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No difference observed in short-interval intracortical inhibition in older burn-injury survivors compared to non-injured older adults: A pilot study

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ABSTRACT

Objective: The study aimed to investigate short-interval intracortical inhibition (SICI) in burns survivors and non-injured controls, and establish whether paired-pulse transcranial magnetic stimulation (TMS) is a sensitive tool to investigate SICI after burn-injury.

Methods: Burn survivors underwent experimental assessments at 6- and 12-weeks after injury, and control participants underwent two equivalent sessions 6 weeks apart. Single-pulse transcranial magnetic stimulation (TMS) was used to record motor-evoked potentials (MEPs) from a hand muscle and paired-pulse TMS was used to measure SICI. Functional measures were obtained for comparison at 12-weeks after injury.

Results: There was no significant difference in SICI between burns survivors and non-injured controls at either 6- or 12-weeks after burn injury. There was no evidence of correlations between SICI and functional outcome measures in burns survivors.

Conclusions: These results show that paired-pulse TMS is a useful method for investigating cortical inhibition following burn injury, and that SICI circuits in the primary motor cortex are not affected by minor burn injury. This study presents details for definitive future studies of primary motor cortex function after minor burn injury.

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1. Introduction

It is well established that the brain is capable of changing—a phenomenon known as neuroplasticity. Structural and functional neuroplasticity underlie the ability to acquire, consolidate and retain motor skills [1], and neuroplasticity has been observed in a variety of musculoskeletal injuries. Indeed, the capacity for neuroplastic change likely impacts the functional

recovery from these injuries [2,3]. The mechanisms underlying neuroplasticity in the motor cortex is of great importance. Neuroplasticity of the primary motor cortex (M1) is thought to be mediated by unmasking of existing, but functionally silent, connections via disinhibition [4–6]. For example, transient deafferentation can lead to a rapid expansion of motor cortical maps coupled with reduced intracortical inhibition [7]. The rapid change in inhibition facilitates the unmasking of otherwise functionally silent connections [8].

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Transcranial magnetic stimulation (TMS) is a form of non-invasive brain stimulation (NIBS) that can be used to measure corticospinal excitability and motor cortical inhibition. In single-pulse TMS, a brief, high current electrical pulse is delivered through a handheld coil placed over the scalp, which induces a magnetic field that passes through the scalp and skull with little attenuation. The magnetic field induces current flow in the underlying brain tissue, and if the stimulation is sufficiently intense, will result in depolarization of the neurons [9,10]. A single, suprathreshold pulse delivered to M1 will depolarize neurons in the underlying brain tissue and elicit a motor-evoked potential (MEP) in the muscle controlled by the cortical representation over which the pulse was delivered. The amplitude of the MEP provides a measure of corticospinal excitability.

Paired-pulse TMS can be used to measure the excitability of inhibitory processes within the M1. One major inhibitory process that has been identified is short-interval intracortical inhibition (SICI) [11]. When a subthreshold conditioning stimulus (CS) precedes a suprathreshold test stimulus (TS) by 1–5ms, the amplitude of the MEP elicited by the TS is suppressed because of the activation of SICI circuits [9,11–15]. Pharmacological studies provide strong evidence that SICI is mediated by GABA_A receptor activity [16,17].

Rehabilitation and recovery from a burn injury is a particularly challenging process for older adults. Age is known to have a significant negative impact on burn victims' morbidity and mortality [18–22]. Ageing has been shown to lead to a decline in both resting-state and task-related GABA-ergic activity in the M1, with declines in resting-state inhibition leading to declines in motor performance [23,24]. It is plausible that functional recovery from a burn injury is impacted by an age-related decline in motor cortex inhibition through the GABA-ergic system. This study aimed to investigate whether SICI is affected after an acute burn injury in older adults compared to a non-injured, age-matched control group, and whether differences in SICI were associated with functional outcome measurements within an older burn injury population. It was hypothesized that burns survivors would have less SICI than non-injured, age-matched controls.

