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Examination of the role of physical activity in children with attention-deficit hyperactivity disorder

PHD THESIS ABSTRACT

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Acknowledgments:

I would like to express my gratitude to Prof. Dr. Judit Balázs for taking supervision of my doctoral program, and for helping me to carry through my planned research. I thank her for her perseverance, expert contribution and advice in helping me with my work over these years. Last but not least, I am thankful for her kindness and encouragement in supporting me through challenging situations.

I would also like to thank Dr. Judit Futó and Dániel Komáromy for their help in data processing and statistical work, thus raising the quality of my publication with their insights.

I would like to thank my fellow doctoral students, Dóra Szentiványi, Olga Lili Horváth, Szabina Velő for their joint work.

I am grateful to the parents and children involved in the research for their successful participation, dedicated time and enthusiasm in facilitating the successful completion of the study.

I would like to thank the principals and teachers of the schools in Budapest for giving me the opportunity to advertise the research, recruit the participants and provide an examination room for the children in the control group.

I would like to thank the colleagues working at Vadaskert Child Psychiatric Hospital and Outpatient Clinic for helping to recruit the clinical sample and for providing space for data collection. Special thanks to Dóra Sarolta Kis for her added support.

I would like to thank my family for their support throughout my doctoral program. I am especially grateful to my husband, Gergely Domokos, for helping me finish my work with his helpfulness, calmness and support.

List of own publications used in my dissertation[1]:

Miklós, M., Futó, J., Balázs, J. (2017). A fizikai aktivitás és a végrehajtó funkciók kapcsolata figyelemhiányos/hiperaktivitás zavar diagnózisú gyermekek körében. *Psychiatria Hungarica, 32*(1), 65-83.

Miklós, M., Futó, J., Balázs, J. (2019a). How Do Parents See? The Relationship between Sport Participation and Quality of Life among Boys with ADHD: A Cross-Sectional Study. *Psychology and Behavioral Science International Journal, 10*(5), 555796. DOI: 10.19080/PBSIJ.2019.10.555797

Miklós, M., Futó, J., Komáromy, D. Balázs, J. (2019b). Executive function and Attention Performance in Children with ADHD: Effects of Medication and Comparison with Typically Developing Children. *International Journal of Environmental Research and Public Health, 16*(20), E3822. DOI: 10.3390/ijerph16203822

Miklós, M., Komáromy, D., Futó, J., Balázs, J. (2020). Acute Physical Activity, Executive Function, and Attention Performance in Children with Attention-Deficit Hyperactivity Disorder and Typically Developing Children: An Experimental Study. *International Journal of Environmental Research and Public Health, 17*(11), 4071. DOI: 10.3390/ijerph17114071

Other related publications in connection with the topic, which are not included in my dissertation:

Kis, D. S., **Miklós, M.**, Fűz, A., Farkas, M., Balázs, J. (2017). A „Fészek": A Vadaskert Gyermekpszichiátriai Kórház és Szakambulancián működő kognitív-viselkedésterápián alapuló program bemutatása. *Psychiatria Hungarica, 32*(4), 423-428.

Szentiványi D., Halász, J., Horváth, L. O., Mészáros, G., **Miklós, M.**, Miklósi, M., Velő, Sz., Vida, P., Balázs, J. (2017). Externalizáló zavarok tüneteit mutató gyermekek életminősége a gyermek saját szemszögéből és a gondviselője megítélése szerint. *Psychiatria Hungarica, 32*(3), 332-339.

[1] The coauthors of the listed publications have consented to the use of the publications in my dissertation.

1. Introduction

1.1. Attention-deficit hyperactivity disorder (ADHD)

Attention-deficit hyperactivity disorder (ADHD) is one of the most common child psychiatric disorders, with a prevalence of 4-12% in the 6-12-year-old age group (Goldman et al., 1998; Brown et al., 2001). The symptoms of ADHD are presented under the "Neurodevelopmental Disorders" section in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5, American Psychiatric Association, 2013).

Although the relevance of several factors has been identified in the development of ADHD, its etiology has not been fully discovered. Previous studies found the role of the frontal regions of the brain, specifically to the prefrontal cortex function in the aetiology of ADHD (Benton, 1991; Heilman et al., 1991). Dysfunctional levels of certain neurotransmitters were also registered in ADHD (Levy, 1991). Abnormal dopamine and noradrenaline levels have been displayed in the prefrontal cortex, an area where abnormal structure and function may be responsible for certain ADHD-like symptoms, such as the lack of inhibition regarding attention and executive control function (Sharma and Couture, 2014, review study). Accordingly, medications with sympathomimetic effect, such as methylphenidate, amphetamine, or atomoxetine, which increase dopamine and noradrenaline levels in the prefrontal cortex, are often used in the treatment of ADHD (Zuvekas et al., 2006; Sharma and Couture, 2014).

Up until now, the combination of certain evidence-based non-medicated (Chronis et al., 2006; Jones and Chronis-Tuscano, 2008; Young and Amarasinghe, 2010) and medicated treatments (Wernicke and Kratochvil, 2002; Brown et al., 2018) is the most effective method in the treatment of the symptoms of ADHD (Goldman et al., 1998; Jensen et al., 2001; Pelham and Fabiano, 2008). The initiation of these treatments is recommended for several reasons, i.e. studies have demonstrated lower levels of quality of life in children and adults with ADHD compared to healthy controls, which can be improved with effective treatment (Danckaerts et al., 2010).

1.2. ADHD, executive functions and other indicators of attentional performance

Similarly to Barkley's theory (1997), many researchers hypothesize the abnormal functioning of executive functions in ADHD (Schachar et al., 1995; Sjöwall et al., 2013), leading to a greater incidence of hyperactive, impulsive, and inattentive behaviours and social problems (Douglas, 1991; Pennington and Ozonoff, 1996; Kofler et al., 2011).

Numerous studies support the impairment of executive functions in ADHD, including working memory, inhibition, planning and strategy creation (e.g., Rapport et al., 2008; Kofler et al., 2011; Sonuga-Barke et al., 2002; Oosterlaan and Sergeant, 1996; Clark et al., 2000). Contrary to the results of these studies, many other researchers question the central role of the impairment of executive functions in the disorder (e.g., Doyle et al., 2000; Boonstra et al., 2005; Nigg et al., 2005; Willcutt et al., 2005). These studies illustrate that there is no comprehensive consensus on the impairment of executive function in ADHD among researchers, which may be due to the use of different measurements examining the same executive function, or the use of diverse research designs. The reliability of the applied tests (tasks measuring executive functions) is also questioned (as not every study reports it), as well as the low sensitivity and limited discriminative ability of tests measuring executive functions (Doyle et al., 2000).

Besides examinations of executive functions, studies have found evidence of the involvement of other cognitive abilities in ADHD, such as alertness (Cao et al., 2008; Abramov et al., 2019), distractibility (Gumenyuk et al., 2005; Cassuto et al., 2013), divided attention (Karatekin, 2004; Fuggetta, 2006) and cognitive flexibility/switching (Lawrence et al., 2004; Toplak et al., 2009). In contrast, other studies did not report serious impairment in these abilities (e.g., the ability of alertness, Tucha et al., 2006; divided attention, Elosúa et al., 2017; flexibility/switching, Goldberg et al., 2005) as it was demonstrated regarding specific executive functions mentioned above.

1.3. ADHD and physical activity

Examining healthy individuals, several studies reported that physical activity increases prefrontal cortex activity (in both children and adults) (Yanagisawa et al., 2010; Basso et al., 2015; Mücke et al., 2018), blood flow (Jørgensnen et al., 1992), the level of catecholamines (Winter et al., 2007; Zouhal et al., 2008; Rethorst et al., 2009) and growth factors (brain-derived neurotrophic factor, BDNF) (Zoladz and Pilc, 2010; Walsh and Tschakovsky, 2018 ; Pedersen, 2019). Due to these immediate biological and neurochemical changes, cognitive function is enhanced by acute physical activity, while morphological changes occur in chronic physical activity in areas of the brain that play an important role in learning (Best, 2010). All these biological processes (that is, the molecular-level mechanisms of the functioning of the brain) are related to learning, cognition and memory (Glikoroska and Manchevska, 2012). Beneficial biological and physiological changes due to physical activity thus affect the brain and cognitive functions, and also promote well-being (Mandolesi et al., 2018).

