

Pediatric obesity and brain health: a novel and important topic – expert opinion of the European Childhood Obesity Group

John Reilly, Professor of Physical Activity and Public Health Science, University of Strathclyde

Obesity is a major public health concern for developed and developing countries. Over the past years, paediatric obesity has more than doubled in children and tripled in adolescents worldwide (1). The consequences of childhood obesity are dramatic, leading to overweight/obesity later in life (2), future morbidity and mortality (3, 4), as well as metabolic, functional, psychosocial or quality of life impairments, among others (5, 6). While most of the time unconsidered, child and adolescent obesity has been also associated with impaired brain health, structure and function (7-10), that can definitely affect individuals' day-to-day social interaction and integration, and even potential occupational success later in life (11).

Cognitive functioning effectively represents all the mental processes that allow individuals to properly perform any task, allowing an active role in the processes of receiving, choosing, transforming, storing, processing and retrieval of information. Specifically, executive function refers to the higher cognitive processes that enable forethought and goal-directed action, and involves inhibitory control, working memory and cognitive flexibility (12). In youth, executive functions, in turn, have been suggested to predict academic performance (13). While the association between obesity and impaired executive function has been widely established in adults (14), this remains less known in children and adolescents. Indeed, while some studies support the existence of executive function deficits in individuals with overweight/obesity, others fail to observe these differences (9). As such, there is still a clear need to better identify not only the cause-effects relationships between obesity and executive function during childhood and adolescence, but also their underlying brain implications, since healthier

This is a peer reviewed accepted author manuscript of the following in-press article: Reilly, J. (Accepted/In press - 2020). Pediatric obesity and brain health: a novel and important topic – expert opinion of the European Childhood Obesity Group. *Pediatric Obesity* .

brain may imply improved executive function, and in turn, better and healthier eating and activity choices (15, 16).

Paediatric obesity may compromise brain health by influencing both brain structure and function (8, 15, 17, 18). Structural neuroimaging studies in paediatric populations showed that obesity has been linked to smaller grey matter volume in brain regions involved in executive function, such as the prefrontal cortex (18). In addition, childhood obesity was associated with differences in white matter organization mainly in frontal and temporal brain regions (8). Resting-state functional connectivity studies identified that adolescent obesity is related to reduced global functional connectivity in the brain regions that are involved in executive function, namely the dorsolateral prefrontal cortex, and involved in emotional memory in the middle temporal cortex (15). In contrast, other studies found no associations or even positive associations between obesity and brain structure (e.g., cortical thickness or gray and white matter volume) (19, 20). Thus, the cause–effect relationship between obesity, brain health and executive function might be positive, negative or neutral and even exist in both directions, as neurocognitive and other psychiatric disorders may also cause obesity, and it is important to take into account the potential bi-directionality of this association.

Collectively, children and adolescents are exposed, in parallel, to both the potential effects of obesity-related biology changes and the establishment of brain–behavior connections. Specifically, childhood and early adolescence are considered critical periods for neurodevelopment, in which youth are sensitive to experience changes in their brain’s structure and function, as well as in the executive function, since the brain matures, develops, learns, and forms connections (19,20). Although multidisciplinary weight loss interventions in children and adolescents with obesity have shown improved response inhibition, sustained attention and enhanced memory as well as reaction time and brain function among others, (21-23), recent studies seem to suggest the particular interest of moderat-to-vigorous-intensity physical activity to improve brain health (24). However, the available

evidence regarding physical activity and other lifestyle behaviors and their influence on brain health in children and adolescents, and particularly in the context of obesity, is still scarce (25).

In that context, and in line with its main objective, that is to analyze and translate scientific evidence into daily practice, the European Childhood Obesity Group (ECOG) gathered experts in the field and dedicated an entire session to this topic during its 29th annual congress (Katowice, Poland; November 13-16 2019; <https://www.ecog-obesity.eu/congress/>). This plenary session proposed clear and deep presentations of the main available and reliable evidence regarding physical activity academic and brain health, including brain structure and function, executive function and academic performance, in the context of pediatric obesity.