2. Methods

2.1. Participants

Sixteen burn injury survivors (10 male, $M=56.8\pm 7.9$ years, range 45–71 years) and thirteen control participants (6 male, $M=62.4\pm 10.3$ years, range 47–83 years) took part in the study. Burn injury survivors were recruited through the State Adult Burn Unit. The inclusion criteria for burn injury survivors were: aged 45 years or older at the time of recruitment; total body surface area of burn injury less than 20%; burn injury occurred less than 6 weeks prior to recruitment. The exclusion criteria for burn injury survivors were: conditions that may confound the measurement of recovery or hinder rehabilitation beyond the burn injury such as neurological incidents (e.g. stroke) and reported musculoskeletal skeletal injury or surgery within the last three months; severe or recent heart disease; sleep deprivation; any contraindication to TMS. Burns participants

underwent normal treatment for their burn injury, through the State Adult Burn Unit Inpatient and/or Outpatient Services, which included an extensive medical history and physical examination, and a functional assessment at twelve weeks after burn injury.

Non-injured volunteers were recruited from the public. The inclusion criteria for these participants were: aged 45 years or older at time of recruitment; no history of a burn injury that received medical treatment. The same exclusion criteria as for the burns survivors applied for control participants.

The protocol was performed in accordance with the Declaration of Helsinki and was approved by the Murdoch University Human Research Ethics Committee (MU HREC Reference: 2016-166), East Metropolitan Health Service (EMHS HREC Reference: 16-012), South Metropolitan Health Service (SIRO HREC Reference: 16-012) and University of Western Australia (UWA HREC RA/4/1/8354). Governance approval was obtained from East and South Metropolitan Health Services. All subjects gave written informed consent prior to testing and were screened for conditions that would contraindicate TMS [25,26].

2.2. Experimental procedures

2.2.1. Transcranial magnetic stimulation

All participants attended two experimental sessions at the TMS laboratory at Murdoch University, six weeks apart; for burns survivors, the sessions were conducted at 6-weeks and 12-weeks after injury. In both sessions participants were seated in a comfortable chair with their right hand resting on a soft pillow on their lap. The first dorsal interosseous (FDI) muscle on the right hand was palpated (participants asked to gently abduct the index finger against resistance for palpation of the muscle), and the overlying skin cleaned with an alcohol-based solution. Surface electromyography (EMG) was recorded from two Ag-AgCl electrodes (with water-based lubricant applied) taped into position; one electrode was placed over the belly of the muscle and one electrode was placed over the tendon insertion. A grounding electrode was attached to the skin over the distal ulna at the wrist. The EMG signal was amplified ($\times 1000$) and band-pass filtered (20Hz – 1kHz) using a CED 1902 signal conditioner (Cambridge Electronic Design Co. Ltd, Cambridge, UK). The signal was then digitized at 2kHz using a CED 1401 analog-to-digital converter (Cambridge Electronic Design Co. Ltd, Cambridge, UK) and was then stored on a computer to allow for later off-line analysis. TMS pulses (monophasic) were delivered using a figure-of-eight coil connected to a Magstim BiStim 200² stimulator (The Magstim Company Limited, Whitland, Wales, UK). The coil was held tangentially to the scalp at an angle of 45° to the sagittal plane with the handle pointed posteriorly to induce a posterior-anterior current flow.

The site for optimal stimulation and the resting motor threshold (RMT) were determined for the right FDI with left M1 stimulation. To determine the optimal stimulation site, suprathreshold pulses were delivered at a number of sites to identify the site from which FDI MEPs were evoked consistently. The optimal site was marked on a tight-fitting material swimming cap to ensure reliable placement of the coil throughout the experimental session. RMT was defined as

the minimum stimulus intensity (as a percentage of the maximum stimulator output) that produced a MEP of at least 50 μ V in at least three out of six trials in which the FDI was completely relaxed [27–30].

2.2.2. Paired-pulse TMS

Three blocks of single- and paired-pulse TMS were delivered. There was a total of 14 single- and 14 paired-pulses per block (order randomised; the interval between trials was 5 s ($\pm 20\%$ jitter)). For single-pulse trials, test stimulus intensity was set to 120% of RMT. For paired-pulse trials the conditioning stimulus intensity was set to 80% of RMT, the test stimulus intensity was set to 120% RMT, and the inter-stimulus interval was 2 milliseconds (ms).

