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Comparison of Postural Features and Muscle Strength between Children with Idiopathic Short Stature and Healthy Peers in Relation to Physical Exercise

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Abstract: Previous research has reported that children with idiopathic short stature (ISS) showed functional and cognitive impairments. The purpose of this study was to compare muscle strength and body posture between children with ISS treated with growth hormone (GH) and healthy peers (healthy children, HC), and to analyze whether these parameters were affected by physical exercise. Eighteen children for the ISS group (mean age: 10.96 ± 1.68 years) and 26 children for the HC group (mean age: 10.19 ± 1.06 years) were recruited for the study. All participants performed the following assessments: handgrip and Sargent test for the muscle strength evaluation; baropodometric and stabilometric test for the posturographic measures. Data were analyzed with analysis of covariance (ANCOVA) using height and weight as covariate. Groups were then stratified into active and inactive and independent *t*-tests were used to determine differences between variables. Significance level was set to $p < 0.05$. Our results showed a significantly lower performance for both hands ($p < 0.01$) and a greater difference of plantar loading distribution between feet in the ISS compared to the HC groups ($p < 0.01$). In relation to physical exercise, the HC active group showed the highest handgrip strength values for both hands among the analyzed groups and, moreover, handgrip strength of both ISS active and inactive groups was significantly lower than corresponding CH peers for both hands. Although ISS and HC inactive groups reported an unequal plantar loading distribution between feet ($p < 0.05$), this asymmetry was not present in both ISS and HC active groups. We assume that GH therapy integrated with physical exercise in young patients with ISS could be suggested to increase muscle strength and body posture improving their quality of life.

Keywords: idiopathic short stature; physical activity; muscle strength; body posture; handgrip test; Sargent test; GH therapy; GH treatment

1. Introduction

Idiopathic short stature (ISS) is defined as a disorder of the short stature disturbances group characterized by a non-identifiable cause in which children present a height greater than 2 standard deviations (SD) below the corresponding mean height for age, gender and population [1,2]. This

growth disorder is multifactorial and includes genetic and epigenetic factors, environmental conditions and constitutional growth delay [2,3]. The presence of no recognizable cause obtained through the diagnostic investigation including medical history, physical examination, laboratory tests, and radiological examinations establishes the diagnosis of ISS [2]. Once the diagnosis has been ascertained, growth hormone (GH) is widely used for the treatment of ISS even in children with no GH insufficiency [4–6]. In order to achieve the maximum possible efficacy of the treatment, clinicians manage the therapy differently among patients with ISS, on the basis of several parameters they have to take into consideration [7]. Nevertheless, although children treated with growth hormone recuperate the height gap, the potential gain of growth rate of the treatment is controversial and, anyhow, they may not achieve normal height [4,8,9].

Previous research showed both intellectual disorders and psychosocial difficulties as well as motor impairments in patients with ISS that negatively influence their quality of life [10]. In particular, regarding the intellectual disorders, some studies reported cognitive retardation that compromises school performances and social behaviours [2]. Instead, as reported by Cohen et al, the psychosocial aspect is affected by the low level of self-esteem that children with ISS could have and episodes of bullying to which they could be subject [5]. Furthermore, studies on short stature in children have demonstrated the association between this disease and functional limitations as motor skills or physical tasks [3,11].

As mentioned above, although GH treatment is managed by clinicians mainly for the purpose of increasing height in these patients, some research works have investigated the influence of GH therapy on various functional and psychological characteristics, as motor skills or cognitive abilities, in children with short stature reporting contrasting results [3,12–16].

Regarding this issue, physical exercise is known to play a key role in GH release representing an effective physiological and non-pharmacological stimulus for the secretion of this hormone [17,18]. Some research groups have investigated fitness characteristics in children with short stature, however, studies aimed at the influence of physical exercise in features such as muscle strength and body posture in these patients are limited [18–21]. Nevertheless, it is widely recognized that physical exercise induces to positive effects on both physiological and psychological aspects in children and, in general, during the whole lifespan [22–25].

For this reason, given the lack of scientific literature on this topic, the aim of the present study was to evaluate any differences in characteristics of muscle strength of upper and lower limbs; body sway; plantar loading distribution between feet in children with ISS treated with GH hormone compared to a healthy age-matched control group. Our hypothesis is that children with ISS could show lesser performances of upper and lower limbs strength and poorer level of body balance and postural control than healthy peers. Moreover, we hypothesize that physical exercise could improve fitness and postural features in children with ISS allowing them to reach equal levels of muscle strength and postural control of healthy children.

