ŁUNIEWSKI, Bartosz, MACKO, Angelika, ŁUNIEWSKA, Maria, LAUKO, Kamil, OLSZAŃSKA, Monika, NOWICKA, Iga and JURCZUK, Aleksandra. Physical activity in the management of obesity in prader-willi syndrome. Quality in Sport. 2025;41:60335. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.41.60335
https://apcz.umk.pl/QS/article/view/60335

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 15.04.2025. Revised: 25.04.2025. Accepted: 06.05.2025. Published: 11.05.2025.

PHYSICAL ACTIVITY IN THE MANAGEMENT OF OBESITY IN PRADER-WILLI SYNDROME

Bartosz Łuniewski – corresponding author

Medical University of Bialystok,

Jana Kilińskiego 1, 15-089 Białystok, Poland

https://orcid.org/0009-0005-8934-6626

e-mail: bartosz.lun12@gmail.com

Angelika Macko

Medical University of Bialystok

Jana Kilińskiego 1, 15-089 Białystok, Poland

https://orcid.org/0009-0007-1274-2481

e-mail: angel1682000@gmail.com

Maria Łuniewska

Mazovian Regional Hospital

Poniatowskiego 26, 08-110 Siedlce, Poland

https://orcid.org/0009-0005-2349-0182

e-mail: maria.luniewska@wp.pl

Kamil Klaudiusz Lauko
Medical University of Bialystok
Jana Kilińskiego 1, 15-089 Białystok, Poland
https://orcid.org/0000-0003-0727-3661
e-mail: kamillauko.research@gmail.com

Monika Olszańska
Medical University of Bialystok
Jana Kilińskiego 1, 15-089 Białystok, Poland
https://orcid.org/0009-0006-2511-505X
email: moniolsza00@gmail.com

Iga Maria Nowicka
Medical University of Bialystok
Jana Kilińskiego 1, 15-089 Białystok, Poland
https://orcid.org/0009-0000-4218-0036
iganowicka7@gmail.com

Aleksandra Jurczuk
Medical University of Bialystok
Jana Kilińskiego 1, 15-089 Białystok, Poland
https://orcid.org/0009-0003-5369-5395
email: aleksandra.jurczuk@sd.umb.edu.pl

Abstract:

Introduction: Prader-Willi syndrome (PWS) is a rare genetic disorder whose most characteristic and dangerous symptom is massive obesity. It develops as a result of neurohormonal abnormalities, abnormal appetite regulation and reduced energy expenditure.

Due to its multifactorial nature, the treatment of obesity in PWS presents particular clinical challenges.

Materials and methods: A review of selected literature in the PubMed database was conducted, using the following keywords: “Prader Willi Syndrom”, “Phisical excercise”, “Obesity”,”Treatment”

Summary: This paper discusses the main mechanisms leading to the development of obesity in PWS, such as hypothalamic dysfunction, endocrine disruption (ghrelin, leptin, GH) and changes in body composition. Current therapeutic strategies - nutritional therapy adapted to the developmental stage of the patient, growth hormone treatment and the potential use of anti-obesity drugs - were analysed. Special attention was given to the role of physical activity, which, despite its limited effect on body weight, significantly improves fitness, muscle strength, body composition and quality of life in patients.

Conclusions: The management of obesity in PWS requires an individualised, multidirectional approach based on collaboration between the specialist team and the family. Given the limited efficacy of available therapies, further research is needed into new treatments - both pharmacological and non-pharmacological - that are better adapted to the metabolic and behavioural specificities of this patient group.

Keywords: Prader Willi syndrome; genetic syndrome; growth hormone; physical activity

1. Introduction:

Prader-Willi syndrome (PWS) is a disease with complex effects on multiple body systems. With an estimated incidence of 1 in 10,000 to 1 in 30,000 in the populations studied, it is the most common syndromic cause of life-threatening obesity and the first recognised genomic imprinting disorder in humans [1]. It results from a deletion on chromosome 15 in the region 15q11.2-q13, which is inherited from the father. There are three main genetic types of PWS: deletion of the 15q11-q13 region of paternal origin (present in approximately 65-75% of cases), maternal disomy of chromosome 15 (present in 20-30% of patients) and genetic stigma defect (observed in 1-3% of cases) [2].

