European Journal of Nuclear Medicine and Molecular Imaging (2024) 51:340–341
https://doi.org/10.1007/s00259-023-06491-y

LETTER TO THE EDITOR

Hormone-induced body-brain interaction and the impact on cognition

Lihua Sun[1,3] · **Pirjo Nuutila**[1,2,3]

Received: 11 October 2023 / Accepted: 21 October 2023 / Published online: 9 November 2023

Hormone-induced interaction between brown adipose tissue (BAT) and brain is an important regulator of feeding behaviour. Traditional thermoregulatory feeding theory has been capable to explain, at least partly, the mechanisms underlying BAT-brain interactions. A recent article by Sun et al. [1], using positron emission tomography (PET) imaging to study the effect of secretin on satiation, reveals a novel glucose-level endocrine communication between BAT and brain. This study demonstrates the usefulness of PET in studying body-brain interactions. It also opens new windows to tag into the nature of inter-organ biochemical interactions, e.g., via measuring glucose consumption or neurotransmission.

It is possible to image any part of the body using a traditional or modern total-body PET scanner. However, due to low temporal resolution of kinetic imaging and dependency of specific radiotracers, usefulness of this technique in revealing clinically meaningful body-brain interactions has not been well studied [2]. Secretin-inspired BAT-brain endocrine communication, as Sun et al. reported, may be a good example on how body-brain interaction should be studied, especially regarding the effect of hormones or drugs (Fig. 1).

Besides, the study by Sun et al. used both PET and fMRI imaging tools, where PET was used to measure glucose consumption levels in the brain and BAT, while behavioural and

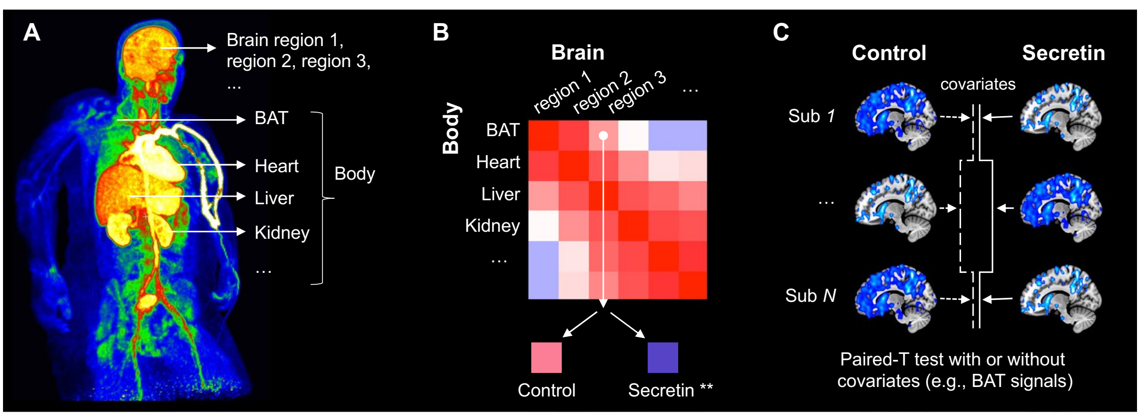

Fig. 1 Positron emission tomography as a method to study the body-brain interaction. **A** Total-body scanner allows for simultaneous measures for brain and peripheral organs (perfusion image using Siemens Biograph Vision Quadra, by Hidehiro Iida). **B** Correlation matrices, between brain regions of interest and peripheral organs, are built for individual conditions (e.g., control vs. secretin). **Only significant correlations may be meaningful. **C** Brain voxel-level analysis can be conducted using paired-T test with covariates (e.g., BAT signals during different conditions). Differentiable brain clusters, compared to analysis without covariates, will be regions showing interactions with the covariates (i.e., BAT signals)

✉ Lihua Sun
lihua.sun@utu.fi

1 Turku PET Centre, University of Turku, Turku, Finland

2 Department of Endocrinology, Turku University Hospital, Turku, Finland

3 Turku PET Centre, Turku University Hospital, Turku, Finland

fMRI measures have been used to evaluate brain cognitive responses related to satiety. These approaches are crucial to investigate the impact of body-brain interactions on cognition. Though previous findings [3, 4] have reported the impact of secretin on cognition and feeding behaviour, it remained unknown what roles the interaction between BAT and brain play in this effect. Therefore, finding by Sun et al.

