TYPE Editorial
PUBLISHED 09 January 2024
DOI 10.3389/fendo.2023.1350462

OPEN ACCESS

EDITED AND REVIEWED BY
James M Olcese,
Florida State University, United States

*CORRESPONDENCE
Katarina Tomljenović Borer
katarina@umich.edu

RECEIVED 05 December 2023
ACCEPTED 11 December 2023
PUBLISHED 09 January 2024

CITATION
Borer KT, De Sousa MJ, Nindl BC, Stanford KI and Pedersen BK (2024) Editorial: Integrative exercise endocrinology.
Front. Endocrinol. 14:1350462.
doi: 10.3389/fendo.2023.1350462

Editorial: Integrative exercise endocrinology

Katarina Tomljenović Borer[1]*, Mary Jane De Sousa[2], Bradley C. Nindl[3], Kristin I. Stanford[4] and Bente Klarlund Pedersen[5]

[1]Department of Movement Science, School of Kinesiology, The University of Michigan, Ann Arbor, MI, United States, [2]Department of Kinesiology and Physiology, College of Health and Human Development, The Pennsylvania State University, University Park, PA, United States, [3]Warrior Human Performance Research Center, School of Health and Rehabilitation Sciences, University of Pittsburgh, Pittsburgh, PA, United States, [4]Department of Surgery, General and Gastrointestinal Surgery, Davis Heart and Lung Research Institute, The Ohio State University College of Medicine, Columbus, OH, United States, [5]Centre of Inflammation and Metabolism/ Centre for Physical Activity Research, University of Copenhagen, Copenhagen, Denmark

KEYWORDS

adipokines, cytokines, exosomes, hepatokines, hormones, myokines, osteokines

Editorial on the Research Topic
Integrative exercise endocrinology

Defining exercise endocrinology is not easy largely because of the many different avenues of inter-organ messaging that exercise elicits in its control of metabolism, physiology, behavior, and survival. Although this messaging has been studied for a long time, it continues to change and evolve. The classical view of exercise signaling included autonomic nerves releasing the neurotransmitter norepinephrine and triggering the release of cortisol and adrenal catecholamines (1) for the control of the metabolic fuel mix appropriate for the type, duration, or intensity of exercise (2, 3) or for activation of the life-saving fight-or flight behavioral and physiological responses (4). Hormones, molecules secreted by endocrine glands and released into circulation (5, 6) such as adrenal norepinephrine, epinephrine, and cortisol (1), pituitary growth hormone (GH) (7, 8), IGF (9), and pancreatic glucagon (10) were considered to be the main exercise-associated messengers. The next insight was that exercise could stimulate messaging by paracrine or autocrine means (5, 6) by molecules made in various tissues and organs and acting on other cells and tissues in their vicinity rather than through circulation. Examples are somatostatin in delta pancreatic cells controlling secretion of glucagon from alpha, and of insulin by beta, cells and somatostatin in the stomach inhibiting gastric cells in the antrum (11, 12). Similarly, IGF-gene expression in the muscle is stimulated by mechanical loading to promote *in situ* hypertrophy (13). Realization that exercise-induced changes in hormone pulsatility can affect physiological outcomes, led to the discovery that increased frequency of GH pulses accelerates mature hamster skeletal and somatic growth (14, 15), and that reduced energy availability associated with exercise reduces in female athletes frequency, and increases the amplitude, of LH pulses and abolishes menstrual cycles (16). More recently, explorations of hormone signaling was extended to various body organs which during exercise release messengers into circulation to specific targets. Cytokine messengers like interferon, interleukins, and tumor necrosis factor control immune system and inflammation (17), while insulin-like growth factors control cellular growth (8). Myokines such as irisin, interleukins, and myostatin are released by the muscle (18, 19), hepatokines such as FGF21 and follistatin by the liver (19), adipokines leptin, adiponectin, and resisting are released by the adipose tissue (19, 20). Osteokines like osteocalcin, carboxyterminal propeptide of type-1 collagen (bone formation osteokine), and carboxyterminal peptide of type 1 collagen (bone resorption osteokine) are released from bone osteoblasts and osteoclasts (19, 21, 22). All of these messengers are to a variable extent affected by exercise and play a role in inter-organ communication and actions (19). Finally, exercise also releases bioactive molecules within the extracellular vesicles and exosomes (23, 24).

The editorial team that evaluated the submitted manuscripts was chosen for their expertise in relevant aspects of integrative exercise endocrinology: endocrine changes in the athletes subjected to energy deprivation (25), secretion of exerkines participating in inter-organ communication (26), effects of exercise-induced IGF-1 isoforms in muscle hypertrophy (27), lipokines facilitating muscle lipid metabolism (28), and GH and PTH pulsatility in acceleration of growth (15) and in anabolic responses of postmenopausal bone (22).