PWS has a variable course in the neonatal period and is mainly characterised by severe muscle weakness (hypotonia), a weak sucking reflex and feeding difficulties. In late infancy or early childhood, an excessive appetite develops which, if uncontrolled, can lead to morbid obesity [3]. Obesity and its complications are a major cause of morbidity and mortality in Prader-Willi syndrome (PWS). Several mechanisms have been proposed to underlie the development of obesity in this disorder, including abnormalities in hypothalamic pathways responsible for satiety control, disruption of the function of hormones that regulate appetite and satiety, and reduced energy expenditure. Despite progress in understanding the genetic basis of obesity in PWS, the available treatment data are still inconsistent. Although obesity prevention should begin in infancy, there are promising reports on the possibility of treating obesity in adult patients with PWS - using modern anti-obesity drugs in combination with lifestyle changes, although the available data in this area are still limited [4].

2. Etiology of obesity in PWS

Obesity is a key symptom of Prader-Willi syndrome (PWS) and a major cause of morbidity and mortality in patients. It develops gradually, starting at two years of age. It is characterised by a multiphasic eating pattern, ranging from feeding difficulties in infancy (phase 1), through a gradual increase in appetite and interest in food (phase 2), to full-blown hyperphagia and compulsive eating (phase 3), which may be partially alleviated in adulthood (phase 4) [5]. The main mechanism responsible for the development of obesity in PWS is the dysfunction of the hypothalamic satiety centre and its hormonal regulatory pathways. This leads to a constant feeling of hunger, hyperphagia and compulsive eating behaviour - such as aggressive food seeking, stealing or eating inedible objects [6]. Behavioural problems with features of autism spectrum disorder have also been observed to exacerbate these difficulties [7]. Brain imaging studies have shown increased activity in reward areas (nucleus accumbens, amygdala) before meals, reduced activity of the hypothalamus and hippocampus in response to food, reduced activation of the prefrontal cortex responsible for impulse inhibition, and impaired functional connectivity between the ventral striatum and limbic structures in people with PWS. This leads to an inappropriate assessment of hunger and satiety and an excessive motivation to eat [8,9].

2.1 Endocrine disorders regulating appetite and adipogenesis

Endocrine disorders play a key role in the development of obesity in people with PWS. The most important hormone is ghrelin, a potent appetite stimulant. In patients with PWS, its levels are elevated from infancy. Initially, its inactive form (UAG) predominates, which explains the lack of appetite, and over time the active fraction (AG) increases, leading to uncontrollable hunger[10]. Despite attempts at ghrelin-lowering pharmacological treatment, it has failed to reduce appetite, indicating persistent changes in the satiety system [11].

Leptin, responsible for the feeling of satiety, is present in PWS patients in amounts proportional to adipose tissue, with no evidence of impaired function[12]. In contrast, adiponectin, beneficial for glucose metabolism and insulin sensitivity, is present in PWS patients at higher levels than in typically obese individuals, which may explain the lower risk of diabetes[13].

Other hormones such as obestatin, peptide YY (PYY) and pancreatic polypeptide (PP) also show some abnormalities, but the data are inconclusive. Also of note is resistin, whose levels are higher than in healthy individuals and may promote fat deposition, although it does not clearly affect insulin resistance [4].

2.2 Other endocrine disorders and body composition

Patients with PWS have a growth hormone deficiency that results in reduced muscle mass, increased fat - especially around the trunk - reduced energy expenditure and weakened muscle strength [14]. PWS is also characterised by hypogonadism, or hormonal failure of the gonads, which also promotes loss of muscle mass and fat accumulation [15]. In addition, hypothyroidism, which often co-exists, further reduces the metabolic rate [16]. Interestingly, despite having a high BMI, people with PWS have less visceral fat and more subcutaneous fat. This specific fat distribution may explain the milder metabolic course - patients with PWS often have better insulin sensitivity and a lower risk of developing diabetes compared to those with typical obesity [17].

3. Treatment of Obesity:

Dietary management of obesity in Prader-Willi syndrome (PWS) plays a key role and should be tailored to the changing nutritional phases of the patient. Children with PWS have a reduced energy expenditure (REE) and require a much lower calorie intake than healthy children - from infancy onwards. During the preschool and school years, an intake of 10-12

kcal/cm of growth is recommended for weight maintenance and 6-8 kcal/cm for weight reduction [18,19]. Best results are achieved with a diet containing ≤45% complex carbohydrates (up to 20g fibre), 30% fat and 25% protein. It is also important to limit access to food and to maintain constant monitoring [20].

