Proactive inhibition does not differentially affect preparatory activation between limbs

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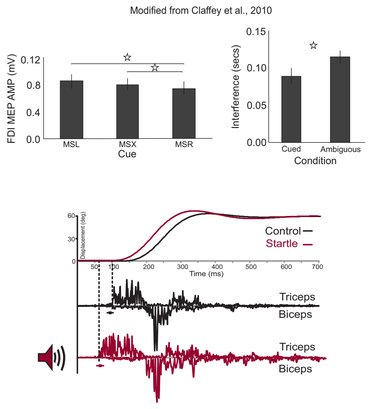
Background

➲ A conditional stop-signal task requires participants to plan and initiate a bimanual limb movement as fast as possible in response to a go-signal, but to inhibit a specified movement/limb in response to an infrequent stop-signal, while the response for all other movements/limbs should nevertheless be made [1,2,3].

➲ Essential to this conditional stop paradigm is that advance information is given about which movement/limb may need to be stopped, allowing participants to prepare in advance which limb might have to be stopped [1,2,3].

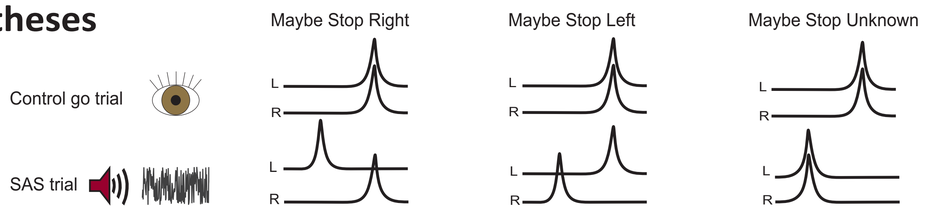
➲ Performance in this task has been linked to a selective stopping mechanism, decribed as proactive inhibition. Hallmarks of proactive inhibition are decreased corticospinal excitability (CE) only in the limb that was cued to maybe stop [4,5,6], and less interference (slowing of RT) in the (other) responding limb [5,7].

➲ A startling acoustic stimulus (SAS > 120 dB) has been shown to provide added activation, resulting in the involuntary triggering of the prepared response [8,9]. A SAS has been shown to simultaneously trigger two independently prepared movements, which enables a SAS to be used to study the activation related to each hand independently [10].



Q: How does proactive inhibition affect preparation and activation related to the initiation of both responses, particularly that of the non-cued limb which does not have to be stopped?

Hypotheses

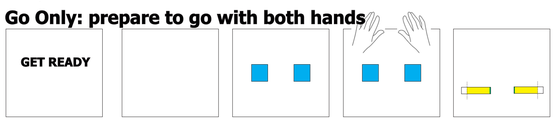


Methods

Exp 1. SAS + simple conditional stop-signal task (n=9)

