Clinical Neurophysiology 127 (2016) 769–778

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Afferent inhibition and cortical silent periods in shoulder primary motor cortex and effect of a suprascapular nerve block in people experiencing chronic shoulder pain

Lynley Bradnam [a,b,*], E. Michael Shanahan [c,d], Kirsty Hendy [a], Amalia Reed [a], Tegan Skipworth [a], Anri Visser [a], Sheila Lennon [a]

[a] Discipline of Physiotherapy, School of Health Sciences, Faculty of Medicine, Nursing and Health Sciences, Flinders University, South Australia, Australia
[b] Applied Brain Research Laboratory, Centre for Neuroscience, School of Medicine, Faculty of Medicine, Nursing and Health Sciences, Flinders University, South Australia, Australia
[c] Department of Rheumatology, Repatriation General Hospital, Adelaide, South Australia, Australia
[d] School of Medicine, Faculty of Medicine, Nursing and Health Sciences, Flinders University, South Australia, Australia

ARTICLE INFO

Article history:
Accepted 23 March 2015
Available online 4 April 2015

Keywords:
Transcranial magnetic stimulation
Short afferent inhibition
Cortical silent period
Chronic shoulder pain
Infraspinatus
Suprascapular nerve block

HIGHLIGHTS

- Novel short afferent inhibition, cortical silent periods (CSPs) and their interaction were demonstrated in the shoulder primary motor cortex in healthy adults.
- Aberrant neurophysiology was observed in patients with chronic shoulder pain.
- Suprascapular nerve block injection immediately normalised short afferent inhibition while further modulation of the CSP by sensory input was apparent 1 week later.

ABSTRACT

Objective: To characterise short afferent inhibition (SAI) and the cortical silent period (CSP) in the primary motor cortex representations of the infraspinatus muscle in healthy adults and people experiencing chronic shoulder pain, to determine the impact of a suprascapular nerve block (SSNB).
Methods: Neurophysiological measures were obtained in 18 controls and 8 patients with chronic shoulder pain, pre and post SSNB and 1 week later. Pain intensity was assessed by a visual analogue scale.
Results: SAI was apparent in controls (all $P < 0.03$) and a CSP was observed which reduced in the presence of SAI (all $P < 0.0001$). Compared to controls, shoulder pain patients demonstrated higher active motor threshold ($P = 0.046$), less SAI ($P = 0.044$), a longer CSP ($P = 0.048$) and less modulation of the CSP by SAI ($P = 0.045$). Higher motor thresholds were related to higher pain scores ($P = 0.009$). The SSNB immediately restored SAI ($P = 0.013$), with a positive relationship between increased SAI and reduced pain ($P = 0.031$). The SSNB further reduced modulation of CSP by SAI at 1 week post injection ($P = 0.006$).
Conclusions: SAI and the CSP were present and demonstrated robust interaction in controls, which was aberrant in patients. The SSNB transiently restored SAI but had no effect on the CSP; however CSP modulation by SAI was further attenuated 1 week post injection.
Significance: The current findings improve understanding of the neurophysiology of the shoulder motor cortex and its modulation by chronic pain. The effect of SSNB in shoulder pain patients should be interpreted with caution until proven in a larger population. Interventions that target intracortical inhibition might increase efficacy in people with chronic shoulder pain.

1. Introduction

Chronic shoulder and upper limb pain is a highly prevalent and recalcitrant condition affecting health-related quality of life in many patient populations (Pope et al., 1997; Hill et al., 2010; Gill

* Corresponding author at: Discipline of Physiotherapy, Flinders University, GPO Box 2100, Adelaide, South Australia 5001, Australia. Tel.: +61 7221 8291.
E-mail address: lynley.bradnam@flinders.edu.au (L. Bradnam).

http://dx.doi.org/10.1016/j.clinph.2015.03.012
1388-2457/

et al., 2013). There is emerging evidence that painful musculoskeletal disorders of the upper limb are accompanied by aberrant cortical neurophysiology (Alexander, 2007; Berth et al., 2009, 2010; Schabrun et al., 2014). It is unclear whether this aberrant neurophysiology normalises in response to interventions targeting upper limb pain. If so, cortical measures might provide intervention targets and useful markers for the impact of treatments targeting pain. A suprascapular nerve block (SSNB) has shown efficacy for rheumatologic (Shanahan et al., 2003, 2004) and post-stroke shoulder pain (Adey-Wakeling et al., 2013), with high patient acceptability and few adverse effects (Shanahan et al., 2012; Shanahan and Smith, 2012). The mechanisms contributing to the clinical efficacy of SSNB are unclear, but might arise from modification of the cortical networks innervating shoulder musculature. It is well known that sensory input influences excitability of cortical networks by modulating intracortical connections within the primary motor cortex (M1) (Chen et al., 1999; Tokimura et al., 2000). Furthermore, an ischemic nerve block produces rapid cortical reorganisation and increases corticomotor excitability in upper limb M1 representations in healthy adults (Brasil-Neto et al., 1993). An investigation into the effect of SSNB on cortical mechanisms is hampered by limited knowledge of the neurophysiology of proximal upper limb muscles. The infraspinatus muscle is an important dynamic stabiliser of the shoulder, active throughout all shoulder movements (Arwert et al., 1997) whose motor control is degraded in painful musculoskeletal conditions (Magarey and Jones, 2003). The cortical representations of infraspinatus have been mapped (Ngomo et al., 2013) and its task-dependent neural control investigated in healthy adults using transcranial magnetic stimulation (TMS) (Roberts et al., 2008; Bradnam et al., 2010b). A study into the cortical neurophysiology of infraspinatus in people with chronic rotator cuff tears revealed higher active motor thresholds in M1 contralateral to the painful shoulder compared to the non-painful side (Ngomo et al., 2015). Cortical maps were similar between the hemispheres in these chronic shoulder pain patients.

