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# Significance of the insula for the evolution of human awareness of feelings from the body

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An ascending sensory pathway that underlies feelings from the body, such as cooling or toothache, terminates in the posterior insula. Considerable evidence suggests that this activity is rerepresented and integrated first in the mid-insula and then in the anterior insula. Activation in the anterior insula correlates directly with subjective feelings from the body and, strikingly, with all emotional feelings. These findings appear to signify a posterior-to-anterior sequence of increasingly homeostatically efficient representations that integrate all salient neural activity, culminating in network nodes in the right and left anterior insulae that may be organized asymmetrically in an opponent fashion. The anterior insula has appropriate characteristics to support the proposal that it engenders a cinemascopic model of human awareness and subjectivity. This review presents the author's views regarding the principles of organization of this system and discusses a possible sequence for its evolution, as well as particular issues of historical interest.

Keywords: homeostasis; interoception; emotion; salience; feelings; self

## Introduction

In prior articles, I presented detailed evidence for a homeostatic afferent neural pathway to insular cortex that underlies human awareness of feelings from the body, and I proposed that the integration of this pathway underpins our awareness of all emotional feelings and our introspective subjectivity.[1–4] Here, I will discuss what appear (to my mind) to be the fundamental principles underlying the organization of this pathway, and I will suggest a plausible sequence for its evolution. Finally, I will offer comments on a few criticisms and other issues of historical interest. For more extensive details and references, the interested reader is referred to prior publications.

## The ascending pathway and its principles of organization

### Spinal cord

I used single-unit electrophysiology and tract-tracing tools to map the ascending projections from spinal and trigeminal lamina I neurons in cats and monkeys. These neurons had conventionally been associated with "pain and temperature," but even-

tually the functional and anatomical characteristics of these projection neurons led me to recognize that they are better described as a pathway that conveys afferent activity relating the physiological condition of the tissues and organs of the body. Such sensory activity is necessary for homeostasis, and this pathway essentially serves as the central afferent complement of the efferent autonomic nervous system. In the periphery, the small-diameter A-delta and C primary afferent fibers that emerge late in development from small dorsal root ganglion cells (B cells) innervate every tissue of the body, and they project to the superficial dorsal horn of the spinal cord or to the medullary nucleus of the solitary tract (NTS). The output neurons from these two regions (i.e., lamina I and the NTS) project to the homeostatic integration sites and preautonomic motor regions in the brainstem. Lamina I neurons also project heavily to the spinal autonomic nuclei, where sympathetic preganglionic neurons are found. Altogether, these substrates provide the sensory and motor components of the hierarchically organized homeostatic (autonomic) nervous system; this conclusion is underscored by the observation that the descending

projections from the hypothalamus (which many view as a master autonomic control center) target exactly these sites. Indeed, the superficial dorsal horn that is part of the homeostatic afferent system is easily distinguishable in myelin-stained transverse sections of the human spinal cord from the deep dorsal horn, where large neurons receive input from large-diameter primary afferents (which emerge early in development from large dorsal root ganglion cells, or A cells) and project to motorneurons in the ventral horn and to motor control sites centrally. Thus, I suggested that the terms *interoception* and *exteroception* be used to differentiate these two systems (i.e., one that controls smooth muscle, as distinct from one that receives large-diameter mechanoreceptive and proprioceptive inputs and controls striate muscle). An important principle of the heirachical homeostatic system is that it has identifiable sensory and motor components that are tightly interconnected centrally.

### Brain stem

In all mammals, the highest level of this homeostatic hierarchy in the upper brain stem consists of the parabrachial nuclei (PB) and the periaqueductal gray (PAG). These sites can be viewed as the lowest level of the so-called limbic system that controls emotional behavior (e.g., see Ref. 5), because together they organize whole-body behaviors that serve life-supporting functions (cardiorespiratory control, ingestion, elimination, reproduction, etc.), as discovered in studies of chronic decerebrate and decorticate animals at the end of the 1800 s (e.g., see Ref. 6). Modern experiments that revealed approach/avoidance columns in the PAG with correlative, opposing cardiorespiratory actions,[7] provide the fundamental pattern for a combined behavioral and autonomic opponent organization, which I and many other authors have envisaged in the forebrain of mammals and all vertebrates (see Refs. 2, 8–10). The principle of opponent organization is found throughout physiology, for example, in color vision, antagonist muscles, hormones controlling water balance, and cardiac function, probably because it provides an energy-efficient method for precise control. Indeed, opponent interaction is present between the lamina I (i.e., "sympathetic") afferent pathway and the NTS (i.e., vagal, or "parasympathetic") afferent pathway already in the medulla and spinal cord,[11,12] and a similar behavioral/autonomic
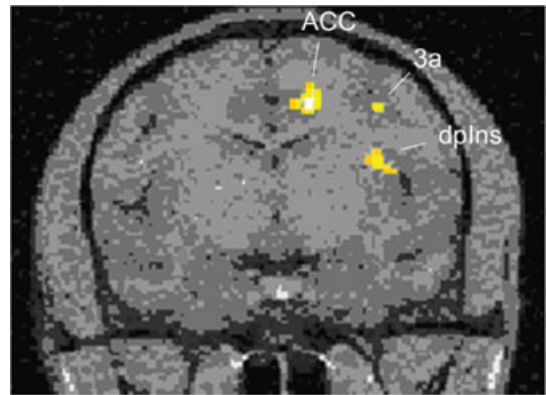