2.3. Functional and quality of life measures

Functional and quality of life measures were obtained from all participants at the second TMS session, which for burn survivors was 12-weeks after injury (median days after injury for Burns Group=88, range=79–103). In addition, all burn survivors completed both the Short-Form Health Survey version 2 (SF-36) and the Burn Specific Health Scale – Brief (BSHS-B) quality of life assessments. The SF-36 is a self-completed questionnaire that is an indicator of overall health status across eight domains [31]; the BSHS-B is a self-completed questionnaire that is an abbreviated outcome scale, designed specifically for burn survivors, used to evaluate burn-specific aspects of health status across nine domains or three broad categorizations [32,33]. Burn survivors who had sustained a burn injury to their upper limb ($n=8$) were also asked to complete the QuickDASH (Disabilities of the Arm, Shoulder and Hand) outcome measure (QuickDASH). The QuickDASH is a self-completed questionnaire that uses eleven items to measure physical function and symptoms in people with any or multiple musculoskeletal disorders of the upper limb [34]. Burn survivors who had sustained a burn injury to their lower limb ($n=6$) were also asked to complete the Timed Up and Go (TUG) test and the Lower Limb Function Index-10 (LLFI). The TUG test involves participants starting in a seated position in a chair, standing, walking three meters quickly to a line identified on the floor, and then returning to the seated position [35,36]. The LLFI is a self-assessment questionnaire that assesses functional status in individuals with lower limb conditions [37]. All of these assessments have been validated for use in a burn injury population [34,38–42]. Some Burns Group participants had both upper and lower limb burn injuries ($n=2$), and therefore completed both upper and lower limb functional measures.

All control participants completed the Short-Form Health Survey version 2 (SF-36) and the Timed Up and Go (TUG) test. (Only the TUG test and SF-36 were assessable across both groups as the BSHS-B, QuickDASH and LLFI are either burn or injury specific and not easily completed by an individual without injury. As noted above, TUG measures were only available from those burn survivors with a lower limb burn injury.)

2.4. Data analysis

Four of the sixteen burn survivors were lost to follow-up after the first TMS session (two participants were unavailable to

attend the second experimental session; one participant had commenced a new medication that contraindicated the use of TMS; one participant's EMG recordings were contaminated by voluntary muscle activity). These four participants did not complete the functional outcome measures (completed at the second TMS session). Their data from the first TMS session, completed at 6-weeks after injury, are included in the analyses comparing Session 1 between groups, but are not included in analyses that compares Session 1 to Session 2 or Session 1 outcomes to functional outcome measures (which were obtained in Session 2, at 12-weeks after injury).

EMG activity was analysed by visual inspection of the offline recordings. Any trial with muscle activity in the 250ms preceding the onset of the MEP was excluded from analysis. The peak-to-peak MEP amplitude (mV) was obtained from the 40ms of EMG activity beginning 15ms after the test stimulus. The total number of trials excluded due to pre-TMS EMG activity was 7.4% ($\pm 5.6\%$). For burns participants, a total of 8.4% ($\pm 6.4\%$) of trials were excluded, and for control participants, a total of 6.2% ($\pm 4.4\%$) of trials were excluded. An independent samples t-test showed that this difference was not statistically significant ($t_{51}=1.33$, $p=0.190$; $BF_{01}=1.45$; $BF_{10}=0.69$).

To test for differences in RMT and MEP amplitude elicited by single-pulse TMS, between groups and across experimental sessions, two-way mixed analysis of variance (ANOVAs) were performed, with within-subject factor of SESSION (Session 1, Session 2) and between-subjects factor of GROUP (burns, control); separate ANOVAs were performed for RMT and MEP amplitude data.

To quantify SICI, the mean MEP amplitude from paired-pulse trials was expressed as the ratio of the mean MEP amplitude from single-pulse trials. The SICI ratios were not normally distributed. Analyses (described below) were performed on the SICI ratios as well as the log-transformation of SICI ratios (that did not violate the assumption of normality); results from the analyses performed on the SICI ratios and the log-transformed ratios did not differ. We report the results of the analyses performed on the non-transformed SICI ratios below.

To test for differences in SICI across the three blocks of trials and across experimental sessions, two-way repeated measures ANOVAs were performed, with within-subject factors of BLOCK (Block 1, Block 2, Block 3) and SESSION (Session 1, Session 2); separate ANOVAs were performed for controls and burns participants. To examine associations between SICI across sessions, correlational analyses were performed on SICI ratios (averaged across the three blocks) from the two sessions, with separate correlations performed for control and burns participants.