Our efforts resulted in publications. Plomgaard et al. presented the regulatory role of glucagon and insulin in the release of hepatokine GDF15. In a clinical study including healthy and anorexic humans, exercise led to increased glucagon to insulin ratio and release of GDF15. Since GDF was also elevated in subjects with anorexia nervosa, this hepatokine may signal chronic energy deprivation. The second manuscript (30) was published by Mohammad et al. describing changes in amyloid-beta precursor protein in an ovariectomized animal. The study with ovariectomized mice demonstrated that voluntary running increased the concentration of an enzyme (BACE1) which limits overproduction of amyloid-beta precursor protein that is implicate in memory loss and Alzheimer disease. The third study was published by Schön et al. about the effects of exercise on growth differentiation factor 11 (GDF11). This cytokine (also called bone morphogenetic protein belonging to TGF alpha family) controls growth, and its gene is found on the chromosome 12. The study reported that an hour of running decreased the concentration of GDF11 in cerebrospinal fluid but not in the blood suggesting cross-talk between the brain and peripheral tissues. The fourth paper was by Hughes et al. presenting an argument that the beneficial increase in bone stiffness arises when the mechanical stimulus of exercise operates during periods of active hormonal influences such as during pubertal growth and administration of PTH analog peritaratide in old age.

This overview of the scope of integrative exercise endocrinology serves, in part, to attract more research in this area of endocrinology and to, hopefully, attract more reports on the Research Topic to this section of Frontiers in Endocrinology.

Author contributions

KB: Conceptualization, Funding acquisition, Supervision, Writing – original draft, Writing – review & editing. MDS: Validation, Writing – original draft. BN: Writing – original draft, Writing – review & editing. BP: Validation, Writing – original draft, Writing – review & editing. KS: Validation, Writing – original draft, Writing – review & editing.

Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. Support by NIH 1 R15 DK066286 grant to KB.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

Publisher's note

References

1. Borer KT. The autonomic nervous system in exercise: An integrative view. In: Tipton CM, editor. *History of exercise physiology,* Champaign, IL, United States: Human Kinetics Publishers (2014). p. 175–210.

2. Romijn JA, Coyle EF, Sidossis LS, Gastaldelli A, Horowitz JF, Endert E, et al. Regulation of endogenous fat and carbohydrate metabolism in relation to exercise intensity and duration. *Am J Physiol* (1993) 265:E380–91. doi: 10.1152/ajpendo.1993.265.3.E380

3. Horton T J, Pagliassotti MJ, Hobbs K, Hill JO. Fuel metabolism in men and women during and after long-duration exercise. *J Appl Physiol* (1998) 85:1823–32. doi: 10.1152/jappl.1998.85.5.1823

4. Rochette L, Vergely C. Hans Selye and the stress response: 80 years after his "letter" to the editor of Nature. *Ann Cardiol Angeiol (Paris)* (2017) 66:181–3. doi: 10.1016/j.ancard.2017.04.017

5. Borer KT. *Exercise endocrinology*. Champaign, IL, United States: Human Kinetics Publishers (2003).

6. Borer KT. *Advanced exercise endocrinology*. Champaign, IL, United States: Human Kinetics Publishers (2013). doi: 10.5040/9781492596172

7. Brockman NK, Yardley JE. Sex-related differences in fuel utilization and hormonal response to exercise: Implications for individuals with type 1 diabetes. *Appl Physiol Nutr Metab* (2018) 43:541–52. doi: 10.1139/apnm-2017-0559

8. Kraemer WJ, Ratamess NA, Hymer WC, Nindl BC, Fragala MS. Growth hormone (s). testosterone, insulin-like growth factors, and cortisol: Roles and integration for cellular development and growth with exercise. *Front Endocrinol (Lausanne)* (2020) 11:33. doi: 10.3389/fendo.2020.00033

9. Nindl BC, Joseph A, Kevin R Rarick KR, Eagle SR, Darnell ME, Allison KF, et al. Differential basal and exercise-induced IGF-I system responses to resistance vs. calisthenic-based military readiness training programs. *Growth Horm IGF Res* (2017) 32:33–40. doi: 10.1016/j.ghir.2016.12.001

10. McCarthy O, Schmidt S, Christensen MB, Bain SC, Nørgaard K, Bracken R. The endocrine pancreas during exercise in people with and without type 1 diabetes: Beyond the beta-cell. *Front Endocrinol (Lausanne)* (2022) 13:981723. doi: 10.3389/fendo.2022.981723

11. Harris AG. Somatostatin and somatostatin analogues: pharmacokinetics and pharmacodynamic effects. *Gut* (1994) 35(3 Suppl):S1–4. doi: 10.1136/gut.35.3_suppl.s1

