

Author's Reply:

We thank the reviewer for the comments and suggestions, providing additional conceptual clarification to this work, and that we will now address point by point. Points 1 and 2 will be addressed together, as both pertain to the distinction between interoception and allostasis.

Comments 1 and 2: We have clarified that allostasis involves not only interoceptive information, but also data from other sensory channels and cognitive processes.

“Conversely, the proactive generation of responses to anticipated homeostatic challenges (i.e., allostasis) depends on predictive capabilities facilitated by an internal model of the body, based on past representations and sensory aspects of interoception (Barrett, 2017), **but also involves non-interoceptive channels (e.g., exteroceptive senses like vision or hearing) and other cognitive processes (e.g., memory) (Sterling, 2012).**”

As we have acknowledged in the text, we also agree with the reviewer that, under a definition of interoception that includes not only sensory aspects but also regulatory signals, the division between interoception and allostasis becomes blurred. Indeed, we believe that at the biological level both processes are deeply intertwined, with any clear division between the two necessarily being difficult to establish. Furthermore, the main goal of our review is to extract data on these phenomena that have potential clinical significance in frontotemporal dementia. Considering these two points, we have decided to not dichotomize metrics into interoceptive or allostatic, but rather report them together, according to the physiological system involved. An index like “heart rate” can be considered as a cardiovascular interoceptive-allostatic marker, as it reflects the dynamic interplay between ascending sensory information from multiple interoceptive channels, descending regulatory signals that control heart rate and can be proactively adjusted in response to anticipated challenges or for adaptive energy regulation, and thus become dysregulated in response to repeated disruptions in homeostasis (serving as an index of allostatic load). We have refined the sentence where we discussed this previously, according to the reviewer’s suggestion, to make this clearer:

“Of note, the interoceptive markers described above, representing sensory events encoded by interoceptive sensory cells in the periphery and brain along with their regulatory signals, are the ones that may become dysregulated in response to repeated homeostatic challenges, thus serving as indices of allostatic load. Given the deep interconnectedness of interoception and allostasis, both sets of markers will be considered together and categorized according to the physiological system involved.”

Comment 3: We acknowledge that visceromotor control can be considered a form of “action” and have modified the sentence to better capture this distinction.

“We will also exclude proprioception and vestibular function from our definition of interoception since they represent the position and movement of the body in space, rather than its physiological condition, and are linked to musculoskeletal action and resulting changes in body posture/movement rather than homeostatic or allostatic regulation.”