

Preparation for voluntary movement in healthy and clinical populations: Evidence from startle

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Abstract

In this review we provide a summary of the observations made regarding advance preparation of the motor system when presenting a startling acoustic stimulus (SAS) during various movement tasks. The predominant finding from these studies is that if the participant is prepared to make a particular movement a SAS can act to directly and quickly trigger the prepared action. A similar effect has recently been shown in patients with Parkinson's disease. This "StartReact" effect has been shown to be a robust indicator of advance motor programming as it can involuntarily release whatever movement has been prepared. We review the historical origins of the StartReact effect and the experimental results detailing circumstances where advance preparation occurs, when it occurs, and how these processes change with practice for both healthy and clinical populations.

Data from some of these startle experiments has called into question some of the previously held hypotheses and assumptions with respect to the nature of response preparation and initiation, and how the SAS results in early response expression. As such, a secondary focus is to review previous hypotheses and introduce an updated model of how the SAS may interact with response preparation and initiation channels from a neurophysiological perspective.

Keywords: Startle; Motor programming; Preparation; Initiation; Subcortical Pathways; Cortical

1. Introduction

The speed with which humans can react to external stimuli is remarkable from a lay-person's point of view. For example, in the 100m sprint at the Olympic Games, athletes regularly record reaction times (i.e., the time between the stimulus and the response) of less than 0.2 seconds. However, it is precisely this delay in reacting that is of interest to researchers. Questions arise as to the nature of the processes occurring between the onset of a stimulus and the onset of a response that allow complex movements to be produced at very short latencies. One way to investigate these processes in the laboratory is through the use of a very loud acoustic stimulus that is capable of producing a reflexive startle response. We are all familiar with being startled by an unexpected loud sound and the fast, involuntary response that goes along with it. Recently, however, researchers have found that when people are preparing to make a controlled, voluntary movement, a startle can elicit that movement with a very short reaction time (RT). The results of this research have been extremely valuable in furthering our understanding of how movement

preparation occurs in both clinical and non-clinical populations. The purpose of this review is to organize and present the knowledge gained from the use of startle methodology in order to provide a clearer picture of how a startle is used and what it can tell us about motor preparation for a variety of tasks and populations.

To examine response preparation we must begin with an understanding of the processes that are involved in producing a movement in response to a "go" stimulus. If we consider a situation where one of a number of possible movements is to be produced in response to the appearance of a "go" stimulus (known as a choice RT task), it was traditionally thought that a performer must identify the stimulus, select the appropriate response, and then prepare and initiate the motor commands associated with the selected response (Donders, 1969), although this view is greatly simplified as will be further explained below. Alternately, if the performer knows in advance what movement is required (known as a simple RT task) processing of information is simplified to only involve stimulus identification and response preparation/initiation. Importantly, this means that response preparation processes can occur before the "go" stimulus (known as pre-programming), during the RT interval (between the "go"

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and movement initiation), or once the movement has already begun (known as on-line programming). One area that has been extensively studied is under what circumstances pre-programming occurs and what are the limits of this advance preparation.

The examination of response preparation has involved a number of experimental protocols, each with their own advantages and limitations. For example, one methodology has involved the use of a movement blocking paradigm whereby participants are asked to make rapid elbow extension movements yet on some trials the movement is unexpectedly blocked (mechanically prevented) at initiation (e.g. Wadman et al., 1979). Although the arm does not move when blocked, a triphasic electromyographic (EMG) pattern is still observed as if the arm had moved, providing strong evidence that the sequence of contractions had been prepared in advance and then released as a unit (Latash and Gottlieb, 1991; Wadman et al., 1979). However, because the blocking paradigm involves perturbing the intended movement, some movement modification due to proprioceptive feedback is observed. Specifically, for arm movements when the movement is blocked, the EMG pattern is modified approximately 100 ms after the agonist onset, which is thought to be the result of reflexive activity. As such, when using the blocking paradigm, the investigation of prepared movements is limited to at most the first 100 ms after EMG onset (Nagelkerke et al., 2000), although earlier changes have been seen when blocking thumb movements (Hallett and Marsden, 1979).

Another line of research examining motor programming examines how manipulation of the required movement affects the latency of movement initiation. For example, Henry and Rogers (1960) found an increase in simple RT with increasing complexity of the required movement. The authors explained this finding via a “memory drum theory,” which suggested that more complex movements (in this case involving programming more action components) required retrieval of more elements from memory, thus increasing RT (see also Sternberg et al., 1978). Expanding on the work by Henry and Rogers, Klapp (1995; 2003) performed a series of studies manipulating response complexity by increasing both the duration and number of response elements. In a simple RT situation, RT did not change for a single component movement of different durations but did increase when extra components of the movement were added. Based on these results, Klapp hypothesized that for simple RT tasks, the internal features of the movement elements could be pre-programmed, while sequencing of movements could not. The suggestion that pre-programming could occur was an important distinction as it suggested that not all response preparation needed to occur after the “go” signal in a simple RT paradigm and thus information processing was not always performed in the same serial order.

It has been shown that the preparatory state of the motor system can also be probed using Transcranial Magnetic Stimulation (TMS). TMS can be used to index the excitability of the motor circuits associated with a particular movement. This is done by measuring the amplitude of a motor evoked potential (MEP) produced in the EMG record following the TMS pulse. As excitability within the pathway increases (e.g. as a result of motor preparation) the size of the MEP produced increases (Hasbroucq et al., 1997; Starr et al., 1988). However while this method can be used to index the excitability of motor pathways involved in a response, it cannot provide additional insight into the structural nature of the motor program that has been prepared.

Building on the evidence that a motor response can be prepared in advance, more recent methodology has allowed the examination of response preparation (more specifically, what has been fully pre-programmed) through the use of a startling acoustic stimulus (SAS). During a simple RT task, replacing the auditory “go” signal with a loud (≥ 124 dB) startling stimulus has been shown to elicit the prepared movement at a much shorter latency, with kinematics and EMG configurations largely unchanged. This effect has become known as the StartReact effect (see Carlsen et al., 2011; Valls-Solé et al., 2008 for reviews) and has been used as a probe for advance preparation as the triggered movement is thought to represent the pre-programmed muscle commands. Although there are several important methodological factors to be considered within this framework such as the required intensity of the acoustic stimulus (Carlsen et al., 2007; Luce, 1986), gender (Kofler et al., 2001), startle habituation (Carlsen et al., 2003a; Valls-Solé et al., 1997), or prepulse inhibition (Valls-Solé et al., 2005; Valls-Solé et al., 2008), this is not the purpose of the current review (for a review of methodological factors related to the StartReact effect, see Carlsen et al., 2011). Rather, it is to summarize the research involving startle methodology and how it can inform us about the process of response preparation. We will begin with a brief historical review of the startle literature and provide evidence that a SAS does indeed act as a trigger for pre-programmed responses. Next we will outline the startle research examining various aspects of response preparation such as what is prepared in advance, when does this preparation occur and how does advance preparation change with practice. We will also summarize research that has been conducted on clinical populations and how startle can be used as a valuable tool to isolate the processes associated with response preparation and response initiation. Lastly, we will introduce a neural model of response preparation that encapsulates and addresses some of the shortcomings of the current explanations provided for the response speeding found in many of the individual startle experiments.

