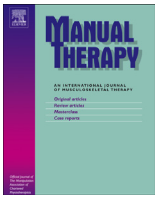
ARTICLE IN PRESS

Manual Therapy xxx (2014) 1–6

Contents lists available at ScienceDirect

Manual Therapy

journal homepage: www.elsevier.com/math



Original article

The role of neuroplasticity in experimental neck pain: A study of potential mechanisms impeding clinical outcomes of training

Bjarne Rittig-Rasmussen [a,*], Helge Kasch [b], Anders Fuglsang-Frederiksen [c],
Peter Svensson [d], Troels Staehelin Jensen [a,b]

[a] *Danish Pain Research Center, Aarhus University Hospital, Aarhus, Denmark*
[b] *Department of Neurology, Aarhus University Hospital, Aarhus, Denmark*
[c] *Department of Clinical Neurophysiology, Aarhus University Hospital, Aarhus, Denmark*
[d] *Clinical Oral Physiology, Department of Dentistry and Department of Oral Maxillofacial Surgery, Aarhus University, Aarhus, Denmark*

ARTICLE INFO

Article history:
Received 12 September 2013
Received in revised form
7 March 2014
Accepted 10 April 2014

Keywords:
Neck pain
Training
Neuroplasticity
Transcranial magnetic stimulation

ABSTRACT

Training is a mainstay in the clinical management of neck pain, yet, effects of various training protocols are only small to moderate and improvements are required. Previous investigations of the nervous system indicate a correlation between neuroplastic adaptation to training and functional recovery. The interaction between neck pain and training thus needs further exploration. This was a randomized experimental study of the effects of experimental neck pain and training on corticomotor excitability. Healthy volunteers were randomized to training and experimental neck pain, training and no pain, and pain and no training. Primary endpoints were corticomotor excitability assessed by transcranial magnetic stimulation and electromyography measured as changes in amplitudes and latencies of motor evoked potentials (MEPs), recorded at baseline and after 30 min, 1 h, and 1 week. Additionally, correlations between changes in MEPs and motor learning, effects of pain and concomitant neck training on pain, muscle strength, and fatigue were investigated. Data were analyzed by repeated measurement ANOVA, paired *t* tests, Grubbs' outlier test and correlation coefficients. Results indicated that neck pain and training significantly enhanced the inhibition of the amplitudes of the MEPs for 1 week. The results indicate that moderate neck pain and training induce long-lasting inhibition of the corticomotor pathways. This inhibition may limit the outcome of neck training in painful conditions in contrast to pain-free training conditions.

1. Introduction

Treatment of neck pain usually includes counseling, self-management, manipulative therapy, and different training protocols, but effects sizes are still only small to moderate, and improvements are necessary (Childs et al., 2008; Haldeman et al., 2009; Leaver et al., 2010; Hagen et al., 2012). Recent studies have looked at possible adaptive neuroplastic changes in the nervous system as tools to assess functional recovery in clinical neurological and musculoskeletal conditions (Traversa et al., 1997; Mano et al., 2003; Tsao et al., 2010; Boudreau et al., 2010a).

Neuroplasticity, as reflected by cortical reorganization and altered excitability of the primary motor cortex, has been investigated using transcranial magnetic stimulation (TMS) and motor evoked potentials (MEPs) (Ziemann et al., 2008). Non-painful tongue or neck training has demonstrated increased corticomotor responsiveness and motor-related brain activity for up to 1 week (Svensson et al., 2006; Arima et al., 2011; Rittig-Rasmussen et al., 2013). In contrast, pain of low to moderate intensity in inactive extremity muscles has been shown to exert an inhibitory effect on the corticomotor responsiveness in terms of instant neural adaptive changes lasting from 30 min to a few hours after the pain induction and is related to impaired muscle function (Le Pera et al., 2001; Farina et al., 2001; Falla et al., 2011; Dube and Mercier, 2011; Bank et al., 2013). The primary motor cortex plays a role in motor learning; however, pain may also interfere with motor learning capabilities, which could be relevant in the process of regaining daily functioning (Boudreau et al., 2007, 2010a; Smyth et al., 2010; Ingham et al., 2011). Likewise, increased strength after short-term strength training appears to be induced by enhanced neural drive in the corticomotor pathways and may be influenced by pain and

---

* Corresponding author. Danish Pain Research Center, Aarhus University Hospital, Norrebrogade 44, Building 1A, DK-8000 Aarhus C, Denmark. Tel.: +45 7846 3380; fax: +45 7846 3269.