Individuals diagnosed with ADHD are characterized by diverse functioning of the aforementioned biological processes and dysfunctional levels of catecholamines and BDNF (Durston and Konrad, 2007; Arnsten, 2009; Lee et al., 2005; Pliszka, 2005; Sharma and

Couture, 2014; Tsai, 2007). Physical activity can reduce the symptoms of ADHD based on the physiological changes it induces, as it has the same mechanisms as stimulant medication (Wigal et al., 2013). Therefore, it is possible that physical activity may exert physiological, neurochemical and, consequently, cognitive functional changes in individuals diagnosed with ADHD, similar to those in healthy individuals, as their prescribed medication moderates the symptoms of ADHD (Hazell et al., 2011), and therefore improves attention and executive functions (e.g., Barnett et al., 2001; Kempton et al., 1999), among others.

1.4. ADHD, quality of life and physical activity

The definition of the World Health Organization (WHO) about quality of life includes the individual's perception of his or her own life situation in the cultural and systemic context in which he or she currently lives (The World Health Organization Quality Of Life Group, 1995). Concerning ADHD, research findings are inconsistent about the areas in which children diagnosed with ADHD rate their quality of life worse than children in the control group (Klassen et al., 2006; Marques et al., 2013). The possible reasons of this inconsistency may be the different measurements applied and also due to the age group of the sample. The importance of information from both sources (that is, child and parent) is highlighted in a study by Klassen et al. (2006), which examined the degree of agreement between parents and their children diagnosed with ADHD regarding physical and psychological areas. The different ratings given by children with ADHD and their parent may be the result of different response styles, whereby children rate with extreme scores more frequently than their caregivers (Davis et al., 2007). In addition, it is important to emphasize that the disorder may not only affect the children's, but also their parents' and siblings' quality of life (Harpin, 2005).

The research of Gapin and Etnier (2014) can be highlighted in that it was the first to examine parents 'perceptions of the effect of physical activity on their children's symptoms of ADHD. The parents' evaluations showed that physical exercise did not have the same effect on all symptoms; it mostly affected inattentive and hyperactive symptoms in a positive way rather than the symptoms of impulsivity.

To the best of my knowledge, up until now there is only one research that analyzed the relationship between physical activity and quality of life. A study by Gallego-Méndez and colleagues (2020) examined the relationship between health-related quality of life and the intensity of physical activity in children diagnosed with ADHD, based on their parents' ratings. Their results showed a positive, significant relationship between the frequency of physical activity and health-related quality of life when examining a sample of children aged 8-14 years.

Furthermore, the parents of children who did not engage in regular sports activity rated their children's health-related quality of life significantly worse than parents with more physically active children (Gallego-Méndez et al., 2020).

1.5. ADHD, physical activity and executive functions

Generally, two forms of physical activity are distinguished and applied in different studies: chronic or acute physical activity (Verburgh et al., 2014). Chronic physical activity includes multiple and prolonged activities, while acute physical activity includes a single, short-term activity (most commonly between 10 and 40 minutes) (Verburgh et al., 2014). In our non-systematic study, we presented 7 studies using chronic and 6 studies using acute physical activity (Miklós et al., 2017). In my doctoral dissertation, additional research using chronic and acute physical activity is presented, published since 2017.

Overall, all but one (Jensen and Kenny, 2004) of the collected 11 studies using chronic physical activity were able to show improvement in at least one area of executive function following long-term physical exercise programs. Of the 11 studies, four showed improvement in inhibition (Chang et al., 2014; Smith et al., 2013; Memarmoghaddam et al., 2016; Pan et al., 2019) and three in task switching (Kang et al., 2011; Pan et al., 2019; Silva et al., 2019). Two studies registered better performance on processing speed (Kang et al., 2011; Verret et al., 2012), sustained attention (Verret et al., 2012; Chou and Huang, 2017), and selective attention (Chou and Huang, 2017; Silva et al., 2019). One study measured improvement in planning and verbal working memory (Gapin and Etnier, 2010), while another showed better performance regarding discrimination skills (Chou and Huang, 2017).

Concerning research using acute activity, it was found that in ten out of twelve studies, at least one of the measured attention or executive functions showed improvement (Medina et al., 2010; Chang et al., 2012; Pontifex et al., 2013; Chuang et al., 2015; Piepmeier et al. et al., 2015; Hung et al., 2016; Gawrilow et al., 2016; Ludyga et al., 2017; Benzing et al., 2018; Ludyga et al., 2020). Seven out of these ten studies demonstrated improvement in inhibition besides the other executive functions measured (Chang et al., 2012; Pontifex et al., 2013; Chuang et al., 2015; Piepmeier et al., 2015; Gawrilow et al., 2016; Ludyga et al., 2017; Benzing et al., 2018). This finding, in turn, may suggest a selective effect of acute physical activity on executive functions, of which inhibitory functions presumably benefit the most.

2. Objectives and hypotheses

In my dissertation, the hypotheses of the examinations concerning my three doctoral topics are the following:

2.1. In the first examination of my doctoral dissertation (Examination 1: E1), we examined the relationship between parental-rated quality of life and regular physical activity in a sample of non-medicated boys diagnosed with ADHD, as well as potential predictors of quality of life. The subject of our study was furthermore the parental self-esteem from the perspective of their children's regular sports activities (Miklós et al., 2019a). I assumed that:

- Non-medicated boys with ADHD who participate in regular sports activities have a better quality of life and fewer behavioural problems than boys with ADHD and without medication who do not engage in regular sports activities, as rated by their parents.
- The parents of boys who do engage in regular sports activities report higher levels of self-esteem compared with those parents whose sons do not engage in regular physical activity.
- The children's problematic behaviour, the severity of attentive and hyperactive/impulsive symptoms (both based on parental estimation) and the parents' self-esteem are predictors of the children's quality of life, as rated by the parents.
- The frequency (hours per week) of sports activity predicts the children's quality of life, as assessed by the parents.

2.2. As a next examination (Examination 2: E2) of my doctoral dissertation, we compared baseline attention and executive function performance between three study groups: a) non-medicated, b) medicated children with ADHD, and c) typically developing control children (Miklós et al., 2019b). I assumed that:

- In all study parameters (performance indicators of alertness, distractibility, divided attention, flexibility, and go/no-go subtests), non-medicated children diagnosed with ADHD perform worse than medicated children with ADHD and typically developing children.
- The performance of the medicated ADHD group do not differ from that of the typically developing group in any of the assessed attention and executive function parameters.

2.3. Finally (Examination 3: E3), we examined the potential effect of acute physical activity on the aforementioned attentional and executive functions in members of the non-medicated and medicated ADHD and the typically developing groups (Miklós et al., 2020). As described in section 1.3. (“ADHD and physical activity”), the results of different studies concerning the effects of physical exercise in healthy individuals, as well as the diverse brain processes and sub-optimal level of neurochemical factors in people with ADHD, as described above, suggest that physical activity may have a beneficial effect on both physiological and physiological parameters in individuals diagnosed with ADHD. Therefore, it is possible that physical activity can improve cognitive and learning abilities to a level of functioning very similar to that of typically developing individuals. Since the effects of physical exercise on physiological parameters are very similar to the pharmacological mechanisms of stimulant medications (Wigal et al., 2013), it can be hypothesized that physical activity may exert similar physiological, neurochemical and, consequently, cognitive functional changes in medicated individuals with ADHD as in healthy individuals. Accordingly, I assumed that:

- The children of all three study groups perform better after physical activity, compared to the video-watching control intervention, in the measured attention and executive function parameters.

