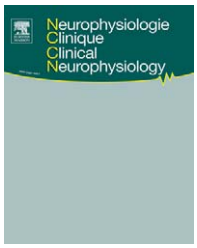
Neurophysiologie Clinique/Clinical Neurophysiology (2011) 41, 73—79

Disponible en ligne sur
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en



ORIGINAL ARTICLE/ARTICLE ORIGINAL

Cortical excitability of amyotrophic lateral sclerosis: Transcranial magnetic stimulation study

Excitabilité corticale et sclérose latérale amyotrophique : étude des stimulations magnétiques transcrâniennes

E.M. Khedr*, M.A. Ahmed, A. Hamdy, O.A. Shawky

Department of Neurology, Assiut University Hospital, Assiut, Egypt

Received 4 November 2010; accepted 21 March 2011
Available online 4 May 2011

KEYWORDS
Transcranial magnetic stimulation (TMS);
Cortical excitability;
Cortical silent period;
Transcallosal inhibition;
Amyotrophic lateral sclerosis;
ALS

Summary
Objective. — The primary purpose of this study was to provide insight into the central changes that occur in amyotrophic lateral sclerosis (ALS) with a view to understanding how these could contribute to symptoms.
Material and methods. — Seventeen patients with definite ALS and 17 control healthy volunteers were included in the study. Clinical examination, amyotrophic lateral sclerosis severity score (ALSSS) and TMS investigations including measurement of resting and active motor threshold (RMT and AMT), motor evoked potential (MEP), input-output curve, contralateral silent period, and transcallosal inhibition (CSP and TI, postulated markers of GABAb function) were measured for each participant.
Results. — There were no significant differences in RMT or AMT in either hemisphere between patients and the control group. Despite this there was a significant negative correlation between ALSSS and RMT and AMT meaning that increased severity was associated with higher thresholds. MEPs were significantly smaller in ALS patients in comparison to the control group ($P = 0.03$). There was a significant decrease in the slope of the I/O relationship of MEP amplitude to TMS intensity in patients group in comparison to controls. ALS patients had a significant prolongation of CSP and TI for both hemispheres. There was a tendency for a significant negative correlation between left TI and ALSSS ($P = 0.051$).
Conclusion. — Measurements of cortical motor excitatory changes in ALS confirm the presence of corticospinal hypoexcitability. Additionally we found increased excitability of presumed intracortical GABAb circuits that correlated with the severity of ALS. We postulate that the disease results in an imbalance between excitation and inhibition in the cortex that can contribute to clinical symptoms.

* Corresponding author.
E-mail address: emankhedr99@yahoo.com (E.M. Khedr).

0987-7053/$ - see front matter © 2011 Elsevier Masson SAS. All rights reserved.
doi:10.1016/j.neucli.2011.03.001

MOTS CLÉS
Stimulation magnétique transcrânienne ;
Excitabilité corticale ;
Période de silence cortical ;
Inhibition transcalleuse ;
Sclérose latérale amyotrophique ;
SLA

Résumé
But de l'étude. — Étudier les dysfonctionnements nerveux centraux associés à la SLA et examiner dans quelle mesure ceux-ci peuvent contribuer à ses symptômes.
Patient et méthodes. — Nous avons inclus 17 patients porteurs de SLA et 17 contrôles. Pour chaque sujet, nous avons réalisé : un examen clinique, la mesure du score de sévérité de la SLA (ALSSS) et des stimulations magnétiques transcrânienne avec les mesures suivantes : seuil moteur au repos (SMR) et sous-activation (SMA), potentiels évoqués moteurs (PEM), courbes de relations entrées-sortie (CRES), période de silence controlatéral et inhibition transcalleuse (ITC et IT, constituant des marqueurs probables de la transmission GABAb).
Résultats. — Les SMR et SMA ne différaient significativement dans aucun hémisphère entre les patients et les contrôles. Néanmoins, nous avons retrouvé une corrélation négative significative entre l'ALSSS et les SMR et SMA, un score de sévérité accrue étant associé à des seuils plus élevés. L'amplitude des PEM était significativement plus faible chez les patients que les contrôles. La pente de la relation amplitude du PEM et intensité de stimulation était significativement plus faible chez les patients. Une prolongation de l'ITC et de l'IT fut retrouvée au niveau des deux hémisphères chez les patients porteurs de SLA avec une tendance à une corrélation négative significative entre l'ALSSS et l'IT sur l'hémisphère gauche ($p = 0{,}051$).
Conclusion. — La mesure des modifications de l'excitabilité du cortex moteur confirme l'existence d'une hypoexcitabilité corticospinale dans la SLA. Nous avons également retrouvé une excitabilité accrue de circuits intracorticaux GABAb, corrélée à la sévérité de la maladie. Nous postulons qu'un déséquilibre entre l'excitation et l'inhibition intracorticale pourrait contribuer à la symptomatologie clinique.