2. Historical origins and initial support for the StartReact effect

While investigating the effects of motor readiness on a startle reaction, Valls-Solé et al. (1995) found that when they delivered a SAS (> 130 dB) at the same time as the visual “go” signal in a simple RT task, the RT was substantially shortened from 152 ms to 80 ms. It was initially thought that these shortened RTs might be the result of increased excitability within the nervous system due to the startle (Valls-Solé et al., 1995), allowing the voluntary response to be propagated more quickly. However, because the fast RTs observed were similar to that of the startle reaction itself (Brown et al., 1991) it was also possible that the observed responses consisted of an early startle reaction component with a superimposed later voluntary component. Therefore as a follow-up study, Valls-Solé et al. (1999) investigated the effect of a SAS on the pattern of muscle activity associated with a wrist flexion movement. EMG data showed that presenting a SAS once again led to a dramatic decrease in premotor RTs (from 171 ms to 77 ms), yet the stereotyped EMG activity associated with the movement was unchanged between control trials and those where a SAS was delivered. These results indicated that the intended response was not simply superimposing and adding on to an early startle response, but that the voluntary response was being produced similarly in the presence of a SAS, albeit with a much shortened latency. It was argued that the prepared action was somehow being driven at the speed of a startle because the observed startle-elicited RTs were 77 ms on average, while RTs of 140 - 180 ms are commonly observed in response to auditory and visual stimuli respectively (Brebner and Welford, 1980). Importantly, because in some of the startle trials the onset of EMG related to the movement occurred less than 65 ms after the SAS, it was suggested that the initiation of these movements was unlikely to have involved the cortex (Valls-Solé et al., 1999). This is due to the minimum calculated time of ~60 ms needed just to transduce the auditory stimulus and for neural transmission, let alone any cortico-cortical transmission (see Carlsen et al., 2004b; Valls-Solé et al., 1999 for timing details). Thus it was suggested that “sufficient detail of the movement characteristics may be stored in brainstem and spinal centres” (Valls-Solé et al., 1999, p. 937) so that it could be, in some cases, released early by the startle.

It might be argued that the large observed RT effect seen in response to startle could be attributed to intersensory facilitation (Nickerson, 1973) or simple stimulus intensity (see Woodworth, 1938). To examine this hypothesis, a study by Carlsen et al. (2007) systematically manipulated the stimulus intensity of the “go” signal from 84dB to 124dB and examined RT when a startle reaction was or was not elicited (as determined by EMG activity in the SCM muscle). Critically, the extent of the RT facilitation did not depend on the intensity of the stimulus if a startle reaction

was elicited. In other words, it was shown that that irrespective of the intensity, when a startle response was elicited by the stimulus, RT was facilitated to a large extent that could not be explained by simple stimulus intensity (Carlsen et al., 2007).

In order to determine whether a SAS was indeed acting to release a stored movement (i.e. motor program, Keele, 1968), Carlsen et al. (2004b) hypothesized that movements with differing characteristics with respect to their EMG timing (onsets and durations of bursts) would retain those differences in startle trials if the SAS was acting to release a stored program. If the SAS was just triggering a “generalized flexion response” with a short latency to onset (Brown et al., 1991; Landis et al., 1939; Yeomans and Frankland, 1996), these different patterns would no longer be evident in the SAS trials. Thus, subjects performed a series of ballistic arm movements to targets of 20, 40, and 60 deg where a 124 dB SAS was randomly presented in 20% of trials in place of the usual (82 dB) auditory “go” signal. Extension movements were employed as they were thought to be the opposite of what would be expected to be seen if indeed the response elicited was a “generalized flexion” (Carlsen et al., 2004b). Similar to what was found by Valls-Solé et al. (1999; 1995), premotor RTs (the time from the “go” stimulus to EMG onset) in startle trials (70 ms) were significantly shorter than in control trials (95 ms). Moreover, results clearly showed that the responses elicited at short latencies by the SAS retained similar EMG phasing characteristics and kinematics to the control movement counterparts. That is, when a 20 deg movement was planned, a 20 deg movement and its associated EMG pattern was elicited by the SAS, and when a 60 deg movement was planned, a 60 deg movement and its (different) associated EMG pattern was elicited (see Figure 1 for example data). These results showed that startle led to the early production of the particular movement that was planned in a simple RT task (Carlsen et al., 2004b) suggesting that a prepared action could be triggered by a SAS. Similar results have since been shown for various types of movements including stepping (MacKinnon et al., 2007; Nieuwenhuijzen et al., 2000; Reynolds and Day, 2007), sit-to-stand actions (Queralt et al., 2008), eye movements (Castellote et al., 2007), and head rotations (Oude Nijhuis et al., 2007; Siegmund et al., 2001).

The above results could still not rule out the original suggestion that increased neural excitability was the genesis of this RT speeding effect by startle (Valls-Solé et al., 1995). Therefore, an experiment was conducted by Carlsen et al. (2004a) where a SAS was delivered in situations where subjects could presumably pre-program the required action in advance (simple RT task) and situations where they presumably would not pre-program (choice RT task). In an equal probability choice RT task the required action is provided by the imperative “go” signal. In this situation, particularly for large possible response sets, the RT benefit of pre-programming a response decreases while simultaneously increasing the possibility of

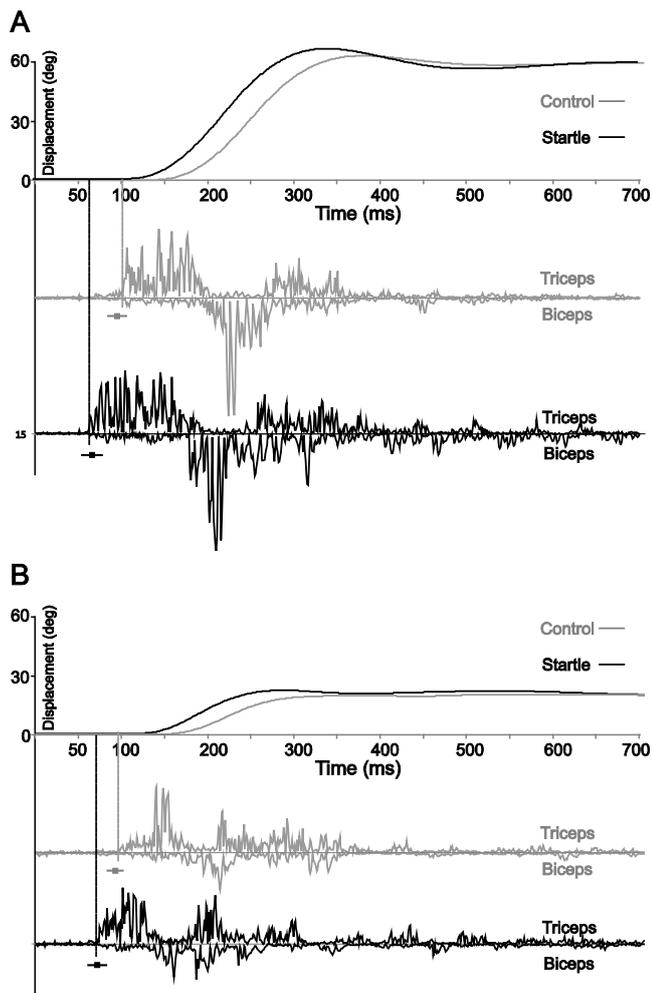


Figure 1. Example raw kinematic and EMG data from a single participant making a 60 deg (panel A) and a 20 deg (panel B) wrist extension movement in a simple RT task. Control trial (82 dB auditory “go”) is shown in grey, Startle trial (124 dB SAS) shown in black, time zero is stimulus onset. Displacement (deg) is shown on top and raw rectified EMG from triceps (positively rectified), biceps (negatively rectified) is shown below. Group mean (+/- SE) EMG onsets are shown (as data point) below each respective raw triceps EMG onset. Note that although RT latency was shortened in the Startle trials (dotted lines), triphasic EMG configuration and kinematics were unaffected. Adapted in part from Carlsen AN, Chua R, Inglis JT, Sanderson DJ, and Franks IM (2004a) Prepared movements are elicited early by startle. *J Mot Behav* 36:253-264. Copyright ©2004 Heldref Publishing Limited.

