Clinical Neurophysiology 128 (2017) 2217–2226

Contents lists available at ScienceDirect

Clinical Neurophysiology

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

Corticomuscular coherence in the acute and subacute phase after stroke

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ARTICLE INFO

Article history:
Accepted 21 August 2017
Available online 22 September 2017

Keywords:
Ischemic stroke
Subacute phase
Hemiparesis
Motor recovery
Corticomuscular coherence
Intermuscular coherence

HIGHLIGHTS

- Corticomuscular coherence (CMC) and intermuscular coherence (IMC) were reduced in acute and subacute stroke compared to healthy controls.
- CMC was localized above the contralateral sensorimotor cortex in both patients and controls.
- Improvement of hand motor performance did not require changes in CMC or IMC.

ABSTRACT

Objective: Stroke is one of the leading causes of physical disability due to damage of the motor cortex or the corticospinal tract. In the present study we set out to investigate the role of adaptations in the corticospinal pathway for motor recovery during the subacute phase after stroke.
Methods: We examined 19 patients with clinically diagnosed stroke and 18 controls. The patients had unilateral mild to moderate weakness of the hand. Each patient attended two sessions at approximately 3 days (acute) and 38 days post stroke (subacute). Task-related changes in the communication between motor cortex and muscles were evaluated from coupling in the frequency domain between EEG and EMG during movement of the paretic hand.
Results: Corticomuscular coherence (CMC) and intermuscular coherence (IMC) were reduced in patients as compared to controls. Paretic hand motor performance improved within 4–6 weeks after stroke, but no change was observed in CMC or IMC.
Conclusions: CMC and IMC were reduced in patients in the early phase after stroke. However, changes in coherence do not appear to be an efficient marker for early recovery of hand function following stroke.
Significance: This is the first study to demonstrate sustained reduced coherence in acute and subacute stroke.

1. Introduction

Stroke results from critically reduced blood flow to the brain tissue due to bleeding or obstruction of arteries. Globally, stroke remains a major cause of disability despite advances in preventive treatment and in acute management (Hankey, 2017). The most common impairment caused by stroke is motor disability affecting approximately 80% of the patients, most frequently seen as hemiparesis (Langhorne et al., 2009). Spontaneous recovery may occur in the following weeks and months after stroke and can be facilitated through rehabilitation involving exercise (Maulden et al., 2005). Despite of this, upper limb motor impairments are often persistent and disabling (Lai et al., 2002) and no rehabilitation program has been proven superior to other programs (Pollock et al., 2014). Strategies aiming at enhancing rehabilitation programs require a greater understanding of the mechanisms of recovery. In the present study we set out to investigate the role of

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Abbreviations: ADP, adductor pollicis; APB, abductor pollicis brevis; CMC, corticomuscular coherence; CST, corticospinal tract; EEG, electroencephalographic; EMG, electromyographic; FDI, first dorsal interosseous; IMC, intermuscular coherence; M1, primary motor cortex; MVC, maximal voluntary contraction.

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https://doi.org/10.1016/j.clinph.2017.08.033

adaptations in the corticospinal tract (CST) for motor recovery of the affected hand during the subacute phase after stroke.

Studies performed in monkeys have demonstrated severe deficits in precise finger movements following selective lesion to the CST (Lawrence and Kuypers, 1968) and diffusion-tensor imaging studies have consistently shown a relation between damaged CST fibres and motor deficits (Stinear et al., 2007; Schulz et al., 2012). In primates most of the neurons in the CST originate in the primary motor cortex (M1) and a subset of these makes direct, corticomotoneuronal connections with spinal motoneurons especially towards distal finger muscles (Porter and Lemon, 1993). Evidence suggest that these direct connections play a key role in fractionated finger movements, which are important for manipulation of small objects (Lemon et al., 2004). It is believed that the direct connections work in parallel with the more indirect connections by adding the final spatiotemporal excitation patterns in order to produce appropriate levels of motoneuronal recruitment and discharge (Lemon et al., 2004). Disconnection of direct and indirect connections in the CST is assumed to be a major cause of impaired hand and finger motor function after stroke (Lemon, 2008).

Estimates of task-related corticospinal connections can be noninvasively determined during finger movements from coherence analysis in human subjects. This measurement allows a statistical analysis to be performed to characterize the functional coupling in the frequency domain (coherence) between cortical oscillatory activity (measured by EEG) and motor activity (measured by EMG) during a task (Halliday et al., 1995). I addition, coherence analysis of surface EMG within and between muscles provides a complementary means of measuring and detecting changes in the CST (Grosse et al., 2002). Previously cross-sectional studies have demonstrated that corticomuscular coherence (CMC) is reduced in the chronic phase after stroke (Mima et al., 2001; Braun et al., 2007; Fang et al., 2009; Rossiter et al., 2013) and furthermore that CMC can increase in the chronic phase after training (Belardinelli et al., 2017), with peripheral electrical stimulation (Lai et al., 2016) and with time (von Carlowitz-Ghori et al., 2014). However the adaptations in the CST during the first 4–6 weeks post-stroke, where the most dramatic improvements occur, have not been investigated. We hypothesized that CMC will be reduced in stroke patients and will increase in parallel to the stroke patient's improvement in functional performance during early recovery.