Based on the discussions that came up from this session, the ECOG and the expert group collectively concluded that: i) brain structure and function; executive function and academic performance definitely need to be considered as important impairments related to pediatric obesity and not only as a secondary complication; ii) preventive and treatment strategies must promote daily physical activity (especially moderate-to-vigorous physical activity), favoring active settings and lifestyle, in order to maintain and improve both brain health, executive function and academic performance ; iii) school-based active strategies, such as more frequent Physical Education lessons, active playgrounds, active classes and active breaks could be encouraged and should aimed at increasing the time devoted to moderate-to-vigorous physical activity. Indeed, such strategies have been shown to increase youth's physical activity level without altering their academic performance and have been shown to improve children's concentration and attention ; iv) physical activity interventions should focus on active games (when possible, with cognitive engagement) to increase enjoyment and adherence, and have long-lasting effects. These active games should focus not only on aerobic exercise, but also on motor skills exercise and muscular strength exercise; v) such interventions should assess potential mediators and moderators to better understand the relationship between physical activity and brain health in children with overweight/obesity; vi) further studies are obviously needed to better understand these

relations between physical activity/physical fitness, brain health and pediatric obesity, and to identify weight loss intervention that can help improve brain health, executive function and academic performance in children with overweight/obesity; vii) integrative studies aiming at multiple lifestyle behaviors (e.g., eating patterns, physical activity, sedentary or sleep behaviors) for the establishment of brain–behavior connections during youth obesity are clearly warranted.

References

1. Garrido-Miguel M, Cavero-Redondo I, Alvarez-Bueno C, Rodriguez-Artalejo F, Moreno LA, Ruiz JR, et al. Prevalence and Trends of Overweight and Obesity in European Children From 1999 to 2016: A Systematic Review and Meta-analysis. *JAMA pediatrics*. 2019 Aug 5:e192430. PubMed PMID: 31381031. Pubmed Central PMCID: PMC6686782. Epub 2019/08/06. eng.
2. Singh AS, Mulder C, Twisk JW, van Mechelen W, Chinapaw MJ. Tracking of childhood overweight into adulthood: a systematic review of the literature. *Obesity reviews : an official journal of the International Association for the Study of Obesity*. 2008 Sep;9(5):474-88. PubMed PMID: 18331423. Epub 2008/03/12. eng.
3. Ortega FB, Lavie CJ, Blair SN. Obesity and Cardiovascular Disease. *Circulation research*. 2016 May 27;118(11):1752-70. PubMed PMID: 27230640. Epub 2016/05/28. eng.
4. Reilly JJ, Kelly J. Long-term impact of overweight and obesity in childhood and adolescence on morbidity and premature mortality in adulthood: systematic review. *International journal of obesity (2005)*. 2011 Jul;35(7):891-8. PubMed PMID: 20975725. Epub 2010/10/27. eng.
5. Esteban-Cornejo I, Ortega FB, Catena A. Neural perspectives on cognitive control development during childhood and adolescence should take into account how obesity affects brain development. *Acta paediatrica (Oslo, Norway : 1992)*. 2018 Apr;107(4):720-1. PubMed PMID: 29280185. Epub 2017/12/28. eng.
6. Lobstein T, Baur L, Uauy R. Obesity in children and young people: a crisis in public health. *Obesity reviews : an official journal of the International Association for the Study of Obesity*. 2004 May;5 Suppl 1:4-104. PubMed PMID: 15096099. Epub 2004/04/21. eng.
7. Bauer CC, Moreno B, Gonzalez-Santos L, Concha L, Barquera S, Barrios FA. Child overweight and obesity are associated with reduced executive cognitive performance and brain alterations: a magnetic resonance imaging study in Mexican children. *Pediatric obesity*. 2015 Jun;10(3):196-204. PubMed PMID: 24989945. Epub 2014/07/06. eng.
8. Ou X, Andres A, Pivik RT, Cleves MA, Badger TM. Brain gray and white matter differences in healthy normal weight and obese children. *Journal of Magnetic Resonance Imaging*. 2015;42(5):1205-13.
9. Yang Y, Shields GS, Guo C, Liu Y. Executive function performance in obesity and overweight individuals: A meta-analysis and review. *Neuroscience and biobehavioral reviews*. 2018 Jan;84:225-44. PubMed PMID: 29203421. Epub 2017/12/06. eng.
10. Esteban-Cornejo I, Tejero-Gonzalez CM, Castro-Pinero J, Conde-Caveda J, Cabanas-Sanchez V, Sallis JF, et al. Independent and combined influence of neonatal and current body composition on academic performance in youth: The UP & DOWN Study. *Pediatric obesity*. 2015 Jun;10(3):157-64. PubMed PMID: 24919886. Epub 2014/06/13. eng.
11. Spengler M, Damian RI, Roberts BW. How you behave in school predicts life success above and beyond family background, broad traits, and cognitive ability. *Journal of personality and social psychology*. 2018 Apr;114(4):620-36. PubMed PMID: 29504796. Epub 2018/03/06. eng.

