Somatic and Endocrinological Changes in Non Medicated ADHD Children

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Abstract: Attention deficit hyperactivity disorder (ADHD) is one of the most commonly diagnosed childhood psychiatric disorders and it constitutes a group of developmental disorders, which are characterized by inadequate level of attention, excessive activity and impulsivity. In connection with neurological and endocrinological changes, children with ADHD can show also changes in the growth and development without consequence to the medication. Differences were found especially in higher weight and BMI. Very few studies were done on this topic and the results of the studies are very different, methods are heterogeneous and insufficient. The most serious absence is the much reduced number of anthropometrics and other characteristics and parameters. Studies usually analyse only BMI, height and weight and do not take into account socio-economic characteristics, feeding customs and other important factors. Many studies are done on changes in growth only associated with medical treatment of children ADHD. However changes in the development and growth can be a manifestation of the disorder itself. Authors of this paper review studies which monitor changes in the development of children with ADHD and compare their results.

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Introduction

Attention deficit hyperactivity disorder (ADHD) is one of the most commonly diagnosed childhood psychiatric disorders [1, 2] and it constitutes a group of developmental disorders [3, 4], which are characterized by inadequate level of attention, excessive activity and impulsivity [5, 6]. It is also a developmental disorder with a probable strong genetical binding [7, 8].

ADHD is manifested in every part of children's behaviour [5]. Biochemical [9, 10], endocrinological [11, 5], neurological [5, 4] and even neuroanatomical [12, 13] changes appear in children with ADHD. In this connection and according to current studies children with ADHD have higher probability of changes in the growth and development [14, 15, 16, 17]. ADHD is claimed to be a disorder with multiple symptomatology and heterogeneous aetiology [5] as some other developmental disorders i.e. autism [18, 19]. Specific changes in the brain development of ADHD children may be caused by disorder itself [4] or they can be caused by other non-related factors [20].

Changes in growth and development in non-medicated children with ADHD are the aim of this paper. There are very few studies on this topic. Results of these studies are inconsistent and methodically heterogeneous and insufficient. Some of the studies describe changes in growth and habitus, other studies contradict that. Many studies are done on changes in growth only associated with medical treatment of children ADHD [21, 16, 22]. However changes in the development and growth can be a manifestation of the disorder itself [23, 2].

The aim of this research was to compare studies done in the topics of growth and development in children with ADHD, without consequence to the medication. The aim was to compare results of those studies; point to potential insufficiency in methods and according to these findings suggests a recommend progress in following studies and also in clinical practise.

ADHD children, growth and obesity

Most of the studies examine possible differences in BMI between children with ADHD and children without ADHD. As the prevalence of childhood obesity increases, identifying groups of children who are at increased risk of overweight is important. Therefore some studies estimated the prevalence of overweight in children and adolescents in relation to attention-deficit/hyperactivity disorder [24]. According to other studies obesity and ADHD demonstrate significant comorbidity [25].

Some research has been conducted to examine the prevalence of obesity in children with developmental disabilities, particularly in individuals with Down syndrome and Prader-Willi syndrome who are reported to have a higher prevalence of overweight than in the general population [26, 27]. However, a few studies have been undertaken to assess the prevalence of overweight in children with other developmental disorders, such as attention deficit hyperactivity disorder

[28]. It is considered that many symptoms of ADHD can be manifested by children with other mental or somatic disorders [4] or in some cases the symptoms of the disorder itself can be a reaction to some traumatic events [29] and show similarity with other traumatic phenomenon i.e. dissociation [30, 31].

The literature on obesity in children with ADHD is sparse. Historically, inquiries into weight status of children with ADHD have focused on the potential for growth suppression associated with the use of stimulant medication [28].

One of the first researches of its kind was specialized on growth in children with ADHD. It was done by McGee et al. [32]. This study included groups of seven-year-old boys (identified as hyperactive-only, aggressive-hyperactive, aggressive-only and non-aggressive/non-hyperactive). Anthropometric data were collected on these groups. Measures included: stature, weight, skeletal maturity, mid-upper arm circumference, triceps and subscapular fat-folds and body-mass index. The hypothesis that hyperactive-only boys would show delayed maturation, as indicated by lower bone-age, was not confirmed. However, these boys had significantly smaller mid-upper arm circumference, triceps fat-fold and body-mass index than the other groups. The results suggest that body leanness may discriminate ‚pure' hyperactive boys from aggressive-hyperactive boys.

