2.3.2

Study 6: Prolonged effects of WBV on cognitive functions in ADHD

ABSTRACT

Adult attention deficit hyperactivity disorder (ADHD) is associated with a variety of cognitive impairments which were shown to affect academic achievement and quality of life. Current treatment strategies, such as stimulant drug treatment, were demonstrated to effectively improve cognitive functions of patients with ADHD. However, most treatment strategies are associated with a number of disadvantages in a considerable proportion of patients, such as unsatisfactory effects, adverse clinical side effects or high financial costs. In order to address limitations of current treatment strategies, Whole Body Vibration (WBV) might represent a novel approach to treat cognitive dysfunctions of patients with ADHD. WBV refers to the exposure of the whole body of an individual to vibration and was found to affect physiology and cognition. In the present study, WBV was applied on 10 consecutive days to an adult diagnosed with ADHD. Neuropsychological assessments were performed repeatedly at three different times, i.e. the day before the start of the treatment, on the day following completion of treatment and 14 days after the treatment has been completed (follow-up). An improved neuropsychological test performance following WBV treatment points to the high clinical value of WBV in treating patients with neuropsychological impairments such as ADHD.
INTRODUCTION

Assessments of neuropsychological functions of adults with attention deficit hyperactivity disorder (ADHD) revealed impairments in various aspects of attention, memory and executive control, including focused and divided attention, vigilance, task switching, fluency, inhibition, prospective memory and working memory (Biederman et al., 2008; Boonstra, Oosterlaan, Sergeant, & Buitelaar, 2005; Fuermaier et al., 2013a; Hervey, Epstein, & Curry, 2004; Schoechlin & Engel, 2005; L. Tucha et al., 2009; O. Tucha et al., 2006; O. Tucha et al., 2005). Furthermore, it could be demonstrated that impairments in these aspects of cognition were associated with impaired occupational functioning and a reduced quality of life (Agarwal, Goldenberg, Perry, & IsHak, 2012; Barkley & Murphy, 2010; Lange, Reichl, Lange, Tucha, & Tucha, 2010). First-line choice of treatment strategies is often stimulant drug treatment e.g. using methylphenidate which was shown to effectively improve symptoms and cognition of adults with ADHD (L. Tucha et al., 2011; O. Tucha et al., 2006; Verster et al., 2010; Vidal-Estrada, Bosch-Munso, Nogueira-Morais, Casas-Brugue, & Ramos-Quiroga, 2012; Wigal, 2009). However, stimulant drug treatment is associated with disadvantages affecting a considerable proportion of patients, such as unsatisfactory effects, adverse clinical side effects (e.g. headache, dry mouth, insomnia) or high financial costs (Adler, Spencer, McGough, Jiang, & Muniz, 2009; Wigal et al., 1999; Wilens, Spencer, & Biederman, 2002). Consequently, there is a general need for alternative or additional treatment options in order to improve the clinical outcome of patients with ADHD.

In this respect, Whole Body Vibration (WBV), i.e. the exposure of the whole body of an individual to vibration, might be interesting. In previous research on healthy individuals, WBV was shown to have beneficial effects on various physiological measures, including balance, mobility, posture control, muscle strength, oxygen uptake, heart rate, blood pressure and blood flow (Bogaerts, Verschueren, Delecluse, Claessens, & Boonen, 2007; Cardinale & Lim, 2003; Cochrane et al., 2008; Lam, Lau, Chung, & Pang, 2012; Stewart, Karman, Montgomery, & McLeod, 2005). Support for the potential value of WBV in improving cognitive performance was provided by studies in mice, demonstrating improved maze learning and enhanced neuronal activity following the application of WBV (Keijser et al., 2011; Van der Zee et al., 2010). The effect of WBV on cognition in humans, however, was not examined in detail. A small number of studies has been performed so far which examined whether cognitive functioning is different when participants perform cognitive tasks while they receive WBV. The results of these studies are not conclusive with some studies finding no effect of WBV (Ljungberg, Neely, & Lundstrom, 2004; Ljungberg & Neely, 2007) and others reporting negative effects of WBV on cognitive functions, such as short-term and long-term memory, arithmetic
problem solving or reasoning (Sandover & Champion, 1984; Sherwood & Griffin, 1992; Sherwood & Griffin, 1990). In contrast, the potential of WBV as an alerting system to improve vigilance was emphasized for particular bands of vibration frequencies (Poulton, 1978). Moreover, with regard to patients with impaired cognitive functions (i.e., patients with traumatic brain injury), proprioceptive stimulation was demonstrated to improve both cognitive performance and physiological processes (Mueller et al., 2002). Considering the latter findings of WBV on human performance, the aim of the present case study was to examine prolonged effects of WBV on cognitive functions in a patient with a diagnosed ADHD. The patient was treated with WBV continuously for 10 days and various neuropsychological functions were assessed in repeated measurements in order to explore prolonged effects of WBV on cognitive functions.

