by the OFC and other medial PFC regions (Fuster, 2001). The OFC includes medial and ventral PFC regions with strong connections to the amygdala and limbic system (Chudasama and Robbins, 2006), by which it integrates affective and cognitive information and mediates motivated goal-directed behaviors (Ochsner and Gross, 2005; Salehinejad et al., 2017b). Recent experimental and theoretical results consistently suggest that the OFC is specifically involved in value-based and economic decision-making (for review see Padoa-Schioppa and Conen, 2017). Additionally, it is part of the default mode network (DMN) which is associated with different aspects of social cognition similar to hot executive functioning (Schilbach et al., 2008) and has a rival interaction with the CEN. While the DLPFC is more involved in top-down biasing of stimuli representations in favor of goal-directed behavior, the OFC is involved in valuing of those representations in decision making (Otero and Barker, 2014) and specifically economic decisions and value comparisons (Padoa-Schioppa and Conen, 2017). Therefore, EF that involve emotion, motivation, reward or valence critically depend on OFC activity and may not benefit much from DLPFC activation (Nejati et al., 2017c). Examples of such EF include temporal discounting or risky decision making that are characterized by uncertainty of action outcomes (Doya, 2008) and value comparisions. Brain imaging studies showed that the OFC along with the anterior insula is activated in response to situations involving risk taking or reward expectation (Mobini et al., 2002; Kuhnen and Knutson, 2005). Moreover, clinical studies have shown an involvement of the OFC in disorders and behaviors