Brain and Cognition 127 (2018) 34–41

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c

Transcranial direct current stimulation enhances retention of a second (but not first) order conditional visuo-motor sequence

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ARTICLE INFO

Keywords:
Implicit sequence learning
Serial reaction time task
Transcranial direct current stimulation
tDCS

ABSTRACT

This study examined the role of the left inferior frontal gyrus in the implicit learning and retention of a 'simple' first order conditional (FOC) sequence and a relatively 'complex' second order conditional (SOC) sequence, using anodal transcranial direct current stimulation (a-tDCS). Groups of healthy adults received either a-tDCS ($n = 18$) over the left inferior frontal gyrus or sham/placebo ($n = 18$) stimulation. On separate days, participants completed a serial reaction time (SRT) task whilst receiving stimulation. On one of the days, participants were presented with a FOC sequence and in another, a SOC sequence. Both the learning and short-term retention of the sequences were measured. Results showed a-tDCS enhanced the short-term retention of the SOC sequence but not the FOC sequence. There was no effect of a-tDCS on the learning of either FOC or SOC sequences. The results provide evidence of prefrontal involvement in the retention of a motor sequence. However, its role appears to be influenced by the complexity of the sequence's structure. Additionally, the results show a-tDCS can enhance retention of an implicitly learnt motor sequence.

1. Introduction

The ability to learn and use information that is sequentially structured contributes to motor, language, reading and social skills (Clegg, DiGirolamo, & Keele, 1998; Perruchet & Pacton, 2006). Sequence learning can take place without the intent to learn or awareness that the acquired information is influencing behaviour. In this context, the learning and use of sequential information is said to be implicit (Cleeremans, Destrebecqz, & Boyer, 1998). The implicit learning and retention of sequences is primarily supported by a cortico-striatal network comprising the basal ganglia, primary and pre-motor cortical areas, as well as the cerebellum (Doyon, Penhune, & Ungerleider, 2003; Hardwick, Rottschy, Miall, & Eickhoff, 2013). Additionally, evidence presented from non-invasive brain stimulation has implicated the prefrontal cortex in motor sequence learning (e.g., Alamia et al., 2016; Clerget, Poncin, Fadiga, & Olivier, 2012; Janacsek, Ambrus, Paulus, Antal, & Nemeth, 2015; Pascual-Leone et al., 1998). In this study, we examined the role of the left inferior frontal gyrus in the implicit learning and retention of sequences using transcranial direct current stimulation.

1.1. Implicit sequence learning on the SRT task

The neural circuitry that underpins implicit sequence learning has been widely studied using the Serial Reaction Time (SRT) task. On the task, participants are seated in front of a computer display in which a visual stimulus or cue repeatedly appears in one of four horizontal locations. The aim is to press one of four buttons on a response box that matches the location of the visual stimulus. The task involves presenting hundreds of trials in which a visual stimulus appears in one of the four locations, which in turn prompts the participant to provide a manual response. Unknown to participants, the visual stimulus follows a pre-determined sequence typically around 6–12 elements in length (for a review of the task see Robertson, 2007).

Research has repeatedly shown that healthy adults (and children) learn the sequence even though they may not be aware of its existence (e.g., Nissen & Bullemer, 1987; Thomas & Nelson, 2001). The typical finding in these groups is that reaction times (RT) become faster after

Abbreviations: a-tDCS, anodal-transcranial direct current stimulation; SRT, Serial Reaction Time; FOC sequence, first order conditional sequence; SOC Sequence, second order conditional sequence

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https://doi.org/10.1016/j.bandc.2018.09.006
Received 10 May 2018; Received in revised form 4 September 2018; Accepted 18 September 2018