making errors. Thus, participants often choose not to pre-program a response when a choice is involved (Donders, 1969; Klapp, 1996). In the experiment by Carlsen et al. (2004a), the upcoming movement was either certain (simple RT: 20 deg right wrist extension), or uncertain and provided by the visual “go” signal (choice RT: 20 deg wrist flexion or extension with either hand). A SAS was delivered in conjunction with the imperative stimulus in 12% of right wrist extension trials, whether simple RT, 2-choice RT, or 4-choice RT trials. Results showed that RT

was only shortened by the presence of a startle for the simple RT trials, that is, only when a response was pre-programmed, supporting the suggestion that the SAS triggered a planned response and did not simply facilitate responses due to increased activation (Carlsen et al., 2004a). While no difference was observed in RTs for Choice RT trials by Carlsen et al. (2004a), other studies have shown some limited RT facilitation in choice RT situations (e.g. Kumru et al., 2006; Maslovat et al., in press; Oude Nijhuis et al., 2007; Reynolds and Day, 2007), suggesting that residual activation in the motor pathways due to startle may play a role in facilitating these responses.

In summary, the presentation of a stimulus that is capable of eliciting a startle reaction can act as an early trigger for a voluntary response that is prepared and ready to be executed, resulting in its early release (Carlsen et al., 2004b; 2007; 2011; Valls-Solé et al., 1999; 2008). Importantly, this StartReact effect can then be used as a probe, or tool, to elucidate the nature of motor response pre-programming.

3. Using the StartReact effect to probe response programming

3.1. Using StartReact to determine in what situations pre-programming occurs

One way in which a startle can be used to examine the nature of motor preparation is to provide information about whether or not a response is pre-programmed in a given situation. As previously shown, the presentation of a SAS led to early response production in a simple RT task but not in a choice RT task (Carlsen et al., 2004a). Not surprisingly this revealed that when the required response was known in advance, a response was pre-planned and ready to be executed, which would be beneficial to the required goal of responding quickly. In contrast, no response appeared to be pre-planned in a choice RT situation benefiting the goal of accurate responses (Carlsen et al., 2004a). However, the situation becomes much more complex when predicting whether or not a response will be pre-programmed in a RT task where the required response is known, but the identity of the imperative stimulus indicates whether a response is to be made or withheld. This task, generally referred to as a “Go / No-go” task, usually involves two stimuli, one of which is the “Go” stimulus (e.g. green light), and one which is the “No-go” stimulus (e.g. red light), whereas the required response is always certain. Donders (1969) proposed that in a Go / No-go task the response did not have to be selected and programmed during the RT interval since it was known in advance. If a beneficial strategy to enable fast responses is to pre-program and store a known response, Carlsen et al. (2008a) hypothesized that the required response would always be pre-programmed in a Go / No-go RT task. However, presenting a SAS in

addition to both the “Go” and “No-go” stimuli did not lead to early response initiation, and led to increased error rates, similar to that obtained when a startle was presented in a choice RT task (Carlsen et al., 2004a). The authors interpreted this result as indicating that a Go / No-go task may be treated similarly to a choice RT task in terms of response programming. That is, participants appeared to wait until after the imperative stimulus to fully prepare the response, suggesting that when participants are presented with the mere *possibility* of not having to respond, a strategy is employed whereby fast responding (i.e., short RT) is balanced with correctness in responding (c.f. Ramautar et al., 2004). This strategy is in contrast to one used by participants in a simple RT task in which maximal advance preparation would be most advantageous to optimal performance of the task. It may be that when confronted with a choice between some mutually exclusive actions, humans are biased toward accuracy (i.e. correctness) of responding, over a small decrease in speed of responding.

The requirement of having to make a choice does not preclude motor preparation before the “go” signal. For example, in a Go / No-go RT task, evidence of increased activation of cortical motor structures was seen in the lateralized readiness potential, a measure of lateralized differences in cortical activation derived from EEG, particularly when Go probability was high (Low and Miller, 1999). Increased activation of subcortical motor circuits, evidenced by the amplitude of the sternocleidomastoid (SCM) response in startle trials, in addition to limited RT facilitation, was also reported for a choice RT task as well as a Go / No-go task (Kumru et al., 2006), although the response was not triggered by the SAS in the same way as in a simple RT task. Thus, although in some cases a response may not be pre-programmed in its entirety for later triggering, there is evidence that some preparation of the motor system is undertaken, evidenced by observed increased activation of related motor circuits.

A startle has also been shown to be useful in revealing the motor preparation that occurs when only part of an upcoming response is known in advance of the “go” signal (e.g. Carlsen et al., 2009). Neurophysiological evidence for partial advance preparation has been provided by the examination of brain activation pattern via EEG (see Leuthold et al., 2004 for a review). However, a pre-cuing paradigm where one aspect of the required response is provided in advance (i.e. pre-cued) can also be used to investigate behavioral outcomes of partial advance preparation (Rosenbaum, 1980). Rosenbaum suggested that when part of a response was known, it could then be pre-programmed leading to shortened RTs. If this were the case the pre-programmed component should be triggered early by a SAS. In contrast to this prediction, it was shown that *multiple full responses* (that were a subset of the full range of response possibilities indicated by the pre-cues) were often elicited by a SAS at short latencies (Carlsen et al., 2009). For example, if the pre-cues provided information

that an extension movement was required but did not provide information regarding which hand would be used to respond, the presentation of a SAS often led to the triggering of simultaneous left and right hand extension responses (Carlsen et al., 2009). Similar results were observed for the pre-cue condition that indicated either a flexion movement with the left hand or extension with the right. That is, when the pre-cue indicated two possible bilateral targets (one for each hand), multiple responses were elicited at short latency by the SAS (Carlsen et al., 2009). This showed that rather than enabling the preparation of part of a response, pre-cues often led to the pre-programming of multiple responses in parallel, particularly when the response possibilities involved one distinct movement for each hand. When the two possible responses involved the same hand (flexion or extension), pre-programming of multiple responses was much less clear, and resembled results observed in a pure choice RT experiment (see Carlsen et al 2004a). This may have been influenced by the instructions to prepare whatever was possible based on the pre-cue. Thus the use of a SAS in this task exemplified the usefulness of the StartReact effect to illuminate exactly what had been pre-programmed depending on cues, response set, and instructions when multiple response options existed.

3.2. Using StartReact to determine when pre-programming occurs

The StartReact effect has not only been used to show what was pre-programmed, but in a similar way it can provide information as to *when* a response is fully programmed and ready for execution. For example, a SAS can be used to determine how long a response is held in readiness. Manipulating the foreperiod duration (i.e. the time between the warning and “go” signals) has been shown to affect RT in different ways. For example, when a “go” signal is certain to occur (e.g., in the 100m sprint start at the Olympics) RT gets shorter as the foreperiod “ages” (i.e., gets longer) since the likelihood of the “go” signal occurring increases with increasing time. However, if there is the possibility of no IS occurring, the shortest RTs are seen in the middle of a range of possible foreperiods (Drazin, 1961; Niemi and Näätänen, 1981). This effect has often been attributed to changes in the state of preparation of the motor system. However, in trials where a SAS was presented in a RT task involving a range of foreperiods from 2500ms – 5500 ms, with 20 % catch trials (where no IS was given), the RT differences were eliminated (Cressman et al., 2006). This indicated that the RT differences seen in control trials were more attributable to perceptual processing and that the movement was fully prepared throughout the range of variable foreperiods up to 5.5 sec.

