Electric and acoustic stimulation during movement preparation can facilitate movement execution in healthy participants and stroke survivors

Running title: Movement facilitation via sensory stimulation

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Abstract

There has been increasing interest in the use of loud acoustic stimulation (LAS) to gain insight into the preparation and initiation of motor actions. Typically, LAS presented during movement preparation in healthy participants culminates in the earlier than normal initiation of the prepared movement and an increase in the magnitude of the response. Recent reports have shown LAS can also facilitate movement in chronic stroke survivors. This suggests that current therapies for motor recovery after stroke might benefit from employing such alternate methods of triggering movement. In this study we sought to test a new way to facilitate motor actions that could be of relevance in clinical settings. Five individuals with chronic motor impairments due to stroke and eight healthy young adults performed a functional reaching task in response to a visual go-signal. On 30% of the trials, LAS or electric stimuli (collectively, sensory stimuli) were unexpectedly presented in synchrony with the go-signal. Both healthy and stroke participants reacted with shorter latencies and executed faster responses when sensory stimulation was synchronised with the go-signal. We have replicated previous findings showing acoustic stimuli can aid movement execution in chronic stroke survivors and demonstrated the same type of effect can be achieved using electric stimulation. Thus, these two types of sensory stimuli can be easily integrated with current devices available to assist people with stroke to engage in rehabilitation efforts.

Keywords: Sensory stimulation, Stroke survivors, reaching, motor control

Introduction

Task-related practice is widely regarded as a crucial step for recovering movement after a neurological injury [22]. However, a lack of sufficient voluntary movement after a stroke can be a limiting factor in the ability of patients to engage in intensive rehabilitation efforts [3]. As a result, there is great interest in investigating training opportunities that can assist stroke survivors in overcoming the limitations of voluntary movement in the early stages of recovery [12, 13]. One option that warrants exploration is the combination of task-oriented training and loud acoustic stimulation (LAS).

Several experiments have demonstrated that LAS can facilitate the initiation and execution of motor actions in the healthy participants, as well as in people with neurological conditions [7, 10, 11, 21]. Although, there is an ongoing debate about the specific neural mechanisms and pathways involved in the phenomenon [1, 9, 14, 15, 17, 18, 20, 21, 23], it is widely agreed that LAS can both speed the initiation and augment the vigour of prepared responses. In other words, the quicker and more forceful response observed when LAS is delivered is more than the simple observation of reflexes in specific muscles: it is the facilitation of the prepared voluntary movement [24].

Recent reports have shown that LAS can facilitate voluntary motor acts in chronic stroke survivors. For example, Honeycutt and Perrault showed that in stroke survivors LAS can improve movement initiation and execution to a level similar to that observed in aged matched controls with no neurological conditions [10, 11]. This indicates that current therapies for movement recovery could benefit from employing alternate methods of assisting movement initiation, which is a factor that limits the engagement of stroke survivors in rehabilitation programs. Similar to LAS, we have recently found that unexpected electric stimulation can also facilitate movement initiation and execution in healthy participants performing arm supination and finger abduction tasks [16], suggesting this form of sensory

stimulation could also be employed in rehabilitation settings and achieve similar outcomes to LAS.

Building on these two approaches, LAS and electric stimuli, we sought to determine whether somatosensory electric stimulation could induce movement facilitation in healthy and chronic individuals with stroke during performance of a functional reaching task [2, 8].

Methods

Participants

Eight healthy young volunteers (mean age = 25, SD = 5.6) and five chronic stroke survivors (mean age = 51.8, SD = 8.5, see Table 1 for further details) with elbow contracture <15 degrees participated in the study. Participants gave written informed consent prior to commencement of the study, which was in accordance with the Declaration of Helsinki and approved by the local Ethics Committee of the University of Queensland. Healthy participants reported normal or corrected to normal vision and stated that they were right hand dominant. Stroke survivors were all right hand dominant and had impairments to the non-dominant arm.