Intracortical mechanisms contributing to aberrant cortical neurophysiology in people experiencing shoulder pain can be explored using TMS. One method with potential relevance for pain physiology is known as short afferent inhibition (SAI). Short AI is the result of inhibition of corticomotor excitability by sensory input, and can be assessed by pairing TMS and peripheral nerve stimulation. Short AI was originally described in the hand motor cortex following stimulation of the median nerve at the wrist (Tokimura et al., 2000). The SAI pathway is only partially elucidated, but is likely to traverse from the periphery directly to the thalamus and M1 (Tokimura et al., 2000), via the primary somatosensory cortex (SI) (Tsang et al., 2014). It is known that SAI is reliant upon cholinergic mechanisms (Di Lazzaro et al., 2000; Sailer et al., 2003) interacting with γ-amino butyric acid (GABA) inhibitory interneurons (Di Lazzaro et al., 2005a). Afferent inhibition is aberrant in neurological disorders including stroke (Di Lazzaro et al., 2012), Alzheimer's disease (Di Lazzaro et al., 2002) and Parkinson's disease (Sailer et al., 2003; Yarnall et al., 2013). In contrast, SAI presents normally in complex regional pain syndrome affecting the hand (Turton et al., 2007). There has been limited use of TMS to measure SAI outside of the hand motor cortex; accordingly SAI in chronic shoulder pain has not yet been investigated. We recently described suppression of corticomotor excitability of the infraspinatus representation by stimulation of the suprascapular nerve (Hendy et al., 2014), facilitating exploration of SAI in the shoulder motor cortex in patient populations.

Intracortical inhibition, mediated by GABAergic interneurons within M1, can also be explored using TMS. One measure is the cortical silent period (CSP), a transient period of electromyography (EMG) suppression following TMS during a voluntary muscle contraction. The late period of the CSP is attributed to GABA-mediated intracortical inhibition (Fuhr et al., 1991; Inghilleri et al., 1993; Roick et al., 1993; Uncini et al., 1993). Modulation of cortical excitability by GABAergic interneurons is critical to the integrity and normal function of neural networks (Jacobs and Donoghue, 1991). Aberrant GABAergic intracortical inhibition would impact on cortical reorganisation (Clarkson et al., 2010) and motor learning (Stagg et al., 2011), with consequences for motor function. Accordingly, the CSP is altered in neurological diseases such as Parkinson's and Alzheimer's disease, Dystonia and Schizophrenia (Curra et al., 2011; Khedr et al., 2011; Lang et al., 2011; Trompetto et al., 2012). The CSP has not been previously described in the shoulder motor cortex or tested in a chronic shoulder pain population. The CSP may elucidate whether GABAergic inhibition within the shoulder motor cortex is altered in people with chronic pain, or if modulation of GABA receptor-mediated inhibition contributes to effects of a SSNB. Finally, sensory inputs mediating SAI also reduce GABA receptor-mediated inhibition, exposed previously by paired-pulse TMS (Udupa et al., 2009, 2014). The interaction between SAI and GABAergic inhibition has not been explored using the CSP or in the shoulder M1 in healthy adults or adults experiencing chronic shoulder pain.

The aim of this study was to characterise SAI and the CSP in M1 representations of infraspinatus in healthy adults, to compare these measures to people experiencing chronic shoulder pain, and to determine the impact of a SSNB. We formed an *a priori* hypothesis that SAI and CSP are present in healthy adults and SAI attenuates the CSP (Udupa et al., 2009, 2014). Our second hypothesis was that SAI is reduced and the CSP lengthened in people with chronic shoulder pain. Our third hypothesis was that these measures will be normalised following SSNB, associated with a reduction in subjective pain intensity. The study findings will further the understanding of cortical neurophysiology in people with chronic shoulder pain and may explain the clinical efficacy of SSNB in this population.

2. Methods

2.1. Participants

Twenty-six participants included eighteen healthy controls (9 male, 8 female) aged 20–68 years (mean 41.3), without history of musculoskeletal or neurological conditions affecting the upper limb or neck and eight patients with chronic shoulder pain (1 male, 7 female, 49–75 years old, mean 64.9) recruited from a Rheumatology Clinic. The dominant hand for each control participant was determined using the Edinburgh Handedness Inventory (Oldfield, 1971). All patients had been diagnosed with chronic rotator cuff pathology consisting of rotator cuff and sub-acromial pathology, subacromial impingement syndrome or tendinopathy on ultrasound. No patients had been diagnosed with a rotator cuff tear and all could perform some degree of lateral rotation of the shoulder. All patients experienced shoulder pain for at least 1 year prior to the study and were identified as suitable candidates for SSNB by the rheumatologist (MS). Ethical approval for the study was provided by the local ethics committee and all participants provided written informed consent.

2.2. Experimental design

Control participants attended a single session to assess cortical neurophysiology. The patients attended two sessions, separated by 1 week. At their first session, baseline TMS measures and visual analogue scale (VAS) for pain intensity in the shoulder at rest were collected (PRE), followed by a SSNB (40 mg depo-medrol