The timing of when advance preparation of a known movement occurs may also depend on the temporal predictability of the “go” signal. Reaction time studies

often use a variable foreperiod to ensure participants are not able to anticipate when the “go” signal occurs and thus must react to the imperative stimulus. This uncertainty would require the participant to prepare the required movement early in the foreperiod such that it can be initiated as soon as possible following the “go” signal. In such studies, presenting a SAS as early as 1500 ms *prior* to the expected “go” signal can elicit the intended response. Specifically, in a simple RT wrist extension task with either a variable foreperiod (2 – 3 sec) or a fixed 3 sec foreperiod it was shown that the required response was elicited in more than 60% of trials when a SAS was delivered 1500 ms prior to the “go” signal. Notably, this proportion of trials where the “voluntary” response was elicited early rose to more than 90% of trials when the SAS occurred only 500 ms prior to the “go” signal (Carlsen and Mackinnon, 2010). This suggested that in a simple RT task, the response was fully planned and ready for execution well before the “go” signal much of the time. Since the proportion of trials where a SAS elicited the motor program increased from 60% to over 90% as the anticipated “go” signal neared, it appeared that the response was likely “programmed” and thus ready for initiation sometime between 2 sec and 1 sec prior to the “go” signal (Carlsen and Mackinnon, 2010). Similar results were shown for stepping initiation, where it appeared that the stepping response was progressively readied sometime between 1400 ms and 100 ms prior to the “go” signal (MacKinnon et al., 2007). In particular, only a small amplitude anticipatory postural adjustment (APA) associated with the stepping response was elicited early by a SAS presented 1400 ms prior to the “go” signal. However, when a SAS was delivered only 100 ms prior to the “go” signal, an APA of similar magnitude to control trials was elicited the along with a full step response (MacKinnon et al., 2007). This indicated that for a RT task involving stepping, the program was likely progressively assembled beginning with the APA component more than 1400 ms before the “go” signal.

In tasks that provided a much higher degree of temporal information about when the subject was meant to respond, the StartReact effect has been used to show that participants wait until much later to program the response. That is, participants wait until just prior to when the response is needed if the time of responding is known to a high degree of accuracy (Carlsen et al., 2003b; 2008b; Carlsen and Mackinnon, 2010). For example, in an anticipation-timing task where participants were asked to respond with a wrist flexion movement when a clock hand reached a target, a SAS was delivered 1500 ms, 500 ms, and 150 ms prior to the time of responding. In contrast to the RT results above for a variable foreperiod task, the SAS rarely led to early responses when presented 1500 ms or 500 ms prior to the target (0% and 18% incidence of early response respectively). However, when presented just 150 ms prior to the target a SAS resulted in early responses in 98% of startle trials (Carlsen and Mackinnon, 2010). Similar results were seen for a stop-signal anticipation-

timing task (Slater-Hammel, 1960), where no response was elicited by SAS as little as 200 ms prior to the target (Carlsen et al., 2008b). However, this may not be an accurate indication of when response preparation may occur in a regular anticipation timing task since, like in a go / no-go task (see above, Carlsen et al., 2008a; Donders, 1969; Kumru et al., 2006), there was the possibility that a response may not be required, so participants may have waited much longer than normal to program the response (see also Coxon et al., 2006). Finally, it should be mentioned that the use of a startle to show that motor preparation is undertaken later if it is known *when* the response is required with higher accuracy is not limited to tasks with an overt timing requirement. A task was performed where an arm extension movement was made through a target (located 55 deg from starting position), and the goal was to open the hand when the target was reached, although visual information about the arm was unavailable (e.g. Cordo, 1990). A SAS was delivered at various points (5, 25 and 45 deg) into the arm movement prior to the target, however, only when the arm was near the target (45 deg) did the SAS result in the early elicitation of the hand opening movement (Carlsen et al., 2003b). Although participants did not overtly use a timing strategy to perform the hand opening movement accurately, the secondary hand opening response was not programmed until just before it was required (i.e. <400ms prior to the target Carlsen et al., 2003b).

3.3. Using StartReact to determine how pre-programming changes with practice

The evidence above shows that the StartReact effect can be cleverly employed to reveal some of the previously inaccessible processes underlying motor preparation such as *what* is programmed and *when* pre-programming is undertaken depending on the task and the timing information available. Another way a startling stimulus can be used is to probe the changes that occur to advance preparation as a result of practice. As previously outlined, during performance of a movement in a simple RT task, pre-programming of the motor response can occur. It then follows to reason that if improvements in performance are observed as a result of practice, they should be at least partially attributable to the pre-programming of more accurate motor commands. To examine this, the startle paradigm has been used to investigate to whether practice can result in changes to motor pre-programming. The underlying assumption is that if changes to preparation occur as a result of practice, startle trials should trigger these changed movements as practice progresses and these changes should mirror difference found in control trials.

One of the first studies that used a SAS to examine practice related to response preparation required participants to perform an asymmetrical bimanual arm extension movement whereby the right limb moved twice the distance of the left limb (Maslovat et al., 2008). While

previous research has shown evidence for interference between the limbs such that both arms move in a similar pattern, this coupling of limbs can be overcome with practice (Sherwood, 1990; 1994; Walter and Swinnen, 1990; 1992). Furthermore, it has been suggested that amplitudes can be independently pre-programmed for each limb during bimanual movements (Heuer, 1986; 1993; Schmidt et al., 1979). It was predicted that early in practice both startle and control trials would produce a more symmetrical movement which would become more asymmetrical with practice. As expected, control and startle trials initially resulted in a symmetrical movement that resulted in overshooting with the left limb, but with practice participants improved at the task and produced a more asymmetrical movement in both startle and control trials. That is, not only did control trials show improvement in performance, these improvements were also reflected in the movements triggered by the startling stimulus following practice. The results of this study confirmed that data from SAS trials are sensitive enough to examine practice effects on response preparation, such that quantitatively different movements are triggered by the SAS as practice progresses. Furthermore this study confirmed that practice-related changes in performance could be attributed to more accurate pre-programmed motor commands.

After demonstrating that advance preparation of an asymmetrical bimanual movement changed with practice, a follow-up study was conducted using a bimanual arm extension task with symmetrical amplitudes but asynchronous initiation of the limbs, whereby the left limb was delayed by 100ms relative to the right limb (Maslovat et al., 2009a). This movement was chosen as it can be considered a very simplified version of a sequenced movement. Sequential movements have a long history of research (e.g., Keele, 1968; Lashley, 1951; Woodworth, 1938), as they allow insight into the processes associated with preparation and execution of multiple component movements. It was unclear if an asynchronous movement would be able to be programmed in advance as it has been suggested that the sequencing of multiple movement components may need to occur following the “go” signal (Klapp, 1995; 2003). However, the results indicated that the movement was prepared in advance as it was triggered by the startling stimulus throughout the practice period. In addition, similar to the results of the asymmetrical amplitude bimanual movement (Maslovat et al., 2008), the between-limb timing requirement improved with practice for both control and startle trials, lending further support to changes in advance preparation being the locus of task improvement for this movement.

