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Megalographia in Children with Cerebellar Lesions and in Children with Attention-Deficit/Hyperactivity Disorder

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Abstract Structural changes of the cerebellum have been reported in attention-deficit/hyperactivity disorder (ADHD) in several studies. The cerebellum is a structure essential for motor coordination and motor learning. Beside behavioral deficits, children with ADHD often show slight motor abnormalities. In the present study, handwriting was examined in both children with ADHD and children with cerebellar lesions. By writing the same sentence several times, letter height increased in the ADHD and cerebellar groups but not in controls. Comparable disorders of handwriting in cerebellar and ADHD children support previous studies, which suggest a contribution of cerebellar dysfunction to motor abnormalities in ADHD. However, an involvement of non-cerebellar dysfunctions in ADHD cannot be excluded.

Keywords Attention-deficit hyperactivity disorder · Cerebellum · Handwriting · Megalographia

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Introduction

During the last three decades, structural and functional changes of the cerebellum have been demonstrated in several psychiatric disorders such as schizophrenia, autism, and dyslexia [1–4]. Likewise, a reduced volume of the cerebellum has been described in attention-deficit hyperactivity disorder (ADHD) [5, 6]. ADHD is a developmental disorder defined by inattention, motor hyperactivity, and impulsivity (Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR)) [7]. Beside behavioral deficits, about half of patients with ADHD exhibit minor motor abnormalities ("clumsiness") [8, 9]. Minor motor abnormalities may be caused by possible cerebellar dysfunction in patients with ADHD. This assumption is supported by the observation of comparable abnormalities in postural control and the timing of conditioned eyeblink responses in children with cerebellar lesions and children with ADHD [10, 11].

A further clinical sign of cerebellar dysfunction is megalographia, also called macrographia, that is an abnormally large handwriting. The first use of the term megalographia is ascribed to Robert Bing [12] by his scholar Marco Petitpierre [13]. Gordon Holmes [14] has already described letters "unequal in size and irregularly spaced" in the handwriting of patients with cerebellar lesions after gunshot injuries in World War I. Likewise, Andre Thomas [15] has stated that handwriting of cerebellar patients was larger than normal. However, Bing seems to be the first who noticed that the height of letters increases during writing and that this was a contrary effect to micrographia with decreasing letter sizes in Parkinson's disease. In ADHD poor handwriting performance characterized by illegibility [16] or reduced fluency is well known [17, 18]. Furthermore, higher speed, inaccuracy, and higher levels of axial pen pressure have been reported [19]. However, a possible megalographia in patients with ADHD has not been examined so far.

The aim of the present study was to investigate if handwriting abnormalities in ADHD can at least in part be explained by cerebellar dysfunction. For that reason, handwriting was tested in children with ADHD and cerebellar lesions and compared to controls.

Patients and Methods

Patients and controls participated in two previous studies [10, 11]. Patient characteristics will be reported only in brief. Ten boys with ADHD that matched the DSM-IV-TR (2000) [7] diagnostic criteria for the combined subtype of ADHD (mean age 12.3±1.3 (10–15) years), six patients with chronic surgical cerebellar lesions following astrocytoma resection (three male, three female; mean age 13.2±1.5 (11–15) years), and 11 healthy control subjects (nine male, two female; 12.1±1.8 (10–15) years) were included. None of the cerebellar children received adjuvant chemotherapy or cranial radiation. Diagnosis was confirmed by histological examination. All children with ADHD were treated with methylphenidate at the time of testing. All subjects and legal representatives gave informed written consent. The study was approved by the local ethical committee.

Mean total score of the international cooperative ataxia rating scale (ICARS) [20] was 8±5.6 (range, 0–14) in the cerebellar group and 1.5±3.2 (range, 0–10) in the ADHD group. Subscores concerning ataxia of upper extremities were 3.3±2.4 (range, 0–6) in the cerebellar group and 0.7±1.5 (range, 0–4) in the ADHD group. One child of the cerebellar and seven children of the ADHD group had normal ICARS scores. None of the control subjects showed total ICARS scores >0. Values in Conners' questionnaires [21] for the assessment of ADHD symptoms was abnormally high in ADHD children at the time of diagnosis (mean Conners' parents total T-score, 69±11 (abnormal, >60), mean Conners' teachers total T-score, 69±11). One patient with a cerebellar lesion showed increased values (Conners' parents total T-score, 69; Conners' teachers total T-score, 73), but mean scores of cerebellar patients were in the normal range (Conners' parents total T-score, 53±10; Conners' teachers total T-score, 53±11). In all control subjects, values were in the normal range (Conners' parents total T-score, 48±5; Conners' teachers total T-score, 48±7). Structural magnetic resonance imaging was performed in all participants and has been reported previously [10, 11].