2. Materials and Methods

2.1. Study Design

In the present observational case-control study, the case group included children with ISS treated with GH hormone, while the control group comprised healthy children (HC). ISS group subjects were enrolled in the Paediatric and Endocrinology Departments of "ARNAS – G. Di Cristina" hospital of Palermo from December 2017 to June 2018, while HC group data were collected in several primary schools of the same city from January 2018 to May 2018.

2.2. Participants

Eighteen children (10 males and 8 females; mean age: 10.96 ± 1.68 years; mean height: 122.28 ± 9.61 cm; mean weight: 24.56 ± 4.44 kg; body mass index: 16.41 ± 2.15 kg/m^2) for the ISS group and 26 children (14 males and 12 females; mean age: 10.19 ± 1.06 years; mean height: 140.08 ± 16.29 cm; mean weight: 39.36 ± 9.83 kg; body mass index: 19.85 ± 4.2 kg/m^2) for the HC group were considered for the

study. Participants were excluded from the study whether they met the following exclusion criteria: orthopaedic lesions; physical injuries; neurological diseases. Three participants from the ISS group were excluded after applying the selection criteria (due to physical injuries and neurological disease: n = 2 and n = 1, respectively). Moreover, to discern the influence of physical exercise on the aforementioned fitness and postural parameters, for data analysis, both groups were stratified into active (i.e., ISS active group vs. HC active group) and inactive (i.e., ISS inactive group vs. HC inactive group). Children who were considered physically active had practiced any type of sport/physical exercise at least 2 times/week for at least 6 consecutive months from the recruitment time.

Parents/legal guardians provided a written informed consent which allowed their minors to participate in the study from which they could withdraw at any time. The study conforms to the Declaration of Helsinki for the use of persons in research and was approved by the Ethical Board of the University of Palermo.

2.3. Maximum Isometric Handgrip Strength Assessment

Through the handgrip test using a mechanical dynamometer (KernMap model 20K1 — Kern®, Kern and Sohn GmbH, Balingen, Germany) each participant performed three trials of 3-second of maximum isometric handgrip strength (MIHS), alternatively with the right hand and the left hand, separated by 60 seconds of rest period. Before starting assessments, participants familiarized with the test and the mechanical dynamometer they would use. Throughout the measurements, each participant, sitting on a chair with back resting, head in neutral position and looking forward, were given strong verbal encouragement by the researcher to perform the MIHS. All measurements were collected by the same researcher. The best recorded MIHS (kg) of the three trials was considered for statistical analysis.

2.4. Explosive-Elastic Lower Limbs' Strength Assessment

The explosive-elastic lower limbs' strength (EELLS) was measured using the Sargent test in which each participant performed three trials of maximum high jump separated by 60 seconds of rest period. Each participant, maintaining an upright position with the lateral side of the body facing the wall and feet side by side, was asked to touch the wall as high as possible with the fingertips of the hand closer to the wall. Afterwards, each of them was instructed to bend the knees and to carry out the maximum high jump, bringing the arms and the hands upwards, and to touch the wall with the fingertips as high as possible. In order to measure the jump height, the same experimenter marked with a chalk the exact point on the wall touched by each participant before the jump and that one reached during the jump. The difference between the two points was calculated and the best recorded value was considered for statistical analysis.

2.5. Stabilometric and Baropodometric Analysis

A stabilometric evaluation, in order to quantify body sway, was carried out using the FreeMed® posturographic system (Sensor Medica®; Guidonia Montecelio, Rome, Italy) comprising the freeMed® Maxi platform and FreeStep® software (version 1.6.007). The stabilometric signal was digitized at 50 Hz. The test procedure was the following: each participant was required to stand barefoot for 51.2 s in an upright position on the platform, forming a 30° angle with the feet and the heels at 3 cm of distance from each other, the arms along the trunk and the head in neutral position looking forward [26]. The test was repeated in two different conditions: with eyes open (EO) and eyes closed (EC). The posturographic system measured the center of pressure (CoP) displacement and calculated the related variables: sway path length (SPL); ellipse surface (ES); speed (S); amplitude of antero-posterior sway along the virtual y-axis (ΔY); and amplitude of medial-lateral sway along the virtual x-axis (ΔX).

A baropodometric evaluation, in order to measure the percentage of plantar loading distribution between feet, was carried out via the same system (FreeMed®; Sensor Medica®; Guidonia Montecelio, Rome, Italy). For the assessment, each participant was instructed to maintain an upright

position for 5 s barefoot with feet positioned side by side, the arms along the trunk and the head in neutral position looking forward.

2.6. Statistical Analysis

Means and standard deviations were described for the total sample and for both the ISS and HC groups. Strength and posturographic measures were analyzed with analysis of covariance (ANCOVA). Each variable was tested across groups using height and weight as covariates. Groups were then stratified into active and inactive (i.e., ISS active and HC active groups; ISS inactive and HC inactive groups), and independent *t*-tests were used to determine differences between variables. All tests were carried out through jamovi software (version 1.2) [27]. Significance level was set to $p < 0.05$.