To further test the limits of advance preparation, a third study was conducted using a SAS in a practice paradigm (Maslovat et al., in press). In this study, a two-component unimanual arm movement was compared to single-component unimanual arm movements to determine if practice resulted in a change in how the movement was prepared. Although the previous work confirmed a

sequenced bimanual movement could be prepared and triggered by the startling stimulus (Maslovat et al., 2009a), research involving multiple-component unimanual movements has shown that only the first element is prepared in advance with the second movement prepared on-line (Adam et al., 2000; Khan et al., 2006; Vindras and Viviani, 2005). However, with practice it has been hypothesized that movement “chunking” would occur such that a multiple component movement can be recoded and controlled by a single motor program that can be fully prepared in advance (as hypothesised by Klapp, 1995). Based on these ideas, it was expected that early in practice there would be a difference in the movement produced between control trials and startle trials as the SAS would only trigger the first component of the two-step movement. However with practice, if the entire movement could be pre-programmed then the startling stimulus would trigger a movement similar to that performed during control trials. Contrary to expectations both single and double element movements were triggered at short latencies by the SAS with similar kinematics EMG pattern as compared to control trials. From this result, Maslovat et al. (in press) concluded that the entire two-component movement was able to be prepared in advance from the start of practice and thus there was no change in *mode* of preparation as a result of practice. Furthermore, it caused the authors to question the assertion that the sequencing of multiple-component movements could not be completed in advance (Klapp, 1995; 2003) and revisit how the SAS acts to initiate the movement, a topic we will return to later.

Collectively, these studies show that the use of a SAS within a learning paradigm can probe preparation processes at various stages of skill acquisition. In addition to providing information as to how specific movements are prepared, the results of these experiments confirm that improvements in performance can be at least partially attributed to changes in the motor preparation process. With practice, participants are better able to prepare in advance the motor commands associated with a movement, such that they are more likely to achieve the goals of the task showing that startle methodology is sensitive enough to also evaluate changes to the process involved in pre-programming as a result of practice.

3.4. Using StartReact in clinical populations

The use of the StartReact effect as a probe for motor planning may also provide some insight into motor dysfunction. For example, in patients with various neurological disorders such as cerebellar ataxia or Parkinson’s disease (PD) it may often be unclear whether associated motor dysfunction is solely the result of a deficiency in planning a motor action or in the execution of the motor output. For example, akinesia, which is a term used to describe the lack of spontaneous voluntary movement, is a common symptom observed in some patients with Parkinson’s disease (PD). In both the upper

and lower limbs, akinesia is characterized by impaired initiation of self-paced movements and prolonged reaction times to external cues. Historically, this slowness in responding has been attributed to deficits in motor response programming (Georgiou et al., 1993; Sheridan et al., 1987), notwithstanding the observation that the presentation of external cues can also have the effect of facilitating movement (e.g. line markings on the ground to facilitate stepping, Griffin et al., 2011; Jiang and Norman, 2006). However, when investigating whether having patients prepare to react would decrease startle response habituation, it was observed that RTs were facilitated in patients with PD and multiple system atrophy (MSA) but not in patients with progressive supranuclear palsy (PSP) (Valldeoriola et al., 1998). The authors suggested that this finding allowed PD and MSA to be easily differentiated from PSP by using a SAS. Importantly, however, this finding may illuminate the underlying processes contributing to akinesia and slowness in PD. Findings from a recent study showed a similar effect on RT in patients with PD. Specifically, in a simple RT task involving a 20 deg arm extension movement to a target, premotor RT was decreased from 170 ms to 99 ms when patients were off their anti-parkinsonian medication, and from 149 ms to 95 ms when on medication (Carlsen, 2010). A similar result was shown whereby patients with Parkinson's disease showed RT and movement speed improvements when subthreshold TMS was applied over motor cortex. The authors suggested that increased cortical excitability provided by the TMS pulse led to faster and more normalized response initiation in the patients (Pascual-Leone et al., 1994). Since it is assumed that StartReact effect is the result of the early triggering of a prepared response it can be concluded that in patients with PD, akinesia and slowness in reacting may be more attributable to deficits in response initiation processes than to response programming processes. However, these startle results are currently preliminary results, so any conclusions should be considered carefully.

4. Model of response preparation & initiation

4.1. Basic features

The evidence presented in the current review has shown that presenting a SAS to subjects preparing to react in a simple RT task results in substantially shorter RTs (i.e. <70 ms) than would normally be expected if normal stimulus-response processing occurred (Carlsen et al., 2004b; Valls-Solé et al., 1999; 2008). This "StartReact effect" was thus suggested to result from a pre-planned movement being released early from subcortical structures (Carlsen et al., 2004a, b; Rothwell, 2006; Valls-Solé et al., 1999; 2008). For this to occur it was suggested that details of the upcoming movement were likely stored in subcortical areas

(likely reticular formation) that were common to both the voluntary response and startle response pathways, and then involuntarily triggered by the startle (Rothwell, 2006; Valls-Solé et al., 1999). While this explanation is appealing, as it provides a mechanism for the StartReact effect, the neural pathways involved are not well described and structures involved in the storage and triggering of the response are unclear. The purpose of this section is to introduce the framework for a model of response preparation and initiation that (1) presents a more formalized neural mechanism for the RT facilitation observed due to SAS (i.e. the StartReact effect), and (2) explains previous data showing how simple RT changes under certain circumstances.

It was traditionally thought that in RT tasks, several processes must occur prior to the response being expressed. First, the "go" signal has to be identified, then the response must be prepared and executed (Schmidt and Lee, 2011). In the case of a simple RT task, no response selection processing needs to occur since the response is known beforehand. Nevertheless, the processes underlying the identification of the "go" signal and the execution of the planned response each take some time to complete resulting in normal simple RTs ranging from 140 ms to 180 ms (Brebner and Welford, 1980). In the model we are proposing, we assume that preparation of the "motor program" and response initiation are separate processes (e.g. Ghez et al., 1990) that each involve a change of neural activation level. Although in some situations these processes may overlap, full motor preparation can occur prior to the "go" signal if sufficient time and information is given between the warning and response signals. These preparatory processes can be observed at a neural level through the examination of event-related brain potentials such as the readiness potential and lateralized readiness potential (see Leuthold et al., 2004 for a review), which have been shown to be dependent on whether movement is expected and /or self-selected (Leuthold, 2003; Praamstra et al., 1995).

Thus, the process of motor program preparation can be conceptualized as increasing activation of a neural network to some level below threshold. Initiation of the movement is then achieved by the input of additional activation of the network beyond threshold, as has been suggested in the saccade literature (e.g., Carpenter and Williams, 1995; Hanes and Schall, 1996; Nazir and Jacobs, 1991). We propose that under certain circumstances the presentation of a SAS can act to provide that additional input, via a subcortically mediated pathway that is faster than the conventional information processing route. However, first it is important to describe the basis of the model involving the two processes in the absence of a SAS.

4.2. Preparation (programming) and initiation processes

As noted above, there are many circumstances where it is beneficial or even essential to prepare a motor action in advance of when it is needed. However, although little neural evidence has been provided to support their existence, many researchers accept motor programs as literal entities (Summers and Anson, 2009). One proposed neural explanation for a motor program is the “cell assembly” (Wickens et al., 1994) which is a group of cortical motor neurons with increased strength of synaptic connections (Hebb, 1949). In this view, a network of neurons with increased synaptic strength act as a functional unit to determine the pattern and combinations of cortical neurons to activate for a given motor action. Importantly, it was suggested that the process of preparation for a discrete action involved activating the appropriate cell assembly to a level below the “ignition point.” As such, only a relatively small input would irreversibly “ignite” the assembly leading to motor output (Summers and Anson, 2009; Wickens et al., 1994).