**Figure 1.** An image of BOLD (blood oxygenation level–dependent) signal in the brain of an anesthetized cynomolgus macaque monkey in response to 45 seconds application of noxious cold (a bag of ice) to the contralateral plantar foot repeated every 2.5 minutes for 18 minutes, thresholded at $P = 0.001$ in a 2-mm-thick structural slice. 3a, area 3a; ACC, anterior cingulate cortex; dpIns, dorsal posterior insula.

opponent organization is present in the medial and lateral portions of the hypothalamus.[13] Thus, the PB and PAG can be viewed as identifiable, complementary sensory and motor regions, respectively, that support homeostasis with a coordinate behavioral/autonomic opponent organization.

### Thalamus

In rodents, the ascending pathway from lamina I and the NTS does not project to specific targets beyond the brainstem; rather, they have widely scattered projections, and the main homeostatic afferent pathway to their forebrains conveys integrated activity from PB to hypothalamus, amygdala, and insular cortex.[14] In primates, however, the high-resolution homeostatic afferent representation of the physiological condition of the body ascends directly from lamina I and the NTS to a pair of specific subnuclei in the thalamus (i.e., VMb and VMpo), as well as to a third site in medial thalamus (MDvc). These regions, in turn, project to three sites in the cortex—the fundus of the superior limiting sulcus of the insula and the fundus of the central sulcus (both by way of VMpo/VMb), as well as the fundus of the cingulate sulcus (by way of MDvc). This pattern is illustrated in Figure 1, which shows functional activation at these three cortical sites induced by noxious cold stimulation of the contralateral foot of an anesthetized monkey. To my mind, the

insular and cingulate cortices that receive these inputs can be regarded as limbic sensory and limbic motor cortices, respectively, because their major descending projections are to PB and PAG, respectively.[5,14,15] The activation in the fundus of the central sulcus (area 3a) could be a viscero-motor (somatic reflex) signal, because area 3a integrates interoceptive, vestibular, and Group I muscle afferent inputs and projects to spinal motor control regions. Overall, this pattern mimics the sensori-motor organization of homeostatic afferent processing in the spinal cord and brainstem (e.g., Ref. 16), consistent with the view that the primary role of neocortex is to model and control sensory integration and motoric action at lower hierarchical levels. Thus, at the thalamo-cortical level in primates, the interoceptive system is distinguished from the exteroceptive system (which is represented in Rolandic sensorimotor cortex), and separate sensory and motor components for the homeostatic system can be identified.

### Insular cortex

The projections of VMpo and VMb extend over the entire posterior-to-anterior extent of the insula in the macaque monkey,[17–19] approximately 12–14 mm. However, in humans, the insula extends approximately 50–60 mm antero-posteriorly, and functional imaging studies indicate that lamina I input (e.g., pain, temperature, or itch stimuli) first activates the most posterior 15–20 mm, while vagal and gustatory input (e.g., gastric distension, salty taste) activates the next 10 mm or so.[3,4,20] In other words, primary interoceptive cortex occupies the entire dorsal insula in monkeys, but only the posterior third in humans. This pathway contains modality-selective components that each generate a distinct "feeling" from the body in humans, including first (pricking) pain, second (burning) pain, cool, warm, itch, muscle ache, gastric distension, vasomotor flush, sweet, salty, and so on. Our positron emission tomography (PET) imaging study of innocuous cool sensation[21] showed that activation in the dorsal posterior insula, which is linearly related to objective stimulus intensity, is accompanied by activation of the mid-insula and the anterior insula, where activity correlates much more strongly with subjective feelings of cool. Indeed, activation in the anterior insula is uniquely associated with subjective feelings of all kinds.[1,3] This pattern suggests a posterior-to-anterior processing gradient in the human insular cortex, which fits with considerable evidence (e.g., Ref. 22), and that subjective feelings are based directly on homeostatic sensory integration, which is consistent with the James-Lange theory of emotion and the "somatic marker" hypothesis.[23,24] To my mind, this pattern also suggests that integration within the insula generates the template for a "feeling," namely, a neural representation of homeostatic sensori-motor conditions that can valuate or quantify energy utilization, thus providing a metric for amodal computation of homeostatic efficiency (a "common currency;" see Refs. 3, 4, 25–27).

