Title: Triggering mechanisms for motor actions: The effects of expectation on reaction times to intense acoustic stimuli.

Running Head: Triggering voluntary actions with sounds.

Authors and Affiliations

Li-Ann **Leow**[1], Aya **Uchida**[1], Jamie-Lee **Egberts**[1], Stephan **Riek**[1], Ottmar V. **Lipp**[2], James **Tresilian**[3] & Welber **Marinovic**[2*]

1 Centre for Sensorimotor Performance, School of Human Movement and Nutrition Sciences, The University of Queensland; 2 School of Psychology, Curtin University, Perth WA 6102, Australia; 3 Department of Psychology, University of Warwick, United Kingdom.

* Corresponding author

Welber Marinovic

School of Psychology, Curtin University, Perth, Australia

E-mail: welber.marinovic@curtin.edu.au

Abstract

Motor actions can be released much sooner than normal when the go-signal is of very high intensity (> 100dBa). Although statistical evidence from individual studies has been mixed, it has been assumed that sternocleidomastoid (SCM) muscle activity could be used to distinguish between two neural circuits involved in movement triggering. We summarized meta-analytically the available evidence for this hypothesis, comparing the difference in premotor reaction time (RT) of actions where SCM activity was elicited (SCM+ trials) by loud acoustic stimuli against trials in which it was absent (SCM- trials). We found ten studies, all reporting comparisons between SCM+ and SCM- trials. Our mini meta-analysis showed that premotor RTs are faster in SCM+ than in SCM- trials, but the effect can be confounded by the variability of the foreperiods employed. We present experimental data showing that foreperiod predictability can induce differences in RT that would be of similar size to those attributed to the activation of different neurophysiological pathways to trigger prepared actions. We discuss plausible physiological mechanisms that would explain differences in premotor RTs between SCM+ and SCM- trials.

Keywords: movement preparation, reaction time, response triggering, StartReact effect.

Introduction

An unexpected startling acoustic stimulus (SAS) delivered during the preparation for a motor action can trigger the prepared response at a latency that is much shorter than normal, a phenomenon termed the StartReact effect (Valls-Solé, Rothwell, Goulart, Cossu, & Munoz, 1999). Because the StartReact effect can reduce deficits in motor initiation and execution in some neurological conditions (Honeycutt & Perreault, 2012; Honeycutt, Tresch, & Perreault, 2015; Marinovic, Brauer, Hayward, Carroll, & Riek, 2016; Nonnekes et al., 2014; Rothwell, 2006; Valldeoriola et al., 1998), it has the potential to be applied in movement rehabilitation interventions. However, there is ongoing debate about what exactly constitutes a true startle response and how the StartReact effect can be differentiated from other well-known phenomena such as the stimulus intensity effect (Pieron, 1914). This debate is theoretically relevant because it concerns our basic understanding of how motor actions are prepared and initiated by the central nervous system (CNS).

Carlsen and colleagues proposed that to ascertain that the neural mechanisms responsible for the StartReact effect are activated, it is essential to observe sternocleidosmastoid (SCM) activity (Carlsen, Dakin, Chua, & Franks, 2007; Maslovat, Franks, Leguerrier, & Carlsen, 2015). Thus, trials where responses are triggered by unexpected startling acoustic stimuli must be divided into trials in which the SAS elicited a SCM response (SCM+ trials) and trials where it did not (SCM–). Although we have highlighted the difficulties with interpretation of data based on a strict adherence to this criterion elsewhere (Marinovic & Tresilian, 2016), it has been generally accepted that SCM activity is important to study the StartReact effect. It has even been proposed that, when analyzing the StartReact effect, trials should be discarded when no activity is detected in this muscle, as the physiological mechanism for movement triggering would be different (Carlsen, Maslovat, Lam, Chua, & Franks, 2011). However, not all studies separating trials based on

SCM activity (SCM+ and SCM-) report statistically reliable differences in reaction times (RT) (Marinovic, de Rugy, Riek, & Tresilian, 2014; Marinovic, Milford, Carroll, & Riek, 2015; Nonnekes et al., 2014) and in some instances the StartReact effect (very short RTs) appears to be observed even with no SCM activity at all (Valls-Solé, Kofler, Kumru, Castellote, & Sanegre, 2005), bringing into question the hypothesis that there is a special startle-evoked mechanism at play only in SCM+ trials. In general, however, it has been proposed that SCM+ trials comprise a distribution of RTs that are on average shorter than those observed for SCM- trials. Alternatively, Marinovic and colleagues have proposed that differences in SCM+ and SCM- activity may be explained by random fluctuations in preparatory activity from trial to trial (Marinovic, de Rugy, Lipp, & Tresilian, 2015; Marinovic & Tresilian, 2016), which could lead to both a reduction in RT and a higher probability of detecting SCM activity when preparation levels are high.

We conducted a systematic mini meta-analysis (see appendix) of studies investigating differences in RT between SCM+ and SCM- trials in StartReact studies, and confirmed statistically that SCM activity is indeed correlated with faster reaction times. The magnitude of the effect is, however, small (-16.9 ms 95% CI [-23.7, -10.1]; see Table 1 in the appendix) and is substantially affected by foreperiod variability (see Table 2 and 3 in the appendix).

It is well known that foreperiod manipulations can strongly affect the level of preparation for an action and, consequently, modulate RT (Niemi & Näätänen, 1981). However, Niemi (1979) showed that foreperiod effects are reduced when the IS is an intense signal in the auditory modality, suggestive of a facilitatory effect of phasic arousal over the neural activity of circuits responsible for the initiation and execution of the voluntary response (Niemi & Näätänen, 1981; Tona, Murphy, Brown, & Nieuwenhuis, 2016). This reduction of foreperiod effects when using an intense acoustic go-signal may reflect the activation of a specific physiological mechanism thought to be involved in the StartReact effect (Valls-Solé, 2012). Here, we sought to revisit this issue and determine whether systematic fluctuations in the level of preparation for action - as indexed by RT measurements - can be observed when the IS is a strong signal in the auditory modality (SAS). This allowed us to evaluate our hypothesis that random fluctuations in preparatory activity from trial to trial (Marinovic, de Rugy, et al., 2015; Marinovic & Tresilian, 2016) are associated with reductions in RT in StartReact studies.