3. Method

3.1. Ethical permission, information about the research and consent

The research presented in my dissertation was approved by the Ethical Committee of the Medical Research Council, Hungary (ETT-TUKEB-5677-1 / 2016 / EKU [89/16]) on 25 January 2016, followed by its extension (ETT- TUKEB-7406-5 / 2017 / EKU). All of the children and their parents took part in this research voluntarily, after being informed about the nature of the study and subsequently providing written consent.

The study was carried out with support from the Hungarian Scientific Research Fund (Hungarian abbreviation: OTKA, No: K-108336).

3.2. Design and procedure

The research design is illustrated in Figure 1.

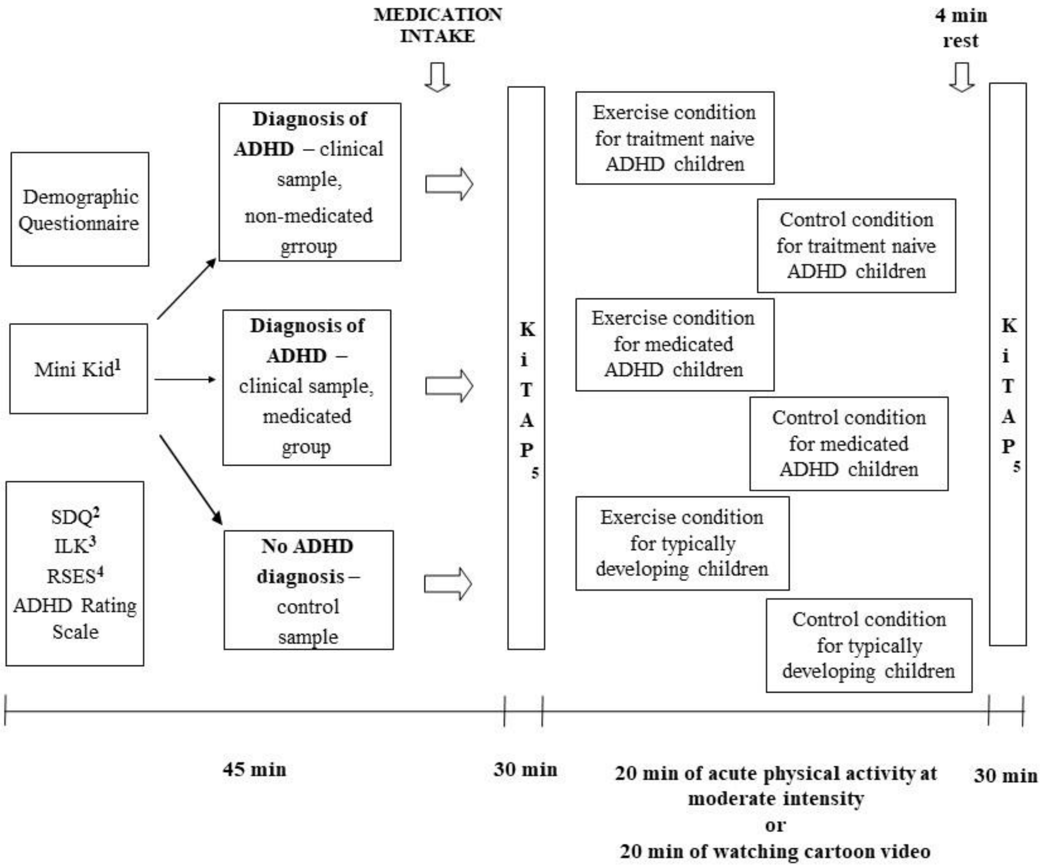

Figure 1. Study design.

MINI Kid[1]: Mini International Neuropsychiatric Interview for Children and Adolescents, SDQ[2]: Strength and Difficulty Questionnaire, ILK[3]: Inventar zur Erfassung der Lebensqualität bei Kindern und Jugendlichen, RSES[4]: Rosenberg Self-Esteem Scale, KiTAP[5]: child version of the Test of Attentional Performance (or Testbatterie zur Aufmerksamkeitsprüfung für Kinder)

The experimental procedure consisted of 5 stages: 1) information provision and consent (also in E1, E2 and E3); 2) diagnostic and questionnaire phase (in E1, E2 and E3: MINI Kid, Demographic Questionnaire; in E1: SDQ, ILK, RSES, ADHD Rating Scale); 3) pre-test (first neuropsychological test session with KiTAP) (for E2 and E3); 4) interventions (physical activity or video-watching control intervention) (only in E3); 5) post-test (second neuropsychological test session with KiTAP) (only in E3).

Previously, the experimental condition, the participants' resting heart rate and blood pressure were recorded. If the measured values met the inclusion criterion, the minimum and maximum target zones of physical activity were calculated, using 60% and 80% of the maximum heart rate (HRmax= 220-age, She et al., 2015; Riebe et al., 2017). This recommendation about the protocol of intensity and physical activity was provided by the head of the Performance

Diagnostics Research Department of the National Sports Medical Institute (Sports Hospital) in Budapest, Hungary. Accordingly, we calculated the minimum target range using the formula (220 - age) x 0.6 and the maximum target range using the formula (220 - age) x 0.8 for each child. Intensity was maintained between these two target values during the activity phase. For this purpose, heart rate was measured during the entire workout with a heart rate monitor chest strap, fastened on the child's chest. The average heart rate during activity was 140.57 BPM (*SD*= 5.92 BPM), which was related to the average intensity at 66.79% (*SD*= 2.91, Min= 60%, Max= 72%), which demonstrates moderate intensity. There was no significant difference between the groups in terms of mean heart rate ($F(2, 72) = .43$, $p > .05$).

The running workout was carried out as an interval training, in which a total time of 20 minutes was divided into 4 × 4-minute periods, with 1 minute slow walking "breaks" between each period. During this physical activity phase, children watched two parts of a 20-minute cartoon series, the same episodes of "Penguins of Madagascar" as participants in the control intervention.

Participants in the control intervention watched the same parts from the "Penguins of Madagascar" as children in the exercise condition, for 20 minutes, while seated.

3.3. Participants

A total of 168 children aged 6 to 12 years were included in the study (E1, E2, and E3). Data collection was carried out from February 2016 to February 2018. The analyses included data from two clinical and one control groups. Convenience sampling was used for all three study groups.

The children participating in the clinical sample were recruited at Vadaskert Child Psychiatric Hospital and Outpatient Clinic in Budapest, Hungary. The control group consisted of typically developing children from elementary schools in Budapest.

Inclusion criteria for the clinical sample included: a) children between 6 and 12 years of age; b) ADHD diagnosis established by a structured diagnostic interview. The clinical sample included two subgroups: 1) a group of children with ADHD never treated with any psychotropic medication, and 2) a group of children with the diagnosis of ADHD receiving adjusted and ongoing medication.

Children from the non-medicated group were seeking professional help for the first time at Vadaskert Child Psychiatric Hospital and Outpatient Clinic. The experimental part of the research could be completed before the child's psychiatrist could recommend the initiation and adjustment of medication treatment regarding ADHD. For this type of clinical group, inclusion criteria also featured the lack of any former treatment with methylphenidate or atomoxetine. In contrast, subjects in the medicated clinical sample had to receive ongoing and adjusted medication (either methylphenidate or atomoxetine) at the time of the experimental progress.

For the control (i.e. typically developing) group, the following inclusion criteria were defined: a) age of 6-12 years; b) lack of previous psychological or psychiatric treatment (stated in the Demographic Questionnaire by the parents) and c) the absence of an ADHD diagnosis, based on the structural diagnostic interview.