Distinct activation of the mid-insula, which may be phylogenetically novel in hominids, is produced not only by interoceptive stimulation, but also by mechanoreceptive and proprioceptive (i.e., exteroceptive), motoric, and hedonic stimulation[3,4] (e.g., see Refs. 28, 29). The evidence suggests that the mid-insula integrates interoceptive activity with other neural inputs to form a combined representation of homeostatically salient features of the individual's internal *and* external environment. The middle insula also initiates the lateralization of sympathetic, energy-consuming activity to the right insula and parasympathetic, energy-nourishing activity to the left insula, which I believe was evolutionarily driven by a preexisting behavioral and autonomic efferent asymmetry that is present in all vertebrates.[4,10] The anterior insula displays strong functional connectivity with the anterior cingulate in many studies, consistent with view that the insula serves as limbic sensory cortex and the cingulate as limbic motor cortex; this view also fits with the idea that, in humans, an emotion can be described as a feeling and a motivation,[30] and it fits with a modern anatomical view of the limbic system.[5]

In the 10 years since the publication of our PET study of cooling sensation, thousands of functional imaging studies have accumulated indicating that the anterior insula of humans is associated with all subjective emotional feelings and all task-related and attention-related aspects of behavior, including subjective time estimation, music appreciation, mental effort, and behavioral salience;[3,4] for detailed reviews, the interested reader is referred to 21 articles in a special issue on the insula that I organized.[31] I proposed that the human anterior insula substantializes what can be called "the sentient self," based on a progressive integration of all neural activity across all networks of the brain

onto the homeostatically relevant representation of inner and outer salience formed in the mid-insula, formed on the basis of the interoceptive template for a "feeling." This proposal fits with the topics reviewed previously, as well as with recent neuroeconomic views of the anterior insula.[32,33] To my mind, this view is strikingly supported by the observation that the "feeling-of-knowing," a mental process representing memory accessibility or familiarity, is parametrically associated with activation in the anterior insula (and anterior cingulate) bilaterally.[34] Recognizing that the brains of humans use approximately 25% of the body's energy budget, and up to 60% in infants,[35] and that energy utilization was a prime arbiter of brain growth in evolution,[36] it makes sense that an integrated representation of the activity in all brain networks was needed in order to improve behavior from the perspective of homeostatic efficiency. I believe that the goal of homeostatic efficiency (with respect to both the individual and the species) provides the best explanation of the progressive posterior-to-anterior integration in the insula and thus the evolution of human awareness. Without specifying the role of insular cortex, others have independently reached similar conclusions regarding the fundamental role of energy efficiency in human evolution (see below; see also Refs. 37,38).

Significantly, there is evidence indicating that the anterior insula has dynamic connectivity; in other words, it is functionally linked with different, widespread portions of cortex during different feelings or different behaviors (e.g., see Ref. 39). In the model of awareness I proposed,[3,4] the representation of the salient "material me" formed in the anterior insula provides the basis of a mental resource of perceptual quanta (or "global emotional moments") that serve as frames of a cinemascopic representation indexed across real time (at a frame rate of approximately 8 Hz). Each "global emotional moment" must be able to store a set of feelings that can represent any pattern of neural activity across the brain, for the purpose of behavioral decision making, and that requires dynamic connectivity. The cinemascopic model also provides an emergent basis for music (viewed as the rhythmic progression of emotionally laden moments) and for the subjective slowing of time under emotional duress.[3,4] Furthermore, the buffers required for comparing feelings across time provide an emergent basis for intro-

spective subjectivity.[4] In other words, in this model, both music and subjectivity are epiphenomena that emerged with the development of the real-time representation of homeostatic salience that constitutes the "material me" across time. Finally, in the homeostatic model I proposed, the opponent organization of positive (energy-nourishing) and negative (energy-consuming) feelings on the left and right sides of the brain, respectively, provides an efficient basis for nuanced control of emotional behavior that matches a preexisting forebrain behavioral asymmetry common to all vertebrates.[10] To summarize, I believe that energy efficiency, the goal of homeostasis, is also the goal of the integration that proceeds from posterior to anterior in the human insula and produced the basis for awareness.