Methods

Participants

Twenty-four volunteers (mean age 19.5 years old, SD = 3.17; 14 female) participated in the experiment. All of them stated that they were right-handed and had normal or corrected to normal vision. Participants gave informed consent prior to commencement of the study, which was conducted in accordance with the Declaration of Helsinki and approved by the local Ethics Committee of the University of Queensland.

Task

To induce systematic variations in preparatory states over time during a trial, we used a marked reaction time task (see Stilitz, 1972) where the IS (a soft or a SAS) was presented together with one of three visual cues (visual time markers). More precisely, we presented a sequence of four brief flashes (50 ms, red square, 200 x 200 pixels) displayed 600 ms apart as shown in Figure 1. The first flash served as the warning signal (WS), whereas subsequent flashes marked the potential temporal location of the IS (600, 1200, or 1800 ms after the WS), and eliminated uncertainty about the temporal aspect of the task. With this task, we expected that RT would decrease as a function of the evolving conditional probability of the presentation of the IS during a trial when its temporal location was unpredictable (Niemi &

Näätänen, 1981; Stilitz, 1972). In other words, reductions in RT were expected to occur as a function of the increasing probability of the IS over time. Participants performed this task in two blocks: a) predictable, and b) unpredictable. In the predictable block, participants were informed that the IS (soft or SAS) would be presented together with the 2nd, 3rd, or 4th flash before the trials began. The order of marker presentation was randomized across participants, and all trials for each IS-marker pairing (2nd, 3rd or 4th) were presented sequentially. Note that to avoid false starts, we also presented catch trials in which the IS was not presented. In the unpredictable block, participants were informed that the IS could be presented together with any of the three temporal markers or not presented at all (catch trials). In each block of trials, participants performed 27 trials (9 trial/marker) in which the SAS was presented, 27 catch trials (9 trials/marker), and 108 control trials (36 trials/marker). The order of the blocks was counterbalanced across participants to avoid sequencing effects.

Procedures and Design

Participants sat in a chair in front of a 22-in Samsung LCD monitor (60 Hz refresh rate, 1280 x 1024 resolution) approximately 1 m in front of them. The task required participants to make isometric abductions of the wrist (radial deviation) as fast as possible upon hearing the IS (see Figure 1). Participants had their right hands snugly fit into a custom-built device (see de Rugy, Loeb, & Carroll, 2012; Marinovic, Poh, de Rugy, & Carroll, 2017) that held the hand and forearm in a neutral position throughout the experiment. To standardize the level of force produced in each trial, participants were asked to move a circular cursor from the centre of the monitor to a target presented at 90^{o} in relation to the cursor origin (see Figure 1). To move the cursor to the target, participants had to apply a contraction equal to 20Ns with their wrists. Forces were measured by a six-degree of freedom force/torque sensor (JR3 45E15A-I63-A 400N60S, Woodland, CA). Veridical feedback on RT was provided on the monitor screen after all control trials to encourage fast responses and also avoid anticipatory reactions. Thus, any response with a RT of more than 200 ms was followed by the text "Too slow", whereas any response with a RT of less than 50 ms was followed by the text "Too quick". Responses that fell within these intervals were followed by a "Good timing" message. When the IS was intense (a SAS), the message displayed was always "Good timing" irrespective of the actual RT value. Catch trials were followed by the message "No movement required".

Prior to the experimental trials in each bock, participants performed 15 practice trials to familiarize themselves with the task. Acoustic stimulation was presented three times during familiarization. Visual stimuli were generated with Cogent 2000 Graphics running in MATLAB 7.5.

Auditory stimuli

The auditory stimuli were generated with MATLAB and presented binaurally through high fidelity stereophonic headphones (Seinheiser model HD25-1 II; frequency response 16Hz to 22kHz; Sennheiser Electronics GmbH & Co. KG, Wedemark, Germany). The input signal to the headphones had a bandwidth of approximately 10 Hz–30 kHz. The soft auditory IS was a 50 ms pure tone (500 Hz) with a peak loudness of 65 dBa, whereas the SAS was a broadband white-noise (rise/fall time shorter than 1.5 ms) with a peak loudness of 114 dBa. Sound intensity was measured with a Bruel and Kjaer sound level meter (type 2205, A weighted; Brüel & Kjaer Sound & Vibration Measurement, Naerum, Denmark) placed 2 cm from the headphone ear cup.

Insert Figure 1 here

Data analysis

The main variable of interest was reaction time (RT). RT was defined as the difference between the time of movement onset and the time the IS was presented. To calculate movement onset times, we first transformed the two-dimensional screen coordinates and filtered it using a low-pass second order Butterworth filter with a cut-off frequency of 10 Hz. Movement onsets were estimated from the tangential speed time series (derived by numerical differentiation of the filtered cursor position data) using an algorithm proposed by Teasdale et al. (1993). Although it is typical to report pre-motor reaction times in the StartReact literature (see our mini meta-analysis in the appendix), our RT measurements using the torque data add only a small delay to our estimates of movement onset time. More precisely, based on data from Marinovic et al. (2017) (26 participants in Experiment 2), the average introduced delay is about 19.3 ms (SD = 4.9), allowing us to estimate how much quicker pre-motor RTs should be based on our RT data. We also analyzed the percentage of false starts as a function of IS timing and predictability. A response was considered a false start if the participant's rate of force development in any given trial - the first derivative of the forces applied on the torque sensor - surpassed 10% of the median rate of force development observed across all trials with a soft IS. The time window to detect a correct response was from the time of the warning signal (1st flash) until 1000 ms after the 3th marker (4th flash). Trials in which RT was lower than 50 ms (anticipatory reactions) or larger than 1000 ms (inattention to the IS) were discarded. Across all participants, approximately 2.9% (SD = 5) of all trials were excluded from further analysis based on this criterion, and the inclusion of all trials did not change the qualitative pattern of results.