Growth hormone

Growth hormone (GH) is currently the only FDA-approved treatment for patients with PWS. Its use is beneficial in reducing fat mass, increasing muscle mass, and improving growth rate and psychomotor development. Studies have shown that starting GH therapy at 3-6 months of age leads to improved IQ and energy expenditure [21]. Treatment should be individualised according to IGF-1 levels, growth rate and body composition. Although it does not lead to complete normalisation of body weight, it significantly improves it [22]. Contraindications to the use of GH include severe obesity and sleep apnoea [23].

Topiramate

Topiramate (anti-epileptic drug) may reduce appetite and improve behaviour - some studies have found a reduction in weight and aggression [24].

Metformin

Metformin, used for insulin resistance, showed an improvement in eating anxiety but did not lead to weight loss. Some patients discontinued treatment due to worsening emotional state [25].

Naltrexone-Bupropion

Naltrexone-bupropion is a combination that affects central appetite regulation; one study showed improved behaviour and reduced BMI in a child with PWS [26].

GLP-1 receptor agonists

GLP-1 receptor agonists (e.g. liraglutide, exenatide) improve glycaemic control, reduce ghrelin levels and promote satiety. Although the effects on BMI were moderate, reductions in appetite and improvements in metabolic parameters were observed [27].

Oxytocin

Intranasal oxytocin has been shown in some studies to improve social and eating behaviour, although not all studies have confirmed this Intranasal oxytocin has

been shown in some studies to improve social and eating behaviour, although not all studies have confirmed this [28].

4. Prevention of obesity

4.1 Dietary and Behavioral interventions

Prevention of obesity in children with Prader-Willi syndrome (PWS) should begin as early as possible, preferably in the first months of life. The main goal is to control caloric intake, which is challenging due to poor patient compliance [29]. Initially, the diet should ensure proper development, but after the first year of life, it is necessary to introduce a low-calorie but well-balanced diet. An important part of prevention is also constant monitoring of access to food to reduce the tendency to sneak food. Effective prevention requires the involvement of a multidisciplinary team and the education of the family and caregivers in the daily management of the child's diet and eating behavior [4].

4.2 The role of phisical activity in PWS

Physical activity (AF) plays a key role in the comprehensive therapeutic management of people with Prader-Willi syndrome (PWS), although its implementation is associated with specific difficulties. Patients with PWS show significantly lower levels of daily exercise than those with non-syndromic obesity. This is due to a combination of syndrome-specific features: deficiency of lean body mass, muscular hypotonia, low physical capacity and limited motivation [30]. Only 5-8% of children and 15-25% of adults with PWS meet the World Health Organisation (WHO) recommendations for moderate to vigorous physical activity (MVPA), which is 60 minutes a day for children [31].

Despite low levels of activity, well-planned exercise interventions have a number of health benefits. Studies have shown that regular exercise improves cardiorespiratory fitness, muscle strength, motor coordination and gait parameters that are typically impaired in people with PWS [32]. Improvements in bone mineral density and lean body mass gain were also seen in children and adults [33]. While exercise alone rarely leads to significant weight or BMI reduction, its impact on overall fitness, metabolism and quality of life cannot be overstated. Importantly, AF in PWS is safe - there have been no reported cases of serious exercise-related side effects [34,35].

From a physiological point of view, it is worth noting that children with PWS do not show the typical increase in growth hormone (GH) after intense physical activity, although IGF-1 levels may increase normally. Therefore, physical activity does not replace GH therapy, but can effectively support it and enhance its effects on muscle development and overall performance [36].

Implementing effective AF programmes requires a personalised approach and the involvement of the entire patient environment - family, therapists, teachers and carers. The best results are achieved when physical activity is part of the daily routine and the patient is involved in the choice of activities [37]. Research shows that children with PWS do best when they can choose their own activities ('player's choice'). The variety of activities is important - from movement games, dance and active video games to group activities or psychomotor therapy. High levels of participation in activities have been observed in both home and institutional settings, provided that the activities are appropriately supervised and adapted to the mood, fatigue and motivation of the participants [38].

In order for physical activity to have a lasting effect, it is essential that parents and carers are provided with both emotional and organisational support (e.g. educational materials, training, counselling). It should also be emphasised that people with PWS and their families often feel isolated and overburdened with therapeutic responsibilities, so the role of the medical team is not only to plan but also to actively support the implementation of physical activity programmes [39].