3. Results

Regarding the anthropometric characteristics (Table 1), our results showed significant differences between ISS group and HC group both for height ($p = 0.001$), and weight ($p = 0.001$) as well as BMI ($p = 0.003$).

Table 1. Descriptive characteristics of the analyzed groups.

Characteristics	ISS	HC	*p*
Age (years)	10.96 ± 1.68	10.19 ± 1.06	0.068
Height (cm)	122.28 ± 9.61	140.08 ± 8.14	0.001 *
Weight (kg)	24.56 ± 4.44	39.36 ± 9.83	0.001 *
BMI (kg/m^2)	16.41 ± 2.15	19.85 ± 4.20	0.003 *

Data are presented as means ± SD; ISS = idiopathic short stature; HC = healthy control; * = significant.

Table 2 reported strength performances of upper and lower limbs measured through the handgrip test and the Sargent test, respectively. Although the ISS participants had lower performance levels compared to those of the HC group, our outcomes showed no significant differences on the explosive-elastic lower limbs' strength (EELLS) between the two groups ($p > 0.05$). However, regarding the handgrip test, the ISS participants showed lower significant values both for the right ($p = 0.001$) and the left ($p = 0.004$) hand compared to the HC group (Figure 1).

Table 2. Upper/lower limbs strength performance and posturographic measures of the analyzed groups.

Measures	ISS	HC	*p*
Limbs' strength			
R MIHS (kg)	8.26 ± 2.86	13.07 ± 4.31	0.001 *
L MIHS (kg)	8.32 ± 3.1	12.03 ± 4.41	0.004 *
EELLS (cm)	13.33 ± 6.06	15.88 ± 5.78	0.165
Posturographic measures			
SPL (mm)	229.08 ± 282.54	315.07 ± 298.87	0.343
ES (mm^2)	733.24 ± 313.66	616.66 ± 201.84	0.141
R Foot load (%)	53.78 ± 8.32	48.42 ± 4.88	0.010 *
L Foot load (%)	46.22 ± 8.32	51.58 ± 4.88	0.010*

Data are presented as means ±SD; R = right; L = left; MIHS = maximum isometric handgrip strength; EELLS = explosive-elastic lower limbs' strength; SPL = sway path length; ES = ellipse surface; ISS = idiopathic short stature; HC = healthy control; * = significant.

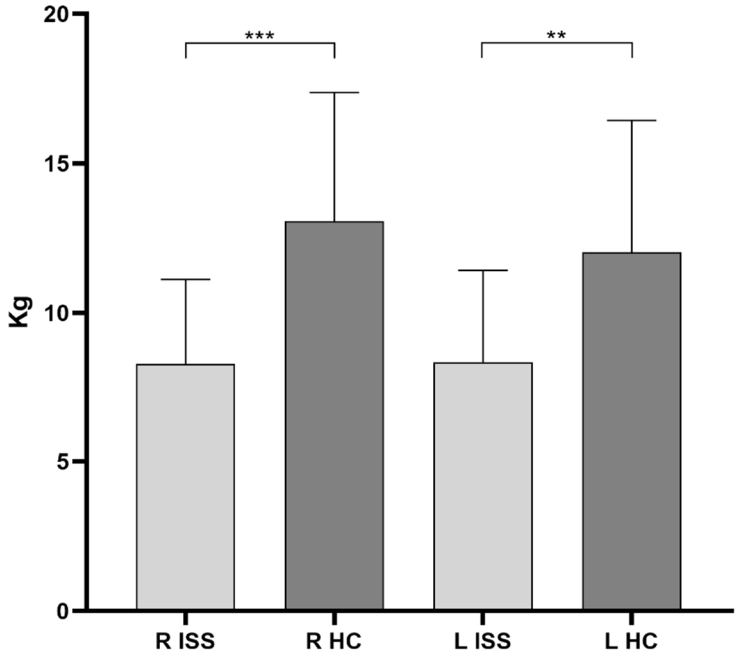

Figure 1. Differences in maximum isometric handgrip strength (MIHS) between the ISS and the HC groups. Figure highlights a significant difference between groups for both hands. R = Right; L = Left.

Furthermore, as presented in Table 2, although we did not find any differences in all the stabilometric parameters, our findings reported a greater difference of plantar loading distribution between feet in ISS compared to the HC group and an opposite plantar loading distribution between feet across the analyzed groups (ISS group: 53.78 ± 8.32 % *vs.* 46.22 ± 8.32 % for the right and the left foot, respectively; HC group: 48.42 ± 4.88 % *vs.* 51.58 ± 4.88 % for the right and the left foot, respectively).