The statistical data analysis was conducted in R (R Core Team, 2016) using the lmer function from the lmerTest package (Kuznetsova, Brockhoff, & Christensen, 2017). The analysis was separated into two phases. First we analyzed the median RT using a 2 (Predictability: Predicable vs. Unpredictable) x 2 (IS intensity: soft IS vs. SAS) x 3 (IS time: 1st, 2nd, and 3rd marker) linear mixed model. For this analysis, we employed the Sattethrwaite approximation (Satterthwaite, 1941) to calculate F-tests and estimate p-values for the main effects and their interactions. Predictability, IS intensity and IS time were treated as fixed factors, whereas participants were treated as a random factor into the model. Q-Q plots of the residuals at each level of the random factor (Participant ID) indicate the assumption of normality of residuals was largely met. The percentage of false starts was analyzed using a permutational analysis of variance using the *ezPerm* function (*ez* Package), and had Predictability and IS time as factors. In the second phase of our analysis, we fitted cumulative distribution functions (CDF) to the data of all participants in both blocks of trials when the IS was intense (SAS). Next, we recorded percentiles that represented the different distributions of responses to the SAS (Fast and Slow) of each CDF for each participant (see details below). These values were then entered into a 2 (Predictability: Predicable vs. Unpredictable) x 2 (Percentile: Fast vs. Slow) x 3 (IS time: 1st, 2nd, and 3rd marker) linear mixed model. Predictability, RT Percentile, and IS time were treated as fixed factors, whereas participants were treated as a random factor into the model. The rationale for this analysis relies on the assumption that the distribution of RTs in response to SAS is bimodal (see (Marinovic & Tresilian, 2016), Figure 4), reflecting the activation of different neurophysiological pathways to trigger prepared responses. Note that, typically, the method of choice to determine if trials were triggered via the mechanism responsible for the StartReact effect is the presence of SCM activity (Honeycutt, Kharouta, & Perreault, 2013). However, given that responses can be elicited rather quickly by a SAS in the absence of SCM activity (Valls-Solé et al., 2005), and slow responses can be observed when SCM activity is detected (Marinovic & Tresilian, 2016), one can conclude that SCM activity is neither necessary nor sufficient to determine whether the StartReact effect was observed. Therefore, separating trials by their latencies is likely to be more indicative of a mechanism that bypasses or activates specific mechanisms in the central nervous system than relying on surface EMG (see also (Dean & Baker, 2017). We decided which percentiles would be representative of Fast and Slow responses by fitting a CDF to the data kindly provided by Honeycutt et al. (2013) (grasp task included in the meta-analysis). The reported values obtained when using SCM to separate trials (SCM+ and SCM-), where a statistically reliable effect was observed, are shown in Figure 3 (dashed lines). For SCM+ trials, Honeycutt and colleagues reported a mean latency of 87 ms, which matched closely the 35th percentile estimate using a CDF. For SCM- trials, they reported a mean latency of 96 ms, which approximately matched the 65th percentile using a CDF (see Figure 3). To further examine the impact of presenting the intense IS (SAS) while preparation levels were expected to vary over time, we also estimate the slope of linear regressions using a bootstrapped procedure (5000 iterations). If the earliest responses (Fast, 35th percentile) were triggered via a distinct mechanism responsible for the StartReact effect, the confidence interval of the bootstrapped distribution should include zero. In contrast, if preparation levels could modulate the latency of the fastest responses across the three IS times, the confidence interval of the bootstrapped slope distribution should not include zero. Additionally, we also calculated the slopes using percentiles representing even faster responses: 5th, 15th, and 25th percentiles (the lower the percentile the faster the RT).

Effect sizes are given as likelihood ratios (LR) and were calculated contrasting the null or main effect models against relevant models of interest (single main effects or interactions).

Results

Initial analysis

Insert Figure 2 here

As expected, there was a main effect of IS intensity on RT ($F_{(1,253)} = 130.08$, $p < .0001$, LR = 63.4), indicating that responses were faster when the IS was intense (SAS). There was also a main effect of temporal predictability of the IS ($F_{(1,253)} = 106.49$, $p < .0001$, LR = 50.7), demonstrating that RTs were shorter when participants knew the likely time of appearance of the IS. The main effect of IS timing was also statistically reliable ($F_{(2,253)} = 39.61$, $p < .0001$, LR = 36.7), indicating responses tended to become faster as the IS appeared later in the trial. As shown in Figure 2A, this main effect was qualified by a significant interaction between IS predictability and IS timing ($F_{(2,253)} = 18.66$, $p < .0001$, LR = 24.36), suggesting the effect of IS timing was stronger in the unpredictable block of trials.

There was a statistically reliable increase in the percentage of false starts as a function of IS time in both blocks of trials (main effect of IS timing: $p = 0.032$). This analysis also indicated a main effect of IS predictability ($p < .001$), indicating that participants had more false starts (≈ 20%) when the temporal predictability of the IS was high as shown in Figure 2B. The apparent interaction between IS time and predictability failed to reach statistical significance ($p=0.094$).

Overall, these results indicate that more intense stimuli result in shorter RTs. However, this effect also depends on the level of preparation for action. In other words, the higher the level of expectation for the IS, the shorter the RT will be. The results also suggest that even though

RTs cannot be much shorter in a highly predictable context, the percentage of false starts indicates preparation levels can still increase over time.

Fast vs. Slow responses to SAS

Insert Figure 3 here

As it can be seen in Figure 3, the average premotor reaction time for SCM+ and SCM- trials is close to the 35th and 65th percentiles, respectively. Further inspection of the means and standard deviations estimated using both methods indicate they produced similar results. In more detail, the average premotor RT (SD) measured using SCM activity was 87.06 ms (14.1) and 95.86 ms (17.2) for SCM+ and SCM- trials, respectively. The estimates we obtained based on the 35th and 65th percentiles were 86.83 ms (14.6) and 95.61 ms (17.02), respectively. Simple t-tests using the averages estimated with both methods yielded very similar results too (SCM activity method: $t_9 = 4.411$, $p = 0.0016$, mean difference = -8.80 ms (6.3), 98% CI [-14.43, -3.17]; Percentiles method: $t_9 = 5.332$, $p = 0.0004$, mean difference = -8.77 ms (5.2), 98% CI [-13.42, -4.13]). Thus, our reanalysis of Honeycutt et al.'s (2013) data suggests that "faster" responses - triggered by different physiological mechanisms - should pertain in average to the 35th percentile, whereas "slower" responses - triggered via slower pathways - would be in average clustered around the 65th percentile. As shown next, these percentiles were used to further analyze our RTs of our experiment.