[Table 1 here]

Procedures and Design

[Figure 1 here]

Participants were seated on a chair beside the device, which offered support to the tested arm as shown in Figure 1. They were restrained by a seatbelt to restrict trunk movements. Bright white and green light emitting diodes (LED) were embedded in a Perspex block (10 cm height by 3 cm depth) to serve as warning and go-signals, respectively. The LEDs were mounted at the rear end of a linear slide to which a potentiometer was attached to transduce displacement. Participants made movement toward the Perspex block which was placed beyond arm's length. The tested arm (affected arm for stroke survivors and non-dominant arm for healthy young) was positioned in pronation and wrist extension (0° to 45°) in a customized thermoplastic splint that prevented active movement. The splint had an aluminium frame that was fixed to a manipulandum connected to the linear track. Participants started their movements from a standardized position and were told to push along the linear slide in the direction of the LEDs until they reached a comfortable distance. The request to reach a comfortable distance rather than the maximal range was to allow examination of whether acoustic and/or electric stimulation can induce participants to move further than normal. Based on previous studies with the Sensorimotor Active Rehabilitation Training (SMART) arm, the number of repetitions during the experimental phase was 60 trials [2, 5, 8], plus 6 no-go trials introduced to control for potential false starts (66 trials total).

In some trials (probe trials), acoustic or electric stimulation was physically synchronised with the go-signal. In control and probe trials, go-signal presentation was always preceded by the warning signal appearance (200 ms duration). The interval between warning and go-signals was 1.4 seconds (± 200ms). Participants were asked to reach a comfortable distance forward as quickly as possible upon the presentation of the go-signal

and remain stationary otherwise (no-go trials). Probe trials comprised 30% of the total number of trials. Feedback on reaction time was given after control trials but not after probe trails. If participants made any movement during no-go trials, the message "*Pay attention*" was presented on the monitor screen. Participants were asked to ignore acoustic and electric stimulation and respond only to the go-signal. If reaction times were shorter than 100 ms in control trials, the message "*Do not anticipate*" was displayed.

Before the beginning of the experiments, participants performed 15 practice trials with the right limb (opposite to the limb tested during the experiment) to familiarise themselves with the task. Acoustic stimulation was presented twice during familiarization and electric stimulation was increased (in 1mA steps) until the intensity the participant could tolerate or up to a maximum of 20mA. Only one participant (stroke survivor) did not reach 20mA and tolerated 14mA. The order of presentation of the trials was randomised so that probe trials were not presented twice in a row or sequentially. The inter-trial interval from the end of one trial to the beginning of the next trial was 5 seconds.

Auditory stimuli

The auditory stimuli were bursts of 50 ms broadband white noise with a rise/fall time shorter than 1 ms. Stimuli were generated on a digital computer and presented binaurally via high-fidelity stereophonic headphones (Sennheiser model HD25-1 II; Germany). The input signal to the headphones had a bandwidth of approximately 10 Hz–30 kHz. Auditory stimuli had a peak loudness of 114 dB. 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 speaker.

Electrical stimulation

Electrical stimulation was implemented using a Digitimer DS7A stimulator (Digitimer Ltd, UK) through a pair of Ag-AgCl electrodes (electrode centre about 10mm apart) applied to the biceps' short-head on the non-dominant or less affected arm (unaffected arm for stroke survivors).

Data analysis

The variables of interest were: reaction time, peak velocity, time to peak velocity and distance moved. Reaction time was defined as the difference between movement onset time and the time of go-signal appearance. Peak velocity was determined as the maximum speed of the reaching movement. Time to peak velocity was defined as the time between movement onset and peak velocity both based on the potentiometer data. Distance moved was defined as the maximum distance the manipulandum moved forward (cm) in the direction of the Perspex block. Peak velocity ratios were analysed using the non-parametric Wilcoxon test, to avoid the detrimental impact of right-skewed outliers. The effects of experimental conditions involving more than two means were initially analysed through one-way ANOVAs with repeated measures. The corrected degrees of freedom were reported when the assumption of sphericity was not met, Huynd-Feldt correction. The differences between control and stimulation trials were further assessed through post-hoc t-tests using the false discovery rate (FDR) correction of p-values introduced by Benjamini and Hochberg [4]. Alpha was set to 0.05 for all comparisons. We report 95% confidence intervals (CI) for the difference of means for all pairwise comparisons.