Data analysis in relation to the practice of physical exercise (Table 3) reported that the HC active group showed the highest handgrip strength values for both hands among the analyzed groups and, moreover, that handgrip strength of ISS active and inactive children was significantly lower than corresponding CH peers for both hands (Table 3). Furthermore, ISS and HC inactive groups reported an unequal plantar loading distribution between feet ($p < 0.05$), while this asymmetry was not present in both ISS and HC active groups (Table 3).

Table 3. Upper/lower limbs strength performance and posturographic measures of the groups stratified according to physical exercise practice.

Measures	ISS Active	HC Active	*p*	ISS Inactive	HC Inactive	*p*
Limbs' strength						
R MIHS (kg)	7.33 ± 2.48	14.03 ± 4.67	0.01 *	8.75 ± 2.92	12.55 ± 4.15	0.01 *
L MIHS (kg)	7.17 ± 2.59	12.81 ± 4.97	0.02 *	8.94 ± 3.16	11.61 ± 4.19	0.07
EELLS (cm)	17.43 ± 7.66	20.56 ± 5.25	0.35	12.17 ± 5.67	13.41 ± 4.43	0.51
Posturographic measures						
SPL (mm)	273.66 ± 432.82	257.07 ± 206.76	0.25	185.78 ± 147.54	345.78 ± 339.56	0.61
ES (mm^2)	831.34 ± 437.48	628.26 ± 239.03	0.92	648.7 ± 208.57	610.53 ± 187.02	0.13
R Foot load (%)	47.14 ± 7.76	51.22 ± 5.74	0.25	45.42 ± 8.6	51.76 ± 4.55	0.02 *
L Foot load (%)	52.86 ± 7.76	48.78 ± 5.74	0.25	54.58 ± 8.6	48.24 ± 4.55	0.02 *

Data are presented as means ± SD; R = right; L = left; MIHS = maximum isometric handgrip strength; EELLS = explosive-elastic lower limbs' strength; SPL = sway path length; ES = ellipse surface; ISS = idiopathic short stature; HC = healthy control; * = significant.

This within-group analysis reported the same asymmetrical loading distribution between feet also for the entire two groups of the study (i.e., ISS and HG groups) as shown in Figure 2.

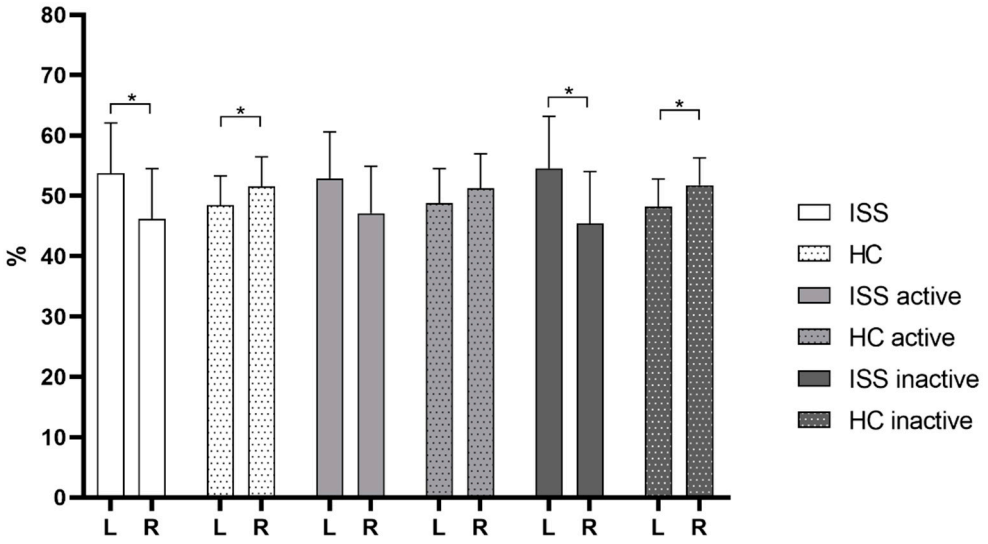

Figure 2. Differences between Left (L) and Right (R) plantar loading distribution within the ISS and the HC group. The values are stratified for each group between active and inactive participants.

4. Discussion

The main purpose of the present study was to evaluate any differences on fitness features such as upper and lower limbs strength, postural characteristics such as body sway, and plantar loading distribution, between the ISS group and the HC group. Moreover, we analyzed whether there were any differences in the aforementioned variables between physically active and inactive children.