For all three study groups, the exclusion criteria were the following: a) intellectual disability or autism spectrum disorder indicated in the medical history or established retrospectively; b) refusal to perform the required tasks and related oppositional behaviour; c) ongoing illness (e.g., abdominal pain, diarrhea); d) current use of other medication(s) (e.g., tiapride, risperidone); e) incomplete diagnostic interview, and f) indication of previous psychological or psychiatric treatment for control children.

In the case of E3, in addition to the above, children with a medical history of a) congenital or acquired heart disease, or b) any other cardiovascular disease, c) asthma and/or diabetes were excluded from the experimental (physical activity) part of the study. Furthermore, children with a resting heart rate above 110 BPM and/or a blood pressure above 130/80 mmHg at baseline were not eligible to participate in the physical activity intervention.

3.3.1. Description of the sample for E2 and E3

In E2 and E3, the data of 50 non-medicated children with ADHD (45 boys and 5 girls, *M*= 8.26 years, *SD*= 1.47, 6-11 years of age), 50 medicated children with ADHD (47 boys and 3 girls, *M*= 9.70 years, *SD*= 1.78, 6-12 years of age) and an additional 50 typically developing children (43 boys and 7 girls, *M*= 8.68 years, *SD*= 1.41, 6-11 years of age) were processed. The total sample consisted mostly of boy participants (135 boys and 15 girls). There was a significant difference between the groups in terms of age ($F(2, 147)= 11.29$, $p<.001$).

In the non-medicated clinical sample, 40 children (80%) were diagnosed with the combined type, 8 children (16%) with the predominantly inattentive type and 2 children (4%) with the predominantly hyperactive/impulsive type of ADHD. From the medicated clinical group, 48 (96%) children had the combined type, 1 child (2%) the predominantly inattentive type and also 1 child (2%) the predominantly hyperactive/impulsive type of diagnosis.

Due to the low prevalence of individuals with the predominantly inattentive and hyperactive/impulsive type of ADHD diagnosis, we only compared the combined type of diagnosis between the two clinical groups with Pearson’s chi-square test and Yates continuity correction. This yielded a significant difference between the two groups ($\chi^2(1) = 4.60$, $p= .03$) regarding this type of ADHD. Thus, there were more children with a combined type of diagnosis in the medicated than in the non-medicated group.

Of the medicated group, 43 children (86%) used methylphenidate treatment, whereas 7 participants (14%) received atomoxetine during the study. The average dosage of methylphenidate was 15.70 mg (*SD*= 7.68), while the average dose for atomoxetine was 39.29 mg (*SD*= 15.66).

3.3.2. Description of the sample for E1

In our first examination (E1), data from 45 boys between the age of 6 and 11 years (*M*= 8.24, *SD*= 1.48) with a diagnosis of ADHD were included from the non-medicated clinical group presented in E2 and E3. Of the treatment-naïve boys with ADHD, 24 engaged in regular sports activity, while 21 did not engage in any sports activity. Sports activity was considered regular if the child had been participating in sports activity for at least a month before his participation in the study, as stated by the parent in the Demographic Questionnaire. There was no significant age difference between the two groups (*U*= 249.50, *Z*= -.06, *p*= .95).

3.4. Measurements

3.4.1. Mini International Neuropsychiatric Interview for Children and Adolescents (MINI Kid) – in E1, E2 and E3

Throughout the research, the Hungarian version of the Children’s Mini International Neuropsychiatric Interview for Children and Adolescents (Child MINI) (Lecrubier et al., 1997; Sheehan et al., 1997; Sheehan et al., 1998; Balázs et al., 2004; Sheehan et al., 2010) was applied to establish (in the case of the non-medicated and medicated ADHD group) and to exclude (as for the control group) the diagnosis of ADHD. For the medicated group, we asked retrospectively about the symptoms of ADHD prior to medication treatment, so the diagnosis was “re-established” at the time of the study.

The Hungarian adaptation of the questionnaire was developed by Balázs and colleagues (2004). Their examination showed an adequate inter-rater and test-retest reliability of the questionnaire for the analyzed psychiatric disorders. The criterion validity of the instrument also proved to be acceptable, when examined with both sensitivity and specificity values (Balázs et al., 2004).

During the study – according to the instructions of the MINI Kid –, children participated in the interview together with their parents, as the presence of a parent is required for admission under the age of 13, who can thus help the child to respond (Balázs et al., 2004; Sheehan et al., 2010).

The interviewer had to attend a short MINI Kid training, after which he/she is able to use the structure diagnostic interview with adequate expertise and confidence.

3.4.2. Inventar zur Erfassung der Lebensqualität bei Kindern und Jugendlichen (ILK) – in E1

We used the Intervertar Lebensqualität Kindern und Jungendlichen (ILK) questionnaire to assess children's quality of life (rated by parents), which was validated by Mattejat and Remschmidt (1998) on a sample of populational and psychiatric patients in Germany.

As a result of the validation of the Hungarian version of ILK, an appropriate Cronbach α value was found concerning the internal reliability for all three versions (child, adolescent, parent) (Kiss et al., 2007). The reliability of the test-retest was also acceptable.

In the parental version, caregivers complete the questionnaire regarding their child's quality of life. In this version (similar to the one designed for children), besides the general quality of life, 6 specific areas are assessed in ILK: school, family, peer relationships, time spent alone, physical health, and mood (Kiss et al., 2007). In the case of a clinical sample, questions assessing the burden caused by the disease or problem, the clinical examinations and treatments are also estimated in the two versions. It should be emphasized that lower values in both versions indicates better quality of life.

The fifth item was found to be different from the rest in the questionnaire, which was supported by its low item-total correlation (r=.15). After excluding this fifth item, the Cronbach α value of .79 indicated an appropriate level of reliability for ILK.

3.4.3. Strength and Difficulty Questionnaire (SDQ) – in E1

The Strength and Difficulty Questionnaire (SDQ) was used to assess the children's problematic behaviour, based on parental ratings. SDQ was developed by Goodman (2001) to examine children's emotional and behavioural characteristics and abilities (prosocial behaviour) between 3 and 16 years.

Each version of the questionnaire (self-administered, parental and teacher version) included 25 items, divided into 5 subscales: Hyperactivity, Emotional Symptoms, Behavioural Problems, Peer Relationship Difficulties and Prosocial Behaviour (Goodman, 2001).

The SDQ problem score can be calculated by the sum of the subscale scores, except for the prosocial subscale. A higher SDQ problem score suggests a higher degree of problematic behaviour.

The validation of the Hungarian version was performed by Turi et al. (2013). The values providing information about the internal consistency of the SDQ subscales ranged from moderate to adequate.
The diagnostic discriminative ability of the Hungarian version also proved to be adequate when comparing clinical with control groups. Therefore, the applicability of the questionnaire was verified to be suitable for clinical sample as well.
In our analysis, the instrument showed a Cronbach α value of .73, supporting the reliability of the questionnaire.

3.4.4. Rosenberg Self-Esteem Scale (RSES) – in E1

Parental self-esteem was estimated by the Rosenberg Self-Esteem Scale (RSES), which is an accepted instrument of global self-esteem (Rosenberg, 1965; Schmitt and Allik, 2005). According to the psychometric examination of the alternative Hungarian translation of the questionnaire (RSES-H), the internal consistency of the measurement was qualified as adequate (Sallay et al., 2014). The questionnaire contains 10 statements that need to be answered on a four-point Likert scale. A higher score equals a higher degree of self-esteem.
The reliability of the instrument was found to be adequate (Cronbach α= .91) in our analysis.

3.4.5. ADHD Rating Scale – in E1

The severity of the two main symptoms of ADHD (inattention, hyperactivity/impulsivity) was estimated using the ADHD Rating Scale developed by DuPaul in 1998. This included 18 items, which can be divided into two subscales: Inattention and Hyperactivity/Impulsivity. The presence of more severe symptoms is indicated by higher total scores. The questionnaire can be filled in by a parent or teacher. The validation made by Faries et al. (2001) was based on evaluation by clinicians. It yielded acceptable levels of inter-rater and retesting reliability, internal consistency, convergent and discriminant validity and sensitivity.
The questionnaire had an appropriate Cronbach α value in our analysis (Cronbach α= .91), confirming its reliability.