While it has been shown preparation of the motor system can occur in advance of the “go” signal when the response is known in advance (Chen and Hallett, 1999; Coxon et al., 2006; Klapp, 1996; MacKinnon and Rothwell, 2000), it is unclear exactly what processes this activation represents. EEG activity over motor cortex (in particular the motor related potential) has been taken as evidence that cortical motor preparation occurs well in advance of motor output when the response is known in advance (Cui and MacKinnon, 2009; Kornhuber and Deecke, 1965; Leuthold et al., 2004), and may well be evidence of cell assembly activation. To minimize RT, it would be most beneficial to raise the neural activation level of the cell assembly to as close as possible to threshold during the foreperiod phase. However, due to the nature of its components, stochastic variability (i.e. “noise”) occurs within the nervous system from such sources as cellular, electrical, or synaptic noise (see Faisal et al., 2008 for a review). Since this variability would be present in the input to the cell assembly, the ongoing level of activation within the assembly would also contain a certain amount of noise, or variability. This variability would restrict the level of activation a participant could achieve during pre-programming as the level would have to be kept low enough so that random noise could not increase activation beyond threshold causing an unintentional trigger of the movement. Thus we propose that the motor programming process can be thought of as the noisy activation of a neural network to a level below the threshold required for cascading output. The amplitude of the stochastic noise may also partially determine the distribution of observed RTs as any given trial would have variability regarding the level of activation achieved during preparation. That is, if activation is constantly changing due to inherent noise in the system, movement initiation processes could occur when the

activation level is relatively high or low (see Figure 2A). This difference in activation would change the amount of extra activation required to achieve threshold, which would result in a longer or shorter RT.

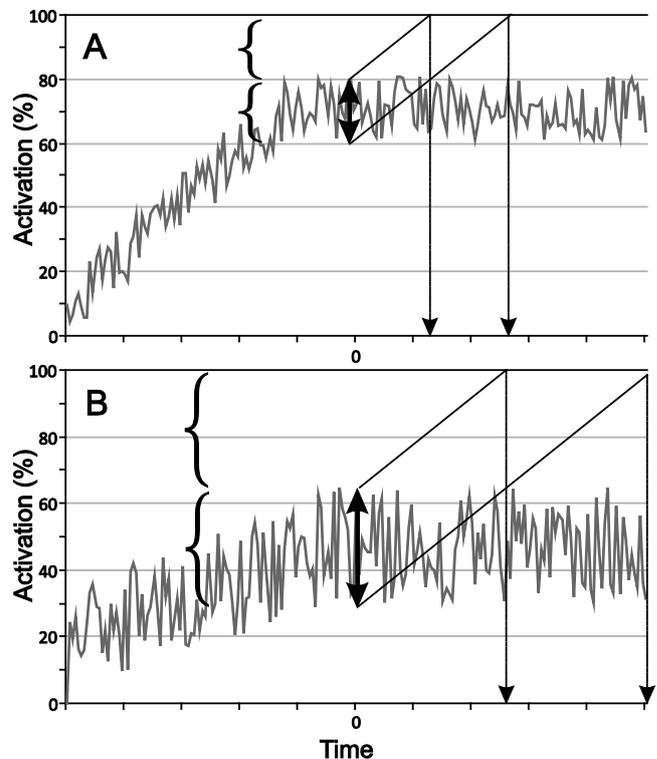


Figure 2. Schematic representation of neural activation related to motor program preparation (grey) and program initiation (black) as a percentage of threshold (e.g. 100%). Panels exemplify situations in which there is lower noise (A) or higher noise (B) – see text for examples. In panel (A) noise is $\pm 10\%$, thus mean activation can achieve a higher level (70%) without risk of accidental triggering (safety margin here is represented as $1\times$ noise amplitude). In panel (B) noise is $\pm 18\%$ so mean activation must be kept lower (47%). Program initiation (onset at time zero, double headed arrow) is represented as a constant increase in activation. Note that noise amplitude affects the width of the distribution (space between dashed arrows) of time taken to reach threshold once initiation process starts as well as the latency of movement initiation.

Following response preparation, movement initiation processes must occur. We consider a prevalent model from the saccade literature whereby initiation involves an increase in neural activation levels over time until a threshold level is reached (Carpenter and Williams, 1995; Hanes and Schall, 1996; Nazir and Jacobs, 1991). This process has been described using the concept of a neural accumulator, whereby differences in initiation time can be attributed to differences in level of preparatory activation with respect to threshold as illustrated in Figure 3A (e.g. in a similar way to differences in threshold level as suggested by Maslovat et al., in press; Nazir and Jacobs, 1991), differences in the rate of activation accumulation as illustrated in Figure 3B (Carpenter and Williams, 1995), or

a hybrid of the two (Pacut, 1977). If one accepts this conceptualization of response preparation and initiation, during simple RT preparation would occur in advance, resulting in neural activation accumulation to a certain level based on the inherent noise in the system. RT would be then be the time required to identify the “go” stimulus and increase neural activation to above threshold. This initiation time would depend not only on the level of activation achieved during preparation but also the rate of activation accumulation.

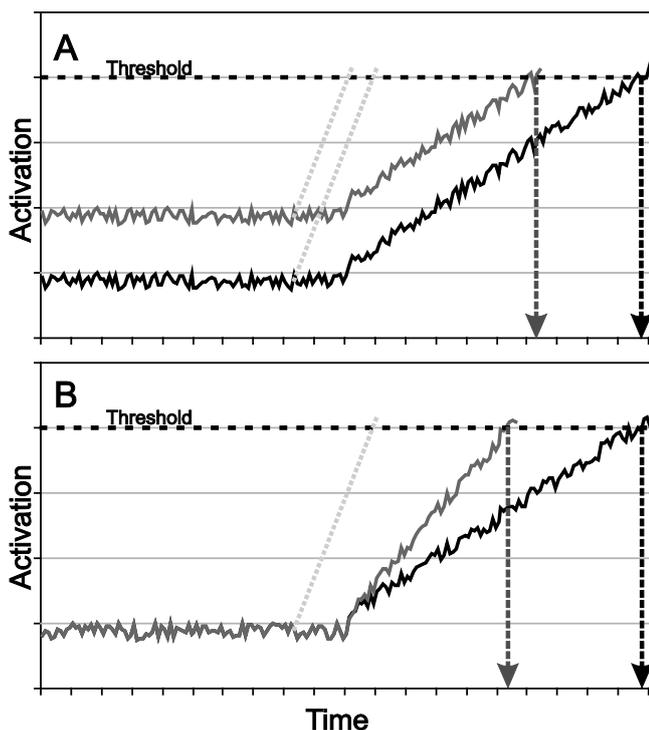


Figure 3. Schematic representation of program initiation activation (arbitrary units). Panel (A) shows the effect of motor program activation level where with higher initial activation (grey), threshold is reached in less time than for lower initial activation (black). Panel (B) shows the effect of rate of activation accumulation related to initiation processes where with a faster rate (grey), threshold is reached earlier than for a slower rate (black). Hypothetical startle initiation (light grey dotted line) is shown in both panels. Note that startle activation starts earlier and proceeds at a faster rate in both cases. See text for further discussion of the model.

4.3. Factors affecting preparation and initiation

Given the explanation we have offered above for preparation and initiation, there are a number of factors that would be expected to affect these processes. For example, it has long been known that increased complexity of movement results in longer RTs (Henry and Rogers, 1960), a result typically attributed to additional programming time. In particular, movements involving multiple components appear to have the largest effect on RT with more components leading to longer RTs (Klapp, 1996; 2003; Maslovat et al., in press), although it has also been shown

for movements with an increased amplitude or accuracy demands (Khan et al., 2008; Lajoie and Franks, 1997). However, these effects are seen even in simple RT situations when the response can presumably be pre-programmed. In order to explain differences in simple RT for more complex movements we consider that rather than increased programming time, these effects may be due to a lower activation level achieved during preparation, thus requiring more time to reach initiation threshold. In other words, perhaps for some movements the activation level during pre-programming cannot be brought as close to threshold. More complex or difficult movements, particularly those involving a sequence of actions, likely involve either larger or more numerous cell assemblies. It is conceivable that this increase in neurons involved would lead to an increase in the amount of noise in the system. With higher amplitude noise, the mean level of preparation (activation) would have to be decreased so that the noise would not accidentally initiate the assembly (see Figure 2B). This model of preparatory activation results in two predictions that are supported in the literature. With the initiation process working at a fixed rate, more complex movements should result in longer RTs, as well as a larger distribution of RTs (e.g. Klapp, 1996; 2003).