E-mail addresses: brr@ki.au.dk, rittig@mail.dk (B. Rittig-Rasmussen).

http://dx.doi.org/10.1016/j.math.2014.04.010
1356-689X/© 2014 Elsevier Ltd. All rights reserved.

Please cite this article in press as: Rittig-Rasmussen B, et al., The role of neuroplasticity in experimental neck pain: A study of potential mechanisms impeding clinical outcomes of training, Manual Therapy (2014), http://dx.doi.org/10.1016/j.math.2014.04.010

the load, velocity, and precision of the movement (Ylinen, 2007; Kidgell et al., 2011; Lindstroem et al., 2012). A number of studies have studied these interactions with focus on the extremity, trunk, and jaw muscles, but the findings have not yet been extended to the neck region (Boudreau et al., 2007; Ingham et al., 2011; Tsao et al., 2011; Schabrun and Hodges, 2012; Bank et al., 2013).

Consequently, the interactions between neck pain, the corticomotor pathways, learning, and muscle fatigue needs to be further investigated in the process of improving the clinical management of neck pain. The present study examined the effects of training on corticomotor control of neck muscles and on motor learning in healthy volunteers randomized to either experimental neck pain or no pain. We hypothesized that experimental pain would impede training-induced corticomotor excitability and motor learning capabilities. Additional experiments investigated the effects of experimental pain and concomitant neck training on experienced pain, muscle strength, and fatigue.

2. Methods

2.1. Subjects

The study included 52 healthy subjects (31 women and 21 men) aged 20–32 (mean ± SD: 23 ± 2) years. The sample size required to detect a difference of primary outcome in MEP amplitude equivalent to a 50% increase was estimated from previous studies (Svensson et al., 2006; Rittig-Rasmussen et al., 2013). Subjects were volunteers recruited among university students. Written consent was obtained from all subjects. Inclusion criteria were absence of any medical, physical, psychological problems and pregnancy. The study was carried out in accordance with the Helsinki Declaration and was approved by the local ethics committee (ID: M-20070213).

2.2. Design

A randomized study with healthy subjects randomized to either hypertonic saline injection and trapezius training (HS + training, $n = 20$) or to isotonic saline injection and trapezius training (IS + training, $n = 20$). A control group (HS; $n = 12$) received hypertonic saline injections and performed no training.

2.3. Training

The subjects performed 20 min of upper trapezius training by elevating and lowering their right shoulder 70 times in a repeated movement path with a load of 10% of their maximal lifting capacity (Fig. 1). The maximal lifting capacity was measured before and after training by a one-repetition maximum test (Verdijk et al., 2009). The training task implied moving a blue line displayed on the screen of a feedback system in synchronization with an ascending/descending line. The subjects were asked to follow the line as closely as possible, and deviations from the feedback curve were recorded to quantify potential motor learning effects. Learning effects were defined as the difference in deviation from the feedback curve between the first 5 repetitions and the last 5 repetitions of the total 70 repetitions.

During the tests and training, the subjects were sitting upright on a high chair, unable to touch the floor in order to provide equal test and training conditions. A calibrated electronic load cell (Veccer load cell, VC4200, Reading, UK) connected to the recording software (Scaletronic, Taastrup, Denmark) continuously recorded the load and deviations from the curve during training. The moving trapezius/shoulder region was connected to the load cell with an inflexible strap, and the force applied to the load cell was electronically measured in kilograms.