3.4.6. Demographic Questionnaire – in E1, E2 and E3

The demographic characteristics of study participants were registered using a unique demographic data sheet that was created specifically for this research.

3.4.7. Test of Attentional Performance for Children (Testbatterie zur Aufmerksamkeitsprüfung für Kinder, KITAP) – in E2 and E3

The Child of Attentional Performance Test (KITAP) was chosen to measure attention and executive functions. KiTAP is a computer-based continuous performance test (Kaufmann et al., 2010; Psychologische Testsysteme, 2011) developed for the same consideration as the adult version, namely, to examine the level of attention and executive function in adults with brain injury. Therefore, it corresponds to the pediatric version of the original test battery (Zimmermann et al., 2005).

The test battery contains 8 tasks, of which 5 were included in the present study: Alertness, Distractibility, Divided attention, Flexibility and Go/no-go. These subtests were chosen because of their shorter execution time, so we were able to maintain children's motivation throughout the whole study.

For each task, it is possible to complete a pre-test, during which the research assistant can make sure that the child has understood the task.

3.4.8. Equipment/instruments used for physical activity and control intervention – in E3

Acute physical activity was performed on a DOMYOS TC7 treadmill in E3. During the workout, continuous heart rate measurement and recording was warranted, using a Polar H7 HR Sensor Wearlink Bluetooth chest transmitter and its associated application, which was placed on the participants' chest during the session of physical activity. Children watched two episodes of the cartoon movie "Penguins of Madagascar" on an iPad, both during the running intervention and in the control condition as well.

3.5. Statistical analyses

3.5.1. Statistical analysis of E1

Regarding E1, statistical analyses were performed using IBM SPSS Statistics 22.0.0. First, we examined the distribution of numerical variables using the Kolmogorov-Smirnov test, which showed a normal distribution of all variables, except for the number of hours spent with sports activity (hours per week).

An independent sample t-test was used for the hypothesis of whether the parents of boys who engage in regular sports activity report a better quality of life and fewer behavioural problems than the caregivers of boys whose children do not engage in regular sports activity.

Further, we examined whether higher global parental self-esteem is declared if the son participates in regular sports activity. The child's total quality of life indicator was derived from the average of the sum of items 1, 2, 3, 4, 6 and 7, as these items proved to be relevant to the quality of life of the children, when examining the reliability of the questionnaire. The parental ratings of the children's quality of life were used in the statistical analysis. The fifth item was found to be different from the rest of the items included in ILK, which fact was confirmed by its low item-total correlation (r= .15).

Multiple regression analysis (stepwise model) was applied to examine the potential predictors of children's quality of life, as assessed by the parent, in which case the condition of multicollinearity was still acceptable.

Subsequently, we used a Univariate of Analysis of Variance, to analyze the effect of the SDQ problem score and regular sports activity on quality of life. In the analysis, the condition of standard deviation homogeneity was verified (Levene's test, p= .65).

Finally, we examined the effect of the frequency of regular physical activity (number of hours per week) on the children's quality of life, as rated by the parent, based on linear regression analysis (enter procedure). The condition for both homoscedasticity and the normal distribution of error terms (Kolmogorov-Smirnov test, p= .20) was verified.

3.5.2. Statistical analysis of E2

Statistical analyses for E2 were performed using the R program (version 3.5.1, R Foundation for Statistical Computing, Vienna, Austria).

Among the parameters of the applied KiTAP subtests, the number of errors and omissions, as well as the median and standard deviation (variability) of the reaction time were analyzed, as suggested by Zimmermann et al. (2005).

On the raw data of the median and standard deviation of the reaction time, Shapiro and Bartlett's test was used to test normality and homogeneity. In case of the normality assumption, we used Tukey power transformation. ANOVA analyses were mainly estimated on the Tukey-transformed data. After estimating these models, the Global Validation of Linear Model Assumptions (GVLMA) package was used to inspect possible assumption violations (Pena and Slate, 2019). Next, the following control variables were added: gender, age, mother's education level, father's education level and the number of months spent doing sports. After adding these control variables, the best-fitting model was selected using stepAIC (executing stepwise model selection based on the Akaike Information Criterion) from the MASS package (support for functions and databases contained in the 4th edition of "Modern Applied Statistics with S" [Venables and Ripley, 2002]). In this manner, all models were estimated, by both forward and backward selection, and the best-fitting model was chosen, based on the lowest Akaike

Information Criterion. The group and age variables were kept in all models, as the former was our focal predictor in this study. On the other hand, we had to address the significant age difference between the groups, so the age variable was controlled in all regressions. As a next step, we tested the linear model's assumptions. Post hoc tests were performed by Tukey's honestly significant adjustment (HSD): pairwise comparisons of the groups were made, and the means of the non-medicated group were compared with the means of the medicated and control groups.

Generalized linear models were used to examine the number of omissions and errors. For all dependent variables, the dispersion parameter was higher than unity, hence we preferred applying negative binomial regressions over Poisson regressions. Next, we tested multiple model specifications. First, we compared the fit of the linear versus quadratic variance functions. Subsequently, due to the large number of zero values measured for the dependent variable, we examined zero-inflation. In addition to the Akaike and Bayesian information Criterion, the comparison of the model fits was based on the likelihood ratio test. Then, from the best-fitting model, the variable parameters of the group were estimated. The next step was to evaluate the group effect and perform the three post hoc tests, using Tukey's HSD correction. Then, based on the significance levels and the Akaike Information Criterion, the control variables listed above were added, followed by a re-evaluation of the group effect and the post hoc testing phase for this larger model. Finally, we compared the data of the non-medicated group with the means of the medicated and control groups.

After estimating the 15 models, we controlled the family-wise error to reduce the chance of the first type of error. Concerning this, we chose the Benjamini and Yekutieli method (Benjamini and Yekutieli, 2001).

3.5.3. Statistical analysis of E3

Statistical analyses of the data from E3 were performed using the R program (version 3.5.1, R Foundation for Statistical Computing, Vienna, Austria).

In the first round, outlier detection was implemented on the bivariate dataset (pre- and post-intervention). The Mahalanobis distance (MD) was used, which measures the extent to which cases are multivariate outliers, based on a Chi-squared distribution.

Second, for each group intervention-combination, density functions were plotted to examine the distribution of each dependent variable, and descriptive statistics were estimated. For continuous variables (median and standard deviation of reaction time), Tukey power transformation was used to reduce the likelihood of having non-normal residuals in the models.

Third, we estimated the mixed-effect models that explain both between-subject factors (group membership and type of intervention) and within-subject variation. The latter was obtained by adding a random intercept to the models, which was calculated for each participant. For the median and standard deviation of the reaction time, Gaussian distributed generalized linear mixed-effect models (GLMMs) were used. After running the regression models, we checked the related diagnostics. Normality violation and heteroscedasticity were checked by visual inspection and, if necessary, by Shapiro-Wilk's and Levene' test.

Poisson or negative binomial distributed generalized linear mixed-effect models were applied to analyze the number of omissions and errors. After estimating the Poisson models, we completed a test to determine potential overdispersion and zero-inflation. In case the overdispersion test was significant, or if the Poisson model did not converge, a negative binomial model was used. If there was still overdispersion in the model, it was modelled by groups (assuming that the overdispersion parameter is not identical for each participant, but is a function of the group membership). When zero-inflation was present in the model, first we modelled it as if it was the same for all participants. If the first step did not lead to an acceptable result, it was modelled as a function of group membership.

Fourth, marginal means were estimated using the Kenward-Roger degree of freedom method, to examine the main and interactional effects of the three independent variables (group, intervention and measurement times).