To test for differences in SICI between groups and across experimental sessions, two-way mixed ANOVAs were performed, with within-subject factor of SESSION (Session 1, Session 2) and between-subjects factor of GROUP (burns, control). Bayesian analyses were conducted, with a default Cauchy prior of zero with an interquartile range of 0.5 [43]. Bayesian factors for the null and alternative hypotheses are presented (BF_{01} and BF_{10} , respectively). Analyses were completed using JASP (Version 0.9.2.0, Netherlands).

Greenhouse-Geisser corrections were used for analyses in which the assumption of sphericity was violated (Mauchly's test of sphericity). Conditional on significant main effects of

interactions, post-hoc analyses were performed. Statistical significance was accepted at $\alpha < 0.05$. Data are presented as mean \pm standard deviation, except in the figures where the standard error of the mean (SEM) is presented.

The relationship between Functional and Quality of Life domain scores and baseline SICI was assessed using correlational analysis.

3. Results

3.1. Participant characteristics

There was no evidence of a difference in age or gender between groups (Age $p = .11$, Gender $p = .40$). The average TBSA of burn size in the burn survivors was 2.14%, with burn size ranging from .12% to 7.25%. All burn injuries in this study had a TBSA of less than 15% and are therefore considered to be minor burn injuries [44]. The location of burn injury included nine upper limb burns (two individuals sustained burns to both upper limbs but are only counted once), nine lower limb burns (buttocks included; four individuals sustained burns to both lower limbs but are only counted once), three thorax burns (chest, abdomen, pelvis (including genitals but excluding buttocks) and back) and three head and neck burns. Only one participant sustained a burn injury over the area targeted by TMS (right hand, first dorsal interosseous muscle). Interestingly, this patient was unable to complete the second TMS session as EMG values were unable to be reliably recorded from this area. This may have been secondary to the changes (maturation) in scarring over this area (this was one of the four burn survivors who was lost to follow-up). Six of the burn survivors underwent surgical management of their injuries, ten did not. The median days between sessions for the burn survivors was 44 (range=32–55), that is, the time between the sessions at 6-weeks and 12-weeks after injury. The median days between sessions for the control participants was 50 (range=39–56).

3.2. Baseline corticospinal excitability

There was no evidence of a difference in RMT or baseline MEP amplitude across sessions or between groups. For control participants, the mean RMT was 52.8% (± 8.0) and 53.6% (± 9.3) of maximal stimulator output for Session 1 and Session 2, respectively. For burns participants, the mean RMT was 53.1% (± 6.9) and 51.8% (± 6.1) of maximal stimulator output at 6-weeks after injury and at 12-weeks after injury, respectively. A two-way RM-ANOVA showed no evidence of an effect of SESSION ($F_{1,23} = .52$, $p = .48$, $\eta_p^2 = .02$), no main effect of GROUP ($F_{1,23} = .30$, $p = .59$, $\eta_p^2 = .01$), and no SESSION*GROUP interaction was observed ($F_{1,23} = .05$, $p = .83$, $\eta_p^2 < .01$).

For control participants, the mean MEP amplitude elicited by single-pulse stimuli was 0.96 mV (± 1.44) and 0.68 mV (± 0.70) for Session 1 and Session 2, respectively. For burns participants, the mean MEP amplitude elicited by single-pulse stimuli was 0.69 mV (± 0.51) and 0.72 mV (± 0.58) of maximal stimulator output at 6-weeks after injury and at 12-weeks after injury, respectively. The RM-ANOVA performed on the single-pulse MEP amplitude data showed no evidence of an effect of SESSION ($F_{1,23} = .74$, $p = .40$, $\eta_p^2 = .03$), no main effect of GROUP

($F_{1,23} = .12$, $p = .73$, $\eta_p^2 = .01$), and no SESSION*GROUP interaction demonstrated ($F_{1,23} = 1.02$, $p = .32$, $\eta_p^2 = .04$).