CASE PRESENTATION

History Taking
The patient was a 25-year-old college student who had a well-documented diagnosis of ADHD. Criteria for an ADHD diagnosis according to DSM-V were fulfilled both currently (nine symptoms of inattention, nine symptoms of hyperactivity/impulsivity) and retrospectively for childhood (six symptoms of inattention, six symptoms of hyperactivity/impulsivity) using the self-report ADHD Rating Scale (American Psychiatric Association, 1994; DuPaul, Power, Anastopoulos, & Reid, 1998; Kooij et al., 2005). The diagnosis for ADHD has been established for the first time in adolescence whereas no comorbid disorders have been diagnosed in the present or in the past. The patient was treated with stimulants for several years (methylphenidate, 4 x 10 mg a day) which, according to the patient’s report, improved his abilities to concentrate and to stay focused when studying. He further reported to be less easily distracted and to be better able to maintain attention over a prolonged period of time when being on his regular medication. Furthermore, the patient received coaching once a week for one hour by a clinician specialized in the treatment of adults with ADHD. The objective of the coaching was to acquire competencies in coping with ADHD symptoms. According to the patient’s experiences, he learned with the support of the coach to schedule daily activities realistically and not to always blame himself when something is going wrong. He also succeeded in achieving more stable academic performance. However, intervention was associated with some disadvantageous. Stimulant drug treatment resulted in adverse side effects such as a decline in appetite, so that he occasionally forgot eating when being on medication. In addition, behavioral based intervention was time and money consuming and the patient often felt exhausted and tired from analyzing own behavior continuously. Even though treatment improved his self-perceived level of cognitive
functioning, the patient complained about an inner restlessness and about the need of a high cognitive effort to stay focused and to get things done in time. He further reported to act impulsively in many situations and to experience problems in switching attention flexibly between tasks.