Finally, Bonferroni adjustment was used to compare the two time points, in order to compare the changes in time between the two types of interventions for all three groups.

4. Results

4.1. The results of E1

4.1.1. The results of the questionnaires

Children's quality of life as assessed by the parents, SDQ problem score and Parents's Self-assessment score (boys with regular sports activity versus those without regular sports activity)

Concerning boys engaging in regular sports activity, parents reported significantly better ($t(43)= -3.87$, $p<.001$) quality of life ($N= 24$; $M= 2.02$, $SD= .59$) than parents whose son did not train regularly ($N= 21$; $M= 2.67$, $SD= .53$). The value of Cohen's d was 1.16, which indicated large effect size.

The SDQ problem score was also significantly lower ($t(43) = -3.27$, $p = .002$) for children who exercised regularly ($M = 16.38$, $SD = 4.84$), compared to those who were inactive ($M = 21.14$, $SD = 4.93$), as reported by parents. A Cohen's d of .97 also implied large effect size.

There was a significantly higher ($t(43) = -2.05$, $p = .047$) self-esteem score regarding parents whose children regularly participated in physical activity ($M = 33.33$, $SD = 4.78$), compared to those whose children did not train regularly ($M = 29.62$, $SD = 7.28$). The magnitude of the effect could be considered as medium, according to a Cohen's d value of .60.

SDQ Problem Score, Hyperactivity Score, and Parental Self-Esteem Score as potential predictors of children's quality of life

Based on the applied multiple regression analysis (stepwise model), among the potential predictors (SDQ problem score, Hyperactivity score, Parental Self-esteem score), the SDQ problem score became the only significant independent variable that was suitable for predicting the children's quality of life, as assessed by the parent ($R^2 = .47$, $F(1,43) = 37.71$, $p < .001$, $\beta = .68$, $p < .001$). Hyperactivity score ($\beta = .12$, $p = .927$) and parental self-esteem score ($\beta = -.99$, $p = .394$) were excluded from the model.

The effect of the SDQ problem score and regular physical activity on children's quality of life, as rated by parents

Both the SDQ problem score entered as a covariant ($F(1,42) = 22.75$, $p < .001$) and the variable of regular sports activity ($F(1,42) = 4.50$, $p = .04$) had a significant main effect on the quality of life of the child, as assessed by the parent.

A lower SDQ problem score was associated with a better quality of life ($r = .68$, $p < .001$). Similarly, the parents of boys engaged in regular sports activity reported a better quality of life ($t(43) = -3.87$, $p < .001$) for their children than parents whose children did not play sports actively.

The examination of the frequency of sports activities (number of hours per week) and the quality of life of the children, as assessed by parents

Regular current sports activity (number of hours per week) was a significant predictor of children's quality of life, as scored by parents, based on the results of linear regression ($R^2 = .16$, $F(1,43) = 8.06$, $p = .007$, $\beta = -.397$, $p = .007$).

4.2. The results of E2

4.2.1. KITAP parameters

The results of the examined parameters of the different KITAP subtests are presented below. In the univariate models, the group variable was always significant. From the other control variables, age reached a significant value in most of the measured parameters (14/15). Of the 15 indicators examined, the number of months spent with sports was significant for three, the mother's education level for two, while the father's education level was a significant predictor for one indicator, in addition to the group and age variables.

Alertness – the median and the variability (standard deviation) of reaction time

With reference to the alertness subtest, the focus was on the median and the variability of the reaction time. After performing the Tukey correction, pairwise comparisons did not yield significant results, nor did the comparison between the average of the medicated and the control groups and the average of the non-medicated group.

When analyzing the variability (standard deviation) of reaction time, the corrected contrast estimates resulted in a significant difference between the non-medicated and the control ($t(146)= 3.66$, $p= .001$) and between the non-medicated and the medicated groups ($t(146)= 3.19$, $p= .005$). There was no significant difference between the drug and the control groups. In addition to these results, the difference between the non-drug and the mean of the drug and the control groups was found to be significant ($t(146)= -3.49$, $p< .001$).

Distractibility – omissions (total, with and without distraction) and errors (total, with and without distraction)

Regarding the distractibility subtest, the following parameters were examined: total omissions, omissions with and without distractor, total errors, error with and without distractor. All analyses were performed using generalized linear negative binomial models.

The corrected contrast showed a significant difference between the non-medicated and the control ($z= 2.75$, $p= .02$) and between the medicated and the control group members ($z= 2.51$, $p= .03$) for the total number of omissions. There was no significant difference between the non-medicated and the medicated groups. There was a marginally significant difference when comparing the mean of the non-medicated group and the mean of the medicated and the control groups.

For the number of omissions made when the distractor was present, a significant difference was observed between the non-medicated and the control groups ($z= 2.47$, $p= .04$) and between the medicated and the control groups (*z*= 2.42, *p*= .04), while the comparison between the non-medicated and the control groups did not yield a significant difference. When contrasting the non-medicated group with the mean of the medicated and the control groups, the difference was not significant.

There was a significant difference between the non-medicated and the control groups after the Tukey corrections (*z*= 3.03, *p*= .007) concerning the number of omissions made without the distractor. Additionally, there was a marginal difference between the medicated and the control groups and no significant difference between the non-medicated and the medicated groups. However, the members of the non-medicated group performed significantly worse than the mean of the other two groups (*z*= -2.92, *p*= .02).

In the examination of all errors, both the non-medicated group (*z*= 3.04, *p*= .007) and the medicated group (*z*= 2.46, *p*= .04) differed significantly from the control group. In contrast, the performance of the non-medicated and medicated groups did not differ significantly. There was also a significant difference in the comparison between the mean of the medicated and the control groups and the non-medicated group (*z*= -2.00, *p*= .05).

Regarding errors made when the distractor was present, after the Tukey correction, the only significant difference was found between the non-medicated and the control groups (*z*= 3.20, *p*= .004). In addition, there was a significant difference when comparing the mean of the medicated and the control groups with the mean of the non-medicated group (*z*= -2.59, *p*= .01).

In the analysis of errors made without the distractor, a significant difference was detected between the non-medicated and the control (z= 2.59, p= .03) and between the medicated and the control groups (z= 2.68, p= .02), while there was no significant difference when comparing the non-medicated and the medicated groups. Comparison of the non-medicated with the medicated and the control groups did not yield a significant difference.

Divided attention – the median of reaction time, the total number of omissions and errors

For the divided attention subtest, the number of total omissions and errors, as well as the median of reaction time was examined.

As for the number of missed target stimuli, a significant contrast was detected between the non-medicated and the medicated (*z*= 3.56, *p*= .001) and between the non-medicated and the control groups (*z*= 5.99, *p*< .001). Marginal differences were measurable between the medicated and the control groups. The non-medicated group performed significantly differently (*z*= -5.66, *p*< .001) when its average was compared with the average of the medicated and the control groups.

In the examination of the number of total errors, there was a significant difference between the non-medicated and the medicated (z= 3.40, p= .002) and between the non-medicated and the control groups (z= 4.82, p<.001) in the post hoc testing. In contrast, there was no significant difference between the medicated and the control groups. However, when comparing the mean of the non-medicated group with the mean of the medicated and the control groups, a significant difference was also detected (z= -4.86, p<.001).

Tukey's corrected contrast on the raw data of median reaction time showed a significant difference between the non-medicated and the medicated (t(146)= 2.51, p= .01) and between the non-medicated and the control groups (t(146)= 2.48, p= .01). There was no relevant difference between the performance of the medicated and the control groups. Comparison of the mean of the medicated and the control groups with the non-medicated group resulted in a significant difference (t(146)= -2.52, p= .01).

Flexibility – the median of reaction time and the total number of errors

Among the subtest parameters, the number of total errors and the median reaction time were included in the analyses.