3.3. SICI

For both control and burn participants, there was no significant differences evident in SICI across the three recording blocks or across sessions. For control participants, the two-way ANOVA showed no main effect of SESSION ($F_{1,12} = 1.44$, $p = .25$, $\eta_p^2 = .10$), no main effect of BLOCK ($F_{2,24} = .32$, $p = .60$, $\eta_p^2 = .03$), and no SESSION*BLOCK interaction was observed ($F_{2,24} = .33$, $p = .72$, $\eta_p^2 = .03$). For burns participants, the two-way ANOVA showed no evidence of an effect related to SESSION ($F_{1,11} = .71$, $p = .42$, $\eta_p^2 = .06$), no main effect of BLOCK ($F_{2,22} = 2.10$, $p = .17$, $\eta_p^2 = .16$), and no SESSION*BLOCK interaction observed ($F_{2,22} = .98$, $p = .35$, $\eta_p^2 = .08$). (One burns participant had a SICI ratio $> 2SD$ from the mean; removing this participant from the analysis did not change the results of the ANOVA.)

Fig. 1 shows SICI ratios from control and burns participants. It is clear from panels (C) and (D) that there are strong positive associations between SICI ratios in the two sessions. For control participants (C), there was a strong positive association between the SICI ratios (averaged across the three blocks) obtained in Session 1 and Session 2 ($r = .88$, $p < .001$, 95% CI = .64, .96). For burn participants (D), there was a strong positive association between SICI ratios obtained at 6-weeks after injury and 12-weeks after injury ($r = .67$, $p = .016$, 95% CI = .16, .90). Note that the insert in Fig. 1D shows the association between SICI ratios at 6- and 12-weeks after injury when the participant with a large SICI ratio is removed ($r = .65$, $p = .031$, 95% CI = .08, .90). At the group level, there was no difference in SICI across session or between groups.

The ANOVA performed on the SICI data showed no main effect of SESSION ($F_{1,23} = 1.67$, $p = .21$, $\eta_p^2 = .07$), no main effect of GROUP ($F_{1,23} = .32$, $p = .58$, $\eta_p^2 = .01$), and no observable SESSION*GROUP interaction ($F_{1,23} = .01$, $p = .81$, $\eta_p^2 < .01$). (One burns participant had a SICI ratio $> 2SD$ from the mean; removing this participant from the analysis did not change the results of the ANOVA.) In addition, Baye's factor analysis was performed to quantify evidence for the null vs alternative for Session 1 ($BF_{01} = 3.19$; $BF_{10} = .31$) and Session 2 ($BF_{01} = 3.72$; $BF_{10} = .27$), which suggest that the empirical data do not provide strong evidence to distinguish SICI in burns participants and control participants.

Functional and quality of life measures were recorded 12-weeks after injury in burn survivors (Session 2) prior to the TMS protocol. There was a significant difference evident for the TUG times between the burn survivors and control participants ($p = .02$), with the mean TUG time of 7.95 s (± 1.38) for burn survivors compared to the mean TUG time of 6.46 s (± 1.13) for control participants. There was no significant difference between groups in SF-36 outcomes. Within the burns participants, there was no significant relationship between SICI and any functional outcomes.

4. Discussion

In this pilot study, control participants and burn participants demonstrated strong positive associations between SICI ratios from the two sessions, suggesting the technique can be used to

