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Research report

Psychomotor retardation is linked to frontal alpha asymmetry in major depression

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ABSTRACT

Background: Psychomotor disturbances are a main clinical feature of major depressive disorder (MDD) but little is known about their EEG signature. One of the most replicated EEG findings in MDD is resting frontal asymmetry in the alpha band (FAA), which is thought to be a correlate of withdrawal behavior and reduced approach motivation. The purpose of this study was to assess psychomotor alterations, alpha band power, FAA and investigate the association between them.
Methods: 20 MDD patients and 19 healthy subjects were enrolled. Alpha power and FAA scores were calculated from a resting state EEG. Wrist actigraphy was recorded from the non-dominant arm for 24 h and activity level scores (AL) were extrapolated from the wakeful periods.
Results: MDD patients had a left-lateralized frontal alpha activity and lower AL scores when compared to healthy subjects. A significant correlation was found between mean FAA and AL scores. A negative covariance between power in the lower alpha range and AL scores over the motor cortex bilaterally was detected.
Limitations: Relatively small sample size. Patients were pharmacologically treated with antidepressants.
Conclusions: This study replicates the finding of left-lateralized FAA and lower AL scores in MDD patients, and establishes the first evidence of significant correlations between alpha power, FAA scores and measures of motor activity, which may be interpreted as an expression of impaired motivational drive in MDD.

1. Background/introduction

Psychomotor disturbances are one of the main clinical manifestations of Major Depressive Disorder (MDD); they have been attributed discriminative diagnostic and some predictive value in terms of response to psychopharmacological treatment (Schrijvers et al., 2008a; Sobin and Sackeim, 1997). Aberrant motor activity in MDD includes psychomotor retardation, agitation, reductions in facial expression as well as slowing of fine motor skills, gait and speech (Krane-Gartiser et al., 2014; Lemke et al., 1999; Michalak et al., 2009; Volkers et al., 2003; Walther et al., 2011). Hand-motor tasks have been used to assess the impact of psychopharmacological treatment on motor function in depression (Hegerl et al., 2005; Mergl et al., 2007), while longitudinal changes in spontaneous motor behavior have been proven useful to monitor treatment outcomes. In the latter context, the use of wrist actigraphy allows continuous recording of various parameters of motor activity in naturalistic settings (Stanley, 2003; Todder et al., 2009; Volkers et al., 2002; Walther et al., 2012b, 2009a, 2009b, 2009c), yielding quantitative measures of the clinical phenomenon under scrutiny. In fact, objectively assessed motor behavior in patients with major depression seems to differ from the observations in clinical interviews, leading to only partial overlap of observer ratings as in the Hamilton Depression Rating Scale (HAMD21; Hamilton, 1960) and actigraphy recordings (Razavi et al., 2011).

The neural correlates of motor activity disturbances in depression have been investigated mostly by means of magnetic resonance imaging (MRI) techniques, showing deficits in structural and functional connectivity between frontal cortical regions and basal ganglia (Bracht et al., 2012; Liberg et al., 2014; Walther et al., 2012a, 2012b). EEG studies addressing the issue are few and mainly investigating the spectral EEG characteristics or the link between action monitoring and psychomotor retardation (Nieber and Schlegel, 1992; Schrijvers et al., 2008b, 2009).

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Table 1
Sociodemographic and clinical features for patients and healthy controls.

	Patients ($N=20$, outpatients=3, inpatients=17)		Healthy subjects ($N=19$)		Total ($N=39$)	
Gender	10 females		11 females		21 females	
Smokers	9		4			
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Age (years)	43.30	14.03	41.05	13.82	42.21	13.79
Number of episodes	5.85	6.09	–	–	–	–
Duration of illness (years)	10.7	10.29	–	–	–	–
AL wake, counts/h	14,170	8246	20,094	7374		
Total HAMD score	25.45	4.95	–	–	–	–
Annual income (CHF)	43,446	32,012	46,452	21,907		
Education years	13.71	2.52	14.21	3.66		