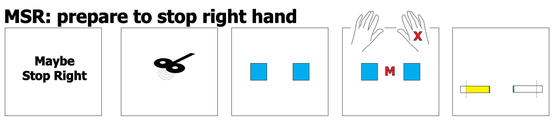
Simple reaction time task

Go Only: prepare to go with both hands

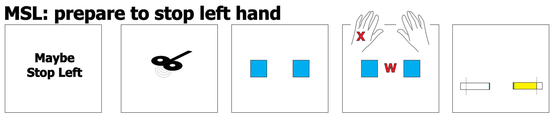


Simple conditional stop-signal task

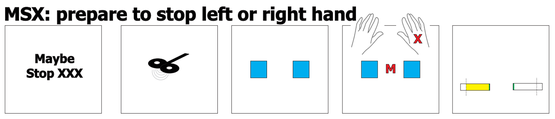
MSR: prepare to stop right hand



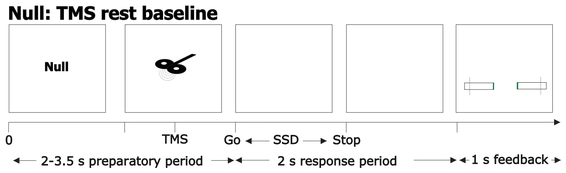
MSL: prepare to stop left hand



MSX: prepare to stop left or right hand



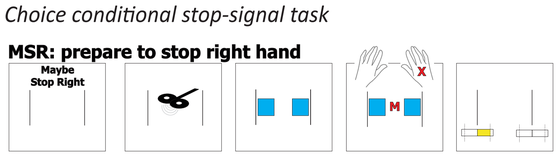
Null: TMS rest baseline



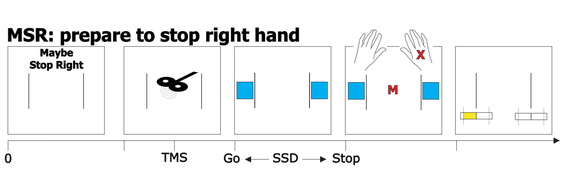
Exp 2. Control choice conditional stop-signal task (n=6)

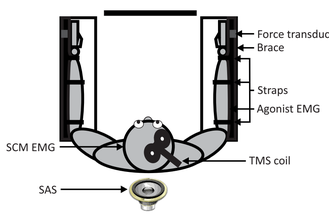
Choice conditional stop-signal task

MSR: prepare to stop right hand



MSR: prepare to stop right hand





Procedure

1. TMS extensor carpi radialis hotspot and resting motor threshold procedure
2. Maximum voluntary isometric force (MVF) test
3. Simple reaction time task - simple bimanual response (40% MVF extension)
4. Conditional stop-signal task - simple bimanual response (40% MVF extension)

Trial Breakdown

MVF - 3 trials
Simple reaction time task - 20 trials
Conditional stop-signal task - 164 trials
- 20 practice trials and 144 testing trials
- 6 testing blocks consisting of 24 trials each
- Each block contained 6 trials per cue type (i.e., MSR, MSL, MSX, NULL)
- 3/6 go trial (50%), 2/6= stop trial (33%), 1/6 = go trial + SAS (17%)

Stimulation

Single pulse TMS 112% of resting motor threshold (mean stimulator output = 49 %)
- TMS delivered 1 s after cue offset on every testing trial
- Counterbalanced left or right hemisphere

Startling acoustic stimulus (120 dB white noise)
- SAS delivered concurrent with go
- Simple reaction time task (5 SAS/ 20 trials)
- Conditional stop-signal task (18 SAS / 144 trials)

Procedure

1. TMS extensor carpi radialis hotspot and threshold procedure
2. Conditional stop-signal task - choice bimanual response (40 deg flexion or extension)

Trial Breakdown: Majid et al., 2013 replication

Conditional stop-signal task - 330 trials
- 90 practice trials and 240 testing trials
- 8 testing blocks consisting of 30 trials
- MSR & MSL: 4/6 go trial (67%), 2/6= stop trial (33%)
- MSX: 8/12 go trial (67%), 4/12= stop trial (33%)
- NULL: 6/6 (100%)

Stimulation

Single pulse TMS 112% of resting motor threshold (mean stimulator output = 46 %)
- TMS delivered 1 s after cue offset on every testing trial
- Counterbalanced left or right hemisphere