**Application of WBV**

In the present study, the patient underwent WBV treatment three times a day (morning – noon – evening) for a period of 10 consecutive days. In each of the three sessions per day WBV treatment was performed for 15 minutes. WBV was applied by using a vibrating platform (Vibe 300; Tonic Vibe, Nantes, France). A wooden chair on a wooden platform was mounted on the Vibe 300. Both the wooden platform and the chair were attached to the Vibe 300 with bolts from underneath the Vibe 300 in order to keep deviations from the vibrating frequency and amplitude on a minimum (Figure 6.1). The manufacturer settings of 30 Hz vibration frequency and 4 mm vibration amplitude were applied as pilot studies showed this setup to be comfortable for the participant as well as efficient. However, the construction of a wooden platform and chair mounted on the vibrating device was assumed to cause some deviations from the manufacturer settings with regard to the vibration frequency and amplitude. The actual vertical displacements (frequency and amplitude) were therefore measured on different locations of the chair (see A, B, C and D in Figure 6.1) based on acceleration data without a person sitting on the chair. The measured displacements (frequency/amplitude) were 30Hz/0.44mm (location A), 30Hz/0.44mm (location B), 30Hz/0.66 mm (location C) and 30 Hz/0.50mm (location D). The modified Vibe 300 was located in a quiet laboratory. During WBV treatment, the participant was instructed to sit on the chair in upright position, the arms on the rest and both feet on the wooden platform. The participant was further instructed to keep body movements to a minimum.
Neuropsychological Assessments
The patient underwent three neuropsychological assessments (repeated measures design), each consisting of standardized neuropsychological tests as well as a self-report of cognitive functioning. The 1st assessment was performed on day 1. WBV treatment sessions were applied between day 2 and day 11 on ten consecutive days (30 WBV treatment sessions in total). The 2nd assessment was performed on day 12 (about 16 hours after the final treatment session has been completed). Finally, a third assessment (follow-up assessment) was performed on day 25. No treatment or other meetings related to the research project were carried out between the 2nd assessment and the follow-up assessment. All three assessments were performed at the same time of the day (starting at around 9 a.m.). Pharmacological treatment was not discontinued for this study so that the patient was on his usual medication throughout the study period (including all assessments and treatment sessions). Neuropsychological tests performed on the three assessment
days included measures of alertness, distractibility, divided attention, vigilance, flexibility (tests of the Testbattery for Attentional Performance, TAP) (Zimmermann & Fimm, 2002), working memory (Digit Span Backward Test from Wechsler Memory Scale (WMS)) (Wechsler, 1987), inhibition ( stroop Color-Word Interference Test) (Stroop, 1935) and a letter fluency test for the assessment of divergent thinking (based on the Controlled Oral Word Association Test) (Benton, Hamsher, & Sivan, 1989; Schmand, Groenink, & van den Dungen, 2008). These test measures were selected because of various reasons: (1) they represent tests which are commonly performed in routine neuropsychological assessment, (2) they measure different aspects of cognition, (3) they have been shown to be sensitive to the impairments of adults with ADHD (Boonstra et al., 2005; Fuermaier et al., 2013b; Schoechlin & Engel, 2005; L. Tucha et al., 2008; L. Tucha et al., 2011; O. Tucha et al., 2006) and (4) they allow repeated measurements (i.e. parallel versions of tests or low susceptibility for practice effects resulting from repeated assessments). Detailed descriptions of all measures can be found in previous studies and in the appendix of this article (Fuermaier et al., 2013a; Fuermaier et al., 2013b; Koerts, Van Beilen, Tucha, Leenders, & Brouwer, 2011; O. Tucha et al., 2006). Moreover, the subjective experience of impairments in attention was measured with a self-report questionnaire (sample of items taken from the Attention Questionnaire) (Schepers, 2007) (see appendix). All three assessments consisted of the same tests and questionnaire with the exception of the letter fluency test of which parallel versions were applied. The duration of testing was about 90 minutes per test session.

Furthermore, six healthy college students (age (in years): 22.8±2.4; gender (f/m): 3/3) were assessed with the same neuropsychological test battery as applied to the patient with ADHD (with the exception of the self-rating of cognitive impairments). College students served as a control group in order to rule out practice effects of repeated measurements. Each control participant was assessed individually for three times, separated by the same time intervals as described for the assessment of the patient with ADHD. However, healthy participants did not undergo WBV treatment.

Neuropsychological Findings
Neuropsychological test performances of the patient and healthy participants are presented in Table 6.1. Inspection of the healthy participants’ performances revealed improvements of functions because of repeated assessments, including measures of vigilance, flexibility, working memory and inhibition, with the best performances logically in the 3rd assessment. The patient with ADHD improved markedly from the 1st to the 2nd assessment in measures of alertness (i.e. variability of performance), divided attention, vigilance, flexibility, inhibition, divergent thinking as well as in self-reported impairments of attention. The considerable beneficial effects of WBV treatment on
vigilance, flexibility, inhibition (interference condition) and verbal fluency are presented in Figure 6.2. Figure 6.2 also shows the mean performances of healthy participants per measure in order to give an indication of the size of potential practice effects. However, WBV treatment did not influence all cognitive measures in the same way. For example, reaction times in the alertness task, the distractibility task as well as the working memory task were (relatively) unaffected by WBV. The improvements of the patient which were found in the 2nd assessment were mostly normalised in the 3rd assessment. With only few exceptions (e.g. variability of reactions in the alertness task and number of errors in the divided attention task), the patient’s performance went back to his initial performance shown during the 1st assessment, including measures of vigilance, flexibility, inhibition, divergent thinking and the patient’s self-reported impairments of attention.