Despite promising results, current evidence is mainly based on studies with small sample sizes and diverse methodologies, making it difficult to draw firm conclusions. More research is needed to compare different forms of activity, their effectiveness in different age groups, and their potential to prevent weight gain, especially during the transition from childhood to adulthood.

5. Summary and Conclusion

The prevalence of obesity in individuals diagnosed with Prader-Willi syndrome is attributable to a multifaceted interplay among genetic, hormonal, and behavioural factors. The early onset of obesity, coupled with difficulties in appetite control, poses a significant challenge to

healthcare providers, as it frequently leads to health complications and even death in this patient group. A multidisciplinary approach is imperative for the treatment of obesity in PWS, encompassing dietary interventions, hormonal therapy, and psychological support.

Physical activity plays a particularly important role, although it rarely leads to significant weight loss. Nonetheless, it improves overall fitness, muscle strength, metabolism and quality of life. The effectiveness of interventions, however, is contingent on an individualised approach, family support, and a meticulously planned routine.

Despite the existence of available therapies, their effectiveness is often limited and variable. Consequently, there is an urgent need for further research into new treatment strategies, both pharmacological and non-pharmacological, that take into account the metabolic and behavioural specificities of PWS patients. A personalised, multidirectional approach is imperative for effectively managing obesity and enhancing quality of life in individuals affected by this condition.

Disclosure

Author's contribution

Conceptualization: Bartosz Łuniewski

Methodology: Bartosz Łuniewski, Angelika Macko, Maria Łuniewska, Monika Olszańska, Kamil Lauko, Iga Nowicka, Aleksandra Jurczuk

Formal analysis: Kamil Lauko, Maria Łuniewska, Monika Olszańska, Aleksandra Jurczuk

Investigation: Iga Nowicka, Maria Łuniewska

Writing-rough preparation: Monika Olszańska, Iga Nowicka

Writing-review and editing: Bartosz Łuniewski, Angelika Macko, Kamil Lauko

Supervision: Bartosz Łuniewski

Receiving funding – not applicable

All authors have read and agreed with the published version of the manuscript.

Funding Statement

The article did not receive any funding.

Institutional Review and Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

Not applicable.

Conflict of Interest Statement

Authors declare no conflicts of interest.

REFRENCES:

1. Nicholls RD, Knoll JH, Butler MG, Karam S, Lalande M. Genetic imprinting suggested by maternal heterodisomy in nondeletion Prader-Willi syndrome. *Nature*. 1989;342(6247):281-285. doi:10.1038/342281a0

2. Angulo MA, Butler MG, Cataletto ME. Prader-Willi syndrome: a review of clinical, genetic, and endocrine findings. *J Endocrinol Invest*. 2015;38(12):1249-1263. doi:10.1007/s40618-015-0312-9

3. Butler MG. Prader-Willi Syndrome: Obesity due to Genomic Imprinting. *Curr Genomics*. 2011;12(3):204-215. doi:10.2174/138920211795677877

4. Muscogiuri G, Barrea L, Faggiano F, et al. Obesity in Prader-Willi syndrome: physiopathological mechanisms, nutritional and pharmacological approaches. *J Endocrinol Invest*. 2021;44(10):2057-2070. doi:10.1007/s40618-021-01574-9

5. Miller JL, Lynn CH, Driscoll DC, et al. Nutritional phases in Prader-Willi syndrome. *Am J Med Genet A*. 2011;155A(5):1040-1049. doi:10.1002/ajmg.a.33951

6. Muscogiuri G, Formoso G, Pugliese G, et al. Prader- Willi syndrome: An uptodate on endocrine and metabolic complications. *Rev Endocr Metab Disord*. 2019;20(2):239-250. doi:10.1007/s11154-019-09502-2

7. Khan MJ, Gerasimidis K, Edwards CA, Shaikh MG. Mechanisms of obesity in Prader-Willi syndrome. *Pediatr Obes*. 2018;13(1):3-13. doi:10.1111/ijpo.12177

8. Holsen LM, Zarcone JR, Brooks WM, et al. Neural mechanisms underlying hyperphagia in Prader-Willi syndrome. *Obes Silver Spring Md*. 2006;14(6):1028-1037. doi:10.1038/oby.2006.118