All participants had to perform handwriting samples on conventional writing paper (8.5×11 in.) using a ballpoint pen. Subjects had to copy the sentence "Eine Katze guckt fröhlich in mein Zimmer" ("A cat looks happily in my room"). The target sentence was shown at the top of the paper. First, to make sure that subjects understood instruction correctly, a practice trial was performed. The practice trial was not included in the analysis. Next, subjects were asked to write the sentence four times, each sentence in a separate line. For analysis, seven letters of various types were selected: (1) two upper case letters ("K" in "Katze" and "Z" in "Zimmer"), (2) three lower case letters ("a" in "Katze," "o" in "fröhlich," and "m" in "Zimmer"), and (3) two lower case letters that are as tall as capital letters ("g" in "guckt" and "l" in "fröhlich"). Vertical extent of each of these letters was measured for each trial with respect to the sentence placement on the page.

For statistical analysis, a univariate repeated measures analysis was calculated using vertical extent of letters as dependent variable, block number (trials 1–4) and letter (positions 1–7 in the sentence) as within-subject factors, and group (ADHD vs. cerebellar vs. control group) as between-subject factor. In post hoc analysis, a univariate repeated measures analysis was calculated comparing ADHD and control group, cerebellar and control group, and ADHD and cerebellar group separately. In another post hoc analysis, univariate repeated measures analysis was calculated for each letter separately. The relationships between the scores of the ataxia rating scale and mean vertical extent of letters, and scores of Conners' scale and mean vertical extent of letters were assessed by means of linear regression analysis separately in each group.

Results

Figure 1 shows representative examples of handwriting and mean letter heights in a child with a cerebellar lesion, a child with ADHD, and a healthy control subject. Repeated measures analysis of variance revealed a significant block effect ($F(3,72)=11.82$, $P<0.001$), i.e., vertical extent of letters increased over the four blocks of handwriting (Fig. 2). Block-by-group effect ($F(6,72)=3.49$, $P=0.004$), reflecting differences between groups in increasing vertical extent of letters, and letter effect, reflecting the different height of the selected letters ($F(6,144)=92.85$, $P<0.001$), were significant. Group effect and all other interaction effects did not reach significance (P values >0.28).

In post hoc analysis, block-by-group effect was significant comparing ADHD and control groups ($F(3,57)=2.86$, $P=0.045$), comparing cerebellar and control groups ($F(3,45)=13.93$, $P<0.001$), but not comparing ADHD and cerebellar groups ($F(3,42)=0.84$, $P=0.48$), i.e., mean letter height increased over the four blocks of handwriting in the ADHD and cerebellar groups but not in controls. Block effects (P values <0.03) and letter effects (P values <0.001)