From data analysis, the anthropometric characteristics of the ISS group were significantly lower than those of the HC group. These results were expected based on the intrinsic definition of short stature (regardless of whether this latter is a primary growth disorder, a secondary growth disorder or, as in the sample we recruited, due to an unknown etiology) [2]. In fact, patients with ISS are characterized by a height shorter than 2 SD below the normal distribution of the corresponding population for age and sex [28,29]. Moreover, as reported by many research groups, children with ISS treated with GH therapy, even if this reduced their height gap, may not achieve the peers' height [4,8].

Considering our findings, the hypothesis we postulated was partially confirmed. Indeed, we found no differences in strength performance of lower limbs and on stabilometric parameters between groups. However, the HC group showed higher significant levels of MIHS, for both hands, than the ISS group. Furthermore, supporting our hypothesis, when ISS and HC groups were stratified into active and inactive, our outcomes reported a symmetrical plantar loading distribution between feet for both within-group analyses (i.e., ISS active group and HC active group); whereas both the inactive groups of ISS and HC showed an unequal loading distribution between the right and the left foot, and this result explains the tendency found for both groups (i.e., ISS and HC).

Relevant level of limbs' strength is fundamental in daily life activities and, moreover, represents a basic quality possessed by physical activity practitioners and athletes in order to maintain physiological body functions and/or enjoy exercise in the best way for the former, and to obtain the best possible results for the latter, respectively [30,31]. In particular, handgrip strength has been considered as marker of health and some studies have demonstrated the correlation between MIHS and global body muscle strength [32,33]. It is widely recognized that a weak handgrip strength can affect children's social and psychological spheres causing difficulties in some basic tasks such as playing or writing [34]. The handgrip strength results we obtained agree with several studies. In particular, since the handgrip test is used for the prognosis of muscle strength in several idiopathic and congenital diseases, our results are in agreement with previous results that reported lower handgrip strength in patients with various diseases both in adults as well as in children [34,35]. However, the main key explanation for the differences we found in the MIHS between the two groups

could be the strict correlation existing between handgrip strength and the anthropometric characteristics, in particular children's height, as demonstrated by many research groups [35,36].

We suppose that we did not find differences on lower limbs' strength between ISS and HC groups thanks to the effectiveness of the GH treatment to which the children with ISS were subjected, according to many previous studies reporting increases in muscle size and muscle strength in children treated [37].

The physiological function of both the nervous and muscular systems can be altered in ISS children with GH hormone deficiency [38,39]. Sartorio et al. have reported that patients with GH deficiency show a reduction of the postural and non-postural muscles strength [40]. Musculoskeletal abnormalities have been demonstrated to influence negatively body posture [41,42]. Several studies have shown poor body balance, abnormalities in postural control and, more generally, impairments in motor skills in patients affected by GH hormone deficiency [3,43,44].

Scientific literature shows many articles have demonstrate that hormonal treatment in children improves cognitive and motor abilities reducing the gap with their healthy peers [45]. In the same way, Mauras et al. reported higher levels of muscle strength after gonadotropin-releasing hormone (GnRHa) treatment in children with short stature [46]. Moreover, several researches demonstrated that long-term GH treatment in children with short stature increases muscle mass improving the related muscle strength [37,47].

These previous researches clearly defined the positive influence of hormone treatment on muscle strength in children with short stature. In accordance with what is written above and given the effects on several human hallmarks, the promotion of the practice of physical exercise can improve muscle strength levels in patients with ISS that are subjected to GH treatment and can prevent the aforementioned issues.

For these reasons, on the basis of our results, we assume that GH therapy integrated with physical exercise in young patients with ISS could be suggested, not only to increase muscle strength and to improve postural features, but also to stimulate the secretion of GH, improving the general quality of life.

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References

1. Deodati, A.; Cianfarani, S. Impact of growth hormone therapy on adult height of children with idiopathic short stature: Systematic review. *BMJ* **2011**, *342*, c7157, doi:10.1136/bmj.c7157.
2. Wit, J.; Clayton, R.; Rogol, A.; Savage, M.; Saenger, P.; Cohen, P. Idiopathic short stature: Definition, epidemiology, and diagnostic evaluation. *Growth Horm. IGF Res.* **2008**, *18*, 89–110, doi:10.1016/j.ghir.2007.11.004.
3. Wheeler, P.G.; Bresnahan, K.; Shephard, B.A.; Lau, J.; Balk, E.M. Short Stature and Functional Impairment. *Arch. Pediatr. Adolesc. Med.* **2004**, *158*, 236, doi:10.1001/archpedi.158.3.236.
4. Bryant, J.; Cavé, C.; Milne, R. Recombinant growth hormone for idiopathic short stature in children and adolescents. *Cochrane Database Syst. Rev.* **2003**, *2003*, doi:10.1002/14651858.cd004440.
5. Cohen, P.; Rogol, A.D.; Deal, C.L.; Saenger, P.; Reiter, E.O.; Ross, J.L.; Chernausek, S.D.; Savage, M.O.; Wit, J.M.; ParticipantsO.B.O.T.2.I.C.W. Consensus Statement on the Diagnosis and Treatment of Children with Idiopathic Short Stature: A Summary of the Growth Hormone Research Society, the Lawson Wilkins Pediatric Endocrine Society, and the European Society for Paediatric Endocrinology Workshop. *J. Clin. Endocrinol. Metab.* **2008**, *93*, 4210–4217, doi:10.1210/jc.2008-0509.