Results

[Figure 2 here]

Figure 2 A and E show mean reaction times for control and the two probe conditions using acoustic (LAS) and electric stimuli. For the stroke survivors, the analysis of variance revealed a statistically reliable effect of condition type on reaction time, $F(2, 8) = 17.99$, $p = 0.001$. The post-hoc test indicated both probe conditions yielded shorter reaction times than control trials ($Control^{stroke}$ – $Electric^{stroke}$, 95% CI [11.6, 134.3]; $Control^{stroke}$ – $Acoustic^{stroke}$ 95% CI [45.25, 162.4]). The post-hoc test also revealed that responses were faster for the LAS than for electric probe trials (LAS^{stroke} – $Electric^{stroke}$, 95% CI [-41.5, -20.2]). A similar pattern of results was found for the healthy young participants. As shown in Figure 2E, there was an effect of condition type on reaction time, $F(2, 14) = 35.21$, $p < 0.0001$. The post-hoc comparisons revealed all pairwise comparisons were statistically significant ($Control^{healthy}$ – $Electric^{healthy}$, 95% CI [31.7, 66.95]; $Control^{healthy}$ – $Acoustic^{healthy}$ 95% CI [39.9, 90.1]; $LAS^{healthy}$ – $Electric^{healthy}$, 95% CI [-28.1, -3.1]).

Figure 2 B and F display mean peak velocity for the three experimental conditions. For the stroke survivors, the ANOVA revealed a statistically reliable effect of condition type on peak velocity, $F(2, 8) = 6.86$, $p = 0.018$. The post-hoc test indicated both probe conditions produced larger peak velocity means in comparison to control trials ($Control^{stroke}$ – $Electric^{stroke}$, 95% CI [-5.3, -0.2]; $Control^{stroke}$ – $Acoustic^{stroke}$ 95% CI [-5.3, -1.2]). The effects on peak velocity were somewhat similar for the healthy young participants. As shown in Figure 2F, there was a reliable effect of condition type on peak velocity, $F(2, 14) = 20.25$, $p < 0.0001$. The post-hoc comparisons showed all pairwise comparisons were statistically significant ($Control^{healthy}$ – $Electric^{healthy}$, 95% CI [-29.7, -12.9]; $Control^{healthy}$ – $Acoustic^{healthy}$ 95% CI [-22.7, -5.4]; $LAS^{healthy}$ – $Electric^{healthy}$, 95% CI [-14.4, -0.15]).

Figure 2 C and G show mean distance moved for control and the two probe conditions. For the stroke survivors, the analysis of variance failed to reach statistical significance, $F(2, 8) = 0.006$, $p = 0.99$. For the healthy young participants, however, the RM ANOVA indicated an effect of the experimental conditions on distance moved, $F(2, 14) = 10.28$, $p = 0.0017$. The post-hoc comparisons revealed participants reached further than in control trials when electric stimulation was presented ($Control^{healthy} – Electric^{healthy}$, 95% CI [-2.05, -0.79]). The pairwise comparison between control and LAS trials approached statistical significance as shown in Figure 2G ($Control^{healthy} – Acoustic^{healthy}$ 95% CI [-1.3, -0. 06].

As shown in Figure 2 D and H, sensory stimulation seemed to shorten time to peak velocity in probe trials for stroke and healthy participants, but the analyses of variance failed to reach statistical significance in both cases (Stroke survivors: $F(2, 8) = 0.64$, $p = 0.55$; Healthy adults: $F(2, 14) = 2.27$, $p = 0.14$).

Discussion

The SMART arm was developed to assist stroke survivors with severe arm impairment to undergo repetitive practice of reaching movements, and has been shown to be effective in increasing upper arm function to a greater extent than traditional therapy alone [2, 8]. In the study reported here, we made use of a training set-up based on the principles of the SMART Arm device to investigate whether sensory stimulation could facilitate movement initiation and execution in both healthy young adults and chronic stroke survivors.