Results

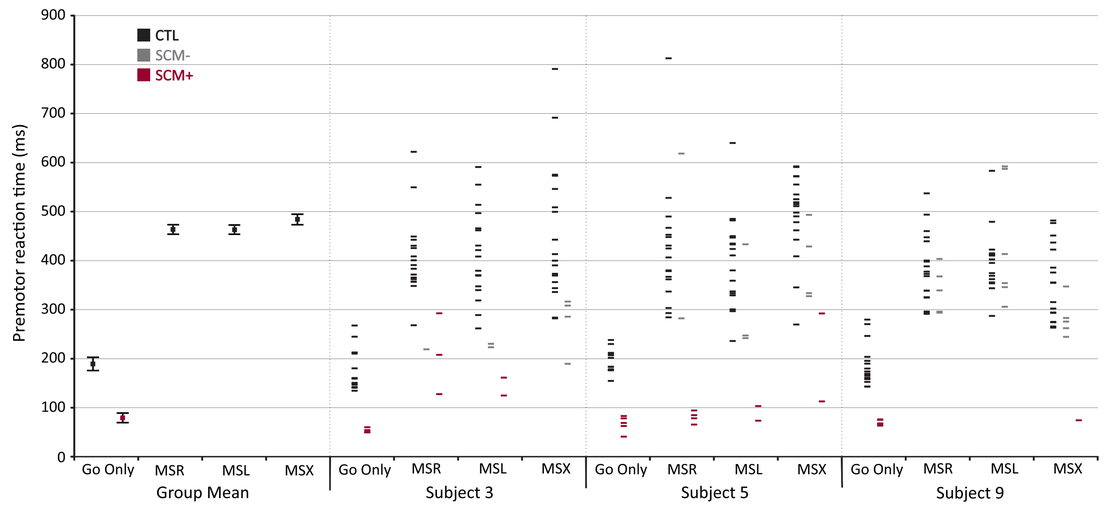


Fig 1. **Premotor reaction time (ms) as a function of trial type during control (CTL) and startle trials (SCM+/-).** Group Mean as well as individual trial data from subjects 3, 5, and 9 are presented. The conditional stop-signal task data from these three subjects are shown as these were the only subjects which a SAS elicited a bilateral startle response (SCM+). Control trials are represented by the dark shades, startle trials which did not result in a bilateral SCM response (SCM-) are represented by the light shade, and startle trials which did result in a bilateral SCM response (SCM+) are represented by the vibrant shade. Go only = simple RT, Maybe stop right = MSR, Maybe stop left = MSL, Maybe stop unknown = MSX. Error bars on group mean data represent within-subject 95% CI.

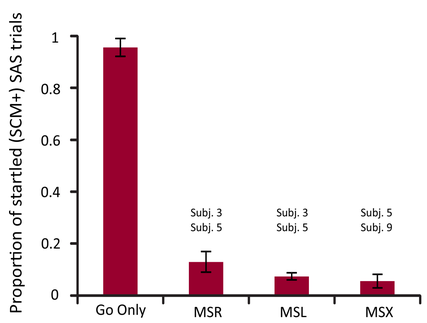


Fig 2. **Proportion of bilateral startled (SCM+) SAS trials as a function of trial type.** The data presented are group means, subjects who had a SCM+ during that trial type are indicated above. Error bars represent within-subject 95% CI.

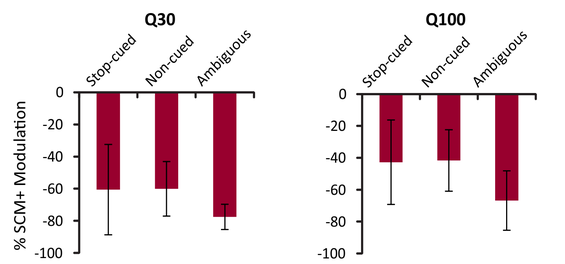


Fig 3. **Within subject % SCM+ modulation of Q30 & Q100 as a function of cue type during the conditional stop-signal task relative to the simple RT task [(stop signal-simple)/simple *100].** The data presented are means (SE) of subjects who had a SCM+ during the conditional stop-signal task. Stop-cued is SCM on the same side which was cued to stop (e.g., right SCM - maybe stop right), Non-cued is the SCM opposite to the cued stop side (e.g., right SCM- maybe stop left), and Ambiguous is SCM during the MSX cue.

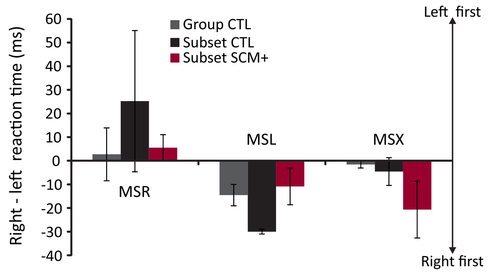


Fig 4. **Mean difference in premotor reaction time (ms) between the right and left response (right - left) during control and SCM+ trials as a function of trial type.** Grey bars are group means during control trials, black bars are the subset mean of subjects who startled during control trials, red bars are the subset mean of SCM+ SAS trials. Error bars = SEM.

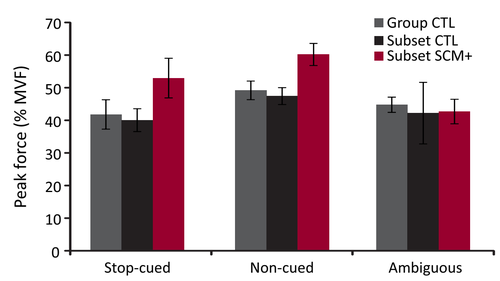


Fig 5. **Peak force (%MVF) achieved for control responses and SCM+ responses as a function of cue type during the conditional stop-signal task.** Grey bars are group means during control trials, black bars are the subset mean of subjects who startled during control trials, red bars are the subset mean of SCM+ SAS trials. Error bars = SEM.