Figure 6.2. Test results of the patient with ADHD and control participants
Patient with ADHD (solid line) received WBV treatment between 1st and 2nd assessment. Healthy participants (dotted line) did not receive WBV treatment.
Table 6.1. Test results of the patient with ADHD (WBV treatment) and control participants (no WBV treatment) on 1st assessment, 2nd assessment and follow-up assessment.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Patient with ADHD</th>
<th>Control participants (M±SD)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st assessment</td>
<td>2nd assessment</td>
<td>Follow-up assessment</td>
</tr>
<tr>
<td><strong>Alertness</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tonic – Reaction time (msec)</td>
<td>206</td>
<td>195</td>
<td>218</td>
</tr>
<tr>
<td>Tonic – Standard deviation (msec)</td>
<td>51</td>
<td>18</td>
<td>24</td>
</tr>
<tr>
<td><strong>Distractibility</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of errors</td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>Divided attention</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of errors</td>
<td>5</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td><strong>Vigilance</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of errors</td>
<td>5</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td><strong>Working memory</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit Span Backward Score</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td><strong>Flexibility</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of errors</td>
<td>6</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td><strong>Inhibition</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Color-Block (sec)</td>
<td>46.3</td>
<td>40.8</td>
<td>49.9</td>
</tr>
<tr>
<td>Color-Word Interference (sec)</td>
<td>71.4</td>
<td>62.1</td>
<td>70.7</td>
</tr>
<tr>
<td><strong>Divergent thinking</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Letter fluency score</td>
<td>38</td>
<td>54</td>
<td>41</td>
</tr>
<tr>
<td><strong>Self-rated impairment of attention</strong></td>
<td>33</td>
<td>27</td>
<td>31</td>
</tr>
</tbody>
</table>

* Testbattery of Attentional Performance (TAP); b Digit Span Backward task; c Stroop Color-Word Interference task; d Controlled Oral Word Association Test; e Items drawn from the Attention Questionnaire.
DISCUSSION

Whole Body Vibration (WBV) was applied to a patient with ADHD on ten consecutive days for three times per day (15 minutes each). WBV was applied passively while sitting on a chair in resting position. This passive application required neither physical exercise nor any physical effort and was therefore easy to administer. A comparison between the 1st assessment (i.e. baseline) and 2nd assessment clearly demonstrated considerable improvements of various measures of cognition. The patient showed improvements in measures of vigilance, divided attention, flexibility, inhibition, divergent thinking (verbal fluency) as well as in self-rated impairments of attention. It can, therefore, be concluded that WBV treatment had a performance-enhancing effect on the patient’s cognition. However, a consistent performance in working memory, distractibility and reaction times (as measured in the alertness task) throughout the different assessments denotes that WBV treatment had not the same beneficial impact on all functions assessed. It is not clear whether the unaffected test performance results from the use of test measures which are not very sensitive to changes or whether this finding indicates that WBV treatment has selective effects on cognition.