Other studies were mainly specialized on only obesity in ADHD children. The study by Holtkamp et al. [33] evaluated a sample of 97 boys with ADHD in Germany. Holtkamp et al. tested the hypothesis that hyperactive boys would have a lower prevalence of obesity than an age-matched healthy male reference population in connection to their increased activity. This study was done during 1999–2001 and included 97 boys with ADHD in age 5.5 to 14.5. 56 boys had other behaviour disorders. BMI was compared. Contrary to expectations, they found that a significant number of subjects with ADHD had a BMI $\geq 90^{th}$ percentile (19.6%) and 7.2% had a BMI $\geq 97^{th}$ percentile. BMI was significantly higher than age-adapted reference values of the German population.

In 2002 Altafas [34] realized study on decreasing obesity among ADHD adults. Altafas (2002) conducted a chart review of 215 adults seen in a weight control clinic (1 year). A sample of 215 patients (90% of whom were female) was divided in two groups: ADHD (27.4%), symptoms of ADHD but did not meet formal diagnostic criteria (33.5%), without ADHD (39.1%). All of the patients with ADHD were classified as having the inattentive type of the disorder. An average decrease in ADHD group was 2,6 BMI (kg/m^2), in group without ADHD was 4 BMI (kg/m^2). Among men whose BMI was more than 40 the difference was more significant. Of those patients with a BMI ≥ 40, 42.6% had ADHD. Loss in group of men with ADHD was 2,9 BMI (kg/m^2), without ADHD 7 BMI (kg/m^2). The authors noted that patients with ADHD were less successful at losing weight than those without ADHD.

Most studies of childhood obesity and psychopathology are cross-sectional or retrospective [17, 24, 28, 34]. The following study was different.

The relations between obesity and psychopathology were monitored by study of Mustillo et al. [35]. This study is one of the very few longitudinal studies. Measures of height and weight were taken annually over 8 years in 9–16 years old children, together with annual information about family characteristics and mental health. Children were divided according to psychiatric diagnoses into 7 groups: conduct disorder, oppositional defiant disorder, depressive disorders (including major depression, dysthymia, and depression not otherwise specified), anxiety disorders (including separation anxiety, generalized anxiety disorder, simple phobia, social phobia, agoraphobia, and panic), bulimia, substance abuse, and attention-deficit/hyperactivity disorder (ADHD). Chronic obesity was more common in children from poor and less-educated families, and it had implications for mental health. Psychopathology was most common in the chronically obese group. However there were no significant associations between obesity trajectory membership and bulimia, ADHD, substance use, conduct disorder, or anxiety, controlling for comorbid psychiatric disorders.

Similar research was done by Curtin et al. [28]. This retrospective study found and compared predispositions to obesity in group of children with ADHD (98) and in group of children with autism (42). Retrospective chart reviews 140 charts of children ages 3–18 years seen between 1992 and 2003 at a tertiary care clinic that specializes in the evaluation and treatment of children with developmental, behavioural, and cognitive disorders. Diagnostic, medical, and demographic information was extracted from the charts: primary diagnoses of ADHD (according to DSM-IV; DSM, 1994), race/ethnicity, age, gender, height, and weight. Information was also collected on medications. Body mass index (BMI) was calculated from measures of height and weight recorded in the child's chart. BMI above 85th percentile was supposed to be the prevalence of at-risk-for-overweigh. BMI value above 95th percentile was supposed to be obesity. The prevalence appeared highest in the 2–5 year old group, but differences among age groups were not statistically significant. The data of this study suggest that the problem of overweight in children with ADHD. However the prevalence of overweight that is similar to children in the general population.

Lam's [14] study aims to investigate whether there is any association between attention deficit hyperactivity disorder (ADHD) tendency and overweight/obesity among adolescents. Children from 13 to 17 were measured. Individual body weight and height were measured, overweight and obesity was determined. In 1429 students were recruited with 85 (6.3%) classified overweight and 42 (3.1%) obese with a mean BMI. There was a significant association between ADHD tendency and obesity among these adolescent. However, the association between ADHD tendency and overweight did not reach a significant level.

