



Is Motor Cortical Excitability Altered in People with Chronic Pain? A Systematic Review and Meta-Analysis



Rosalind S. Parker^{a,b,*}, Gwyn N. Lewis^a, David A. Rice^{a,c}, Peter J. McNair^a

^a Health & Rehabilitation Research Institute, Faculty of Health and Environmental Sciences, Auckland University of Technology, Private Bag 92006, Auckland 1142, New Zealand

^b Department of Physiotherapy, Waitakere Hospital, Auckland 0650, New Zealand

^c Waitemata Pain Service, North Shore Hospital, Auckland 0622, New Zealand

ARTICLE INFO

Article history:

Received 11 November 2015

Received in revised form 2 March 2016

Accepted 30 March 2016

Available online 4 April 2016

Keywords:

Chronic pain

Cortical excitability

Intracortical

Transcranial magnetic stimulation

Systematic review

Meta-analysis

ABSTRACT

Background: Chronic pain is characterised by maladaptive neuroplasticity in many systems, including the motor system. There is evidence that patients with chronic pain demonstrate altered corticospinal and intracortical excitability; however, findings are inconsistent and existing literature in this area has not been systematically reviewed.

Objective: To systematically review studies examining corticospinal and intracortical excitability using transcranial magnetic stimulation in people with chronic pain compared to healthy controls and to provide a meta-analysis of study outcomes.

Methods: Databases were searched for controlled studies evaluating corticospinal and intracortical excitability in chronic pain conditions. Outcome measure data were entered into separate meta-analyses and effect sizes calculated. A subgroup analysis based on the type of chronic pain population was also performed.

Results: Forty-three studies were included, encompassing a pooled total of 1009 people with chronic pain and 658 control participants. Significant effect sizes ($P < 0.05$) indicated that in chronic pain populations the duration of the silent period and the extent of short-interval intracortical inhibition were both reduced and short-interval intracortical facilitation was enhanced. The subgroup analysis revealed that only the neuropathic pain group exhibited significant effect sizes for these outcome measures. Effect sizes for the remaining outcome measures were not significant.

Conclusions: There is evidence of motor cortex disinhibition in chronic pain populations, suggestive of a disruption in GABA-mediated intracortical inhibition. Disinhibition was more pronounced in populations with neuropathic pain. These findings provide new insights into the relationship between chronic pain and motor cortex excitability, which may have meaningful implications for the future treatment of chronic pain conditions.

© 2016 Elsevier Inc. All rights reserved.

Introduction

Chronic pain is the most common cause of disability worldwide, with 17–46% of the population affected [1–4]. Increasingly, there are calls for chronic pain to be recognised as its own disease entity, rather than the symptom of a disease [5–7]. This follows increasing evidence of maladaptive neuroplasticity [8–10] and altered neurotransmitter concentrations [11–13] at spinal and supraspinal levels of the nociceptive system. These changes are common across many different chronic pain conditions [9,10,14] and are

thought to underlie the chronic pain experience, resulting in ongoing allodynia and hyperalgesia due to a persistent increase in the synaptic efficacy of nociceptive pathways.

While less established than the changes in nociceptive pathways, there is an increasing focus on dysfunction and maladaptive neuroplasticity of the motor system in individuals with chronic pain. Deficits in motor performance are common across a range of chronic pain conditions, with evidence of muscle weakness [15,16] and central activation deficits [17], impaired coordination [18,19] and force control [20,21] as well as abnormal muscle activation patterns [18,22] and kinematics [18] during functional activities. While some of these deficits may arise through adaptations in peripheral tissue (e.g. muscle atrophy, metabolic changes) or altered spinal reflex excitability [23], there is mounting evidence of pain-related

* Corresponding author. Tel.: 0064 9 921 9999 ext 8157.
E-mail address: roz.parker@aut.ac.nz (R.S. Parker).

plasticity in sensorimotor areas of the brain, including the primary motor cortex [24–26].

The excitability of the primary motor cortex and corticospinal tract can be examined using single and paired pulse transcranial magnetic stimulation (TMS). Using these techniques, it is possible to measure changes in intracortical circuits within the primary motor cortex, such as GABA mediated inhibition and glutamate mediated facilitation, as well as the overall excitability of the corticospinal tract. Altered intracortical and corticospinal excitability can modify motor output and may therefore be important to several aspects of motor performance. Furthermore, it is possible that these changes contribute to the chronicity of the pain experience itself. For example, reorganisation of the primary motor and sensory cortices has been shown to occur in a range of chronic pain conditions, including phantom limb pain [27], back pain [24], carpal tunnel syndrome [28], osteoarthritis [25] and complex regional pain syndrome (CRPS) [29,30]. The extent of motor cortex reorganisation is positively associated with chronic pain intensity [27] and interventions aimed at reversing reorganisation have been shown to reduce pain, with the extent of this reversal associated with the amount of pain relief experienced [27,31]. Importantly, cortical reorganisation is thought to be initiated by changes in intracortical excitability, with a reduction in GABA-ergic intracortical inhibition and enhanced glutamatergic facilitation allowing reorganisation to occur [32–34]. Furthermore, there is evidence that pain relief in chronic pain populations receiving non-invasive brain stimulation may be related to post-stimulation induced restoration of normal corticospinal and intracortical excitability [35,36]. Finally, motor impairment in chronic pain has been related to the extent of primary motor cortex reorganisation [24,25], and improvements in physical disability following successful treatment of chronic pain have been associated with a reversal of changes in primary motor cortex thickness [37] and corticospinal excitability [38]. Collectively, these findings highlight the importance of better understanding the relationship between chronic pain and motor cortex excitability, as this may have meaningful implications for the future treatment of chronic pain conditions.