12. Diamond A. Executive functions. *Annual review of psychology*. 2013;64:135-68. PubMed PMID: 23020641. Pubmed Central PMCID: PMC4084861. Epub 2012/10/02. eng.
13. Bull R, Espy KA, Wiebe SA. Short-term memory, working memory, and executive functioning in preschoolers: longitudinal predictors of mathematical achievement at age 7 years. *Developmental neuropsychology*. 2008;33(3):205-28. PubMed PMID: 18473197. Pubmed Central PMCID: PMC2729141. Epub 2008/05/14. eng.
14. Dye L, Boyle NB, Champ C, Lawton C. The relationship between obesity and cognitive health and decline. *The Proceedings of the Nutrition Society*. 2017 Nov;76(4):443-54. PubMed PMID: 28889822. Epub 2017/09/12. eng.
15. Moreno-Lopez L, Contreras-Rodriguez O, Soriano-Mas C, Stamatakis EA, Verdejo-Garcia A. Disrupted functional connectivity in adolescent obesity. *NeuroImage Clinical*. 2016;12:262-8. PubMed PMID: 27504261. Pubmed Central PMCID: PMC4969269. Epub 2016/08/10. eng.
16. Harding IH, Andrews ZB, Mata F, Orlandea S, Martinez-Zalacain I, Soriano-Mas C, et al. Brain substrates of unhealthy versus healthy food choices: influence of homeostatic status and body mass index. *International journal of obesity (2005)*. 2018 Mar;42(3):448-54. PubMed PMID: 29064475. Epub 2017/10/25. eng.
17. Augustijn M, Di Biase MA, Zalesky A, Van Acker L, De Guchtenaere A, D'Hondt E, et al. Structural connectivity and weight loss in children with obesity: a study of the "connectobese". *International journal of obesity (2005)*. 2019 Jul 26. PubMed PMID: 31350442. Epub 2019/07/28. eng.
18. Raji CA, Ho AJ, Parikshak NN, Becker JT, Lopez OL, Kuller LH, et al. Brain structure and obesity. *Human brain mapping*. 2010 Mar;31(3):353-64. PubMed PMID: 19662657. Pubmed Central PMCID: PMC2826530. Epub 2009/08/08. eng.
19. Yokum S, Ng J, Stice E. Relation of regional gray and white matter volumes to current BMI and future increases in BMI: a prospective MRI study. *International journal of obesity (2005)*. 2012 May;36(5):656-64. PubMed PMID: 21894161. Pubmed Central PMCID: PMC3982917. Epub 2011/09/07. eng.
20. Sharkey RJ, Karama S, Dagher A. Overweight is not associated with cortical thickness alterations in children. *Frontiers in neuroscience*. 2015;9:24. PubMed PMID: 25698918. Pubmed Central PMCID: PMC4316697. Epub 2015/02/24. eng.
21. Vantieghem S, Bautmans I, Guchtenaere A, Tanghe A, Provyn S. Improved cognitive functioning in obese adolescents after a 30-week inpatient weight loss program. *Pediatric research*. 2018 Aug;84(2):267-71. PubMed PMID: 29907854. Epub 2018/06/17. eng.
22. Delgado-Rico E, Rio-Valle JS, Albein-Urios N, Caracuel A, Gonzalez-Jimenez E, Piqueras MJ, et al. Effects of a multicomponent behavioral intervention on impulsivity and cognitive deficits in adolescents with excess weight. *Behavioural pharmacology*. 2012 Sep;23(5-6):609-15. PubMed PMID: 22785438. Epub 2012/07/13. eng.
23. Anderson YC, Kirkpatrick K, Dolan GMS, Wouldes TA, Grant CC, Cave TL, et al. Do changes in weight status affect cognitive function in children and adolescents with obesity? A secondary analysis of a clinical trial. *BMJ open*. 2019 Feb 19;9(2):e021586. PubMed PMID: 30782863. Pubmed Central PMCID: PMC6367974. Epub 2019/02/21. eng.
24. Valkenborghs SR, Noetel M, Hillman C, Nilsson M, Smith J, Ortega F, et al. The Impact of Physical Activity on Brain Structure and Function in Youth: A Systematic Review. *Pediatrics*. 2019 Oct;144(4). PubMed PMID: 31554668. Epub 2019/09/27. eng.
25. Erickson KI, Hillman C, Stillman CM, Ballard RM, Bloodgood B, Conroy DE, et al. Physical Activity, Cognition, and Brain Outcomes: A Review of the 2018 Physical Activity Guidelines. *Medicine and science in sports and exercise*. 2019 Jun;51(6):1242-51. PubMed PMID: 31095081. Pubmed Central PMCID: PMC6527141. Epub 2019/05/17. eng.