Consistent with recent results in the literature, our results showed LAS shortened reaction time in both stroke survivors and healthy adults (see [10, 11]). They also indicate movement speed was augmented in both groups of participants with both types of stimulation. Thus, importantly, our results showed electric stimulation can also facilitate movement in healthy people and stroke survivors. This is an important finding as current

advice for the use of acoustic stimulation suggests 25% as the maximum percentage of trials with LAS in order to avoid habituation effects [6]. More precisely, now that we have demonstrated electric stimulation can also be used to facilitate movement initiation (Figure 2A and E) and execution (Figure 2B and F) in chronic stroke survivors, it may be possible to use a higher percentage of trials with startle when the delivery of sensory stimulation is distributed across more than one sensory modality within a single session. This is especially relevant in rehabilitation programs in which stroke patients require greater facilitation of movement due to the significant damage to motor pathways arising from the motor cortex and could benefit of additional activation of agonist muscles induced via unexpected sensory stimulation mediated by different sensory modalities.

The effects on reaction time and peak velocity were similar for both groups of participants, however, distance moved increased only for healthy young participants and not for the stroke survivors. One potential explanation for this discrepancy might be that stroke survivors opted for executing further and longer reaches than healthy young participants from the outset (compare Figure 2C and 1G), making it less likely that we could observed an effect on movement distance when they were already closer to maximum distance reached in control trials (a ceiling effect). In the present study, we asked participants to reach to a comfortable distance, in future experiments distance moved should be controlled so as to evaluate whether the effect observed in healthy participants can also be detected in stroke survivors. Requiring stroke survivors to produce shorter movements in the beginning of intervention protocols may also decrease muscle fatigue and allow a larger number of repetitions per session.

Our findings point to new avenues for clinical investigation of the efficacy of using sensory stimulation, particularly in neurological conditions that result in deficits in movement initiation and execution and demonstrates that a simple technique which capitalises on the

natural responses of the motor system can be easily coupled with current devices used in rehabilitation programs.

Limitations

While our results indicate sensory stimulation is beneficial to facilitate movement in healthy young adults and stroke survivors, we should acknowledge some limitations of our study that require attention in future investigations. First, our stroke survivors were all in the chronic phase after stroke and, therefore, more studies are required to determine whether the types of sensory stimulation we employed can be beneficial in the acute and subacute rehabilitation phases post-stroke. Second, it is clear from our results that healthy young adults performed better than stroke survivors as indicated by RT and peak velocity. Thus, we cannot ascertain whether electric and acoustic stimulation made our stroke survivors return to normal levels consistent with aged matched controls. Third, despite observing the same pattern of results in both groups of participants, our sample size was limited and further experiments should assess a larger cohort. Last, we did not have access to the details of the stroke (e.g. volume and area involved) nor assessment of the presence of some impairments, such as spasticity measured by the Tardieu scale. Thus, it remains unclear whether the facilitation of movement via sensory stimulation is particularly beneficial to lesions of specific brain areas or people who present with or without spasticity.

Conflict of Interest Statement

WM, TC, SR have no potential conflicts of interest to be disclosed. SB and KH are involved in SMART Arm Pty Ltd.

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Tables

Table 1: Details of the stroke survivors.

ID#	Sex	Age	Affected limb	Months since stroke	Type of stroke	MAS total	Modified Rankin Scale
1	Male	68	Left	59	Ischemic	13	2
2	Female	59	Left	18	Haemorrhagic	1	3
3	Female	20	Left	47	Ischemic	18	1
4	Male	49	Left	27	Ischemic	1	2
5	Male	63	Left	30	Ischemic	18	1

Figure caption

Figure 1: Illustration of the experimental set-up.