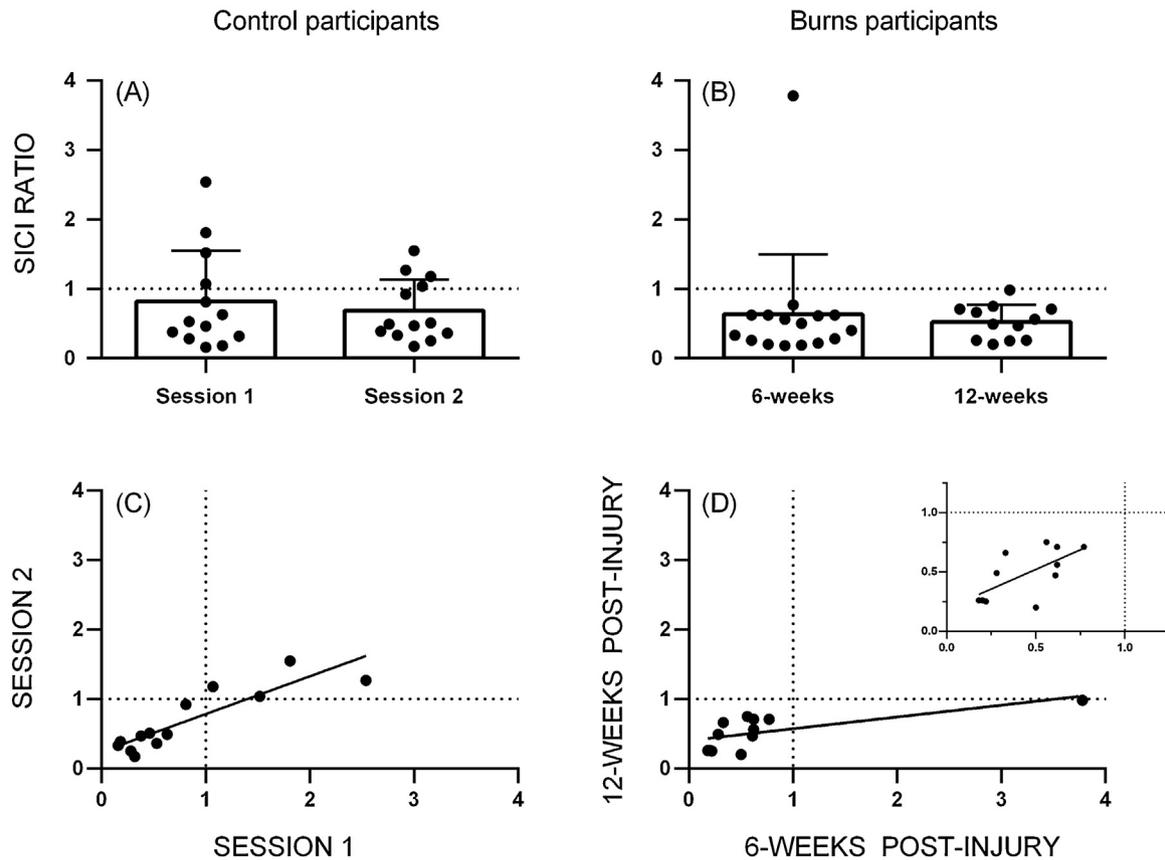


Fig. 1 – Top row shows mean (SEM) SICI ratios for control participants (A) and burn participants (B) in the two sessions. Bottom row shows associations between SICI ratios in Session 1 and Session 2 for control participants (C) and between SICI ratios 6-week after injury and 12-weeks after injury for burn participants (D).

reliably measure intracortical inhibition in these populations. When comparing SICI across groups, there was no difference evident in SICI between burn survivors and non-injured control participants.

4.1. No difference in SICI between burn survivors and non-injured control participants.

In this study, there was no evidence of a difference in SICI between burn survivors and non-injured control participants. Given that SICI is mediated by GABA_A receptor activity [17,45,46], the current findings suggest that a minor burn injury does not lead to a change in GABA_A mediated inhibition in the hand area of M1 between 6- and 12-weeks after injury. At first glance, the absence of a difference in SICI between burn survivors and non-injured controls is somewhat surprising given that there is a reduction in SICI following peripheral changes such as amputation and short-term deafferentation using ischemic nerve block [8,47]. However, there are two plausible explanations for the lack of difference in SICI in the current sample of burn survivors and non-injured control participants.

First, SICI in the current study was measured from a hand muscle (right FDI), but only one of the burn survivors had a burn to their right hand, and one had a burn to the volar surface of all fingers bilaterally. Experiments studying mechanisms of cortical

neuroplasticity secondary to deafferentation measured inhibition acting on the muscle immediately proximal to deafferentation [8]. Similarly, measures of inhibition in amputees were obtained from muscles just proximal to the amputation site [8,47]. Furthermore, in amputees, a significant decrease in SICI in the amputated limb has been shown compared to the intact limb, but SICI in the intact limb is not significantly different to non-injured subjects [47]. Notwithstanding the differences in amputation and burn injury, it is reasonable to speculate that a decrease in SICI in burn survivors relative to non-injured control participants may be observed if SICI acting on muscles immediately proximal to the area of burn injury is measured. It would be valuable for future research to examine SICI in upper-limb burn injury survivors, comparing SICI in the burn-injured and non-injured upper-limb.