Introduction

Amyotrophic lateral sclerosis (ALS) is a degenerative disorder of the motor system. Lower motor neuron (LMN) involvement may be detected by electromyography (EMG), whereas clinically, upper motor neuron (UMN) involvement may be elusive. Alteration of cortical excitability and intracortical inhibition (ICI) has been demonstrated in a number of cases, but in the majority of patients there were no significant changes in corticomotor thresholds (MT) and/or central motor conduction time (CMCT) in early stages of the disease [19]. Motor cortex hyperexcitability has been demonstrated in conjunction with a shortened cortical silent period (CSP) after single-pulse TMS [9]. It was suggested that the reduced CSP represents a shift in the balance of excitatory and inhibitory inputs to cortical output neurons responsible for voluntary action, due to degeneration of cortical interneurons. Impairment of short and long interval intracortical inhibition (SICI and LICI) is considered as being due to depletion of specific subpopulations of intracortical GABAergic neurons and can be seen in motor cortex reorganization following progressive neuronal loss [35,36]. However, we cannot exclude that other networks also participate.

Occasionally, mirror movements have been observed in ALS patients, suggesting an involvement of transcallosal fiber tracts in ALS. Additionally, ipsilateral motor evoked potentials (IMEP) have been demonstrated in ALS patients [15]. TMS can evaluate callosal function [17] by measuring the ipsilateral silent period (TI), which reflects transcallosally mediated inhibition of motor cortical output neurons [8,32].

The primary purpose of this study was to provide insight into the central changes that occur in ALS with a view to understanding how these could contribute to symptoms.

Material and methods

Seventeen cases with ALS were recruited according to the El Escorial criteria (El Escorial World Federation of Neurology, 1994) [5], evidence of lower motor neuron (LMN) as well as upper motor neuron (UMN) involvement is essential for the diagnosis of ALS. The mean age was 56.9 ± 9.9 years ranging from 32 to 75 years old, 13 were males. The mean duration of illness was 15.9 ± 8.97 months ranging from 9 to 36 months. Amyotrophic lateral sclerosis functional rating scale (ALS-FRST) [7] and Amyotrophic Lateral Sclerosis Severity Score (ALSSS) [13] were assessed for each patient, the lower the score the more impaired the patient. MRI was performed for each patient to exclude those with cervical spondylosis.

Seventeen age-matched healthy volunteers (61.1 ± 6.7 ranging from 49 to 70 years old), 13 males were studied as control group. All participants or their caregivers (if the patient could not write [illiterate or due to severe hand muscles weakness] gave their written informed consent before participation after full explanation of the study. The local ethical committee of Assiut University Hospital approved the study protocol. Each subject was submitted to the following: clinical examination and battery of electrophysiological examination to measure the cortical excitability as follow.

Electrophysiological investigations

Subjects sat in a comfortable chair. Electromyographic (EMG) recordings from the first dorsal interosseous muscle (FDI) of both hands were acquired with silver-silver chloride surface electrodes, using a muscle belly-tendon set-up, with a 3 cm diameter circular ground electrode placed on the wrist. A Nihon Kohden Machine model 9400 (Japan) was used to collect the signal. EMG parameters included a bandpass of