Applying EEG-based vigilance measurement in a case of adult attention deficit hyperactivity disorder

Received 31 July 2012; Reviewed 4 September 2012; Revised 11 September 2012; Accepted 11 October 2012;
First published online 10 December 2012

Introduction

Adult attention-deficit hyperactivity disorder (ADHD) is characterized by inattentiveness, hyperactivity, mood lability, hot- or short-temper, impaired stress tolerance, disorganization and impulsivity (Wender, 1995). Due to the reduction of externalizing symptoms in adulthood and the absence of hyperactivity in the predominantly inattentive subtype, ADHD is more difficult to diagnose in adults (Nierenberg et al., 2005) and often unrecognized or mistakenly attributed to other psychiatric conditions (Kessler et al., 2006). Adult ADHD overlaps in symptom profiles and is highly co-morbid with other psychiatric disorders, including major depressive disorder (MDD), bipolar disorder (BD) and substance abuse, making the discrimination of symptoms more complicated (Wilens et al., 2009) and warranting the search for facilitating diagnostic tools.

Case report

S. M., a male student aged 26 yr, was admitted to our hospital with a diagnosis of bipolar depression. The diagnosis of BD was made 4 yr earlier after first-time consumption of cannabis induced a manic syndrome leading to compulsory admission. This was followed by two further admissions and on-going out-patient treatment for recurrent depressive episodes. The patient had been treated with a combination of 1000 mg valproic acid and 40 mg citalopram daily for the previous 18 months and prior to this mirtazapine (up to 60 mg) and venlafaxine (up to 225 mg) daily. There was a family history of BD in his mother. On admission he had marked reduction in self-confidence, frequent feelings of inadequacy, high drive, a feeling of inner tension, reduced ability to concentrate, depressed mood and recurrent suicidal ideation. Further, we ascertained feelings of inadequacy, frequent daily changes between excitation, depressed and euthymic mood and irritability, culminating in severe impairment in relationships and in his studies. A Hamilton Depression Rating Scale (HAMD) score of 10 and Beck Depression Inventory (BDI)-II of 19 supported a mild depressive syndrome. Additionally, all aspects of the Utah criteria of adult ADHD were fulfilled (Wender, 1995). First-grade school reports as well as anamnesis from his parents pictured a keen and astute but also distractible and disobedient child. He pursued motocross racing from his 12th birthday, indicating risk-taking behaviour in the course of adolescence. Questionnaire scores for ADHD showed conflicting results. On self-report, German versions, the WURS-K self-assessment of childhood ADHD was negative. For symptoms in adulthood an ADHD-self-report (ADHD-SB) score of 15 supported the diagnosis, whereas the adult ADHD self-report scale symptom checklist (ASRS-v1.1), English version, was positive for three of the required threshold of four of seven items, Findings on the observer version of Conner’s Adult ADHD Rating Scales (CAARS-O:SV), English version, slightly pointed towards ADHD in the inattention/memory problems subscale (T score 57) and impulsivity/emotional lability subscale (T score 56). Medication with valproic acid and citalopram were discontinued and the patient was monitored in a drug-free state for 7 d. During that time he reported an increase in drive, reduction of tiredness, increased thought content and frequency. Based on a clinical diagnosis of ADHD, methylphenidate (10 mg) daily was commenced and increased to 2 x 10 mg after 7 d. During the treatment with methylphenidate, the patient reported a persistent feeling of contentment, balanced mood and drive as well as more organized thoughts. The BDI-II, HAMD-17 and CAARS-O:SV all showed subclinical scores after 1 and 2 wk treatment. EEG recordings every 15 min under quiet rest with eyes closed and a visual continuous performance test (CPT; for details see Minkwitz et al., 2011) were performed on day 7 without medication (T1), day 7 on 10 mg methylphenidate (T2) and day 7 on 20 mg methylphenidate (T3) as well as at follow-up after 4 months outpatient treatment with 10 mg methylphenidate (T4). To determine regulation of vigilance in the sense of ‘brain arousal’ the computer-based Vigilance Algorithm Leipzig was used to classify 1-s EEG segments into stage W with dominant beta power, stage A with dominant alpha power and lower stages B and C with low-amplitude non-α power (stages according to Bente and Roth; for details, see Hegerl et al., 2012). This algorithm has recently been validated with functional magnetic resonance imaging and fluorodeoxyglucose positron emission tomography (for details see Olbrich et al., 2012). In the course of treatment of S. M., the ratio of stages W:B and A:B increased whereas switches between stages and
Distribution of vigilance stages (%). Increase of high vigilance stages W and A from 52 to 78% during the treatment and decrease of low vigilance stage B from 48 to 22% from T1 to T4. No stages C occurred during the four measures. Segments containing artefacts were excluded from calculations.