Swanson et al. [36] analyzed data from over 4400 subjects from 18 studies, Subjects were 6–17 years old and their weight and height were included in the analyses. Average height was on 51st percentile, weight on 61st percentile.

Growth patterns for children with ADHD were considerably different from current norms. According to these results children are taller and larger than expected at an early age. Age-matched stimulant users are both shorter and lighter than their untreated counterparts, suggesting some stimulant-related growth suppression.

Study by Waring et al. [24] was a cross-sectional analysis of 62 887 children and adolescents aged 5 to 17 years from the 2003–2004 National Survey of Children's Health, a nationally representative sample of children and adolescents in the United States. Attention-deficit disorder/attention-deficit/hyperactivity disorder was determined by response to the question „Has a doctor or health professional ever told you that your child has attention-deficit disorder or attention-deficit/ /hyperactive disorder, that is, ADD or ADHD?" Children and adolescents were classified as underweight, normal weight, at risk of overweight, or overweight according to BMI for age and gender. After adjustment for age, gender, race/ethnicity, socioeconomic status, and depression/anxiety, children and adolescents with attention-deficit disorder/attention-deficit/hyperactivity disorder not currently using medication had 1.5 times the odds of being overweight.

Hubel et al. [17] investigated a possible association between attention-deficit/hyperactivity disorder (ADHD) and overweight by measuring weight status and energy expenditure (basal metabolic rate, BMR) in 39 8–14 years ADHD-boys with hyperactivity. Weight and height were measured and BMI values were calculated. BMR was determined by indirect calorimetry. Significant differences were obtained between the ADHD- and the control-group. Both BMI and BMR were higher in the group of ADHD-boys. The authors supposed that impulsive behaviour in ADHD-boys with hyperactivity may lead to an increased food intake.

Empirical evidence of Bazar et al. [25] has contradicted prior presumptions that the hyperactivity of ADHD would decrease the risk of obesity. They supposed that obesity and ADHD represent different manifestations of the same underlying dysfunction, a phenomenon they term environmental oversampling syndrome. Oversupply of information in the form of nutritional content and sensory content may independently predispose to both obesity and ADHD. Moreover, the pathogenic mechanisms of these conditions may overlap such that nutritional excess contributes to ADHD and cognitive hyperstimulation contributes to obesity. Environmental oversampling syndrome may represent an even more inclusive concept that encompasses various metabolic, inflammatory, and behavioural conditions. Apparently disparate conditions such as insulin resistance, diabetes, hypertension, syndrome X, obesity, ADHD, depression, psychosis, sleep apnoea, inflammation, autism, and schizophrenia may operate through common pathways, and treatments used exclusively for one of these conditions may prove beneficial for the others.

The comparison of the studies

In children with ADHD appear some differences in physique, growth and development. Differences were found especially in weight and BMI. According to

above mentioned studies children with ADHD have higher BMI than norms. However very few studies were done and methods used in the studies are very heterogeneous. Table 1 presents basic parameters and results of studies analyzing growth changes in non-medicated ADHD children.

The studies are very heterogeneous. Different and insufficient number of anthropometric parameters was used in all analysed and presented studies and also the age range of subjects is not optimal. None of the studies brought significant results or clearer insight into the question. So further studies with a complex design and proper psychiatric and anthropometric methodology is needed.

Discussion

Results of compared studies are different and in some cases contradictory. According to current studies we can say that there are some specific and in some cases significant differences in development and statue, especially BMI, in children with ADHD. Increased activity and active living does not have to have effect on weight in children with ADHD. According to previous studies children with ADHD have higher values of BMI than norms or controls. Increased activity of children with ADHD does not have to be necessarily active motion but activity which is demonstrated by low level of attention and concentration or fragmentariness. These characteristics may be more typical for this disorder. The reasons for

