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LATE CORTICAL DISINHIBITION IN RELAXED VERSUS ACTIVE HAND MUSCLES

A. CAUX-DEDEYSTÈRE,[a] P. DERAMBURE[a] AND H. DEVANNE[a,b*]

[a] *Université de Lille, Centre Hospitalier Régional Universitaire de Lille, Neurophysiologie Clinique, F-59037 Lille Cedex, France*

[b] *Université du Littoral Côte d'Opale, F-62228 Calais Cedex, France*

Abstract—Recent research suggests that long-interval intracortical inhibition (LICI) is followed by a transitory period of late cortical disinhibition (LCD) that can even lead to a net increase in cortical excitability. The relationship between LICI/LCD and voluntary drive remains poorly understood. Our study aims at investigating the influence of index abduction on LICI and LCD in an actively engaged muscle and a neighboring muscle, while varying the intensity of the conditioning stimulus (CS). Motor-evoked potentials (MEPs) were recorded from the first dorsal interosseus (FDI) and abductor digiti minimi (ADM) muscles in 13 subjects. Paired-pulses were delivered with 10 different interstimulus intervals (ranging from 60 to 290 ms). Whatever the condition (relaxed or active FDI), the test stimulus was set to evoke an MEP of 1 mV. The time course of conditioned MEP amplitude was compared for relaxed and active conditions when the CS intensity was set to (i) 130% of the rest motor threshold (RMT) or (ii) to evoke the same size of MEP under both conditions. LICI lasted longer (i.e. disinhibition occurred later) at rest than during abduction when evoked either by similar or matched conditioning stimuli. No post-LICI facilitation was observed at rest – even when the CS intensity was set to 160% RMT. In contrast, long-interval intracortical facilitation (LICF) was observed in the quiescent ADM when FDI was active. LICF may then be associated with voluntary activity albeit with lack of topographic specificity. © 2015 IBRO. Published by Elsevier Ltd. All rights reserved.

Key words: motor cortex, late cortical disinhibition, long-interval intracortical facilitation, voluntary activity.

INTRODUCTION

Over the past two decades, many studies have used paired-pulse transcranial magnetic stimulation (TMS) protocols to study intracortical inhibitory and facilitatory networks and the latter's underlying relationship with motor behavior. It has been suggested that intracortical inhibitory and excitatory mechanisms have a role in the modulation of cortical excitability prior to and during voluntary movements, so that the corticospinal drive meets the task's requirements (Floeter and Rothwell, 1999). For example, the short-interval intracortical inhibition (SICI) that can be observed when a subthreshold conditioning stimulus (CS) is delivered 1–4 ms before the test pulse has been extensively investigated. After SICI was first evidenced at rest (Kujirai et al., 1993), it was found that this intracortical inhibition decreases before movement onset (Reynolds and Ashby, 1999) and during tonic voluntary contraction (Ridding et al., 1995; Ortu et al., 2008). Furthermore, SICI is weaker during complex tasks (Kouchtir-Devanne et al., 2012) than during simple isometric contraction and thus is thought to correspond to a mechanism by which cortical motor neuron activity is fine-tuned to allow precise movements. The mechanism referred to as long-interval intracortical inhibition (LICI) was observed initially by Valls-Solé et al. (1992) and later by Wassermann et al. (1996) with interstimulus intervals (ISIs) ranging from 50 to 200 ms. Although LICI was not as extensively investigated as SICI, several studies have highlighted its potential significance in motor control. For example, LICI evoked in the first dorsal interosseus (FDI) muscle is weaker when the muscle is engaged in a thumb-index precision grip than during index abduction (Kouchtir-Devanne et al., 2012). LICI also appears to be shorter and weaker during active contraction than at rest (Wassermann et al., 1996; Chen et al., 1997). More recent studies (using paired TMS protocols) have also revealed that LICI is progressively suppressed at longer ISIs and may even be followed by a period of long-interval intracortical facilitation (LICF), corresponding to a net increase of cortical excitability. Late cortical disinhibition (LCD) is a newly reported phenomenon that is thought to reflect the period of time during which LICI (which decreases more or less rapidly) is combined with the possible recruitment of facilitatory cortical interneurons responsible for the subsequent LICF. LCD has been reported to occur at rest (Cash et al., 2010, 2011) and during voluntary activity (Caux-Dedeystère et al., 2014), and may reflect post-movement synchronization of facilitatory cortical interneurons (Cash

*Correspondence to: H. Devanne, CHRU de Lille, Neurophysiologie Clinique, Hôpital Roger Salengro, F-59037 Lille Cedex, France. Tel: +33-3-20-44-63-54; fax: +33-3-20-44-63-55.

E-mail address: herve.devanne@chru-lille.fr (H. Devanne).

Abbreviations: ADM, abductor digiti minimi; CS, conditioning stimulus; EMG, electromyogram; FDI, first dorsal interosseus; GABA, gamma aminobutyric acid; ISI, interstimulus interval; LCD, late cortical disinhibition; LICF, long-interval intracortical facilitation; LICI, long-interval intracortical inhibition; MEP, motor-evoked potential; MVC, maximal voluntary contraction; RM-ANOVA, repeated-measures analysis of variance; RMT, resting motor threshold; SICI, short-interval intracortical inhibition; TMS, transcranial magnetic stimulation.