Additionally, there is now compelling evidence that acute pain directly alters both motor performance and motor cortex excitability. Numerous studies have shown that acute, experimentally induced pain can modify motor performance in otherwise healthy individuals, with evidence of deficits in muscle strength [39–41], endurance [42], force control [43–47], and kinematic changes during functional tasks such as walking [48] and stair descent [49]. In addition, a number of studies [50–55] have shown that experimentally induced pain can modify corticospinal and intracortical excitability, emphasising the strong relationship between the nociceptive and motor systems.

The effects of chronic pain on motor cortex excitability are more variable, and in some cases opposite to those observed in acute pain. Several studies have reported impaired intracortical inhibition in people with chronic migraine [56–58] and neuropathic pain [35], suggesting that chronic pain is associated with a reduction in GABA-ergic intracortical inhibition. In contrast, other studies have revealed no differences in cortical inhibitory function or corticospinal excitability between chronic pain and healthy populations [59–62]. There is further inconsistency regarding whether intracortical facilitation is influenced in patients with chronic pain [35,63–65]. Thus, it is currently difficult to develop firm conclusions on the effects of chronic pain on the corticomotor system and what level of the neuraxis these changes may occur.

To our knowledge, no previous systemic review has been conducted on this matter. Thus, the goal of the current study was to systematically review studies examining corticospinal and intracortical excitability in people with chronic pain compared

to healthy controls, and to provide a meta-analysis of study outcomes.

Methods

Search strategy

The search strategy was designed to identify studies that compared measures of corticospinal and intracortical excitability obtained using TMS between people with chronic pain and pain-free control participants. To be classified as chronic pain, participants were required to have experienced pain for three months or more. Studies were required to apply TMS to the primary motor cortex and to include any of the following outcome measures: resting motor threshold (RMT), corticospinal excitability, cortical silent period duration, or short- or long-interval intracortical inhibition or facilitation (SICI, LICI, SICF, LICF). All outcome measures were required to be assessed in a resting target muscle except for the cortical silent period. Intervention studies were included if baseline measures of corticospinal and/or intracortical excitability were provided, and only these measures were analysed in this review.

The following databases were searched: MEDLINE, CINAHL Plus, Biomedical Reference Collection, Health Business Elite, Health Source, Psychology and Behavioural Sciences Collection, SPORTDiscus and Scopus. The search terms used were: (“pain” OR “neuralgia” OR “fibromyalgia” OR “FMA” OR “CRPS” OR “complex regional pain” OR “irritable bowel” OR “IBS” OR “temporomandibular disorder” OR “arthritis” OR “whiplash” OR “headache” OR “migraine”) AND (“transcranial magnetic stimulation” OR “cortic* excitability” OR “TMS”). Results were limited to journal articles published between 1985 and December 2015. Included articles were required to be published in the English language, involve human adult participants, and have a full text available. The full text of relevant studies was retrieved and reference lists were searched for additional citations.

Information extracted

Information extracted from the identified studies included the pain population, number of participants, any subgroups of participants, target muscle, type of coil, and the outcome measures used (RMT, corticospinal excitability, silent period duration, SICI, LICI, SICF, LICF). Authors were contacted for more information when appropriate data were not provided in the published paper. Corticospinal excitability measures included any assessment of motor evoked potential (MEP) size from a set stimulus intensity that was matched between the two groups, while all intracortical excitability measures were derived from paired-pulse stimulation (see Table 1 for details of included outcome measures).

Risk of bias assessment

The selected studies were assessed for methodological quality and reporting by two independent reviewers (RP, GL) using the TMS checklist devised by Chipchase and colleagues [66]. The checklist consists of 30 criteria assessing variables relating to the participants, the experimental methodology, and the analysis. Points were awarded if the study a) reported and b) controlled each of the criteria. Four of the criteria are applicable to studies using paired-pulse techniques and were only evaluated in studies using these techniques. In addition, the checklist was adapted by removing the criterion relating to the time between testing days and adding the requirement for studies to control the gender of participants by matching the chronic pain and control groups. The study quality score was calculated as a percentage of the criteria met out of the total applicable criteria.

Download English Version:

<https://daneshyari.com/en/article/6005160>

Download Persian Version:

<https://daneshyari.com/article/6005160>

[Daneshyari.com](https://daneshyari.com)