Second, whilst the results of the current study did not provide any evidence of a difference in GABA_A mediated inhibition between burn survivors and non-injured control participants, it is possible that other types of inhibition are altered following minor burn injury. Indeed, a recent study examined differences in the cortical silent period (period of inactivity in the EMG following a suprathreshold TMS pulse to a voluntarily contracted muscle) between burn survivors and non-injured controls [48] (this previous study was completed by our group; the samples of burn participants and control

participants in our previous study and the current study were completely independent). The cortical silent period is primarily mediated by GABA_B receptor activity [49-52]. Garside et al. [48] demonstrated a significantly shorter cortical silent period in the burned arm of burns survivors with an upper limb injury compared to uninjured controls in those who were injured less than two years ago, those with partial thickness burns, those with upper limb burns only and those with burns than less than 10% TBSA. As in this study, EMG recordings were taken from the FDI muscle in all participants in the Garside et al. [48] study, regardless of burn location. The research suggests that there is a reduction in GABA_B mediated intracortical inhibition in burns survivors compared to non-injured controls. Given the possible role of intracortical inhibition mediated by GABA_B receptor activity future research should examine long-interval intracortical inhibition (LICI). An inter-stimulus interval of 100-200ms between conditioning and test stimuli can reduce MEP amplitude secondary to LICI, with pharmacological evidence showing that LICI is mediated by GABA_B receptor activity [51,53-55].

4.2. Associations between baseline SICI and functional and quality of life measures

No significant relationship was evident between baseline SICI ratios and functional or quality of life measures within the burn survivors. This result is likely primarily influenced by the small sample in this study. However, it is possible that the functional and quality of life measures used may not be sufficiently sensitive to detect associations between SICI and motor function. SICI measurements were taken from a hand muscle, whereas functional and quality of life measures were either limb specific or very generalised (i.e. overall wellbeing). Associations may be identified if more specific measures of motor function were measured, or if SICI was obtained from the area of injury specifically.

4.3. Limitations

In this study SICI was only measured with a single conditioning stimulus intensity and a single inter-stimulus interval (ISI). SICI is dependent on the intensities of the conditioning stimulus. Variation of the conditioning stimulus intensity results in a U-shaped variation in SICI magnitude. The descending arm of this U-shape reflects increasing inhibition with increasing stimulus intensity, with the ascending arm reflecting decreasing inhibition with continuing increases in stimulus intensity [56]. Obtaining the full SICI curve as a function of conditioning stimulus intensity provides a measure of both the sensitivity of circuits that mediate SICI (that is, the descending limb) and the magnitude of SICI (that is, maximal inhibition). In the current study, SICI was measured at a single conditioning stimulus intensity that likely corresponds to maximal inhibition; it would be valuable to measure SICI as a function of CS intensity in burn survivors and non-injured controls to determine whether the sensitivity of SICI circuits is altered following a burn injury. Furthermore, measures of SICI are influenced by short-interval intracortical facilitation (SICF). SICF provides a measure of intracortical facilitatory processes. SICF can be measured when the

preceding stimulus (set to produce a 1mV MEP alone) precedes a second stimulus (set at 90% of RMT). The extent of SICF induced is dependent upon the ISI between stimuli, with research showing that ISIs of 1.5ms, 2.5-3.1ms and 4.5ms elicit significantly larger MEP amplitudes than a control MEP elicited by the preceding stimulus alone [56]. Although SICI measured at an ISI of 3ms is likely to be influenced more by SICF than SICI measured at an ISI of 2ms, SICF would still have some influence on SICI measured at an ISI of 2ms. Burn injury may alter the balance between motor cortical inhibition and excitation, and therefore future research should examine SICI at different conditioning stimulus intensities and ISIs, taking into account the possible effect of SICF.

Finally, it is important to note that this is a pilot study, and was underpowered to detect anything except a large effect. The means and variance of SICI from the current study were used to perform power calculations to determine the required sample sizes to detect small and medium effects at 6- and 12-weeks after injury, respectively (G*Power 3.1.9.2). At 6-weeks after injury, a sample of 437 would be required to detect a small effect size (Cohen's $d=0.22$ with 80% power at alpha 0.05). At 12-weeks after injury, a sample of 100 would be required to detect a medium effect size (Cohen's $d=0.47$ with 80% power at alpha 0.05). Further research should obtain more comprehensive measures of SICI in a larger number of burn participants, controlling for burn injury site.

5. Conclusion

The results of the current study show no difference in SICI between burn injury survivors and non-injured control participants. In addition, the current study provides no evidence to suggest that SICI is associated with functional recovery of a minor burn injury. The current pilot study presents details for definitive future studies of primary motor cortex function after minor burn injury.

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Declarations of interest

None.

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