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et al., 2010). Recent evidence suggests that the induction of long-term potentiation plasticity is facilitated when repetitive TMS pulses are delivered during the disinhibition period (Cash et al., 2014). Better knowledge of the LCD's time-dependent profile is therefore of particular value for further improving the efficacy of repetitive TMS protocols.

The time profiles of LICI/LCD at rest and during active contraction have not previously been compared. The primary objective of the present study was thus to analyze the influence of index tonic voluntary abduction on LICI and LCD in FDI at different CS intensities. We also investigated the topographic specificity of LCD and LICF by recording the responses of a neighboring muscle (the abductor digiti minimi, ADM) not engaged in the index abduction task. Throughout the text, conditioned Motor-evoked potentials (MEPs) return to baseline i.e. the weakening of LICI will be referred to as LCD. Post-LCD facilitation (corresponding to the net increase in cortical excitability after LCD, when present) will be referred to as LICF (see Fig. 1).

EXPERIMENTAL PROCEDURES

Participants

Thirteen subjects (including six females) aged between 20 and 46 (mean ± SD age: 24.92 ± 7.26) participated in the study after providing their written, informed consent. None of the subjects was taking any medication or was suffering from a neurological or psychiatric disorder. The study was approved by the local independent ethics committee (*Comité Consultatif de Protection des Personnes Nord Ouest*, Amiens, France) and complied with the tenets of the Declaration of Helsinki.

Electromyographic recordings

Participants were seated in a comfortable chair, with their forearms resting on a height-adjustable table. Ag–AgCl surface electrodes were used to record the electromyographic (EMG) activity of the FDI and ADM muscles of the dominant hand in a belly-tendon montage. The electrodes were positioned over the body of each the two muscles and (for the ADM and FDI, respectively) the first metacarpophalangeal joint of the fifth finger or the thumb. A large ground electrode was attached to the wrist. The EMG signals were amplified (×1000), high-pass filtered at 10 Hz and low-pass filtered at 1000 Hz (Digitimer, Hertfordshire, UK) prior to sampling at 2 kHz with a 1401 MicroMKII device (Cambridge Electronic Design, Cambridge, UK). Data were stored on a computer for subsequent off-line analysis using customized SIGNAL software (Cambridge Electronic Design). Subjects first produced maximal voluntary contraction (MVC) of the FDI (abduction of the index finger) in three successive trials. A 1401+ device and customized SPIKE2 software (both from Cambridge Electronic Design) were used to record and display the root mean square of the low-pass filtered (100 Hz) EMG signal from the FDI as a percentage of the MVC–EMG signal.

Stimulation procedures

TMS was performed using a figure-of-eight focal coil (external diameter: 9.5 cm) connected to two Magstim 200 stimulators (The Magstim Company Ltd, Whitland, UK) via a Bistim module. Stimulation was applied over the optimal scalp point for the FDI of the dominant hand, i.e. the site that yields the strongest MEPs for the FDI at a given suprathreshold intensity. This scalp point was determined by moving the coil while the subject relaxed his/her hand muscles. To ensure constant coil positioning throughout the series, the FDI's hotspot was marked on a swimming cap worn by the subject. The coil was held tangentially to the scalp, with the handle pointing backward and laterally (at a 45° angle from the midline). We then measured the resting motor threshold (RMT) of the FDI, defined as the lowest possible stimulus intensity capable of eliciting MEPs > 50 μV in at least 5 of 10 trials in the muscle at rest. In all experimental series, single pulses and dual pulses were

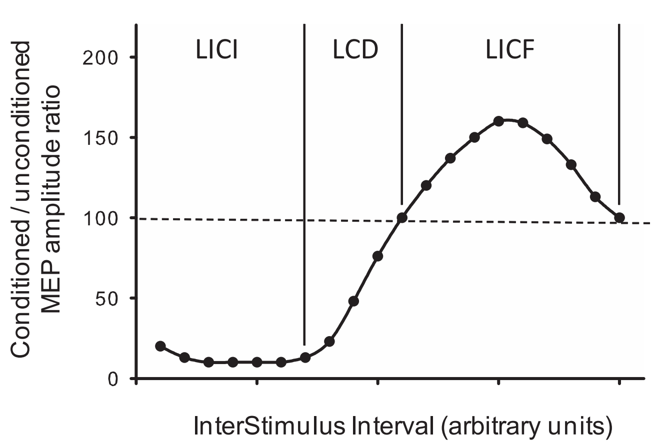

Fig. 1. Theoretical curve describing the time-dependent modulation of conditioned MEPs as a function of the time interval between conditioning and test pulses. After the period of LICI, the conditioned MEP's return to baseline corresponds to LCD. The LCD may then be followed in some cases by a net increase in cortical excitability (corresponding to LICF).