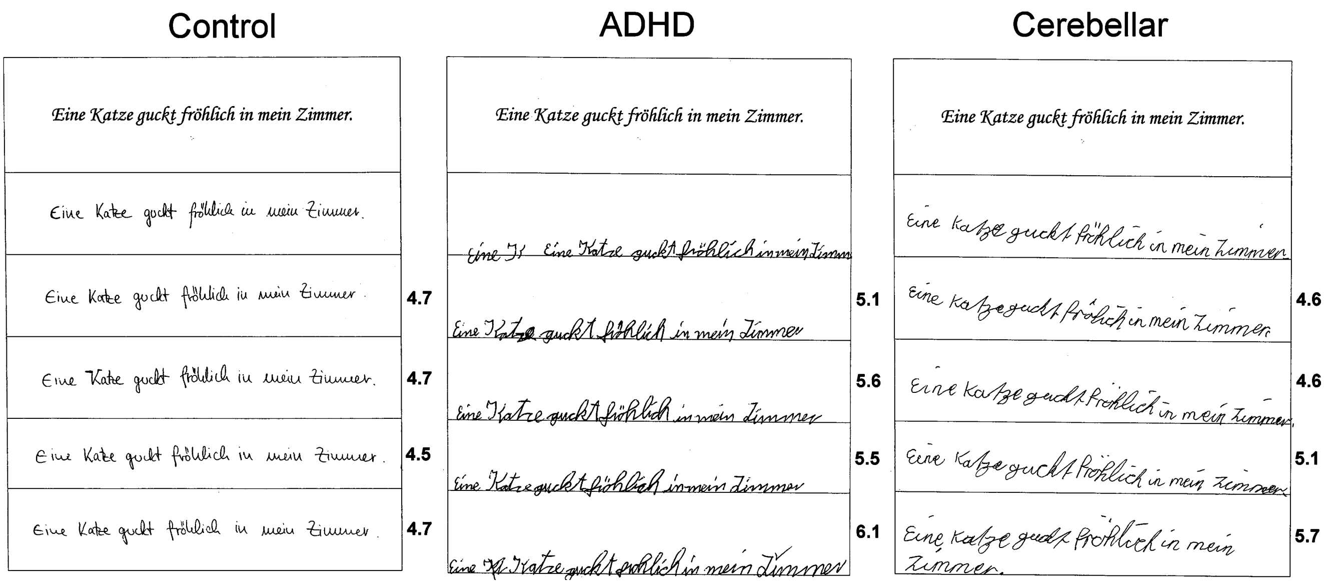

Fig. 1. Representative examples of handwriting from a child with a cerebellar lesion, a child with attention-deficit/hyperactivity disorder, and a healthy control subject. Mean letter heights in millimeter are written next to each line for each subject

were significant in these comparisons. All group effects and interaction effects were not significant (*P* values >0.07).

Separate analysis of each letter revealed for the last four letters in the sentence ("o", "l", "Z", and "m") significant block effects (*P* values <0.01) and for two of them ("l" and "m"), significant block-by-group effects (*P* values <0.03). All other *P* values for block, group, or block-by-group effect were not significant.

Linear regression analysis revealed no significant correlation of mean letter height with ICARS score, subscores concerning ataxia of upper extremities, or Conners' scores in children with cerebellar lesions, children with ADHD, or controls (*P* values >0.09). To exclude gender effects, univariate repeated measures analysis was performed with gender as covariate revealing no gender and no interaction effects (*P* values >0.3).

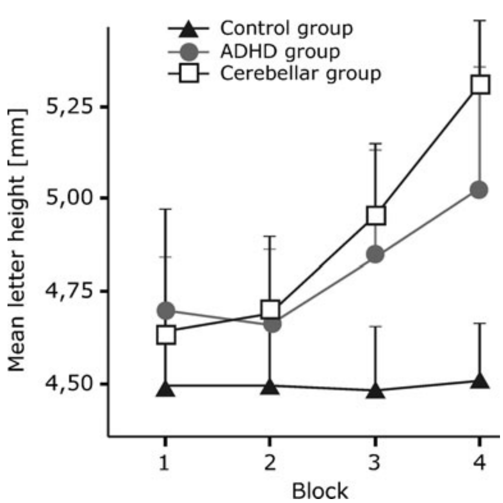

Fig. 2. Mean letter height±standard deviation of all seven analyzed letters over the four blocks in the group of all control subjects (*black triangles*), attention-deficit/hyperactivity disorder patients (*gray circles*), and cerebellar patients (*white squares*)

Discussion

In the present study, size of handwriting in children with ADHD was compared to children with cerebellar lesions and controls. Mean letter height was not different between groups. However, letter height increased during repeated writing of the same sentence in the ADHD and cerebellar groups but not in controls. Separate analysis of each of the selected letters revealed a significant increase only of the letters at the end of each sentence suggesting an increase of letter height not only across but also within each sentence.

Results of the present study are in accordance with the description of megalographia in cerebellar patients by Robert Bing [12], who did not only describe a larger size of handwriting but also an increase of letter height during writing. In contrast to micrographia in Parkinson's disease, descriptions of megalographia in literature are rare. Larger handwriting, but no increase of letter height, has been reported in patients with Huntington's disease, which mainly affects the striatum [22]. Another study reported larger handwriting in adults with high-functioning autism [23].

Autism, like ADHD, is a multifocal disorder. In both, dysfunction of the cerebellum, the striatum, and the frontal lobe have been described [3, 5]. Therefore, it cannot be excluded that non-cerebellar dysfunction, in particular, dysfunction of striatum and frontal lobe, contribute to macrographia in children with ADHD. However, comparable findings in cerebellar and ADHD patients suggest that cerebellar dysfunction explains at least parts of the observed megalographia in ADHD. Furthermore, in the same ADHD and cerebellar patients, comparable abnormalities were observed in a postural task and eyeblink conditioning [10, 11]. Because all children with ADHD were treated with methylphenidate at the time of testing, effects may be diminished. Methylphenidate results in more accuracy and better legibility of handwriting but also in decreased handwriting fluency [18].

The present finding of the comparable impairment in handwriting of children with cerebellar lesions and ADHD supports previous studies suggesting a contribution of cerebellar dysfunction to motor abnormalities in ADHD. However, an involvement of non-cerebellar dysfunctions in ADHD cannot be excluded.

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Conflicts of interest The authors reported no potential conflicts of interest. The authors have no financial disclosures.

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