Insert Figure 4 here

As shown in Figure 4, the estimated RT at the 35th percentile of the CDF were faster than those at the 65th percentile (main effect of RT percentile*:* ($F_{(1,257)} = 12.49$, $p = .0004$, LR =

37.2). The pattern of results is similar to that observed when contrasting the soft and intense IS (see Figure 2A). More specifically, we observed a statistically reliable main effect of IS predictability ($F_{(1,257)} = 75.2$, $p < .0001$, LR = 50.8), and also a main effect of IS time ($F_{(1,257)} = 70.03$, $p < .0001$, LR = 38.5). The interaction between IS predictability and IS time was also statistically significant ($F_{(1,257)} = 30.1$, $p < .0001$, LR = 23.4), again suggesting that the effect of IS time was more pronounced in the unpredictable than the predictable block of trials.

To further examine whether changes in preparation levels over the course of a trial could impact the RT to an intense IS, we bootstrapped the slope of a linear regression for the RT estimates in the 35th percentile for both blocks of trials. As shown in Figure 4B, the mean slope of the bootstrapped linear regression in the unpredictable block was much further away from zero (mean = -0.033, 98%CI [-0.042, -0.026]) than that obtained for the predictable block of trials (mean = -0.006, 98%CI [-0.016, 0.002]), suggesting IS predictability can also affect the latency of responses initiated with very short latencies. Note that the estimates for the unpredictable block of trials changed little when we calculated the slopes using percentiles representing even faster RTs (5th percentile: mean = -0.022, 98%CI [-0.029, -0.016]; 15th percentile: mean = -0.023, 98%CI [-0.029, -0.018]; 25th percentile: mean = -0.029, 98%CI [-0.037, -0.022]).

In summary, we have demonstrated here that even the fastest responses to a SAS are affected by the level of preparation for action. The higher the level of preparation, the shorter the RT. Clearly, this effect is more pronounced when the IS is less predictable, but the range of the bootstrapped slopes was also negative in the predictable block of trials. In the unpredictable block of trials, these results were independent of the percentile analyzed.

Discussion

Our mini meta-analysis (see appendix) revealed that premotor RTs are indeed shorter in SCM+ than in SCM- trials. The estimated magnitude of this effect across the studies is on average (≈17 ms) large enough to entertain the possibility that motor programs are triggered via a pathway that bypasses some cortical areas of the brain (Carlsen, Chua, Inglis, Sanderson, & Franks, 2003; Valls-Solé et al., 1999), but not large enough to completely rule out cortical involvement (Marinovic & Tresilian, 2016). It is also clear from our meta-analysis comparing SCM- and control trials that foreperiod variability is critical for the average difference among the studies analyzed. Our experiment was designed to target this issue more directly. First, however, it is important to consider why fast responses would be triggered via a different (faster) physiological pathway.

Why would responses be initiated earlier when SCM activity is detected?

Maslovat et al. (2015) proposed that the detection of SCM activity indicates that a more direct neural circuit, associated with the startle reflex, was responsible for involuntarily triggering the prepared response. Thus, when responses occur without SCM activity (SCM-), the longer neural circuit - involving the auditory cortex - would trigger the motor response. This model would explain why responses are faster when SCM activity is observed. Interestingly, the StartReact effect can still be observed when the startle reflex is reduced due to the presentation of a less intense stimulus before the go-signal (pre-pulse inhibition, PPI) (Valls-Solé et al., 2005). This result is counterintuitive because it suggests that the more direct neural circuit is still activated when the transient activation of the midbrain nuclei by the prepulse stimulus exerts long-lasting inhibition of the giant neurons of the caudal pontine reticular nucleus and inhibits the neural circuit of the startle reflex (Fendt, Li, & Yeomans, 2001). Note also that SCM+ trials can have relatively long latencies, suggesting SCM activity is neither necessary nor sufficient to produce the StartReact effect (Marinovic & Tresilian, 2016). Alternatively, we have suggested that the apparent correlation between SCM activity and premotor RT could be a result of variations in the build-up of preparatory activity from trial to trial (Marinovic, de Rugy, et al., 2015). More precisely, it seems plausible that in some trials, the peak of preparatory activity could be either reached sooner than expected (and remain constant until the go-signal arrives) or at the expected time of the go-signal, whereas on other trials the go-signal could reach peak slightly later. If we assume that the build-up of preparatory activity during the foreperiod facilitates SCM muscle activity, then it could be the case that SCM+ trials simply indicate a higher level of preparatory activity, resulting in responses being initiated earlier when preparatory activity is relatively higher. This hypothesis would explain why responses with SCM activity are faster than those without it, eliminating the requirement for different neural circuits involved in response triggering. We experimentally tested the effect of varying the levels of preparation during the course of a trial on the latency of responses triggered by a loud startling stimulus.

The effect of predictability and conditional probability on reaction times to SAS.

To induce systematic fluctuations of the overall state of preparation for an action over the time course of a trial, we employed a marked reaction time task (see (Stilitz, 1972). This task was expected to make participants alter the level of preparation for an action as a function of the conditional probability of the IS being presented in the unpredictable block of trials. More specifically, in any given trial, the probability that the IS would appear with the next time marker should increase, resulting in an increased level of preparation for action. In agreement with this prediction, RTs decreased linearly as the IS was presented later on a trial in the unpredictable blocks of trials (see Figure 2), and this was true for RTs to the soft and loud ISs (SAS). This effect was clearly reduced in the predictable block of trials, however, responses still seemed faster when the IS was delivered later in the trial (together with the last marker), and the probability of a false start increased linearly as the time between warning and IS time increased. Thus, our task successfully led participants to increase the overall level of preparation over time. To avoid the possibility that participants completely anticipated the time to initiate their action and respond to the IS only, we introduced catch trials in which no IS was presented and responses should be withheld. Our analysis of false starts showed that participants had more false starts in the predictable than in the unpredictable block of trials. This is an important observation because it indicates that when the IS is certain to appear and the foreperiod is predictable, participants are more likely to exhibit anticipatory reactions that can be mistaken for very fast responses to the IS in the context of the StartReact effect. Interestingly, despite the fact that participants knew in advance the time of the IS in the predictable block of trials, the probability of falsely starting a response increased as the IS was presented later. This suggests that preparatory activity could still increase over time, and that participants do not simply engage in motor preparation after the 3rd flash (last 600 ms before the 3rd IS marker) in the predictable block of trials. If this is the case, RT is not really a sensitive measure of motor preparation when the foreperiod is predictable and the IS intense as RTs can be very close to the limit of the human capability. Note that the mean RT in the predictable block for the 3rd IS marker was 103 ms (% of false starts = 26), which would correspond to a premotor RT of about 84 ms (see our estimate of the neuromechanical delay in the Data Analysis section). This estimate would be 96 ms in the unpredictable blocks of trials, when the percentage of false starts was below 5%. To further examine whether preparation levels would affect the latency of responses to SAS, we calculated the 35th and 65th percentiles for these responses. The results of this analysis indicated that even the fastest responses to SAS are affected by rising preparation levels. Here the fastest RT in the predictable block of trials would correspond to a premotor RT of about 76 ms in the predictable block of trials (RT to the 3rd IS marker), and 87 ms in the unpredictable block of trials. These estimates are within the range of what one expects when analyzing the StartReact effect. Moreover, the difference between responses at the 35th and 65th percentiles, assuming a bimodal distribution of trials, was 19.5 ms in the predictable block and 22 ms in the unpredictable block of trials. These values are well within the expected range we obtained in our mini-meta-analysis (95% CI [-23.7, -10.1], see Table 1 in the appendix) suggesting this might be a valid method to separate trials in the context of the StartReact effect where entire datasets are often discarded from analysis when participants do not display clear SCM activity.