2. Materials and methods

2.1. Participants

We examined 19 patients (mean age 61 years, range 31–86 years, 2 females, 1 left-handed) with clinically diagnosed stroke and 18 control participants with no history of stroke (mean age 65 years, range 33–88 years, 5 females, 0 left-handed). The stroke patients had unilateral mild to moderate motor weakness of the hand (7 dominant hand affected). We excluded patients with hemorrhagic stroke, those unable to perform the pinch grip task and those with language/cognitive deficits sufficient to impair cooperation in the experiment. Motor strength of the affected hand was graded according to the modified MRC scale (Medical Research Council, 1986). A full written consent was obtained from all participants in accordance with the Declaration of Helsinki. The study was approved by the Ethics Committee of Region Zealand (protocol-number: SJ-459).

2.2. Experimental design

Patients attended two sessions at approximately 3 days (Time 1; T1) and 38 days (Time 2; T2) post stroke. Hand preference before stroke was determined by handedness questionnaire (Oldfield, 1971) and cognitive ability and neglect were evaluated based on the mini mental state examination (Folstein et al., 1975) and a general clinical assessment. During the experiment the patients were seated in an adjustable chair with their forearms resting comfortably on a table. Patients were scored on the Grooved Pegboard Test (Strauss et al., 2006) before they were instructed to control a lever placed in front of them with their affected thumb and index finger. Visual feedback of the force exerted was provided on a computer screen and the patients completed 3 maximal pinch grip contractions (MVC). A dynamic pinch task was then performed with the affected hand (Fig. 1A). Patients were instructed to track a moving target (a ramp) as accurately as possible, by applying force to the levers (Fig. 1B). A cursor moved automatically across the screen from left to right at a constant velocity and force applied to the levers moved the cursor upward. The force level of the ramp plateau (y-axis) was set to an individual level (10%MVC) lasting 3 s followed by a rest interval of 3–5 s. Patients performed 3 × 50 trials with 60 s of rest in between. Before recording, patients were acquainted with the setup and trained to control the lever. The force was measured with a load cell (UU2-K30, Dacell, Korea) and the trials were recorded by Signal software (CED, Cambridge, UK) and stored for later analysis. Control participants attended one session and they used either left or right hand in order to match the side of the affected hand in the stroke group.

2.3. Electrophysiological measurements

Data recorded included EEG activity from 64 electrodes and EMG activity from the affected hand (ActiveTwo, BioSemi, Amsterdam, The Netherlands) using acquisition software ActiView (version 6.05). Active EEG electrodes were mounted in a headcap (Headcap BioSemi, The Netherlands) with an electrode configuration complying with the 10–10 system. Three pairs of bipolar active EMG surface electrodes were placed on the affected (active) hand over first dorsal interosseous muscle (FDI), adductor pollicis (ADP) and abductor pollicis brevis (APB) muscles (interelectrode distance, 15 mm). EMG was recorded as part of the EEG dataset and so had the same pre-processing parameters. In BioSemi the ground electrode is formed by the Common Mode Sense active electrode and the Driven Right Leg passive electrode during acquisition. Offset values were below ±25 microV and recordings were set to AC and sampled at 2048 Hz.

2.4. Statistical analysis

Data analyses were performed using Matlab R2015a (MathWorks, MA, USA), with the toolbox EEGLAB v13.4.4b (Swartz Center for Computational Neuroscience; http://sccn.ucsd.edu/eeglab/) and the toolbox Statistical Parametric Mapping (SPM12). All files were imported to EEGLAB and a 5 Hz high-pass filter were applied. This high-pass filter was applied in order to eliminate movement artifacts below 5 Hz. Higher cutoff frequencies have recently been shown to result in a decrease of the reliability and agreement of the coherence variables (van Asseldonk et al., 2014). Channels with significant drift or excessive 50 Hz noise were removed using visual inspection of the EEG signals before data was re-referenced to average reference. The analysis was based on the steady contraction period during the ramp plateau, in which the strongest coherent activity in the beta band has been shown before (Kilner et al., 1999). The interval between 0.85 and 2.85 s after ramp onset showed a stable force production across participants and was used for further analysis of CMC and intermuscular coherence (IMC). The data were visually inspected and trials were discarded if a force reaction was clearly missing. Because coherence strength may relate to the number of trials across participants an