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CORTICAL INVOLVEMENT IN THE STARTREACT EFFECT

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Abstract—The rapid release of prepared movements by a loud acoustic stimulus capable of eliciting a startle response has been termed the StartReact effect (Valls-Solé et al., 1999), and premotor reaction times (PMTs) of $<$70 ms are often observed. Two explanations have been given for these short latency responses. The subcortical storage and triggering hypothesis suggests movements that can be prepared in advance of a ''go'' signal are stored and triggered from subcortical areas by a startling acoustic stimulus (SAS) without cortical involvement. Alternatively, it has been hypothesized that the SAS can trigger movements from cortical areas through a faster pathway ascending from subcortical structures. Two experiments were designed to examine the possible role of the primary motor cortex in the StartReact effect. In Experiment 1, we used suprathreshold transcranial magnetic stimulation (TMS) during the reaction time (RT) interval to induce a cortical silent period in the contralateral primary motor cortex (M1). Thirteen participants performed 20° wrist extension movements as fast as possible in response to either a control stimulus (82 dB) or SAS (124 dB). PMTs for startle trials were faster than for control trials, while TMS significantly delayed movement onset compared to No TMS or Sham TMS conditions. In Experiment 2, we examined the StartReact effect in a highly cortically represented action involving speech of a consonant–vowel (CV) syllable. Similar to previous work examining limb movements, a robust StartReact effect was found. Collectively, these experiments provide evidence for cortical (M1) involvement in the StartReact effect.

Key words: motor cortex, motor preparation, speech, startle, StartReact, transcranial magnetic stimulation.

INTRODUCTION

The processes of movement preparation and initiation have been examined using methodology involving the use of a loud acoustic stimulus, capable of eliciting a startle reflex (for recent reviews see Valls-Sole et al., 2008; Carlsen et al., 2011, 2012). Using a wrist movement in response to a visual imperative stimulus (IS), Valls-Solé et al. (1995, 1999) sometimes presented a very loud ($>$130 dB) startling acoustic stimulus (SAS) at the same time as the IS. These ''startle'' trials produced fast premotor reaction times (PMT; time from the onset of the IS to the onset of the voluntary muscle activity) without changing the whole triphasic electromyographic (EMG) pattern or the movement kinematics (see also Carlsen et al., 2004b), a result known as the ''StartReact'' effect. The time course of such reactions following a SAS ($<$70 ms; see Valls-Solé et al., 1999; Carlsen et al., 2004b) has been hypothesized to be too fast to invoke cortical activity leading these authors to propose a process of subcortical triggering. They suggested that, at least for simple movements, sufficient details of the movement can be prepared and stored in advance, and then triggered by the startling stimulus from subcortical areas with limited involvement of the cortex. This subcortical triggering is thought to be mediated by the reticular formation, given this area in the brainstem is common to both the startle reflex and voluntary movement pathways (Yeomans and Frankland, 1995; Rothwell et al., 2002).

A number of recent experiments have provided data in support of subcortical involvement in the StartReact effect. One line of evidence has been through the examination of the StartReact effect for movements which are more dependent on cortico-motoneuronal connections such as finger abduction as compared to movements requiring muscles with a higher degree of innervation from reticulospinal pathways such as arm extension or coordinated grasp (e.g., Lawrence and Kuypers, 1968a,b; Davidson and Buford, 2006; Lemon, 2008; Baker, 2011). Although it is likely that both reticulospinal and corticospinal tracts are involved in a

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Abbreviations: AG1, first agonist; CV, consonant–vowel; EMG, electromyographic; ECR, extensor carpi radialis longus; FCR, flexor carpi radialis; HSP, hereditary spastic paraplegia; IS, imperative stimulus; nRPC, nucleus reticularis pontis caudalis; PMTs, premotor reaction times; PPN, pedunculopontine nucleus; RT, reaction time; SP, silent period; SSANOVA, smoothing spline analysis of variance; SAS, startling acoustic stimulus; SCM, sternocleidomastoid; TMS, transcranial magnetic stimulation.