The average slope of the linear regression function calculated using a bootstrapped procedure was -0.033 in the unpredictable block of trials, which means RTs could increase by up to 19.8 ms if one mistimed the peak of preparatory activity by 600 ms. This estimate is more than enough to account for a substantial proportion - if not all - of the RT advantage when SCM activity is detected via surface EMG. Of course, the slope was very close to zero, when the IS was highly predictable, but here responses were already so fast that it can be difficult to detect reliable effects so close to the neurophysiological limits of the system to react voluntarily to the IS. Thus, these results are in agreement with our hypothesis that the build-up in preparatory activity during the foreperiod does facilitate the RT of very fast reactions, and - as previously demonstrated by different groups (Bohlin & Graham, 1977; Brunia, 1993; Valls-Solé et al., 1995) - this can increase the chances of observing SCM muscle activity.

Conclusion

In conclusion, RTs on trials in which SCM activity is observed (SCM+) are faster than those without it (SCM-). Although the mean difference between SCM+ and SCM- trials is big enough to suggest separate neural pathways for movement triggering, the average premotor RT in SCM+ trials (simple RT tasks) is not short enough (≈90 ms) to rule-out cortical involvement. Our experimental data demonstrated that responses initiated very quickly by SAS are still affected by the immediate level of preparation during a trial, and could partially - or completely - explain why SCM+ trials tend to be faster than SCM- trials. Our experimental task and approach to distinguish fast (StartReact) and slow (voluntary reactions) responses to SAS is a promising method to advance our knowledge about the mechanisms involved in the preparation and initiation of motor actions.

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Figure captions

Figure 1: Sequence of events during a trial. The first flash served as a warning signal (WS) and lasted for 50 ms. Subsequent flashes were presented 600 ms apart. The second, third, and fourth flashes also lasted 50 ms, and represented the 1st, 2nd, and 3rd temporal markers. The target was presented simultaneously with the WS and served to motivate participants to produce at least 20N of force in all trials. A moving cursor controlled by the participants represented the forces applied during the trial. To produce the minimum force required participants had to make the cursor intersect the target. Participants were asked to make an abduction of the wrist (radial deviation) as fast as possible upon hearing the imperative stimulus (IS). In the illustrative figure, the IS was presented in synchrony with the 2nd marker, and upon response onset the cursor moved towards the target.

Figure 2: **A.** Reaction time. **B.** False starts. Error bars represent the within participants standard error of the mean (Morey, 2008).

Figure 3: Plot showing the cumulative distribution function (CDF) of reaction times reported in Honeycutt et al. (2013) (Grip task). Data represent the CDF for all trials in which a SAS was presented, irrespective of SCM activity. The green dashed line represents the reported average premotor RT in trials without SCM activity (SCM-). The red dashed line represents the reported average premotor RT in trials with SCM activity (SCM+). Error bars represent the within-participants standard error of the mean (Morey, 2008).

Figure 4: **A.** Reaction time for fast (35th percentile) and slow (65th percentile) trials as a function of IS time in both blocks of trials (Predictable and Unpredictable) for responses elicited by the intense IS (SAS = 114dBa). Error bars represent the within-participants

standard error of the mean (Morey, 2008). **B.** Histograms of the bootstrapped distributions of the slopes for fast RTs. Dashed black lines indicate the boundaries of the 98% confidence intervals of the linear regression slope.

Appendix - *Mini meta-analysis*

Methods

We conducted a Scopus search of research articles citing either Valls-Solé et al.'s (1999) seminal paper on the StartReact effect or Carlsen et al.'s paper (2007) suggesting that responses for which SCM activity was observed were triggered differently from responses without such activity. Because we wanted to more precisely estimate the magnitude of the "true" StartReact effect in comparison to stimulus intensity effects, our analysis only included experimental studies that reported premotor reaction times in SCM+, SCM-, and control trials (trials for which the SAS was replaced by either a less intense acoustic or visual go signal). We performed separate meta-analyses comparing the reaction time means of both SCM+ vs. SCM- trials and SCM- vs. control trials. Meta-analyses were performed using the random effects model, calculating Q-statistics as an indicator of heterogeneity. Standardized effect sizes for the mean change in premotor reaction time were calculated using raw score standardization with heteroscedastic population variances proposed by Bonett (2008). For all meta-analyses we used the R package METAFOR (Viechtbauer, 2010). Sample size calculations to obtain a power of 80% and an α-error of 0.05 were performed using G*Power 3.1 (Faul, Erdfelder, Lang, & Buchner, 2007).

Results

The initial search yielded 210 research articles, of which ten were included for the meta-analysis. Manuscripts were excluded from analysis if (1) SCM activity was not recorded or (2) a comparison between trials in which SCM+ and SCM- was not conducted (e.g. only SCM+ trials were analyzed). For one of the included studies, additional data was kindly provided by the authors (Honeycutt, Kharouta, & Perreault, 2013) to allow the computation of correlation coefficients between change scores. Means and standard deviations of premotor reaction times were provided in the text of the papers or extracted from plots using WebPlotDigitiser 3.8. For six studies, we could not obtain the data to calculate correlation coefficients between change scores (Carlsen, Chua, Inglis, Sanderson, & Franks, 2003, 2009; Carlsen et al., 2007; Honeycutt et al., 2015; Maslovat et al., 2015; Tresch, Perreault, & Honeycutt, 2014). Sensitivity analysis using correlation coefficients from 0.05 to 0.95 showed only small differences in our estimates (≈ 2 ms), thus, we adopted an averaged correlation coefficient of 0.81 for the studies for which data was not available. This value represents the averaged correlation coefficient based on the studies we had available data.