6. Kelnar, C.; Albertsson-Wikland, K.; Hintz, R.; Ranke, M.B.; Rosenfeld, R. Should We Treat Children with Idiopathic Short Stature? *Horm. Res. Paediatr.* **1999**, *52*, 150–157.
7. Wit, J.; Reiter, E.; Ross, J.; Saenger, P.; Savage, M.; Rogol, A.; Cohen, P. Idiopathic short stature: Management and growth hormone treatment. *Growth Horm. IGF Res.* **2008**, *18*, 111–135, doi:10.1016/j.ghir.2007.11.003.
8. Finkelstein, B.S.; Imperiale, T.F.; Speroff, T.; Marrero, U.; Radcliffe, D.J.; Cuttler, L. Effect of Growth Hormone Therapy on Height in Children With Idiopathic Short Stature. *Arch. Pediatr. Adolesc. Med.* **2002**, *156*, 230, doi:10.1001/archpedi.156.3.230.
9. Schena, L.; Meazza, C.; Pagani, S.; Paganelli, V.; Bozzola, E.; Tinelli, C.; Buzi, F.; Bozzola, M. Efficacy of long-term growth hormone therapy in short non-growth hormone-deficient children. *J. Pediatr. Endocrinol. Metab.* **2017**, *30*, doi:10.1515/jpem–2016–0297.
10. Sandberg, D.E. Quality of life and self-esteem in children treated for idiopathic short stature. *J. Pediatr.* **2003**, *143*, 691, doi:10.1067/s0022-3476(03)00395-0.
11. Quitmann, J.; Bullinger, M.; Sommer, R.; Rohenkohl, A.C.; Silva, N. Associations between Psychological Problems and Quality of Life in Pediatric Short Stature from Patients' and Parents' Perspectives. *PLoS ONE* **2016**, *11*, e0153953, doi:10.1371/journal.pone.0153953.
12. Jeong, H.R.; Shim, Y.S.; Lee, H.S.; Hwang, J.S. The effect of growth hormone treatment on height in children with idiopathic short stature. *J. Pediatr. Endocrinol. Metab.* **2014**, *27*, doi:10.1515/jpem–2013–0461.
13. Dahlgren, J. Metabolic Benefits of Growth Hormone Therapy in Idiopathic Short Stature. *Horm. Res. Paediatr.* **2011**, *76*, 56–58, doi:10.1159/0003301655.
14. Yackobovitch-Gavan, M.; Gat-Yablonski, G.; Shtaif, B.; Hadani, S.; Abargil, S.; Phillip, M.; Lazar, L. Growth hormone therapy in children with idiopathic short stature–the effect on appetite and appetite-regulating hormones: A pilot study. *Endocr. Res.* **2018**, *44*, 16–26.
15. Gardner, M.; Boshart, M.; Yeguez, C.; Desai, K.; Sandberg, D. Coming up short: Risks of bias in studies assessing psychological outcomes associated with growth hormone therapy for short stature. *J. Clin. Endocrinol. Metab.* **2016**, *101*, 23–30, doi:10.1210/jc.2015-3256.
16. Chaplin, J.E.; Kriström, B.; Jonsson, B.; Tuvemo, T.; Albertsson-Wikland, K. Growth Hormone Treatment Improves Cognitive Function in Short Children with Growth Hormone Deficiency. *Horm. Res. Paediatr.* **2015**, *83*, 390–399, doi:10.1159/000375529.
17. Hunter, W.M.; Fonseka, C.C.; Passmore, R. Growth Hormone: Important Role in Muscular Exercise in Adults. *Sci.* **1965**, *150*, 1051–1053, doi:10.1126/science.150.3699.1051.
18. Pagani, S.; Cappa, M.; Meazza, C.; Ubertini, G.; Travaglino, P.; Bozzola, E.; Bozzola, M. Growth hormone isoforms release in response to physiological and pharmacological stimuli. *J. Endocrinol. Investig.* **2008**, *31*, 520–524, doi:10.1007/bf03346401.
19. Curtis, V.; Allen, D.B. Boosting the Late-Blooming Boy. *Sports Heal. A Multidiscip. Approach* **2010**, *3*, 32–40, doi:10.1177/1941738110386705.
20. Krzykała, M.; Czerniak, U.; DeMuth, A. [Physical and motor development of preschool children in aspect of short stature]. *Pediatr. Endocrinol. Diabetes Metab.* **2008**, *14*, 135–140.
21. Tomaszewski, P.; Milde, K.; Sienkiewicz-Dianzenza, E.; Nowicki, D. [Physical fitness of short-statured children at the early-school age]. *Pediatr. Endocrinol. Diabetes Metab.* **2007**, *13*, 125–128.
22. Liu, M.; Wu, L.; Ming, Q. How Does Physical Activity Intervention Improve Self-Esteem and Self-Concept in Children and Adolescents? Evidence from a Meta-Analysis. *PLoS ONE* **2015**, *10*, e0134804, doi:10.1371/journal.pone.0134804.
23. Bidzan-Bluma, I.; Lipowska, M. Physical Activity and Cognitive Functioning of Children: A Systematic Review. *Int. J. Environ. Res. Public Heal.* **2018**, *15*, 800, doi:10.3390/ijerph15040800.
24. Harridge, S.D.R.; Lazarus, N. Physical Activity, Aging, and Physiological Function. *Physiol.* **2017**, *32*, 152–161, doi:10.1152/physiol.00029.2016.
25. Battaglia, G.; Giustino, V.; Messina, G.; Faraone, M.; Brusa, J.; Bordonali, A.; Barbagallo, M.; Palma, A.; Dominguez, L.-J. Walking in Natural Environments as Geriatrician's Recommendation for Fall Prevention: Preliminary Outcomes from the "Passiata Day" Model. *Sustainable* **2020**, *12*, 2684, doi:10.3390/su12072684.
26. Scoppa, F.; Gallamini, M.; Belloni, G.; Messina, G. Clinical Stabilometry Standardization: Feet Position in the Static Stabilometric Assessment of Postural Stability. *Acta Medica. Mediterr.* **2017**, *33*, 707–713, doi:10.19193/0393-6384_2017_4_105.