One of the most investigated EEG markers in MDD is resting frontal alpha bandwidth asymmetry (FAA) (Gollan et al., 2014; Stewart et al., 2010; Thibodeau et al., 2006), a pattern of relatively less left than right resting fronto-cortical activity (probed by relatively greater left than right alpha band activity in depressed patients). It is thought to reflect withdrawal behavior and reduced approach motivation (Davidson, 1998) and show both trait- and state-like features (Allen et al., 2004). FAA has been shown to differentiate between healthy subjects and depressed patients even when in remission (Henriques and Davidson, 1990) and to have a modest heritability (Anokhin et al., 2006). It has been proposed to probably reflect a state-independent risk factor for the development of the disorder (Coan and Allen, 2004). However, some reports contradict the association with MDD (Carvalho et al., 2011; Gold et al., 2013; Reid et al., 1998), and there is no substantial agreement as to its potential as a biomarker (Olbrich and Arns, 2013). Therefore, we wanted to assess the presence (or absence) of FAA in a cohort of MDD patients and healthy controls for lower and upper alpha, given the fact that a previous study showed different effects in those two sub-bands (Jaworska et al., 2012). Moreover, the aims of the present study were to evaluate the quantitative motor activity of the two groups and to investigate the correlation between potential motor disturbances and resting state EEG signatures, focusing mainly on alpha band. Alpha waves were observed for the first time over occipital areas during waking relaxation states with eyes closed and were thought to be the neurophysiological representation of the "idling" brain (Berger, 1929). The current interpretation is that they may inhibit cortical areas not in use or contribute to the coordination of different neuronal networks (Palva and Palva, 2007). A peculiar variant of the alpha wave is the mu-rhythm (or Rolandic, or sensorimotor rhythm), which oscillates at a main frequency of 8–13 Hz, can be recorded over the sensorimotor cortex at rest, is reduced by movement or somatosensory stimulation and seems to be generated by sources other than that of occipital alpha (Pineda, 2005). Thus, we hypothesized a correlation between motor activity and alterations in the resting state EEG alpha spectrum, particularly over the motor cortex. Moreover, we expected that patients with MDD would show an asymmetric left-lateralized pattern of frontal alpha band activity when compared with controls, together with reduced motor activity. Finally, we expected an association between motor activity and FAA, both of them being frequent neurophysiological and clinical findings in depression and related to reduced motivational drive.

2. Materials and methods

2.1. Subjects

Twenty patients with a diagnosis of MDD were included after admission to the inpatient and outpatient departments of the University Hospital of Psychiatry in Bern, Switzerland. Diagnoses were made using the Structured Clinical Interview for DSM IV-TR (SCID-1) by experienced psychiatrists. Clinical assessment was performed using the 21 items version of the Hamilton Depression Rating Scale (HAMD; Hamilton, 1960), the Montgomery–Åsberg Depression Rating Scale (MADRS; Montgomery and Åsberg, 1979), the Beck Depression Inventory (BDI; Beck et al., 1961), the Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989) and the Edinburgh Handedness Inventory (Oldfield, 1971). HAMD scores at enrollment were >18. Patients with diagnoses of bipolar disorder or comorbid personality disorders were excluded from the study after assessment with SCID – 1 and 2 and review of the case files. The Unified Parkinson's Disease Rating Scale (UPDRS; Fahn et al., 1987) was used to exclude patients with Parkinson syndrome. Further exclusion criteria were history of significant head trauma, history of electroconvulsive therapy, substance abuse or dependence other than nicotine.

All patients but one received one or more antidepressant drugs (amitriptyline 25–225 mg, $n=2$; escitalopram 20 mg, $n=1$; clomipramine 75 mg, $n=1$; doxepin 100–200 mg, $n=2$; mirtazapine 15–45 mg, $n=5$; sertraline 100–200 mg, $n=2$; venlafaxine 150–300 mg, $n=2$; and venlafaxine and mirtazapine combination 150–300 mg/30 mg, $n=4$). Seven patients received adjunctive agents for augmentation (lithium=2; lamotrigine $n=1$, quetiapine $n=4$), and nine patients received zolpidem 10 mg at night.

In total, 19 adults without psychiatric history, alcohol/drug abuse (assessed with non-patient version of the SCID [SCID-IV/NP]) were enrolled as controls, matched for age, gender, education and income. The two groups did not differ in smoking status. Healthy subjects were also excluded in case of any first-degree relatives with history of any affective disorder. Participants were between 21 and 66 years of age. Demographic characteristics are shown in Table 1. The majority of the participants had been included in a previous report on AL and cerebral blood flow (Walther et al. 2012b).

2.2. Actigraphic recordings

Participants wore a wrist actigraph (Actiwatch, Cambridge Neurotechnology, Inc., Cambridge, U.K.) on the non-dominant arm for 24 h for continuous recording of motor activity. The piezo-electronic sensor converts acceleration into movement counts. Data was sampled in 2 s intervals. Participants provided sleep log