Differences between SCM + and SCM - trials

Table 1: Meta-analysis of studies comparing SCM+ and SCM- trials (n = 115)

Authors (Year)	N	Observed Diff. [95% CI]
Maslovat et al (2015)	13	-39.1 [-59.18, -19.08]
Carlsen et al (2003)	12	-19.4 [-26.8, -12.1]
Carlsen et al (2007)	10	-5.6 [-13.3, 2.1]
Carlsen et al (2009)	14	-25.7 [-33.1, -18.4]
Honeycutt et al (2013)	10	-9.5 [-14.1, -4.9]
Tresch et al (2014)	20	-23.6 [-33.9, -13.4]
Honeycutt et al (2015)	10	-25.7 [-44.4, -7.0]
Kirkpatrick et al (2018)	9	-8.76 [-13.6, -3.9]
Marinovic et al (2014)	7	-13.1 [-25.8, -0.5]
Marinovic et al (2015)	10	-22.0 [-53.8, 9.8]
Random Effects Model		**-16.9 [-23.7, -10.1]**

The difference in premotor reaction time between SCM+ and SCM- trials was -16.9 ms (95% CI [−23.7, −10.1], $t = 5.61$, $p = 0.0003$) and the heterogeneity was also statistically significant (Q test $\chi2 = 35.78$, $df = 9$, $p < 0.0001$). As shown in Table 1, the direction of the effect is consistent across all studies; that is, responses are typically released earlier when SCM activity is detected. This is consistent with the proposal that truly startled responses (SCM+) should be faster than non-startled responses (SCM-). Intensity of the SAS was not a statistically reliable moderator of the effect, $F(5, 4) = 1.44$, $p = 0.37$. An estimate of the standardized effect size (Bonett, 2008) suggests that this effect is large to medium (point estimate: -0.79, 95% CI [-1.14,-0.44]). A sample size estimate based on the average effect size (i.e., one-tailed t-test) indicates this effect could be detected with 12 participants. However, a more conservative estimate of the required sample size to detect a medium effect size (i.e., close to the lower bound of the confidence interval of the standardized effect size) would be 34 participants, indicating most studies to date would be underpowered to detect medium sized effects. The estimated average premotor reaction time in SCM+ trials based on the nine studies using simple RT tasks was 88.5 ms (95% CI [83.5, 93.4]).

Differences between SCM- and Control trials

Because three experiments used either a visual go-signal in control trials (Marinovic, Milford, Carroll, & Riek, 2015; Maslovat et al., 2015) or no go-signal (Marinovic, de Rugy, Riek, & Tresilian, 2014), we limited our comparisons between SCM- and control trials to the seven experiments which used a soft go-signal (≈ 80dBa) in control trials. This analysis showed that the difference in premotor reaction time between SCM- and control trials across these studies was -43.1 ms (95% CI [−63.2, −23.18], $t = 5.28$, $p = 0.0019$) but the heterogeneity was also statistically significant (Q test $\chi2 = 37.96$, $df = 6$, $p < 0.0001$, see Table 3). The standardized effect size (Bonett, 2008) indicates that this effect is large (point estimate: -1.47, 95% CI [-2.18,-0.76], Q test $\chi2 = 14.69$, $df = 6$, $p = 0.02$), and can be detected - one-tailed t-test - with relatively small sample sizes (≈ 13 participants; based on the lower bound of the effect size confidence interval). As can be seen in Table 2, however, the raw mean differences in premotor reaction times of the studies can be divided into two subgroups according to the variability of the foreperiod (time between warning-signal and the go-Signal). For the three studies with lower foreperiod (≤ 500 ms) variability (see Table 2 and Figure 3), the difference in the mean premotor RT between SCM- and control trials was -26.8 ms (95% CI [-44.5, -9.21], $t = 6.55$, $p = 0.022$; Heterogeneity: Q test $\chi2 = 3.08$, $df = 2$, $p = 0.21$). The standardized effect size showed that this effect is medium to large (point estimate: -1.09, 95% CI [-2.00, -0.17], Q test $\chi2 = 2.25$, $df = 2$, $p = 0.32$). In studies with relatively larger foreperiod (≥1000 ms) variability, the difference between SCM- and control trials was -58.5 ms (95% CI [−86.03, −30.99], $t = -6.76$, $p = 0.006$; Heterogeneity: Q test $\chi2 = 9.84$, $df = 3$, $p = 0.019$), more than double the estimate obtained for the lower variability subgroup as shown in Table 3. Here the standardized effect size (Bonett, 2008) was the largest with a point estimate of -1.99 (Q test $\chi2 = 7.06$, $df = 3$, $p = 0.069$), explaining the large confidence interval for this effect size (95% CI [-3.48, 0.50]). It is worth mentioning that the difference between Higher and Lower foreperiod variability subgroups in terms of RT latencies in controls trials is diminished by the lower RTs in Kirkpatrick et al.'s (2018) study where participants practiced for 10 days, and we analyzed here only data from the last day when RTs were reliably faster than on the 1st day of the study. If we exclude Kirkpatrick et al.'s data from our analysis of subgroups, the difference between Higher and Lower foreperiod variability subgroups is more than doubled (Higher = 68.1 ms, Lower = 32 ms).

Table 2: Average time between soft warning-signal and loud go-signal (foreperiod) and its variability.