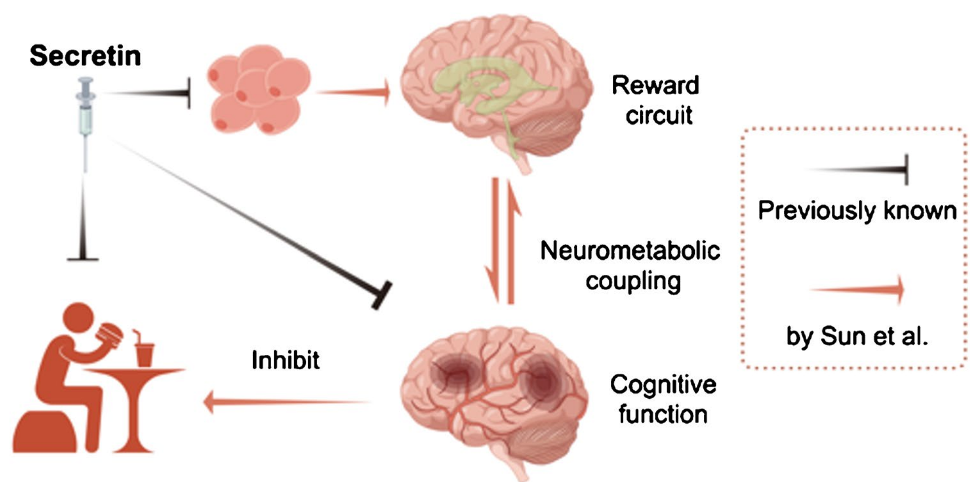

Fig. 2 Secretin induced body-brain interaction is an important step that leads to ultimate changes in cognition and eating behaviour (by Figdraw)

(Fig. 2) is a very significant step that addresses the role of BAT-brain interaction.

PET-fMRI fusion analysis has been increasingly used in neuroimaging studies [5]. After showing that secretin tuned the BAT-caudate interaction regarding glucose consumption, Sun et al. studied the neurometabolic coupling, further showing that the caudate glucose consumption levels modulate both brain reward responses and cognitive control function. This finding proves the importance of secretin effect to BAT-brain interaction, and ideally gears this interaction with corresponding cognitive functions.

Brown adipose tissue function is far beyond its role as a heat-organ [6]. The thermoregulatory feeding theory [7] proposes that BAT-generated temperature change is detected by the brain, leading to corresponding functional adaption in the central nervous system. Indeed, evidence shows that hypothalamic thermo-receptors are upregulated when secretin activates BAT [4]. In contrast, Sun et al. propose that endocrine communication is also underlying this functional BAT-brain axis. This finding further highlights the complexity of how BAT communicates with the brain. In the meanwhile, this endocrine communication may function as a biomarker for studying the effect of relevant neuronal/cellular signalling pathways (e.g., neurotransmission) that are crucial for glucose metabolism.

Accumulative evidence brings up the impact of gut hormones to cognitive functions and feeding behaviour. Here, we propose that body-brain interaction is an important target of gut hormone functions. As obesity has become one of the leading public health challenges of the twenty-first century [8], better understanding of gut hormone effect to body and brain functions is a crucial step with both neuroscientific and clinical significance.

Declarations

Competing Interests Authors report no competing interests.

References

1. Sun L, Laurila S, Lahesmaa M, Rebelos E, Virtanen KA, Schnabl K, et al. Secretin modulates appetite via brown adipose tissue-brain axis. Eur J Nucl Med Mol Imaging. 2023;50:1597–606. https://doi.org/10.1007/s00259-023-06124-4.
2. Reed MB, Ponce de Leon M, Vraka C, Rausch I, Godbersen GM, Popper V, et al. Whole-body metabolic connectivity framework with functional PET. NeuroImage. 2023;271:120030. https://doi.org/10.1016/j.neuroimage.2023.120030.
3. Laurila S, Sun L, Lahesmaa M, Schnabl K, Laitinen K, Klen R, et al. Secretin activates brown fat and induces satiation. Nat Metab. 2021;3:798–809. https://doi.org/10.1038/s42255-021-00409-4.
4. Li Y, Schnabl K, Gabler SM, Willershauser M, Reber J, Karlas A, et al. Secretin-activated brown fat mediates prandial thermogenesis to induce satiation. Cell. 2018;175(1561–74): e12. https://doi.org/10.1016/j.cell.2018.10.016.
5. Sun L, Lukkarinen L, Putkinen V, Karlsson HK, Hirvonen J, Tiihonen J, et al. Mu-opioid receptor system modulates responses to vocal bonding and distress signals in humans. Philos Trans R Soc Lond B Biol Sci. 2022;377:20210181. https://doi.org/10.1098/rstb.2021.0181.
6. Virtanen KA, Nuutila P. The importance of human brown adipose tissue volume. Nat Rev Endocrinol. 2021;17:453–4. https://doi.org/10.1038/s41574-021-00522-0.
7. Himms-Hagen J. Role of brown adipose tissue thermogenesis in control of thermoregulatory feeding in rats: a new hypothesis that links thermostatic and glucostatic hypotheses for control of food intake. Proc Soc Exp Biol Med. 1995;208:159–69. https://doi.org/10.3181/00379727-208-43847a.
8. Stanaway JD, Afshin A, Gakidou E, Lim SS, Abate D, Abate KH, et al. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet. 2018;392:1923–94.