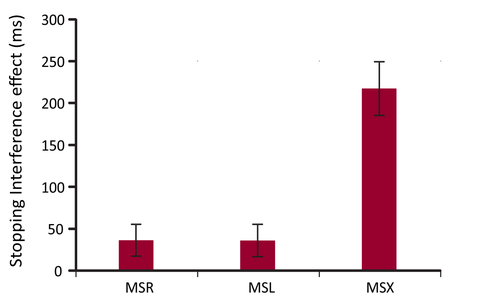


Fig 6. **Group mean stopping interference effect as a function of trial type during the conditional stop-signal task (Exp 1).** The stopping interference effect indicates the delay in RT relative to go of the continuing hand during stop-trials. The reduced interference during Maybe Stop Right (MSR) & Maybe Stop Left (MSL) trials compared to Maybe Stop Unknown (MSX) indicates the use of selective proactive inhibition. Error bars represent within-subject 95% CI.

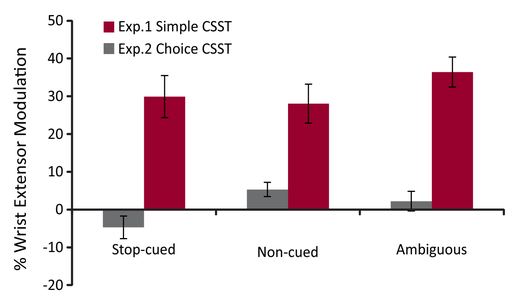


Fig 7. **Group mean modulation of MEP amplitude relative to null trials for each conditional stop-signal task cue type [(cue-null)/null *100].** The red bars are data from Exp 1. which only had a single known bimanual response and the grey bars are data from Exp 2. which had a 2 choice bimanual response. Note the elevated and similar level of excitability for stop-cued and non-cued hands in Exp 1., whereas Exp 2. demonstrates a significant reduction in excitability in the stop-cued hand compared to the non-cued hand. Error bars represent within-subject 95% CI.

Discussion

➲ Presentation of the SAS during the conditional stop-signal task rarely resulted in a startle response (SCM+).

➲ It appears that if a startle response was elicited, both left and right responses were initiated simultaneously regardless of inhibitory cue.

➲ Behavioural results revealed that proactive inhibition was used for task performance, as indicated by the small stopping interference effect in MSR & MSL conditions.

➲ Exp 1. TMS results revealed that corticospinal excitability (CE) was not different between non-cued and stop-cued limbs, and was significantly higher than at rest.

➲ Exp 2. TMS results revealed that CE was significantly reduced in the stop-cued hand compared to the non-cued hand.

➲ Despite behavioural evidence of proactive inhibition of a single response, the results suggest that preparatory activation related to the initiation of the two responses was not different between limbs.

➲ The difference in CE results between Exp 1. & 2. and the large decrease in the startle response suggests that proactive inhibition is suppressing subcortical regions, with large increases in cortical activation related to the initiation of the response in Exp 1. masking the small inhibitory effect typically seen in CE.

References

1. Aron & Verbruggen (2008). *Psych Sci*, 9(11), 1146-1153. **2.** Jahfari et al. (2010). *J Cog Neurosci*, 22(7), 1479-1492. **3.** Claffey et al. (2014). *Neuropsychologia*, 48, 541-548. **4.** Cai et al. (2011). *J Neurosci*, 31(16), 5965-5969. **5.** Greenhouse et al. (2012). *J Neurophysiol*, 107(1), 384-392. **6.** Majid et al. (2013). *J Neurosci*, 33(33), 13259-13269. **7.** Jahfari et al. (2011). *J Neurosci*, 31(18), 6891-6899. **8.** Carlsen et al. (2012). *Clin Neurophysiology*, 123, 21-33. **9.** Maslovat et al. (2015). *Neurosci Let*, 606, 151-155. **10.** Carlsen et al. (2009). *Psychophysiol*, 46(2), 241-251.