Authors (Year)	Average foreperiod (sec.)	Foreperiod variability (+/-seconds)
Carlsen et al. (2003)	2.5	0
Carlsen et al. (2007)	2.5	0
Carlsen et al. (2009)	2.5	0.5
Honeycutt et al (2013)	2.5	1
Tresch et al (2014)	2.5	1
Honeycutt et al (2015)	2.5	1
Kirkpatrick et al (2018)	2.5	1

Table 3: Meta-analysis of studies comparing SCM- and control trials in which the go-signal was acoustic (n = 85)

Authors (Year)	N	Observed Diff. [95% CI]
Lower Variability		
Carlsen et al (2003)	12	-17.1 [-29.9, -4.3]
Carlsen et al (2007)	10	-31.6 [-42.6, -20.6]
Carlsen et al (2009)	14	-28.9 [-29.9, -4.3]
Random Effect Model		**-26.8 [-44.5, -9.21]**
Higher Variability		
Honeycutt et al (2013)	10	-73.3 [-92.4, -54.1]
Tresch et al (2014)	20	-71.3 [-92.5, -50.1]
Honeycutt et al (2015)	10	-54.0 [-79.8, -28.3]
Kirkpatrick et al (2018)	9	-38.1 [-54.2, -22.0]
Random Effects Model		**-58.5 [-86.0, -31.0]**
RE Model All studies		**-43.2 [-63.2, -23.2]**

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Marinovic, W., Milford, M., Carroll, T., & Riek, S. (2015). The facilitation of motor actions by acoustic and electric stimulation. *Psychophysiology*. doi:10.1111/psyp.12540

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Figure 1

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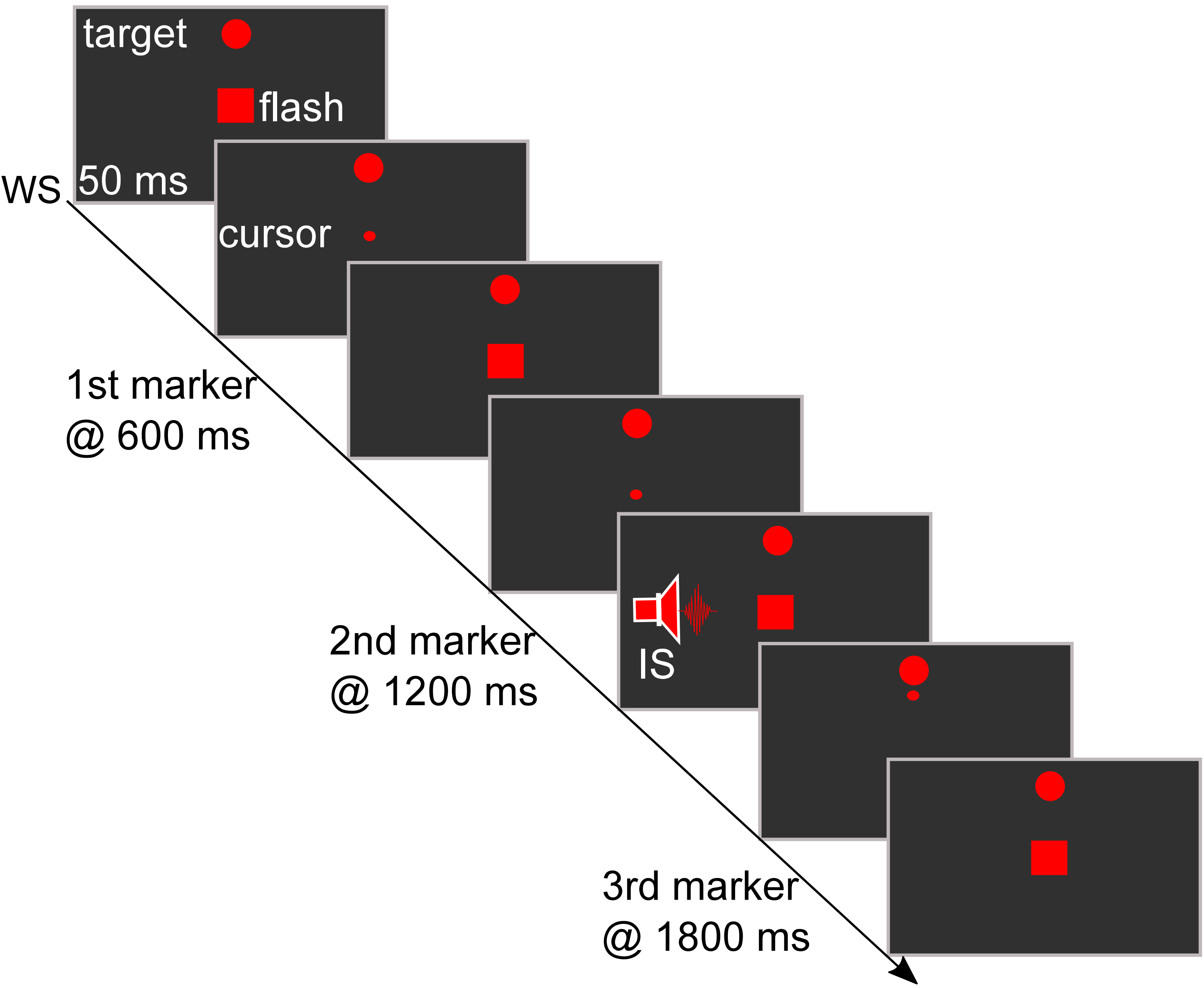