Figure 2: Top half shows results for stroke survivors. Bottom half shows results for healthy young adults. **A** & **E** – Reaction time as a function of experimental conditions. **B** & **F** – Peak velocity as a function of experimental conditions. **C** & **G** – Distance moved as a function of experimental conditions. **D** & **H** – Time to peak velocity as a function of experimental conditions. Error bars represent the 95% CI. Confidence intervals were calculated following Morie's [19] suggestion for repeated measures designs. * Marks statistically significant differences between means. ^ $p = 0.06$. CTL = control trials; Elec. = Electric trials; LAS = loud acoustic stimulus trials.

Figures

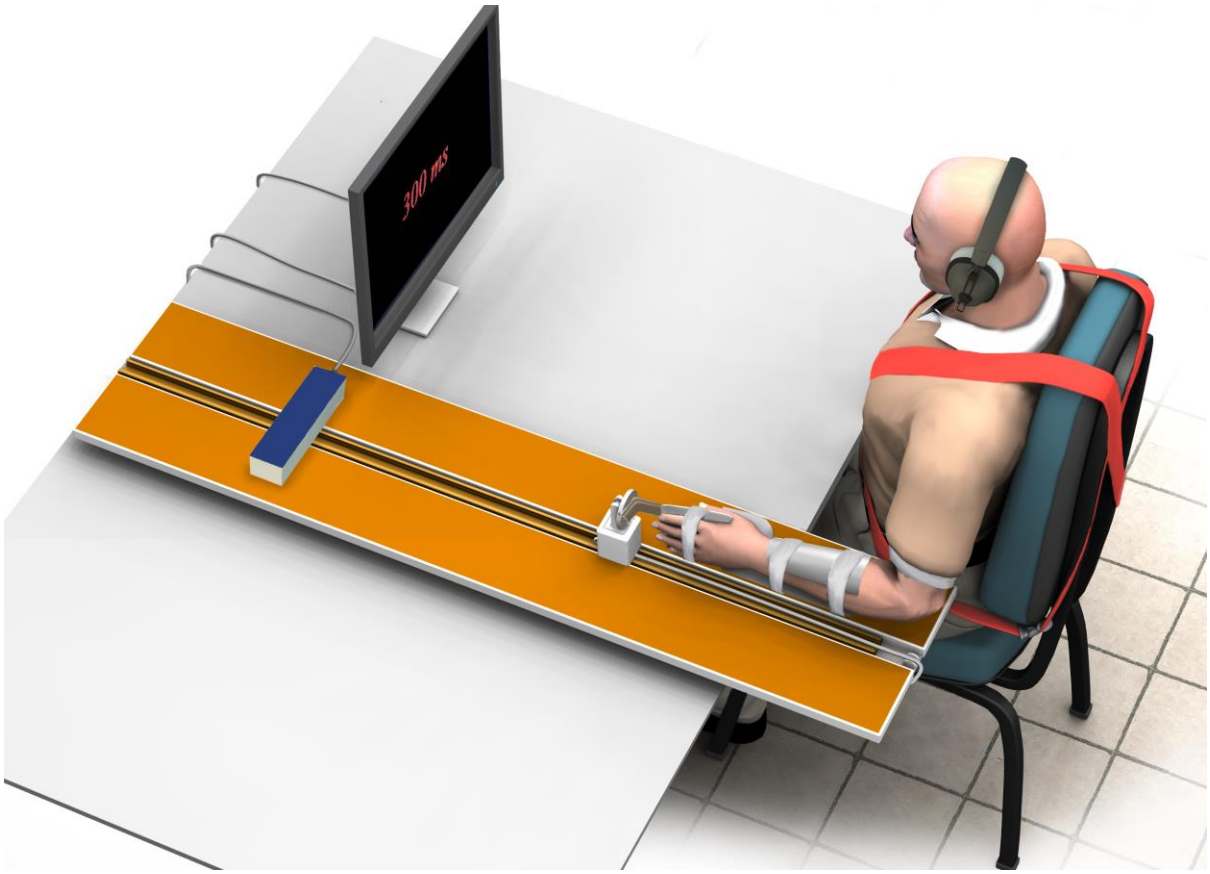

Figure 1

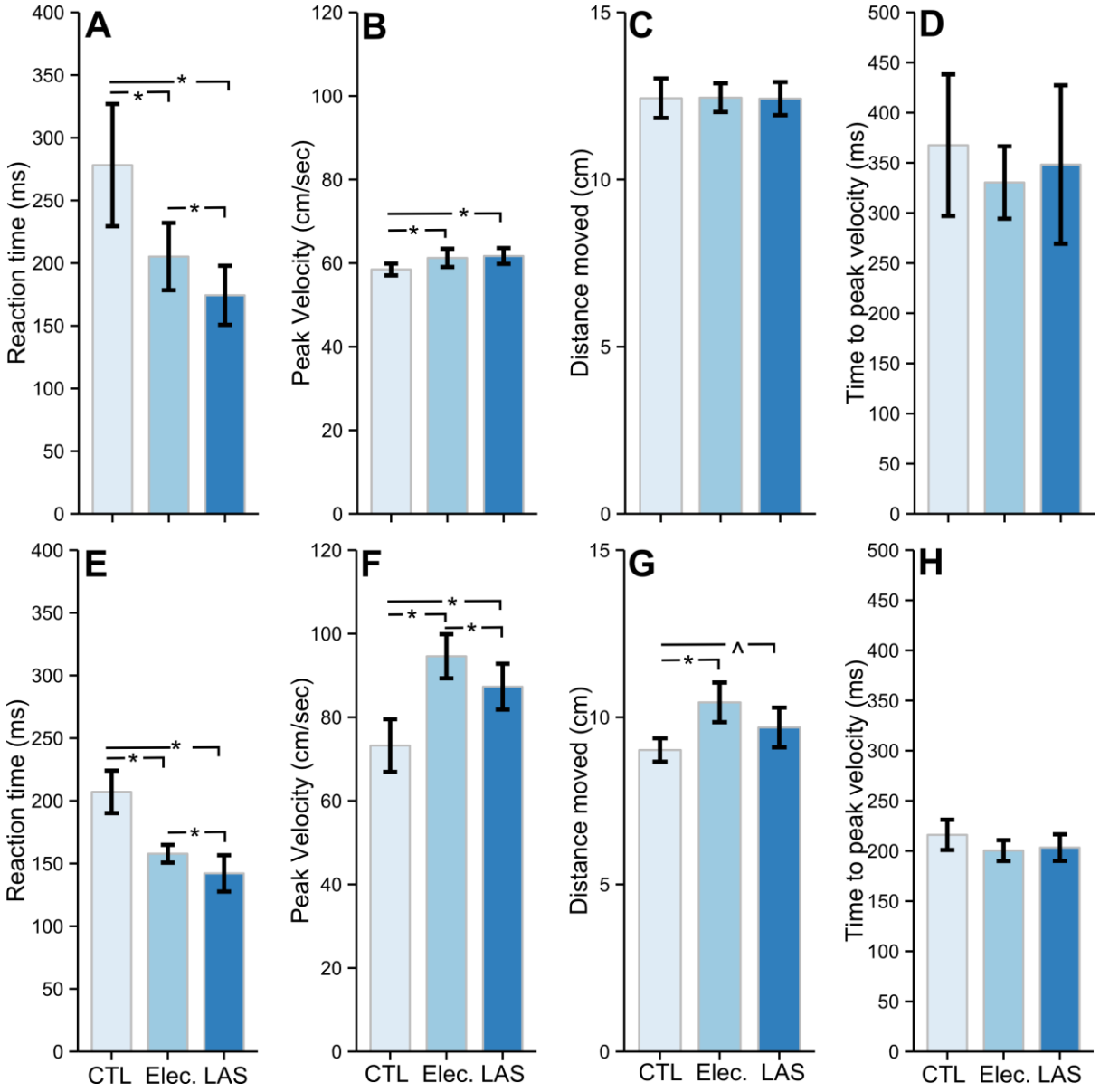
A
B
C
D
E
F
G
H
Reaction time (ms)
Peak Velocity (cm/sec)
Distance moved (cm)
Time to peak velocity (ms)
CTL
Elec.
LAS

Figure 2