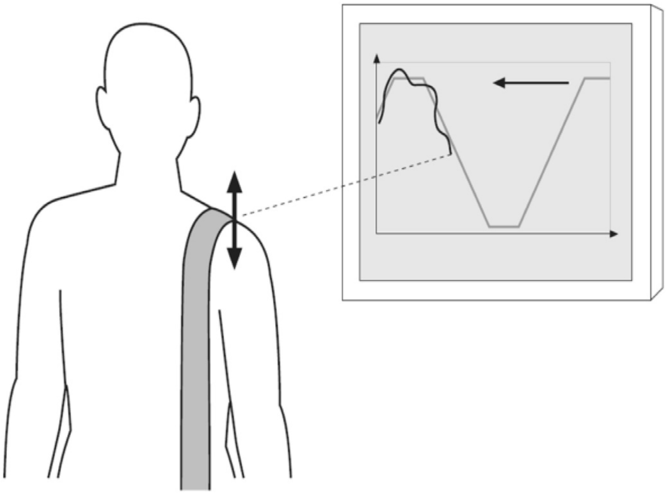


Fig. 1. Neck training: The task was to follow the moving ascending/descending line on the feedback screen as closely as possible by a controlled dynamic concentric/eccentric activation of the right trapezius muscle.

2.4. Transcranial magnetic stimulation and electromyography

Transcranial magnetic stimulation (TMS) (Magstim 200, Magstim Company, Whitland, UK) and electromyography (EMG) (Viking Select, Viasys Healthcare, Dublin, Ohio, USA) were used to stimulate and monitor the right trapezius muscle and the right abductor pollicis brevis muscle (Ziemann et al., 2008; Chipchase et al., 2012). In all 3 groups, the abductor pollicis brevis muscle functioned as a within-subject inert control muscle. Amplitudes and latencies of the MEPs were recorded at baseline and after 30 min, 1 h, and 7 days.

TMS was delivered with a figure-of-eight coil to the left hemisphere. The coil was applied tangentially in a 45° posteroanterior direction to the sagittal midline of the skull, corresponding to the motor representation of the right abductor pollicis brevis muscle and the trapezius muscle. The “hot spot”, i.e., the point where the lowest intensity of TMS evoked a response, was found and marked with a pen to ensure identical localization in the subsequent stimulations. Motor thresholds were defined as the minimum stimulus intensity induced by TMS that produced 5 discrete MEPs discernible from the background EMG activity (MEP $> 50\ \mu$V, peak to peak). Motor thresholds and TMS intensity were determined, and stimuli were equivalent to 120–140% of the individual motor thresholds. Motor thresholds were determined in the same way in all 3 groups with a standardized pre-activated trapezius muscle and with the abductor pollicis brevis muscle at rest.

Subsequently, the subjects held a 4 kg dumbbell in the right hand with the arm hanging freely. This was done to preactivate and facilitate the MEP response from the trapezius muscle. Surface recording electrodes (Neuroline 720; Ambu, Ballerup, DK) were placed over the muscle belly of the right upper trapezius, midway on a line between C7 and the acromion process, and over the belly of the right abductor pollicis brevis muscle. The reference electrodes placed over the right acromioclavicular joint and the proximal phalanx of the right index finger. The ground electrode (Neuroline Ground; Ambu, Ballerup, DK) was placed on the right deltoid muscle.

Stimuli were repeated ≈4–6 times with increasing intensity, until no further increase in amplitude was obtained corresponding to the plateau of the stimulus response curve (Groppa et al., 2012; Pearce et al., 2013), and then 10 stimuli were delivered with interstimulus intervals of 5–10 s and averaged. MEPs were

Please cite this article in press as: Rittig-Rasmussen B, et al., The role of neuroplasticity in experimental neck pain: A study of potential mechanisms impeding clinical outcomes of training, Manual Therapy (2014), http://dx.doi.org/10.1016/j.math.2014.04.010