Supplementary information S2

Box S2 | An example of how interoceptive perceptions arise in the brain

A man is walking alone down a dark street. Based on past experience (relayed from agranular regions of the default mode network / hippocampal memory system), visceromotor cortices initiate a variety of partially completed predictions described by some probability density function. The man sees a stranger in his peripheral vision who suddenly crosses the street and begins to walk towards him at a faster pace. The stranger removes an item from his pocket and holds it in his hand. Visually perceiving this gesture involves many different processes (i.e., categorizing it, which includes, among other things, potentiating activity in the deep laminae of agranular visceromotor cortex that results in visceral predictions that alter the man's autonomic and metabolic state, thereby preparing his body to respond to the threat.) Although the brain initially generates many predictions, each with its own prior probability (based on past experiences or learning in this situation or situations similar to it), the particular circumstances of the man's interaction with the stranger, the state of the environment, and the state of his internal milieu in that particular moment serve as 'evidence' in the Bayesian sense, making some predictions more likely, and some less likely.

The changing activation in visceromotor cortices serves simultaneously as (a) autonomic outputs relayed via thalamic and brainstem nuclei to alter vagal tone, thereby increasing heart rate, respiration, and modifying other (primarily) vagally-mediated interoceptive systems in the service of preparing to fight or run and (b) interoceptive predictions of forthcoming viscerosensory changes that are relayed to supragranular layers of viscerosensory cortex. The resulting viscerosensory changes in heart rate, respiration, etc., are more slowly relayed through ascending vagal pathways via the brainstem and thalamus primarily to stellate cells in granular/dysgranular posterior and mid insula. Cells in the supragranular layer (most likely in layer IIIb) of the mid/posterior insula then compute the difference between the ascending viscerosensory information and the received prediction signals, resulting in prediction error signals that may eventually be relayed back to the agranular visceromotor cortices, where they serve to alter the empirical priors in computations of subsequent interoceptive predictions/outputs (i.e., the posterior probability estimates).

The process of influencing agranular cortices via prediction error is slow, due to the fact that the prediction errors are computed in dysgranular/granular cortices, and because precision weighting cells in mid/posterior insula bias the system against incorporating prediction errors into visceromotor predictions (via the modulation from anterior insula and portions of the anterior cingulate cortex that particulate in the control networks). This bias may have developed due to evolutionary pressures that favored a visceromotor system that is future-oriented, meaning that visceromotor predictions are allostatic, rather than simply homeostatic. The interoceptive experience of viscerosensory changes in response to a threatening stranger thus arises from allostatic interoceptive predictions made by agranular visceromotor cortices. The functional consequence is that the man will continue to feel tense and activated (even afraid; see Supplementary Box 3) for some period after he has left the dark street.