9. Holsen LM, Savage CR, Martin LE, et al. Importance of reward and prefrontal circuitry in hunger and satiety: Prader-Willi syndrome vs simple obesity. *Int J Obes 2005*. 2012;36(5):638-647. doi:10.1038/ijo.2011.204

10. Beauloye V, Diene G, Kuppens R, et al. High unacylated ghrelin levels support the concept of anorexia in infants with prader-willi syndrome. *Orphanet J Rare Dis*. 2016;11(1):56. doi:10.1186/s13023-016-0440-0

11. Tauber M, Coupaye M, Diene G, Molinas C, Valette M, Beauloye V. Prader-Willi syndrome: A model for understanding the ghrelin system. *J Neuroendocrinol*. 2019;31(7):e12728. doi:10.1111/jne.12728

12. Butler MG, Moore J, Morawiecki A, Nicolson M. Comparison of leptin protein levels in Prader-Willi syndrome and control individuals. *Am J Med Genet*. 1998;75(1):7-12.

13. Haqq AM, Muehlbauer MJ, Newgard CB, Grambow S, Freemark M. The metabolic phenotype of Prader-Willi syndrome (PWS) in childhood: heightened insulin sensitivity relative to body mass index. *J Clin Endocrinol Metab*. 2011;96(1):E225-232. doi:10.1210/jc.2010-1733

14. Aycan Z, Baş VN. Prader-Willi syndrome and growth hormone deficiency. *J Clin Res Pediatr Endocrinol*. 2014;6(2):62-67. doi:10.4274/Jcrpe.1228

15. Noordam C, Höybye C, Eiholzer U. Prader-Willi Syndrome and Hypogonadism: A Review Article. *Int J Mol Sci*. 2021;22(5):2705. doi:10.3390/ijms22052705

16. Heksch R, Kamboj M, Anglin K, Obrynba K. Review of Prader-Willi syndrome: the endocrine approach. *Transl Pediatr*. 2017;6(4):274-285. doi:10.21037/tp.2017.09.04

17. Goldstone AP, Thomas EL, Brynes AE, et al. Visceral adipose tissue and metabolic complications of obesity are reduced in Prader-Willi syndrome female adults: evidence for novel influences on body fat distribution. *J Clin Endocrinol Metab*. 2001;86(9):4330-4338. doi:10.1210/jcem.86.9.7814

18. Miller JL, Tan M. Dietary Management for Adolescents with Prader-Willi Syndrome. *Adolesc Health Med Ther*. 2020;11:113-118. doi:10.2147/AHMT.S214893

19. Alsaif M, Elliot SA, MacKenzie ML, Prado CM, Field CJ, Haqq AM. Energy Metabolism Profile in Individuals with Prader-Willi Syndrome and Implications for Clinical Management: A Systematic Review. *Adv Nutr Bethesda Md*. 2017;8(6):905-915. doi:10.3945/an.117.016253

20. Miller JL, Lynn CH, Shuster J, Driscoll DJ. A reduced-energy intake, well-balanced diet improves weight control in children with Prader-Willi syndrome. *J Hum Nutr Diet Off J Br Diet Assoc*. 2013;26(1):2-9. doi:10.1111/j.1365-277X.2012.01275.x

21. Carrel AL, Moerchen V, Myers SE, Bekx MT, Whitman BY, Allen DB. Growth hormone improves mobility and body composition in infants and toddlers with Prader-Willi syndrome. *J Pediatr*. 2004;145(6):744-749. doi:10.1016/j.jpeds.2004.08.002

22. Festen DAM, Wevers M, de Weerd AW, et al. Psychomotor development in infants with Prader-Willi syndrome and associations with sleep-related breathing disorders. *Pediatr Res*. 2007;62(2):221-224. doi:10.1203/PDR.0b013e31809871dd

23. Passone CBG, Pasqualucci PL, Franco RR, et al. PRADER-WILLI SYNDROME: WHAT IS THE GENERAL PEDIATRICIAN SUPPOSED TO DO? - A REVIEW. *Rev Paul Pediatr Orgao Of Soc Pediatr Sao Paulo*. 2018;36(3):345-352. doi:10.1590/1984-0462/;2018;36;3;00003

24. Consoli A, Çabal Berthoumieu S, Raffin M, et al. Effect of topiramate on eating behaviours in Prader-Willi syndrome: TOPRADER double-blind randomised placebo-controlled study. *Transl Psychiatry*. 2019;9(1):274. doi:10.1038/s41398-019-0597-0