In some cases, different RTs can be observed even with the same required movement complexity. Specifically, novel (or not well-practiced) movements tend to result in longer RTs compared to once that same movement is well-learned (Klapp, 1995; Maslovat et al., in press). A similar argument to the one made for more complex movements may also apply to the role of practice on motor preparation and RT. It has been suggested that the threshold for initiation may be higher for novel movements (Maslovat et al., in press; Nazir and Jacobs, 1991) resulting in longer RTs. If instead we consider the threshold level to be fixed, a difference in RT following practice may indicate that preparation activation level of novel movements may not achieve the same level as those well-practiced (similar to differences suggested between complex and simple movements). Presumably, this activation level difference is because the cell assembly for a less practiced movement would not have as strong of synaptic connections as a well-learned movement. Cell assemblies are thought to be formed via synaptic modification, which strengthens the connections between cells that are repeatedly co-activated (Wickens, 1993; Wickens et al., 1994). We suggest that for novel movements the weaker neural connections would have a net result of a more noisy system. This increased noise would in turn limit the maximum achievable level of preparatory activation as explained above. Because of the lower activation level and increased noise, RTs should be longer and more variable. Importantly, this view predicts that as the movement becomes more well learned, RTs should become shorter (due to a higher achieved level of preparatory activation) and less variable (due to lowered noise) which is exactly what is described in motor learning literature (Klapp, 1995; Maslovat et al., in press).

An argument may also be made for increased noise in the nervous system of patients with neurological disorders. As previously described, patients with PD typically have slowed RTs. Indeed, slow RTs observed in PD have traditionally been attributed to deficits in motor programming or preparation (Georgiou et al., 1993; Sheridan et al., 1987). It may be that the disease state leads to increased noise and thus a lower level of preparatory activation manifesting as slowed RTs as described above. Support for this hypothesis has been provided by research showing decreased duration and amplitude of the readiness potential in PD populations (Shibasaki et al., 1978; Simpson and Kharabet, 1987).

To summarize, we propose that the level of activation achieved in preparatory processes may depend on the inherent noise in the system, which may depend on the complexity of the movement, experience with the movement, and neurological disease. These effects can be seen in RT distributions for various tasks or populations, but assume a constant increase in initiation activation following the imperative stimulus. There is evidence, however, that differences in initiation time can occur as a result of differences in the rate of activation accumulation (Carpenter and Williams, 1995; Hanes and Schall, 1996). The most predominant means by which the rate of accumulation would be increased is by stimulus intensity which is well known to result in decreases in RT (Luce, 1986; Woodworth, 1938). It has been suggested that higher stimulus intensities lead to increased neural activation of sensory circuits (Carlsen et al., 2007; Levick, 1973; Maslovat et al., 2009a; Nissen, 1977), which likely alters the accumulation rate such that thresholds are reached in less time as compared to lower intensity stimuli (e.g. see Figure 3; see also Grice, 1968; Maslovat et al., in press).

5. A Possible Mechanism for the RT Facilitation Effect of a SAS

5.1. Neural mechanism

As we return to the explanation of why startle trials produce movements at such short latencies, it may be tempting consider startle trials as an extreme case of stimulus intensity. If a more intense stimulus leads to quicker initiation times as described above, then surely a SAS would substantially reduce initiation time and thus RT. While we believe stimulus intensity may partially contribute to a reduction in reaction time for startle trials we do not believe this is the complete explanation. This is based on evidence that stimulus intensity effects are separate to those involved in the involuntary release of a prepared movement (Carlsen et al. 2007). As previously explained, the results of this study showed that the reduction in RT due to a SAS could not be explained solely by a stimulus intensity effect, providing evidence that the

initiation process when startled is likely different to that of faster neural accumulation due to a louder imperative stimulus. In addition, when stimulus intensity is increased (without eliciting a startle response) initiation times are reduced but the observed latency of the response is still within the time period whereby cortical processing could occur. Conversely, the RTs associated with a SAS occur at a latency that would likely preclude cortical processing.

Previous hypotheses regarding the mechanism for RT facilitation by a SAS involve the subcortical storage of a motor program (e.g. Carlsen et al., 2004b; Rothwell, 2006; Valls-Solé et al., 1999). In contrast, here we propose that a SAS acts to facilitate RT by quickly and directly increasing the activation of the initiation mechanism via a subcortically mediated ascending pathway such that the cortically stored response (in the form of a cell assembly) is triggered without the usual cortical processing. One appeal of this hypothesis is that it does not rely on a second, subcortical representation of the movement. In order for the startle to initiate a cortically readied and stored motor program, sufficient ascending activation would have to interact with the structures normally involved in response initiation. There is some evidence that the thalamus is instrumental in the initiation of prepared responses. For example, Haider et al. (1969) measured brain potentials directly from thalamic and cortical sites using intracerebral electrodes during stereotaxic surgery while subjects performed a simple RT task. The cortical areas showed activity similar to the motor related potentials such as the CNV (e.g. Leuthold et al., 2004). However, two separate thalamic wave complexes were observed from the thalamic motor relay nuclei: a first wave emerged after the warning signal related to programming onset, and a second wave was observed between the “go” signal and the response onset thought to be responsible for response initiation (Haider et al., 1969). In this way, thalamus may be responsible for providing the necessary input to a cortical cell assembly to result in response initiation (see Haider et al., 1969 for a figure depicting the implicated motor pathways). As such, it is possible that that ascending activation generated by the startle reflex in reticular formation directly increases activation of the motor relay nuclei in the thalamus to a sufficient degree to act as an early and involuntary response trigger.

Some recent evidence has been provided that cortical areas are involved in the motor preparatory aspect of the StartReact effect, through the use of transcranial magnetic stimulation (TMS). When subthreshold TMS was applied over motor cortex RT improvements were seen in both healthy controls and PD patients suggesting that the TMS pulse led to increased cortical excitability (Pascual-Leone et al., 1994). On the other hand, suprathreshold TMS over motor cortical areas has been shown to induce a silent period whereby a suppression of EMG activity is observed for a brief period of time (Pascual-Leone et al., 1994, 1999). This TMS-induced “silent period” has been recently used to examine whether a motor program is indeed stored

in subcortical structures. If motor commands are stored subcortically, then a cortical silent period should not affect startle elicited RTs. However, two recent studies showed a significant delay in startle trial RTs when TMS was applied to the motor cortex (Alibiglou et al., 2009; Stevenson et al., 2011). While this preliminary data should be treated with caution, it does suggest that cortical pathways may be involved in mediating the rapid release of a planned movement by a SAS. While this result is inconsistent with subcortical storage of motor commands, it fits the hypothesis presented here that a SAS acts as a subcortically mediated trigger for a cortically stored motor program.

While TMS has been shown to delay startle trial RTs, it does not affect the latency of the startle response indicators (i.e. SCM; Alibiglou et al., 2009; Stevenson et al., 2011). This has been taken as evidence that the descending pathway for the generalized startle response is distinct from the suggested ascending pathway involved in the release of the prepared movement. This result is corroborated by the work examining pre-pulse inhibition (see Valls-Solé et al., 2008 for a review), whereby the startle response can be significantly suppressed when the SAS is preceded by a low intensity electrical stimulus to the finger (Valls-Solé et al., 2005) or a 84dB auditory tone (Maslovat et al., 2009b). The pre-pulse did not affect the RT at which the movement was triggered, providing additional evidence that the startle response and StartReact effect are physiologically different. Functional magnetic resonance imaging (fMRI) has also been used during pre-pulse inhibition of the startle response, indicating the importance of the thalamus in the circuitry of sensorimotor gating (Campbell et al., 2007; Hazlett et al., 2001; Kumari et al., 2005).