27. The jamovi project (2020). jamovi (Version 1.2) [Computer Software]. Retrieved from https://www.jamovi.org.
28. Bryant, J.; Baxter, L.; Cave, C.B.; Milne, R. Recombinant growth hormone for idiopathic short stature in children and adolescents. *Cochrane Database Syst. Rev.* **2007**, *2007*, CD004440, doi:10.1002/14651858.CD004440.pub2.
29. Wit, J.M.; Ranke, M.B.; Kelnar, C.J.H. *ESPE Classification of Paediatric Endocrine Diagnoses: Supplement Issue: Hormone Research 2007, Vol. 68, Suppl. 2. S. Karger 2007.*.
30. Eika, F.; Blomkvist, A.W.; Rahbek, M.T.; Eikhof, K.D.; Hansen, M.D.; Søndergaard, M.; Ryg, J.; Andersen, S.; Jorgensen, M. Reference data on hand grip and lower limb strength using the Nintendo Wii balance board: A cross-sectional study of 354 subjects from 20 to 99 years of age. *BMC Musculoskelet. Disord.* **2019**, *20*, 21, doi:10.1186/s12891-019-2405-7.
31. Hasegawa, R.; Islam, M.M.; Lee, S.C.; Koizumi, D.; Rogers, M.E.; Takeshima, N. Threshold of lower body muscular strength necessary to perform ADL independently in community-dwelling older adults. *Clin. Rehabil.* **2008**, *22*, 902–910, doi:10.1177/0269215508094713.
32. Bohannon, R.W.; Magasi, S.R.; Bubela, D.J.; Wang, Y.-C.; Gershon, R.C. Grip and knee extension muscle strength reflect a common construct among adults. *Muscle Nerve* **2012**, *46*, 555–558, doi:10.1002/mus.23350.
33. Ortega, F.B.; Silventoinen, K.; Tynelius, P.; Rasmussen, F. Muscular strength in male adolescents and premature death: Cohort study of one million participants. *BMJ* **2012**, *345*, e7279, doi:10.1136/bmj.e7279.
34. Mahmoud, A.G.; Elhadidy, E.I.; Hamza, M.S.; Mohamed, N.E. Determining correlations between hand grip strength and anthropometric measurements in preschool children. *J. Taibah Univ. Med Sci.* **2020**, *15*, 75–81, doi:10.1016/j.jtumed.2020.01.002.
35. Bohannon, R.W. Muscle strength. *Curr. Opin. Clin. Nutr. Metab. Care* **2015**, *18*, 465–470, doi:10.1097/mco.0000000000000202.
36. Molenaar, H.M.; Selles, R.W.; Zuidam, J.M.; Willemsen, S.P.; Stam, H.J.; Hovius, S.E.R. Growth Diagrams for Grip Strength in Children. *Clin. Orthop. Relat. Res.* **2009**, *468*, 217–223, doi:10.1007/s11999-009-0881-z.
37. Berndt, C.; Schweizer, R.; Ranke, M.B.; Binder, G.; Martin, D. Height, Muscle, Fat and Bone Response to Growth Hormone in Short Children with Very Low Birth Weight Born Appropriate for Gestational Age and Small for Gestational Age. *Horm. Res. Paediatr.* **2014**, *82*, 81–88.
38. Mainenti, M.; Vigário, P.S.; Teixeira, P.F.S.; Maia, M.D.L.; Oliveira, F.P.; Vaisman, M. Effect of levothyroxine replacement on exercise performance in subclinical hypothyroidism. *J. Endocrinol. Investig.* **2009**, *32*, 470–473, doi:10.1007/bf03346488.