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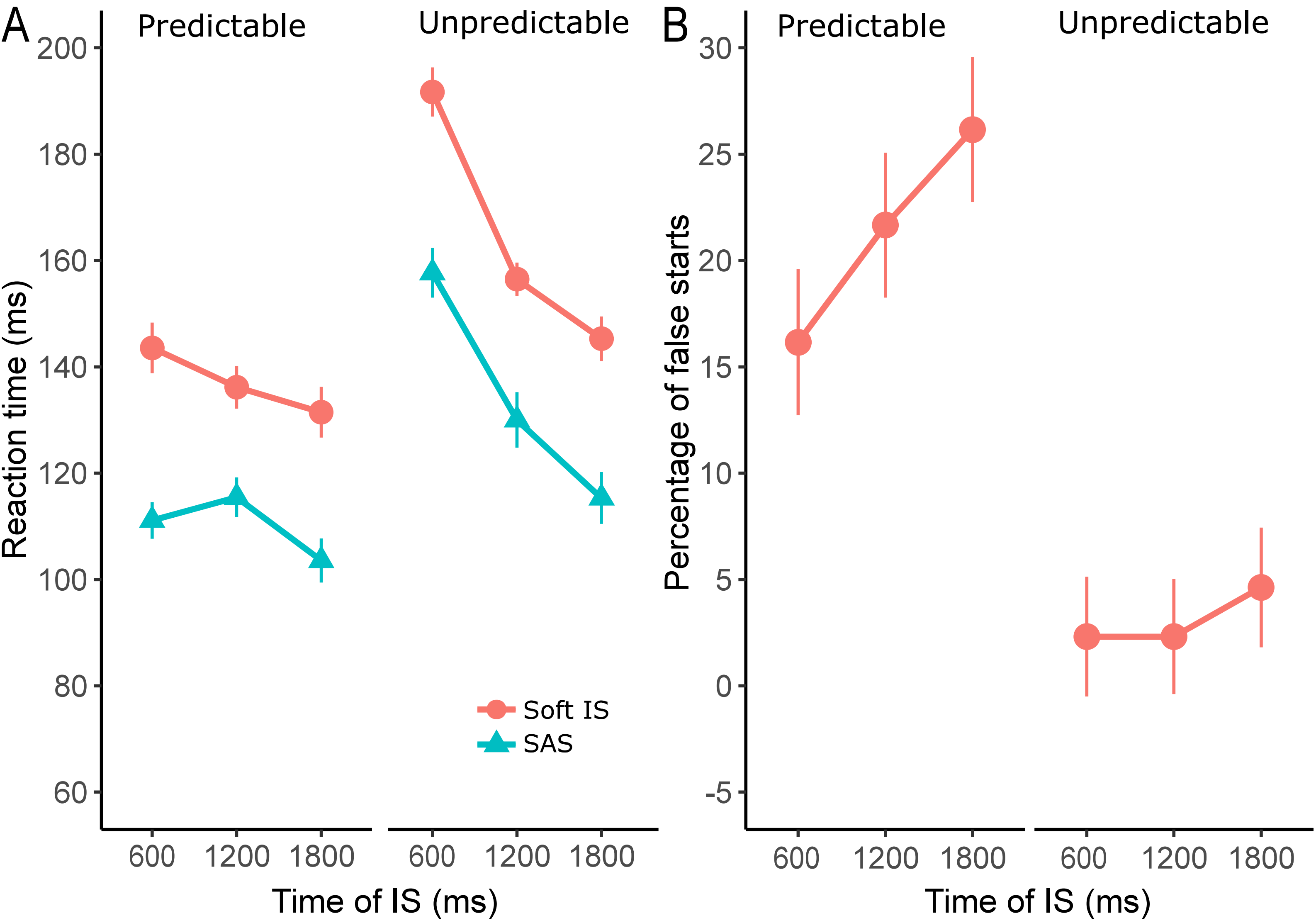

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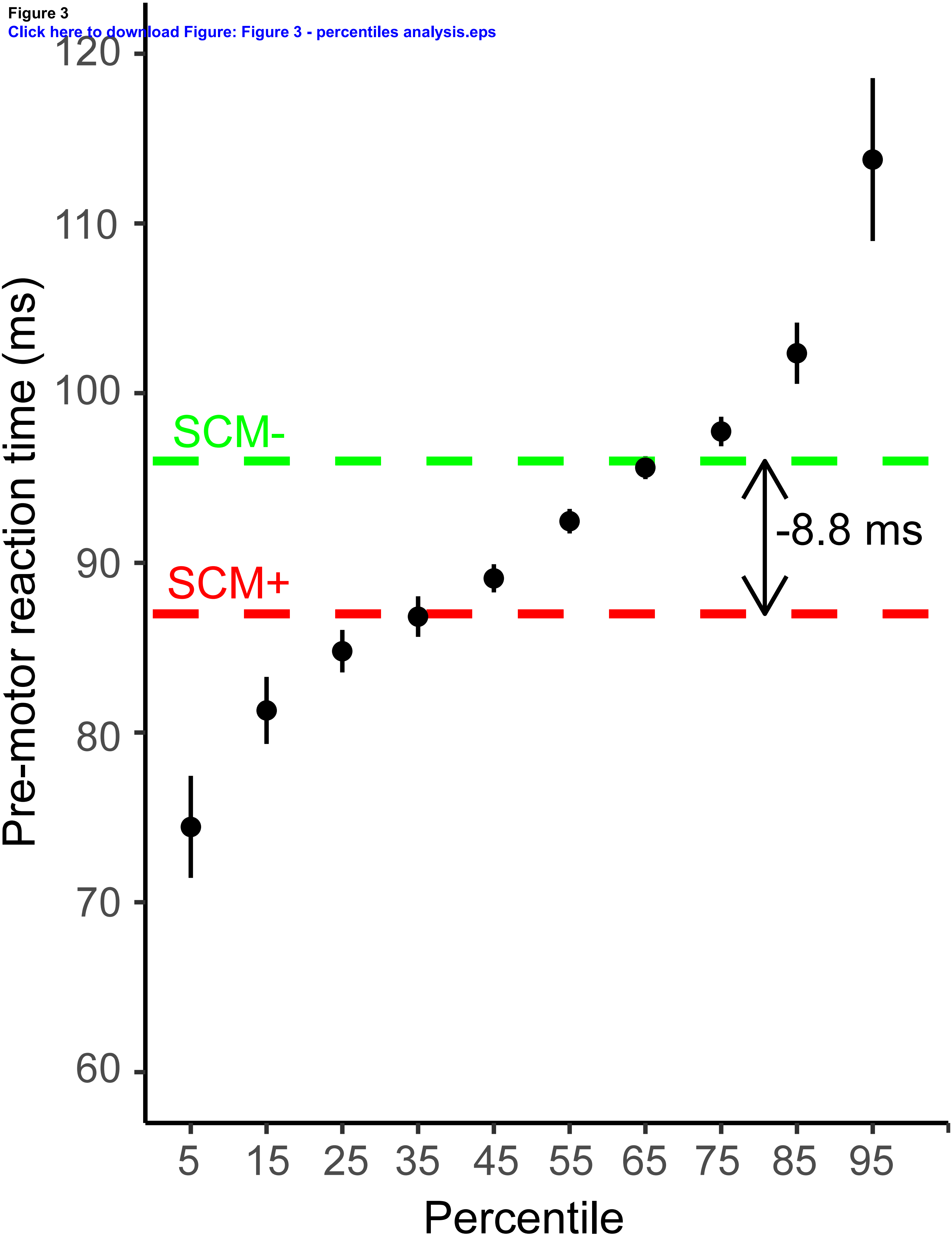

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