Since we are suggesting that the activation associated with a SAS produces an involuntary, subcortical trigger for a cortically prepared response it is important to identify possible neural pathways associated with the startle response and how they interact with a thalamic trigger of a movement. The startle response pathway includes the activation of subcortical brain structures via connections between the cochlear nucleus and the caudal reticular formation, with the giant neurons of the nucleus reticularis pontis caudalis (nRPC) acting as control neurons for the startle reflex (Davis, 1984; Koch, 1999; Yeomans and Frankland, 1996). The nRPC neurons conduct to the various levels of the spinal cord, along the reticulo-spinal tract, and activate motor neurons both monosynaptically and disynaptically via interneurons (see Yeomans and Frankland, 1996 for a figure depicting these pathways). This motor activation then produces the measurable EMG response and movement associated with the startle reaction. The startle related activation is not only descending, however, and ascending activation may influence the motor system via a fast pathway. The required ascending pathway for direct response initiation may involve ascending projections from the pontine reticular formation to thalamus. Indeed it has previously been shown that motor systems are influenced by ascending reticular activation via reticulo-thalamo-

cortical circuits (McDowell et al., 2006; Skinner et al., 2004) or indirect activation through basal ganglia (Takakusaki et al., 2004). Increased activation of thalamus would then provide the required input to the cortical cell assembly to trigger the prepared movement as explained above. Furthermore, the onset of activation would occur earlier due to the shortened pathway, and the slope of accumulation would be steeper (see Figure 3 for a schematic illustration) resulting in much faster RTs as observed.

A calculation of the time required for response triggering via direct activation of a reticulo-thalamo-cortical pathway can be estimated based on earlier studies. First, it has been shown that an acoustic stimulus can result in activation of lateral lemniscus (LL, at the level of the Pons) at a latency of 5-7 ms (Erwin and Buchwald, 1986; Stelmack et al., 2003). This is in contrast to the 35 ms required for an auditory tone to reach the auditory cortex (Erwin and Buchwald, 1986) for voluntary triggering of the response. Second, using brain stem auditory evoked responses, it was shown that another 5-10 ms are required for conduction between LL and thalamus (Stockard et al., 1977). Third, conduction between thalamus and primary motor cortex takes another 2-4 ms. Finally, it has been shown using TMS that conduction time from primary motor cortex to the limb muscles is approximately 25 ms (Pascual-Leone et al., 1994; Rothwell, 1997). Conservatively adding these values gives a minimum time of 46 ms for nerve conduction, which can then account for the RT values observed in response to a SAS.

5.2. Empirical support for a subcortical triggering model from Startle Literature:

The above model suggests that activation related to motor programming and activation related to initiation are distinct processes that can be manipulated independently. The StartReact effect has provided a way in which these processes can be separated. We believe the SAS acts to increase initiation activation to a level which will reach the threshold to trigger a movement, but only if sufficient response preparation has occurred. For example, in a choice RT task the current model predicts that little or no motor program (i.e. cell assembly) activation would be present prior to the SAS, due to uncertainty of the required movement. Thus, the activation of the initiation mechanism would not release a response in this case (Carlsen et al., 2004a), in contrast to when a preparation activation was high, as in a simple RT task (Carlsen et al., 2004b; Valls-Solé et al., 1999). Similarly, knowledge of the timing of the “go” signal would affect *when* preparation activation would occur and thus *when* a SAS would initiate a movement (Carlsen and Mackinnon, 2010). RT deficits seen in patients with PD have often been attributed to deficits in response programming (Georgiou et al., 1993; Sheridan et al., 1987); however, evidence suggests that it is the initiation process that is the genesis of the RT slowness.

This assertion is based on preliminary data showing that presenting a SAS to PD patients (either “on” dopaminergic medication or after overnight withdrawal) in a simple RT task results in dramatic RT decreases to below 100 ms (Carlsen, 2010). This data indicates that the response preparation is intact as the SAS is able to directly trigger the response. Similar data has been shown for PD patients in a button pressing task (Valdeoriola et al., 1998). If we return to the data presented earlier regarding a Go / No go paradigm, recall that a SAS did not lead to early response initiation (Carlsen et al., 2008a). The authors concluded that this situation was treated in a similar manner to a choice RT task in terms of response preparation. However, the current model may allow us to slightly modify that conclusion, as rather than no preparation occurring (as in a choice RT task), it is possible that preparation occurred but at a low level due to uncertainty as to whether the response was to be performed or not. This lowered activation level may not have been sufficient to cause movement initiation upon presentation of the SAS.

The case where no response is elicited by a SAS presents a challenge, since it is less clear whether this is because no preparation has occurred (i.e., choice RT) or because preparation is occurring but not at sufficient activation to allow for movement initiation (i.e., Go / No-go RT). One way to determine if motor preparation is occurring is through the examination of whether or not participants habituate to the startle response. Evidence has been shown in humans that most components of the startle response are no longer seen after only 2-6 random presentations of a SAS (Brown et al., 1991). However, when participants are involved in a simple RT task, habituation of the startle response is delayed indefinitely. For example, Valls-Solé et al. (1997) showed that the magnitude of the startle response greatly diminished (habituated) after only five presentations of a SAS if participants were sitting quietly, sitting in a busy environment, or focused on an upcoming signal. However, when the same participants were preparing a wrist flexion movement in a simple RT task, little habituation occurred after five trials. This has been further shown in simple RT tasks where the startle response is still expressed even after as many as 20-60 presentations (Carlsen et al., 2003a; Carlsen and Mackinnon, 2010; Maslovat et al., in press). Since preparation of a movement appears to result in a decrease in startle habituation, the startle circuits must be influenced by increased activation in voluntary response circuits (Carlsen et al. 2003a). Therefore, the startle response itself can provide a measure as to whether some preparation has occurred. For example, when a SAS was presented well before the required movement when the timing of the “go” signal was known, a much smaller startle response was observed than when presented nearer to, or concurrent with, the “go” signal (Carlsen et al., 2008b; Carlsen and Mackinnon, 2010). Presumably this lowered startle response was due decreased preparation occurring well in advance if it was known when the

movement would be required (Carlsen et al., 2008b). This lowered motor preparation results in greater habituation compared to when the time of responding is uncertain. In this way, the startle response itself can be separated by the StartReact effect and used as a further gauge of the preparation process undertaken by the participant.

6. Summary and Conclusions

In conclusion, here we have provided an account of the observations made when presenting an unpredictable SAS in various tasks ranging from simple and choice RT tasks to anticipation timing movement tasks. It has been clearly shown that when a participant is ready to make a motor response, that a SAS can act to release that movement early and seemingly, involuntarily due to the short RTs observed – the StartReact effect. Thus the SAS can be used as a tool to probe for motor preparation. However, the data from these startle experiments raises several questions about the nature of response preparation, response initiation, and how the SAS interacts with these processes resulting in early expression response expression. Here we conclude that the process of response preparation can be viewed as increased activation of a network of cortical neurons whose inherent noise depends on factors such as the complexity of the movement to be made and the robustness of the connections. Furthermore, it is argued that under normal circumstances, this network would be initiated via thalamo-cortical activation. Finally it was suggested that the startle response provides sufficient ascending activation via reticulo-thalamo-cortical pathways to involuntarily trigger the prepared response. This model of preparation and initiation (including startle initiation) can be used to explain the pattern of data observed when a SAS is presented in various RT tasks and may suggest several new testable hypotheses.

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