39. Macfaul, R.; Dorner, S.; Brett, E.M.; Grant, D.B. Neurological abnormalities in patients treated for hypothyroidism from early life. *Arch. Dis. Child.* **1978**, *53*, 611–619, doi:10.1136/adc.53.8.611.
40. Sartorio, A.; Narici, M.; Conti, A.; Monzani, M.; Faglia, G. Quadriceps and hand-grip strength in adults with childhood-onset growth hormone deficiency. *Eur. J. Endocrinol.* **1995**, *132*, 37–41, doi:10.1530/eje.0.1320037.
41. Battaglia, G.; Bellafiore, M.; Bianco, A.; Paoli, A.; Palma, A. Effects of a dynamic balance training protocol on podalic support in older women. Pilot Study. *Aging Clin. Exp. Res.* **2009**, *22*, 418–424, doi:10.1210/jc.2005-1209.
42. Bellafiore, M.; Battaglia, G.; Bianco, A.; Paoli, A.; Farina, F.; Palma, A. Improved postural control after dynamic balance training in older overweight women. *Aging Clin. Exp. Res.* **2010**, *70*, 614–618, doi:10.1203/PDR.0b013e3182321128.
43. Kempers, M.; Veer, L.V.D.S.; Van Der Sanden, M.W.G.N.; Kooistra, L.; Wiedijk, B.M.; Faber, I.R.; Last, B.F.; De Vijlder, J.J.M.; Grootenhuis, M.A.; Vulsma, T. Intellectual and Motor Development of Young Adults with Congenital Hypothyroidism Diagnosed by Neonatal Screening. *J. Clin. Endocrinol. Metab.* **2006**, *91*, 418–424, doi:10.1210/jc.2005-1209.
44. Hauri-Hohl, A.; Dusoczky, N.; Dimitropoulos, A.; Leuchter, R.H.-V.; Molinari, L.; Caflisch, J.; Jenni, O.G.; Latal, B. Impaired Neuromotor Outcome in School-Age Children With Congenital Hypothyroidism Receiving Early High-Dose Substitution Treatment. *Pediatr. Res.* **2011**, *70*, 614–618, doi:10.1203/pdr.0b013e3182321128.
45. Donze, S.H.; Damen, L.; Mahabier, E.F.; Hokken-Koelega, A.C.S. Improved Mental and Motor Development During 3 Years of GH Treatment in Very Young Children With Prader-Willi Syndrome. *J. Clin. Endocrinol. Metab.* **2018**, *103*, 3714–3719, doi:10.1210/jc.2018-0068.

46. Mauras, N.; Hayes, V.; Welch, S.; Rini, A.; Helgeson, K.; Dokler, M.; Veldhuis, J.D.; Urban, R.J. Testosterone Deficiency in Young Men: Marked Alterations in Whole Body Protein Kinetics, Strength, and Adiposity1. *J. Clin. Endocrinol. Metab.* **1998**, *83*, 1886–1892, doi:10.1210/jcem.83.6.4892.
47. Schweizer, R.; Schwarze, C.P.; Binder, G.; Georgiadou, A.; Ihle, J.; Ranke, M.B.; Martin, D.D. Cortical Bone Density Is Normal in Prepubertal Children with Growth Hormone (GH) Deficiency, but Initially Decreases during GH Replacement due to Early Bone Remodeling. *J. Clin. Endocrinol. Metab.* **2003**, *88*, 5266–5272, doi:10.1210/jc.2003-030432.