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ORIGINAL ARTICLE/ARTICLE ORIGINAL

# Altered cortical excitability in anorexia nervosa



Altération de l'excitabilité corticale dans l'anorexie nerveuse

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#### **KEYWORDS**

Anorexia nervosa; Transcranial magnetic stimulation (TMS); Cortical excitability; Cortical silent period; Intracortical inhibition; Neuropsychiatry

#### Summary

Objectives. — Recent EEG and positron emission tomography (PET) studies have reported hyperactivation of the right hemisphere in anorexia nervosa (AN). The aim of the present study was to test this notion by examining cortical excitability in subjects with AN using transcranial magnetic stimulation (TMS).

Methods. — We investigated thirteen patients meeting the DSM IV diagnostic criteria for AN and 14 controls age and sex matched. Each subject was assessed clinically using the Eating Disorder Inventory (EDI), the Eating Attitude Test (EAT) and Beck's Depression Inventory (BDI-II). TMS measures involved resting and active motor thresholds (RMT, AMT) as well as motor evoked potentials (MEP), cortical silent period duration (CSP), transcallosal inhibition (TCI), and short latency intracortical inhibition (SICI) of the first dorsal interosseous muscle (FDI) were assessed. Cortical esophageal MEP latencies (CL) were also recorded.

Results. — The RMT and MEP onset latency of the FDI and the esophagus as well as duration of the TCI were significantly reduced in anorexic patients compared to the control group. There were no significant differences neither in AMT nor CSP between patients and controls. Moreover, we found significant negative correlations between the EAT scores and RMT, and TCI duration. Although anorexic patients had significantly higher BDI score, there was no correlation between it and cortical excitability.

Conclusion. — Anorexic individuals are characterized by pathologically increased motor and esophageal cortical excitability that significantly correlates with clinical symptoms of anorexia nervosa.

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#### **MOTS CLÉS**

Anorexie nerveuse; Stimulation magnétique transcrânienne; Excitabilité corticale; Période de silence corticale; Inhibition intracorticale; Neuropsychiatrie

#### Résumé

But de l'étude. — Plusieurs études récentes en EEG et en PET-scan ont montré une hyperactivation de l'hémisphère droit dans l'anorexie nerveuse (AN). Notre étude vise à réexaminer cette notion en testant l'excitabilité corticale des patients présentant une AN, au moyen de la stimulation magnétique transcrânienne (SMT).

Méthodes. — Nous avons étudié 13 patients remplissant les critères DSM-IV d'AN, comparés à 14 sujets témoins appariés par l'âge et le sexe. Chaque patient était évalué cliniquement au moyen des tests suivants: Eating Disorder Inventory (EDI), Eating Attitude Test (EAT) Beck's Depression Inventory (BDI-II). Les mesures réalisées par SMT incluaient: le seuil moteur au repos (SMR) et sous-activation volontaire (SMA), les potentiels évoqués moteurs (PEM), la durée de la période de silence corticale (PSC), l'inhibition transcalleuse (IT), l'inhibition intracorticale de courte latence (ICCL) du premier interosseux dorsal (PID). Nous avons également mesuré le temps de latence (TL) des PEM œsophagiens.

Résultats. — Le SMR et le temps de latence des PEM œsophagiens et du PID étaient significativement réduits dans le groupe AN par rapport aux contrôles. Il n'y avait pas de différences significatives au niveau des SMA et PSC. On a également retrouvé des corrélations négatives significatives entre les scores EAT et le SMR, le TL et IT. Bien que les patients anorexiques présentaient un score BDI plus élevé, celui-ci n'était pas corrélé à l'excitabilité corticale. Conclusions. — Les sujets anorexiques présentent une excitabilité corticale motrice et oesophagienne accrue, corrélée aux symptômes cliniques de l'AN.

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#### Introduction

Anorexia nervosa (AN) is a serious mental disorder. Core symptoms are severe food restriction, intense fear of gaining weight or becoming fat, and disturbance in the way one's body weight or shape are experienced. AN is associated with a myriad of physical and psychological comorbidities, high levels of mortality and disability [1]. Significant advances have been made over the last decade in our understanding of the neural correlates of AN, with research highlighting both structural [9,25,37]; and functional [6,30,34,39] alterations in the brain. These neuroimaging studies reveal gray and white matter alterations, and disturbances in limbic, frontal and parietal areas, in addition to alterations in the functioning of neurotransmitters including serotonin and dopamine at different stages of AN.

A number of recent studies have observed hyperactivity in areas of the cerebral cortex. Electroencephalographic (EEG) measures suggest hyperactivation of the right hemisphere [16], whilst positron emission tomography (PET) mapping of serotonergic activity around 5-HT1A receptors revealed increased clusters of serotonergic binding, predominantly in right fronto-temporal regions [10]. A review of the anatomical and metabolic impairments described the pathological profile as "most frequently a right posterior hypometabolism, followed by a right anterior hypermetabolism, both associated with right abnormal EEG spiking" [5]. Interestingly, anorexic patients rated drawings of female body shapes, in different weight categories, as more aversive than healthy control subjects, and the ratings correlated positively with activity in right prefrontal cortex [32]. These findings are consistent with the hypothesis of heightened cortical arousal in anorexia nervosa [4,14] that leads to enhanced focalization of attention and higher anxiety levels. This hyperaroused state has also been observed in obsessive-compulsive disorders (OCD) [33]. The aim of the present study was to use transcranial magnetic stimulation (TMS) as a physiological measure of cortical excitability and test its relationship with the clinical symptoms of AN.

#### Materials and methods

#### Subjects

The experimental group consisted of 13 anorectic patients (12 females). The mean age was,  $21.3 \pm 7.6$  with range (16-39 years). Diagnosis was established with the eating disorders module of the Structured Clinical Interview for DSM IV – axis I Disorders/Patient version [8]. Patients met the principal eligibility criterion required: a body mass index between  $14-18.5 \,\mathrm{kg/m^2}$ . The control group consisted of 14 age-matched healthy volunteers (13 females) with a mean age of 23.0  $\pm$  3.6 years, with range (19–30 years). None of the patients suffered from any other clinically relevant disorder; however most of them were receiving antidepressant drugs; selective serotonin reuptake inhibitors (SSRI) for few months without improvement (10 patients); those patients continue on the SSRI throughout the study. The patients and the control subjects were asked not to take other drugs that affect motor cortex excitability (dopaminergic, psychotropic, antiepileptic, or hormonal drugs, estrogen) at least two weeks before the study. All female patients and control subjects were asked not to be menstruating through the days of the study. Demographic and clinical information were measured for each participant.

The study was approved by the Institutional Ethical Committee of Assiut University Hospital. Prior to the

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