Only the difference between the non-medicated and the control groups was significant (z= 3.95, p< .001) for the total number of false reactions (errors). In addition, a marginal difference was detected between the non-medicated and the medicated groups, while the performance of the medicated and the control groups did not differ significantly from each other. There was also a significant difference in the mean of the non-medicated group compared to the medicated and the control groups (z= -3.64, p<.001).

The Bartlett's test (to test the homogeneity of variances) performed on the transformed data of the median reaction time became significant (Bartlett's K-squared= 10.59, df= 2, p= .005). When the age of the subjects was included as a variable, heteroscedasticity was removed from the error phase, so regular standard errors were used. There was a significant difference only between the medicated and the control groups (t(146)= 2.37, p= .05) in the post hoc testing. Furthermore, there was a marginally significant difference between the non-medicated and the control groups. Comparison of the non-medicated group with the other two groups did not result in a significant difference.

Go/no-go – the median of reaction time and the total number of errors

The number of false reactions (errors) and the median of reaction time were included in the analyses.

Regarding the number of errors, Tukey's corrected contrast analysis showed a significant difference between the non-medicated and the medicated (z= 2.43, p= .04) and between the non-medicated and the control groups (z= 3.61, p< .001). The difference between the medicated and the control group was not significant. In addition, the comparison regarding the mean of the non-medicated group with the mean of the other two groups indicated a significant difference (z= -3.56, p< .001).

Group-wise contrasts on the transformed data of the median reaction time did not yield any significant differences after the Tukey correction. Comparison between the mean of the non-medicated group with the mean of the medicated and the control groups did not produce a significant difference either.

4.3. The results of E3

4.3.1. KITAP parameters

Significant baseline differences between the types of intervention were found only regarding the errors in the go/no-go task (Wilcoxon W= 2141, p= .02; physical activity condition: M= 2.17, control condition: M= 3.26). Table 1 lists the relevant main effects and interactions.

Table 1: The main effects and interactions of the KITAP parameters

KITAP subtests	Main effects and interactions	Df	F/χ^2 values	*p* values
Alertness	**Median of reaction time**			
	Group	2	3.76	***p*<.05**
	Time	1	94.29	***p*<.001**
	Intervention: time	1	3.51	*p*>.05 (marginally)
	Variability of reaction time			
	Group	2	14.17	***p*<.001**
	Time	1	84.42	***p*<.001**
Distractibility	**Total omissions**			
	Group	2	20.03	***p*<.001**
	Omissions with distractor			
	Group	2	15.17	***p*<.001**
	Intervention	1	3.66	*p*>.05 (marginally)
	Omissions without distractor			
	Group	2	16.88	***p*<.001**
	Total errors			
	Group	2	20.86	***p*<.001**
	Time	1	69.31	***p*<.001**
	Group: time	2	8.87	***p*<.05**

Table 1 continuing: The main effects and interactions of the KITAP parameters

KITAP subtests	**Main effects and interactions**	**Df**	***F/χ²* values**	***p* values**
Distractibility (continuing)	**Errors with distractor**			
	Group	2	10.64	***p*<.01**
	Time	1	10.79	***p*<.01**
	Group: time	2	5.97	*p*>.05 (marginally)
	Group: intervention: time	2	5.18	*p*>.05 (marginally)
	Errors without distractor			
	Group	2	17.85	***p*<.001**
	Time	1	33.62	***p*<.001**
	Group: time	2	11.33	***p*<.01**
Divided attention	**Median of reaction time**			
	Group	2	12.80	***p*<.001**
	Time	1	28.88	***p*<.001**
	Total omissions			
	Group	2	40.02	***p*<.001**
	Intervention	1	6.34	***p*<.05**
	Time	1	3.63	*p*>.05 (marginally)
	Intervention: time	1	8.91	***p*<.01**
	Total errors			
	Group	2	14.37	***p*.001**
	Group: time	2	10.07	***p*<.01**
	Group: intervention: time	2	9	***p*<.05**
Flexibility	**Median of reaction time**			
	Group	2	4.56	***p*<.05**
	Time	1	89.32	***p*<.001**
	Group: intervention	2	2.93	*p*>.05 (marginally)
	Total errors			
	Group	2	8.62	***p*<.05**
	Time	1	16.50	***p*<.001**
Go/no-go	**Median of reaction time**			
	Group	2	2.73	*p*>.05 (marginally)
	Time	1	6.06	***p*<.05**
	Group: time	2	3.26	***p*<.05**
	Intervention: time	1	3.86	*p*>.05 (marginally)
	Total errors			
	Group	2	25.49	***p*<.001**
	Intervention	1	4.98	***p*<.05**
	Time	1	3.99	***p*<.05**

Table 1 continuing: The main effects and interactions of the KITAP parameters

KITAP subtests	**Main effects and interactions**	**Df**	***F/χ²* values**	***p* values**
Go/no-go (continuing)	**Total errors (continuing)**			
	Intervention: time	1	3.60	*p*>.05 (marginally)

Table 2 shows the significant and non-significant differences between the two interventions.

Table 2: Differences between the effects of physical activity and control intervention („+” = significant difference, „-” = non-significant difference)

	Non-medicated group	**Medicated group**	**Control group**
Alertness			
Median of reaction time	-	+	-
Variability of reaction time	-	-	-
Distractibility			
Total omissions	-	-	-
Omissions with distractor	-	-	-
Omissions without distractor	-	-	-
Total errors	+	-	-
Errors with distractor	+	-	-
Errors without distractor	-	-	-
Divided attention			
Median of reaction time	-	-	-
Total omissions	+/-	-	-
Total errors	-	+	-
Flexibility			
Median of reaction time	-	-	-

Table 2 continuing: Differences between the effects of physical activity and control intervention („+” = significant difference, „-” = non-significant difference)

	Non-medicated group	Medicated group	Control group
Flexibility (continuing)			
Total errors	-	-	-
Go/no-go			
Median of reaction time	-	-	-
Total errors	-	-	-

5. Discussion

5.1. Discussion of E1

Our results supported our previous hypothesis that the parents of non-medicated boys with ADHD who engage in regular sports activity report a better quality of life, fewer emotional and behavioural problems and a higher level of self-esteem than parents whose treatment-naïve children with ADHD do not do sport regularly. As a consequence of these results, it can be assumed, on the one hand, that regular sports activity has the potential to reduce the frequency of problematic behaviours, thereby increasing children's quality of life and parental self-esteem. On the other hand, it is possible that a parent with higher self-esteem is more likely to help and support his/her child's participation in physical activity, or to see his/her child's quality of life or problematic behaviour less negatively.

Additionally, as mentioned above, parents whose children exercise regularly have a higher self-esteem compared to parents whose child does not engage in regular physical activity. In their study, Alizadeh et al. (2007) reported that the parents of children diagnosed with ADHD have lower self-confidence, less warmth and involvement towards their child. The positive effect of a child's regular sports activity on parental self-esteem may therefore protect the parent from the negative consequences of the disorder.

From all the applied variables, only the SDQ problem score proved to be a suitable predictor of the child's quality of life, as scored by the parent. Besides, the variable of regular sports activity also had a significant main effect on the child's quality of life, as assessed by the parent. Our results suggest that participation in regular sports activity can help the child to deal with his or her behavioural problems and be associated with a better quality of life, based on parental estimation. Physical activity may reduce the symptoms of ADHD due to the physiological changes it induces, as its mechanisms are similar to the effects of stimulant medication (Wigal et al., 2013).

However, it is still questionable whether treatment-naïve children with ADHD are able to participate in regular sports activities because of their moderate level of problematic behaviours, or, conversely, whether their behavioural symptoms are reduced as a result of sports activity. It can be assumed that there are fewer behavioural problems regarding ADHD with regular sports activity, which could also be related to a better quality of life.