Discussion

In this case of adult ADHD, clinical improvement of symptoms was achieved with methylphenidate treatment, following an inadequate therapeutic response for 4 yr due, in our opinion, to the inappropriate diagnosis of an affective disorder. Initial misdiagnosis of mania with prescription of valproic acid may have contributed to continuing inappropriate therapy because drug-associated lassitude and drowsiness may have obscured the most obvious ADHD symptom of hyperactivity. On the other hand, due to its range of side-effects the serotoninergic antidepressant, citalopram, may have reinforced symptoms of ADHD rather than its intended effect of diminishing depressive symptoms. Response to antidepressants in ADHD is limited to buproprion, the most obvious ADHD symptom of hyperactivity. On the other hand, due to its range of side-effects the serotoninergic antidepressant, citalopram, may have reinforced symptoms of ADHD rather than its intended effect of diminishing depressive symptoms. Response to antidepressants in ADHD is limited to buproprion, whereas therapy with psychostimulants has high response and remission rates in ADHD.

A pathogenetic model explaining the mode of action has recently been proposed outlining the connection between overlapping symptoms of ADHD and mania and EEG-based vigilance dysregulation (Hegerl and Hensch, 2012). Externalizing symptoms such as hyperactivity, distractibility and sensation-seeking behaviour are interpreted as an autoregulatory attempt to stabilize vigilance. Unstable vigilance regulation has been found in both mania (state factor) and ADHD (trait factor). Unstable vigilance is characterized by reduced EEG stages A and W and increased proportions of vigilance stages B and C during a 15-min EEG under quiet rest with eyes closed.

In our patient, the EEG-recording revealed unstable vigilance regulation in the unmedicated state. Medication with methylphenidate led to stabilization of vigilance and improved performance in the CPT, with a concomitant reduction of clinical symptoms. Our results are supported by previous findings suggesting a predictive value of vigilance regulation on the treatment outcome with psychostimulants in ADHD (Sander et al., 2010) and mania (Schoenknecht et al., 2010). There, stabilization of vigilance was accompanied by the decline of clinical symptoms. Serial determination of EEG-based vigilance regulation may assist the assessment of pharmacotherapeutic effects but may also be used prospectively to support the discrimination of adult ADHD from MDD, the differential diagnosis in this case report. In MDD, patients show a hyperstable vigilance regulation with higher proportion of stage A1 compared to healthy controls (Hegerl et al., 2012) and contrary to the unstable vigilance observed at baseline in the present case.

In conclusion not only affective disorders but also ADHD should be considered in the diagnosis of young adults complaining of lability of mood, irritability and impulsivity. Previous medication regimes need to be reconsidered critically in terms of enhancement or masking of symptoms of ADHD. Therapies with psychostimulants can be monitored using determination of EEG-vigilance, since vigilance and wakefulness regulation may have a pathogenic role in ADHD as well as BD.

Statement of Interest

H.H. received speaker honoraria from AstraZeneca, Lilly, Bristol-Myers Squibb and Servier, consulting fees from Bristol-Myers Squibb and chemical substances for study support from AstraZeneca, Novartis and Wyeth. U.H. received in the last 3 yr honoraria as speaker or advisor from Lilly, Wyeth, Lundbeck, Bristol-Myers Squibb, Takeda and Sanofi-Aventis as well as a consultant for Nycomed.

References


Fig. 1. Distribution of vigilance stages (%). Increase of high vigilance stages W and A from 52 to 78% during the treatment and decrease of low vigilance stage B from 48 to 22% from T1 to T4. No stages C occurred during the four measures. Segments containing artefacts were excluded from calculations.


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