The present effects of WBV on cognition are meaningful since functions of attention and executive control are crucial for many tasks in everyday life and were found to be considerably impaired in patients with ADHD (Boonstra et al., 2005; Fuermaier et al., 2013a; O. Tucha et al., 2006). However, as the patient was assessed with the same test battery for three times, practice effects in repeated measurements accounted for a potential explanation of the improvements found in neuropsychological test performance (O. Tucha et al., 2006). In this respect, two arguments can be brought forward to address this issue and thereby to contradict the possibility of practice effects to be responsible for the observed improvements. First, if there would be a practice effect of repeated assessments, one would assume that there is a more or less linear increment in performance, meaning that participants are better in the 2nd assessment than in the 1st, and even better in the 3rd than the 2nd assessment. An exception from this assumption might occur if a participant reaches a very high level in a test procedure in the 2nd assessment so that further improvement is hardly possible. In this case, one would assume that the participant’s performance remains on a comparably high level at the 3rd assessment. The results of the patient presented in this case report, however, improved considerably from the 1st to the 2nd assessment and decreased markedly from the 2nd to the 3rd assessment. This performance profile is clearly compatible with the treatment regimen applied to the patient who received WBV treatment between the 1st and 2nd assessment but not between the 2nd and 3rd assessment. Second, further support is given by the performances shown by healthy participants who were also tested three times in
the same time intervals as the patient with ADHD. The improvements displayed by the healthy participants which are obviously the result of practice effects are considerably smaller than the improvements shown by the patient. It is therefore very unlikely that the patient’s improvements can be attributed to practice effects.

As the beneficial effects of WBV were found in a patient who was currently treated with methylphenidate, this case report demonstrates that a combined application of WBV treatment with conventional treatment methods is possible. Furthermore, WBV treatment appears to be a very effective treatment, because it could significantly improve cognition despite the patient already being on medication. Whereas many conventional treatment methods are time and money consuming, WBV represents a relatively inexpensive method which can be applied easily and thereby allows administration in private and institutional settings (i.e. at home, in school or at work place). Moreover, according to our own pilot work on a large number of participants (n > 200), no adverse side effects or discomfort are currently known to be caused by passive WBV treatment. However, despite improvements of cognition were found 16 hours after WBV treatment, the effects were not permanent as the 3rd assessment (14 days following WBV treatment) revealed. This indicates that repeated and regular treatment would be necessary to really support patients with ADHD in their daily lives. At the moment, it is unclear whether regular treatment persists to have beneficial effects on cognition in patients with ADHD.

In addition, we currently do not know what the underlying mechanisms of the effects of WBV treatment on cognition are. These problems should be addressed in future research by examining the effect of WBV treatment in groups of patients with ADHD and by determining factors and underlying mechanisms of the effects of WBV on cognition.

In conclusion, the present study demonstrated for the first time prolonged beneficial effects of WBV on various aspects of cognition in a patient with ADHD. WBV treatment was shown to have long-lasting effects on cognitive performance (for at least 16 hours) and thereby emphasizes its potential for the treatment of patients with ADHD. Moreover, WBV is easy to apply and may not interfere with conventional treatment methods such as stimulant drug treatment. However, even though WBV was shown to considerably improve neuropsychological test performance of an adult with ADHD, it remains unknown to what extent the improvements as measured in neuropsychological tests can be generalized to cognitive functioning in daily life. Future research on the effects of WBV on cognitive functioning of patients with ADHD therefore appears necessary.
APPENDIX

Alertness
In the task for *tonic alertness* (Zimmermann & Fimm, 2002), participants were asked to respond as quickly as possible by pressing a button when a visual stimulus (a cross of about 1.2 by 1.8 cm) appeared on a computer screen. A total of 40 stimuli were undertaken. The mean reaction time and the variability of reaction time were calculated as measures of tonic alertness.

Distractibility
In *distractibility* task (*Incompatibility*, Zimmermann & Fimm, 2002), arrows pointing to the left or right were presented briefly on the left or right side of the fixation point in the center of the computer screen. The participants were requested to press a response button as quickly as possible on the side indicated by the direction of the arrow, independent of the position of the arrow. The number of errors (omission plus commission) was calculated as a measure of distractibility as the capacity to reject irrelevant information.