12. Shamsi BH, Chatoo M, Xu XK, Xu X. Chen XQ.Versatile functions of somatostatin and somatostatin receptors in the gastrointestinal system. *Front Endocrinol (Lausanne)* (2021) 12:652363. doi: 10.3389/fendo.2021.652363

13. DeVol DL, Rotwein P, Sadow JL, Novakofski J, Bechtel PJ. Activation of insulin-like growth factor gene expression during work-induced skeletal muscle growth. *Am J Physiol* (1990) 259:E89–95. doi: 10.1152/ajpendo.1990.259.1.E89

14. Borer KT, Kuhns LR. Radiographic evidence for acceleration of skeletal growth in adult hamsters by exercise. *Growth* (1977) 41:1–13.

15. Borer KT, Nicoski DR, Owens V. Alteration of pulsatile growth hormone secretion by growth-inducing exercise: involvement of endogenous opiates and somatostatin. *Endocrinology* (1986) 118:844–50. doi: 10.1210/endo-118-2-844

16. Loucks AB. Energy availability, not body fatness, regulates reproductive function in women. *Exerc Sport Sci Rev* (2003) 31(3):144–8. doi: 10.1097/00003677-200307000-00008

17. Malkowska P, Sawczyk M. Cytokines as biomarkers for evaluating physical exercise in trained and non-trained individuals: A narrative review. *Int J Mol Sci* (2023) 24:11156. doi: 10.3390/ijms241311156

18. Pedersen BK, Febbraio MA. Muscle as an endocrine organ: focus on muscle-derived interleukin-6. *Physiol Rev* (2008) 88:1379–404. doi: 10.1152/physrev.90100.2007

19. Gonzalez-Gil AM, Elizondo-Montemayor L. The role of exercise in the interplay between myokines, hepatokines, osteokines, adipokines and inflammation for energy substrate redistribution and fat mass loss: A review. *N 12: Nutrients* (2020) 12:1899. doi: 10.3390/nu12061899

20. Takahashi H, Alves CRR, Stanford KI, Middelbeek RJW, Nigro P, Ryan RE, et al. TGF-β2 is an exercise-induced adipokine that regulates glucose and fatty acid metabolism. *Nat Metab* (2019) 1:291–303. doi: 10.1038/s42255-018-0030-7

21. Borer KT, Zheng Q, Jafari A, Javadi S, Kernozek T. Nutrient intake prior to exercise is necessary for increased osteogenic marker response in diabetic postmenopausal women. *Nutrients* (2019) 11:1494. doi: 10.3390/nu11071494

22. Zheng Q, Kernozek T, Daoud-Gray A, Borer KT. Anabolic bone stimulus requires a pre-exercise meal and 45-minute walking impulse of supratreshold speed-enganced momentum to prevent or mitigate postmenopausal osteoporosis within circadian constraints. *Nutrients* (2021) 13:3727. doi: 10.3390/nu143113727

23. Whitham M, Parker BL, Friedrichsen M, Hingst JR, Hjorth M, Hughes WE, et al. Extracellular vesicles provide a means for tissue crosstalk during exercise. *Cell Metab* (2018) 27:237–251.e4. doi: 10.1016/j.cmet.2017.12.001

24. Nederveen JP, Warnier G, Di Carlo A, Nilsson MI, Tarnopolsky MA. Extracellular vesicles and exosomes: insights from exercise science. *Front Physiol* (2021) 11:604274. doi: 10.3389/fphys.2020.604274

25. De Souza MJ, Strock NCA, Ricker NCA, Koltun NJ, Barrack M, Joy E, et al. The path towards progress: A critical review to advance the science of the female and male athlete triad and relative energy deficiency in sport. *Sports Med* (2022) 52:13–23. doi: 10.1007/s40279-021-01568-w

26. Pedersen BK. Physical activity and muscle-brain crosstalk. *Nat Rev Endocrinol* (2019) 15:383–92. doi: 10.1038/s41574-019-0174-x

27. Pierce JR, Martin BJ, Rarick KR, Alemany JA, Staab JS, Kraemer WJ, et al. Growth hormone and insulin-like growth factor-i molecular weight isoform responses to resistance exercise are sex-dependent. *Front Endocrinol (Lausanne)* (2020) 11:571. doi: 10.3389/fendo.2020.00571

28. Stanford KI, Lynes MD, Takahashi H, Baer LA, Peter J Arts PJ, Francis J May FJ, et al. 12,13-diHOME: An exercise-induced lipokine that increases skeletal muscle fatty acid uptake. *Cell Metab* (2018) 27(5):1111–20. doi: 10.1016/j.cmet.2018.03.020