Additionally, the focus was on the number of hours spent weekly with regular physical activity, which also appeared to be a significant predictor of the children's quality of life, as rated by parents. It is conceivable that a higher number of hours of physical exercise increases a child's quality of life, as assessed by a parent. There is lay and common knowledge about ADHD and physical exercise, that the latter moderates the accumulated, excess energies, thus having a positive effect on hyperactive children. Positive emotions may be generated in parents, that their child with ADHD is not only exercising to stay healthy, but their symptoms of the disorder are being "treated" as well.

It would be important for future studies to discover the motivational factors that promote the child's commitment to physical activity and play a role in maintaining that commitment, as we find that regular sports activity is an important factor in the quality of life of these children, in addition to behavioural problems.

5.2. Discussion of E2

Based on this study, comparing typically developing children, treatment-naïve and medicated children with ADHD, the strongest relationship with the measured attention and executive functions was shown by the existence of a diagnosis of ADHD, the age of the participants, physical activity (number of months spent with it) and the educational level of their parents.

In general, treatment-naïve children with a diagnosis of ADHD performed worse on most parameters related to various attentional and executive functions (12/15) than the members of the medication and the typically developing group. For most indicators (10/15), no significant difference was detected between the medicated and the control groups.

The averages achieved by the medicated group were in most cases closer to those of the control group than to those in the non-medicated group, except for omissions without the distractor in the distractibility task and the median of reaction time in the Go/no-go task. The strongest positive effects of medication were seen in terms of alertness, divided attention and performance in the Go/no-go task.

Thus, the members of the non-medicated group produced a significantly worse performance compared to participants in the medicated and the control groups for almost all parameters, which together indicates the impaired attentional and executive functions of treatment-naïve ADHD.

5.3. Discussion of E3

To the best of my knowledge, this is the first study to examine the effect of acute physical activity on various aspects of attentional and executive functions in groups of non-medicated and medicated children diagnosed with ADHD and typically developing children within the same study design. The main effect of the group was significant in 14 out of 15 parameters for both interventions and both measurement times, implying a significantly worse performance by the non-medicated group.

In sum, 20 minutes of acute physical activity had a positive and significantly different effect on 2 of the 15 parameters in the medicated group, which are the following: the median of reaction time in the alertness subtest and error rates in the divided attention task. In connection with two other parameters, positive effects were measured in the group without medication, which are: total errors and errors made with the distractor, both in the distractibility task. Regarding divided attention, although the number of omissions did not change after physical activity in the non-medicated group, significantly more omissions were measurable after the control condition. Our results only partially support the hypothesis that acute physical activity has a beneficial effect on attention and executive functions, as there was not a strong, significant difference between the two interventions for all parameters examined.

In my opinion, the characteristics of the intervention we used (type, form, intensity, duration) may have contributed to the detection of a small number of parameters that resulted in significant improvement. The majority of studies using a similar design (acute physical activity at moderate intensity for 20 minutes) did not demonstrate an improvement in all areas of executive function after physical activity (see subsection 1.5.).

Limitations for E1

The results obtained in the study can only be interpreted in the light of the limitations. First, due to the cross-sectional arrangement of the research, no causal conclusion or relationship can be drawn between the symptoms of the disorder, active participation in sports and the quality of life of the child, as assessed by the parent. Second, the results of the study cannot be generalized to the entire population diagnosed with ADHD, as the present study sample only examined data from non-medicated boys. Third, because the study analyzed only a clinical sample, the results obtained cannot be generalized to the group of children who are typically developing. Fourth, this study included only parental-filled measures to estimate the children's quality of life, problematic behaviour and the severity of their symptoms.

Limitations for E2 and E3

First, there was a significant difference between the three study groups in terms of parents' educational level. This may be due to the convenience sampling used. Second, members of the medicated ADHD group were significantly older than participants in the non-medicated and typically developing control groups. In E2 and E3, this could potentially have affected the results. Taking this into account, the age variable in E2 was controlled during each regression analysis, so that significant differences in the expected direction appeared in the performance indicators in the first-round neuropsychological tests. In the case of E3, the effect of the significant difference in age between the groups was not detectable to a significant extent because the number of expected significant results was quite low. Third, children belonging to the control group were able to complete the examination mainly in the afternoon, after their daily school obligations, while children from the ADHD group were examined primarily in the morning, due to the therapeutic programs in the hospital in which they had to participate. Fourth, children with a history of intellectual disability or autism spectrum disorder and/or previous psychological or psychiatric treatment and whose structural diagnostic interview did not rule out a diagnosis of ADHD were excluded from the control group. However, children from any study group who met the criteria or sub-threshold criteria for any other psychiatric disorder after completing the MINI Kid were not excluded from the experiment process. Fifth, though intellectual disability was an exclusion criterion for all three groups, this diagnosis was based on medical history, and the level of intelligence was not assessed during the research process. Sixth, during the study, participants in the medication group were on medication previously prescribed and adjusted for them, containing either the active ingredient methylphenidate or atomoxetine. Accordingly, the measurement of symptom severity was not performed in the absence of medication treatment, as withholding atomoxetine for the purpose of the study would have raised ethical issues. Seventh, there was a significant difference in the combined diagnosis of ADHD between the two clinical groups. However, this result is not surprising in some respects, as the number of children with presumably the highest number of symptoms (combined type ADHD) are on medication (the MINI Kid retrospectively asked about pre-medication symptoms at the time of the study), while the "less severe" cases (predominantly inattentive or hyperactive/impulsive type) were not treated with medication, thus becoming members of the non-medicated group with ADHD. Eighth, the roles of study coordinator and investigator were performed by one person (myself). As a result, the blind arrangement could not be realized. Finally, although there were 50 individuals in each of the three study groups, providing sufficient strength for the study, in order to confirm the significant research results and to prove the assumed but not detected effects and results, it is necessary to repeat this study on a larger sample.

6. Summary, new results and directions

Among the results of my doctoral work, the following confirm the results of previous studies:

- A higher numbers of problematic behaviours are associated with a lower quality of life in children diagnosed with ADHD.
- Treatment-naïve children with a diagnosis of ADHD performed worse in the parameters of most attention and executive function tasks (12/15), compared to groups of medicated and typically developing children, resulting in impaired attention performance and executive function.
- For most of the subtest parameters examining attention and executive function (10/15), the performance of medicated children with ADHD did not differ from the group of typically developing children; a result highlighting the importance of medication in ADHD.

Results obtained during my doctoral work which are considered to be contrary to the results of previous studies:

- Acute physical activity had a significant, positive effect on medically treated children with a diagnosis of ADHD on 2 out of 15 parameters when compared with the control intervention, which are: the median of reaction time in the alertness subtest and total errors in divided attention.
- In the group of treatment-naïve children with a diagnosis of ADHD, acute physical activity had a beneficial effect on 2 out of 15 parameters, compared with the control intervention: total errors and errors with the distractor, both in the distractibility subtest.
- Regarding the divided attention subtest, acute physical activity did not affect the number of omissions; however, control intervention significantly increased them in children with a diagnosis of ADHD not receiving medication.

New results:

- Participation in regular sports activities can be linked to a better quality of life and less problematic behaviour in non-medicated children with ADHD, as well as higher self-esteem by their parents.

Future research will need to focus on measuring children's quality of life in addition to parental assessment. In terms of quality of life, it would also be important to carry out a comparison with the non-clinical sample, and to include a sample of girls. In addition, a longitudinal research arrangement could highlight the relationship between children's quality of life and regular sporting activity more accurately and in more detail.

In future studies, it would be important to examine the different types of ADHD diagnoses (combined type, predominantly inattentive and predominantly hyperactive/impulsive type), as well as the different comorbidities associated with ADHD, to analyze their potential impacts on executive functions. In addition, the severity of symptoms should be emphasized, as should the potentially different effects of diverse medications on executive functions.

Further studies using physical activity should be able to discover and determine the optimal form, intensity and duration of the physical activity, in order to become potential adjunctive therapy – besides evidence-based treatment – for children diagnosed with ADHD.

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