Divided attention
The *divided attention* task (Zimmermann & Fimm, 2002) required participants to concentrate simultaneously on a visual and an acoustic task presented by a computer. In the visual task, a series of matrices (consisting of a regular array of 16 dots and crosses (4x4)) was presented in the center of the computer screen. The participants were asked to press the response button as quickly as possible whenever the crosses form the corners of a square. In the acoustic task, the participants had to listen to a continuous sequence of alternating high and low sounds. The participants were requested to press the response button as quickly as possible when irregularities of the sequence occurred. The number of errors (omission plus commission) was calculated as a measure of divided attention.

Vigilance
In the task for *vigilance* (Zimmermann & Fimm, 2002), a horizontal bar was presented at the center of a computer screen. The horizontal bar continuously moved upwards and downwards from the center for irregular distances. A target stimulus was defined if the distance for which the horizontal bar moved upwards was considerably larger than in the majority of other movements. The participants were requested to press a response button as quickly as possible when a target event occurred. A total of 2800 stimuli (movements of the bar) were presented. The target rate was about one target stimulus per minute for a total of about 36 targets. The time intervals between target stimuli were irregular. The number of errors (omission plus commission) was calculated as a measure of vigilance.
The task measured vigilance by requiring the participant to remain alert and ready to react to infrequently occurring target stimuli over a relatively long and unbroken period of time.

**Flexibility**

In the flexibility task (Zimmermann & Fimm, 2002), participants were required to place each hand on a separate response button while viewing a computer screen, on which a letter and a digit number (of about 12 by 16mm) were displayed simultaneously. The distance between the letter and the digit number was 5 cm. The participant was instructed to respond by alternately pressing the button that was on the same side of the screen as the letter, and then pressing the button that was on the same side of the screen as the number (i.e. letter – number – letter – number etc.). After each response, a new letter and number appeared, randomly assigned to either side of the screen. A total of 100 trials were presented. The number of errors (omission plus commission) was calculated as a measure of flexibility.

**Working memory**

The Digit Span Backward task, a subtest of the Wechsler Memory Scale (Wechsler, 1987), was applied as measure of working memory. Series of numbers were read to the participants who were required to repeat the digits in the reversed order. The number of correctly repeated sequences was registered.

**Divergent thinking**

Divergent thinking was measured with a test for letter fluency (based on the Controlled Oral Word Association Test (Benton et al., 1989; Schmand et al., 2008)). In this test, participants were asked to produce, within one minute, as many different words as possible beginning with the same letter. This task was performed three times (three trials), each time with another letter for which words had to be produced. The total number of correctly produced words in all three trials was registered as a measure of letter fluency. Parallel versions of the test differed in the letters which have been used (K-O-M; D-A-T; P-G-R).

**Inhibition**

Inhibition was measured with the Stroop Color-Word Interference task (Houx, Jolles, & Vreeling, 1993; Stroop, 1935). The Stroop Color-Word Interference task consisted of two conditions. First, in the Color Block condition, colored rectangles (rectangles printed in yellow, green, blue and red) were presented on a card and the participants were required to name the color of the rectangles as fast as possible. Second, in the Color-Word
Interference condition, color words (YELLOW, GREEN, BLUE and RED) were presented and printed in mismatching ink (e.g. RED printed in blue ink). The participants were required to name the color of the words as fast as possible and to ignore the meaning of the printed word. Each condition consisted of the same number of stimuli. The time in seconds to complete each condition was registered.

Self-rated impairment of attention
The participants’ experienced problems of attention in the academic setting (i.e. studying, attending lectures) were measured with a sample of items taken from the Attention Questionnaire (Schepers, 2007). Participants were presented with eleven statements describing problems of attention (e.g. “Thoughts interfere with my concentration when attending a lecture”) and were asked to indicate how often these problems currently occurred compared to a normal (“average”) state. The scale ranged from 1 (far less often than normal) to 5 (far more often than normal). The sum score of all items was calculated as a measure of self-rated impairment of attention.
2.4 Public perceptions and beliefs towards adult ADHD: Stigmatization