25. Miller JL, Linville TD, Dykens EM. Effects of metformin in children and adolescents with Prader-Willi syndrome and early-onset morbid obesity: a pilot study. *J Pediatr Endocrinol Metab JPEM*. 2014;27(1-2):23-29. doi:10.1515/jpem-2013-0116

26. Puri MR, Sahl R, Ogden S, Malik S. Prader-Willi Syndrome, Management of Impulsivity, and Hyperphagia in an Adolescent. *J Child Adolesc Psychopharmacol*. 2016;26(4):403-404. doi:10.1089/cap.2015.0240

27. Ng NBH, Low YW, Rajgor DD, et al. The effects of glucagon-like peptide (GLP)-1 receptor agonists on weight and glycaemic control in Prader-Willi syndrome: A systematic review. *Clin Endocrinol (Oxf)*. 2022;96(2):144-154. doi:10.1111/cen.14583

28. Kabasakalian A, Ferretti CJ, Hollander E. Oxytocin and Prader-Willi Syndrome. *Curr Top Behav Neurosci*. 2018;35:529-557. doi:10.1007/7854_2017_28

29. Crinò A, Fintini D, Bocchini S, Grugni G. Obesity management in Prader-Willi syndrome: current perspectives. *Diabetes Metab Syndr Obes Targets Ther*. 2018;11:579-593. doi:10.2147/DMSO.S141352

30. Butler MG, Theodoro MF, Bittel DC, Donnelly JE. Energy expenditure and physical activity in Prader-Willi syndrome: comparison with obese subjects. *Am J Med Genet A*. 2007;143A(5):449-459. doi:10.1002/ajmg.a.31507

31. Bellicha A, Coupaye M, Hocquaux L, Speter F, Oppert JM, Poitou C. Increasing physical activity in adult women with Prader-Willi syndrome: A transferability study. *J Appl Res Intellect Disabil JARID*. 2020;33(2):258-267. doi:10.1111/jar.12669

32. Vismara L, Romei M, Galli M, et al. Clinical implications of gait analysis in the rehabilitation of adult patients with “Prader-Willi” Syndrome: a cross-sectional comparative study (“Prader-Willi” Syndrome vs matched obese patients and healthy subjects). *J Neuroengineering Rehabil*. 2007;4:14. doi:10.1186/1743-0003-4-14

33. Rubin DA, Wilson KS, Orsso CE, et al. A 24-Week Physical Activity Intervention Increases Bone Mineral Content without Changes in Bone Markers in Youth with PWS. *Genes*. 2020;11(9):984. doi:10.3390/genes11090984

34. Shields N, Bennell KL, Radcliffe J, Taylor NF. Is strength training feasible for young people with Prader-Willi syndrome? A phase I randomised controlled trial. *Physiotherapy*. 2020;106:136-144. doi:10.1016/j.physio.2019.01.016

35. Capodaglio P, Cimolin V, Vismara L, et al. Postural adaptations to long-term training in Prader-Willi patients. *J Neuroengineering Rehabil*. 2011;8:26. doi:10.1186/1743-0003-8-26

36. Morales JS, Valenzuela PL, Pareja-Galeano H, Rincón-Castanedo C, Rubin DA, Lucia A. Physical exercise and Prader-Willi syndrome: A systematic review. *Clin Endocrinol (Oxf)*. 2019;90(5):649-661. doi:10.1111/cen.13953

37. Shields N, Westle A, Bennell KL, Taylor NF. Physiotherapists perceived developing positive rapport facilitates participation in exercise among people with Prader-Willi Syndrome: a qualitative study. *Disabil Rehabil*. 2020;42(24):3475-3480. doi:10.1080/09638288.2019.1597176

38. Rubin DA, Wilson KS, Honea KE, et al. An evaluation of the implementation of a parent-led, games-based physical activity intervention: the Active Play at Home quasi-randomized trial. *Health Educ Res*. 2019;34(1):98-112. doi:10.1093/her/cyy035

39. Bellicha A, Coupaye M, Mosbah H, Tauber M, Oppert JM, Poitou C. Physical Activity in Patients with Prader-Willi Syndrome-A Systematic Review of Observational and Interventional Studies. *J Clin Med*. 2021;10(11):2528. doi:10.3390/jcm10112528