Table 1 – The comparison of the studies

Study	Avg age	Measurement	Results	Country
McGee, Birkbeck, Silva, 1985	7	stature, weight, skeletal maturity, mid-upper arm circumference, triceps and subscapular fat-folds and body-mass index	smaller mid-upper arm circumference, triceps fat-fold and body-mass index	New Zealand
Holtkamp et al., 2004	5,5–14,5	BMI	higher BMI	Germany
Altafas, 2002	adults	BMI	higher BMI	USA
Mustillo et al., 2003	9–16	BMI (height, weight)	no significant higher BMI	USA
Curtin et al., 2005	3–18	BMI	no significant higher BMI	USA
Lam, Yang, 2007	13–17	BMI	higher BMI, but no significant	China
Swanson et al., 1998	6–17	height, weight	higher values of height and weight	USA
Waring et al., 2008	5–17	BMI	higher BMI	USA
Hubel at al., 2006	8–14	BMI, basal metabolism BMR	higher BMI, BMR	Germany

differences in weight are still unclear. Endocrinological and neurological changes can be the most important factor (dopamine and insulin receptor activity). It is possible that the important cause of the higher incidence of obesity in subjects with ADHD are more serious problems with losing weight [34] resulting from either endocrinological changes or ADHD specific lifestyle. Mustillo [35] questioned if psychopathology can occurred by obesity or presence of psychopathology can cause predisposition to obesity. This question is also not answered yet. Studies on this topic have many insufficiencies. The most serious we consider the much reduced number of anthropometrical and other characteristics and parameters. Studies usually worked only with BMI, height and weight. Study by McGee et al. [32] was the one of very few studies which included complex anthropometric measurement. Also criteria for overweight may differ among studies. Furthermore, the data reported by Altfas et al. [34] and Agranat-Meged et al. [37] underscore the importance of understanding and preventing the problem of overweight in children with ADHD, before they become adults. Studies which were done did not work with craniometrical measurements. That we suppose to be serious insufficiency because psychological and developmental disorders are often connected with changes in brain. Also height and weight of parents of children were not taken into consideration and neither was the birth weight and height. These are important factors which can show more about the development in children with this diagnosis. Most of the studies do not take into account environment where child grows up and lives, socio-economic characteristic, feeding customs. Mustillo's study points to an importance of other factors and family characteristic as education, financial situation, social area, feeding habits etc. [35]. Hubel at al. [17] measured also BMR (basal metabolism rate). Cortese et al. [38] says that there ADHD might lead to obesity via abnormal eating behaviour, impulsivity associated with binge eating might contribute to ADHD in obese patients, or, alternatively, both obesity and ADHD might be an expression of common underlying neurobiological dysfunctions, at least in a subset of subjects.

Other weak point of most of the studies is wide range of age. From anthropometric point of view that is one of the most serious problems of presented studies because developmental disorders are always related to age specific changes in development and maturation. For next studies we would recommend to include children of less wide range of age, and especially not in puberty.

It is necessary to mention that the majority of mentioned studies were conducted in the USA where higher percentage of children suffers from obesity in general. However measured children were always compared with given population norms so the studied differences are always relative to them.

The obesity may also be often connected with the socio-economical characteristics. In most of the cases unfortunately we can not judge the relations of obesity in children with ADHD to socio-economical factors because the mentioned

studies do not take them into account. Despite this fact we consider these factors as one of the most important parameter for further researches.

Many studies also worked with medication and growth. That can detect an effect of medication and secondary effect of medication but does not say anything about the diagnosis and relations. Before we investigate changes in growth in children with ADHD using medication and relations between medication and growth changes, it is necessary to deal with the question of manifestation on development of ADHD itself. According to mentioned studies, children with ADHD show some changes in statue, growth and development.

Spencer [23] pointed that growth deficit in children with ADHD appeared during treatment can be a manifestation of this disorder and not only manifestation of secondary effect of the treatment. Most of the previous studies suggest that the stimulant-associated height deficits in ADHD are temporary and early manifestation of ADHD itself and not complication of therapy, and the small risk of lost centimetres may be the price worth paying for many children to gain improved learning and social function [2]. The examination of these children might be a helpful approach in the understanding to the relationship between obesity and its contributing neurophysiological, psychological and behavioural factors.

Conclusions

According to the resume of presented studies it is unclear whether children with ADHD show differences in anthropometrics characteristics or in growth generally. The main difference against normal population is usually based on BMI factor. Most of the studies which have been done on these topics have mostly methodological insufficiencies. Usually there are some not mentioned important factors which can play an important role in the developmental changes (i.e. complex anthropometrics measurement, craniometry, socio-economical factor, feeding). These findings lead to the conclusion that further research reflecting complexity of the problem should be done.

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