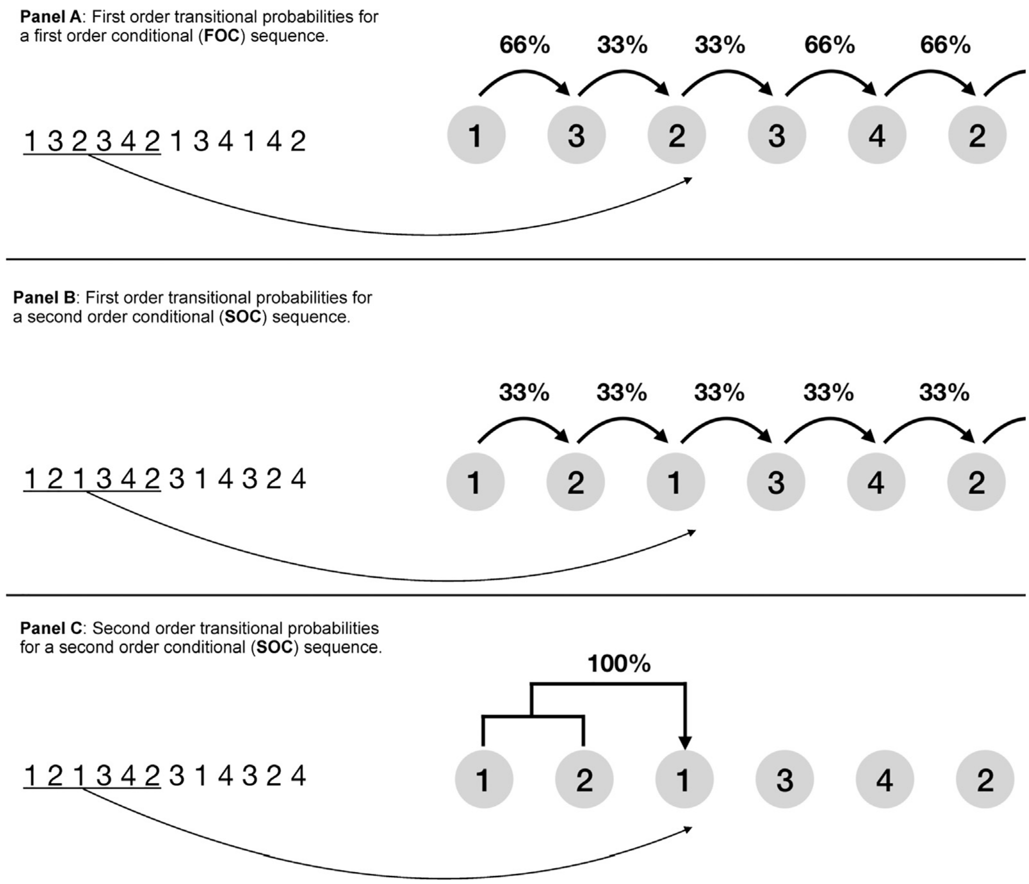

Fig. 1. Overview of transitional probabilities between elements in FOC and SOC sequences. Panel A shows first order transitional probabilities for a FOC sequence. For a FOC sequence, first order transitional probabilities reveal the structure of the sequence. This is not the case for a SOC sequence (Panel B). For this sequence, all first order transitional probabilities are equal. Instead, the structure is revealed by chunking consecutive elements or representing elements in hierarchy as shown in Panel C. All panels show the first six positions of 12 element sequence previously used by Deroost et al. (2010).

completing blocks of trials in which the sequence is repeatedly presented. These faster RT are not solely attributable to improvements in responding to the visual stimulus. This becomes evident in a block of trials presented at the end of the task in which the visual stimulus appears randomly in one of the four horizontal positions. When participants have learnt the sequence, RT slow down on the random block of trials. This rebound increase in RT from sequence to random trials is thought to occur because participants can no longer use knowledge of the sequence when responding to the stimulus (Robertson, 2007).

1.2. The effects of transcranial direct current stimulation on SRT task performance

Transcranial direct current stimulation (tDCS) has been used to study the neurological correlates of sequence learning and retention on the SRT Task. tDCS is a method of non-invasively modulating brain activity via a weak (e.g., 0.5–2 mA) direct current. During stimulation, the current from the anode electrode spreads through the cortex in the direction of the cathode or return electrode (Miranda, Lomarev, & Hallett, 2006). The positive charged current, causes the depolarisation of the resting membrane potential of affected neurones. The current does not cause action potentials. However, when a stimulated neural area becomes active (e.g. from completing a mental or motor task), there is an increase in neural firing rate and functional connectivity compared to when no stimulation is applied (Nitsche et al., 2008; Nitsche & Paulus, 2000; Peña-Gómez et al., 2012; Stagg & Nitsche, 2011). This increase in neural excitability by anodal stimulation, has been linked to enhancement effects of motor and cognitive functions in healthy controls (Coffman, Clark, & Parasuraman, 2014; Reis et al., 2008).

Several studies have examined whether a-tDCS can modulate implicit sequence learning and retention on the SRT task (Savic & Meier, 2016). Initial evidence (Nitsche et al., 2003) indicated that administering a-tDCS over the primary motor cortex whilst participants completed the SRT task enhanced implicit sequence learning, but, not all studies replicated this finding (Hashemirad, Zoghi, Fitzgerald, & Jaberzadeh, 2016; Kang & Paik, 2011; Kantak, Mummidisetty, & Stinear, 2012; Kuo et al., 2008). However, there is more consistent evidence suggesting a-tDCS over the primary motor cortex enhances the retention of a sequence (Hashemirad et al., 2016; Savic & Meier, 2016). Retention of the sequence on the SRT task is tested by presenting participants with blocks of trials comprising sequence and random stimulus presentations after the initial learning phase. For example, 5-minutes, 30-minutes or 24-hours after exposure to the sequence (Kang & Paik, 2011; Meier & Cock, 2014). In Savic and Meier's (2016) review of the literature, three out of three studies investigating the effects of a-tDCS on the retention of sequences via stimulation over the primary motor cortex all found significant enhancement effects (Ferrucci et al., 2013; Kang & Paik, 2011; Kantak et al., 2012). These results suggest that a-tDCS may enhance or stabilise the initial neural representation of the sequence following learning. As a consequence, knowledge of the sequence is less likely to decay or be overwritten with new information.

1.3. The role of the left inferior frontal cortex in sequence processing

The left inferior frontal gyrus may also play a role in the learning and retention of sequences on the SRT task. A number of models propose this structure may be specialised for building and processing verbal and visual sequences that are hierarchically structured or include non-adjacent dependencies (e.g., Fiebach & Schubotz, 2006; Friederici, Bahlmann, Heim, Schubotz, & Anwander, 2006; Koechlin & Jubault, 2006; Wilson, Marslen-Wilson, & Petkov, 2017). One source of evidence supporting this claim was presented by Bahlmann, Schubotz, Mueller, Koester and Friederici (2009). In this fMRI study, participants viewed a