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synergistic manner for all movements, movements more heavily dependent upon the corticospinal system would be less likely to show a reduction in reaction time (RT) in response to a SAS, if the StartReact effect is being mediated through a subcortical triggering mechanism. Indeed, both Carlsen et al. (2009) and Honeycutt et al. (2013) found a typical StartReact effect for the more reticulospinal-based movements; however in the finger abduction task there was little if any reduction in PMT on startle trials when a startle response was observed in the sternocleidomastoid (SCM+) as compared to when no startle indicator was observed (SCM−), which the authors argued was due to the cortically dependent nature of the task. Additionally, deep brain stimulation of the pedunculopontine nucleus has been shown to restore the StartReact effect in Parkinson's disease patients (Thevathasan et al., 2011), suggesting subcortical involvement in the release of a prepared movement. Lastly, Nonnekes et al. (2014) examined the StartReact effect in patients with hereditary spastic paraplegia (HSP), a condition in which corticospinal tracts are degenerated. Although RT to a visual stimulus was delayed in HSP patients as compared to healthy controls, both groups exhibited a similar response to the SAS, confirming an intact StartReact effect. This result supported the notion of subcortical triggering of a stored response through the reticulospinal tract, although the authors acknowledged that subcortical motor preparation likely also involves some cortical processing.

While there has been growing indirect evidence for subcortical storage and triggering, contrasting research has implicated cortical involvement in the StartReact effect. For example, Alibiglou and MacKinnon (2012) questioned the viability of the subcortical triggering hypothesis by investigating whether a single, suprathreshold pulse of transcranial magnetic stimulation (TMS) delivered to the primary motor cortex (M1) could influence the rapid triggering of a movement by a SAS. The premise of the methodology used by these authors was that TMS can delay voluntary RT for a brief period of time due to inhibitory processes in cortical mechanisms (e.g., Day et al., 1989). When TMS was applied prior to the onset of a startle-induced movement there was a significant delay in the early release of the movement In addition, the onset of SCM activity following a SAS, used as the indicator of startle, was not affected by TMS. The authors concluded that M1 does mediate the StartReact effect and response initiation was thus delayed when a cortical silent period (SP) was induced; however, the activity of the subcortical startle reflex pathway was not influenced. Furthermore, Marinovic et al. (2014) examined corticospinal excitability in response to a loud acoustic stimulus and found in addition to early response triggering, increased intracortical facilitation occurred during movement preparation, suggestive of a cortical role in the StartReact effect. Collectively, these observations may be explained through an activation model where the SAS increases cortical activation through an ascending reticulo-thalamo-cortical pathway (Maslovat et al., 2011; Carlsen et al., 2012). In this manner the SAS acts as a faster and non-voluntary trigger for a prepared movement; however, initiation occurs through the same cortical pathways involved in voluntary movement initiation.

In the following experiments we examined the involvement of cortical areas in the StartReact effect using two complementary experimental approaches. In Experiment 1, we extended and replicated the work of Alibiglou and MacKinnon (2012) but implemented a number of methodological changes to provide additional information pertaining to the involvement of cortical areas in the StartReact effect (see Methods, Experiment 1). In Experiment 2, we examined the StartReact effect for a highly cortically represented action involving speech of a consonant–vowel (CV) syllable. If movements are stored and triggered from subcortical structures by the SAS, it would be predicted that tasks requiring cortical involvement during movement initiation would not be subject to a StartReact effect.

METHODS – EXPERIMENT 1

In contrast to Alibiglou and Mackinnon (2012), who presented the SAS at 200 ms prior to the IS, we chose to replace the IS with the startling tone to avoid StartReact responses being triggered prior to the IS. In addition, we introduced a sham TMS condition to ensure participants were not affected by the audible and vibratory click that the TMS pulse produced, as recent evidence has shown that the sound click made by discharging the TMS coil may be sufficient to generate a response in reticular formation neurons (Fisher et al., 2012). We delivered TMS pulses at two time frames prior to EMG activation, 70 ms and 50 ms. We chose a time frame closer to the EMG onset than chosen by Alibiglou and MacKinnon as the closer the stimulation occurs relative to the overt response, the longer the RT delay (Day et al., 1989; Romaiguère et al., 1997; Hashimoto et al., 2004). We predicted the TMS pulse at 50 ms prior to the response would produce a longer RT delay as compared to the 70-ms pulse, providing additional evidence that the cortical SP is mediating the RT delay and thus cortical involvement in the StartReact effect.

Participants

Eighteen participants with no obvious upper body abnormalities or sensory or motor dysfunctions volunteered to participate in this study. All participants gave written informed consent, and the study was conducted in accordance with the ethical guidelines set by the University of British Columbia. Participants were right handed based on a laterality quotient greater than .60 on the Edinburgh Handedness Inventory (Oldfield, 1971). However, only data from thirteen participants (6 male, 7 female; age 22 ± 3 years) were employed in the final analysis. Five participants did not show activation in the SCM muscle during any startle trials (which is thought to be the most reliable indicator of a startle response), and thus were excluded from the