## A putative sequence for the evolution of human awareness

The steps I suggest for the evolution of human awareness might be obvious by now. The primary constraint on biological evolution is the need for efficient utilization of hard-won energy in an uncertain environment.[37] Organizing information increasingly well within the entropic nature of the world requires reversal of the thermodynamic flow of free energy.[38]

Thus, I suggest the following evolutionary sequence: the first step occurred with the development of the neural crest, which is the source of B cells and the interoceptive superficial dorsal horn. A common transcription factor appears at the same time during ontogeny in B cells and in the cells that emerge from the lateral horn to create the superficial dorsal horn (DRG11[40]), which links these components clearly. The second step occurred with the development of the PB and PAG in the brain stem, where homeostasis first generates whole-body behaviors. The third step must have been the production of homeostatically more-efficient behavior due to the integration and learning provided by the telencephalic circuit that modulates the brainstem PB and PAG (insula, cingulate, amygdala, septum, hypothalamus). We might assume that this forebrain circuitry first appeared in the brains of early mammals, because it exists in the rat brain, although there is similar, albeit rudimentary, circuitry in fish and reptiles. The next major step was provided by improved afferent access to the forebrain, which probably occurred in early primates,

because a nucleus that appears equivalent to the VMpo/VMb of macaque monkeys and humans can be seen in the thalamus of both strepsirhine and haplorhine primates, but not in rats or cats.[41] Thus, primate encephalization apparently forged a direct ascending pathway for high-resolution homeostatic afferent information to reach the insular cortex, and this advance must have enabled a large increase in behavioral homeostatic efficiency. Notably, all primates have a lateral sulcus,[42] and, in fact, primates are the only animals that have a distinct lateral sulcus and insular lobe; this suggests, on the basis of the tension model of cortical morphogenesis,[43] that the interoceptive cortex serves as a tensile anchor for cortical gyrification. Indeed, I find it striking that all three of the sulci labeled in Figure 1—the lateral sulcus, the central sulcus, and the cingulate sulcus— are present only in haplorhine and most consistently in anthropoid primates (Old World monkeys, apes, and humans). To my mind, this observation suggests that gyrification in anthropoid primate brains brought these three homeostatic afferent regions as close together as possible, thus forming the fundus of each of these sulci, in order to optimize energy-efficient homeostatic processing. This view offers a much more parsimonious explanation for the observation that the lateral fissure is the first cortical sulcus formed during human fetal development,[44] instead of the inference that it is a primordial representation of evolutionary progression.

The fourth step of this hypothetical sequence was the integration (and lateralization) of afferent activity representing both the inner and outer environments in the region that becomes the mid-insula of humans; this step would, again, have conserved energy by matching a preexisting vertebrate behavioral/autonomic efferent forebrain asymmetry. The fifth step then was the integration of activity across all neural networks to form a complete representation of energy utilization in the body and brain, that is, a "global emotional moment" representing homeostatic salience. This step may correspond with the prominence of von Economo neurons in the anterior insula of hominids.[45] Finally, in the model I proposed, the replication of this quantal resource, indexed for real time (by theta wave oscillations), produced the basis for a sentient self within a specious present and the comparators necessary for efficient decision-making, which also provide the basis for introspective subjectivity.

It is noteworthy that no cynomolgus macaque monkey has been reported to recognize itself in a mirror.[46] I believe that being able to recognize oneself in a mirror requires the capacity for emotional identification with the actions and displays seen in the mirror, and that this can only be provided by a functional, emotionally valid neural representation of the self. Bonobos, siamangs, cetaceans, and elephants have passed the mirror test for self-recognition, as have a particular order of birds (corvids; see Ref. 46). To my mind, it is exciting to recognize that, additionally, these species are all capable of maintaining a rhythm and/or of using music communally, which is consistent with the model of awareness I have proposed.

## Issues of historical interest

### Homeostatic afferents

As far as I know, the first proposal that the dorsal root ganglion B cells that project to the superficial dorsal horn serve as homeostatic afferents was made in a theoretical essay by Prechtl and Powley.[47] Sadly, their proposal was sharply criticized by nearly all discussants. Unfortunately, they did not know that lamina I projections unmistakably provide the central continuation of the system they perceived.

The first detection of the ascending homeostatic afferent pathway in primates was the demonstration by Norgren and colleagues that the NTS projects directly to VMb in the monkey[17] rather than simply to PB as in the rat. They recognized this projection as phylogenetically distinct, but its evolutionary significance was a mystery. After I identified the topographically coherent lamina I projection to the adjoining VMpo with anterograde labeling,[17] it became apparent that together VMb and VMpo provide a complete representation of all homeostatic afferent activity.[1,48]

### VMpo

The concept that a distinct interoceptive pathway underpins affective feelings from the body in humans (such as pain) represents a paradigm shift from the prevailing concepts in the field of somatosensation, and this concept arouses resistance on two main issues. First, the identification of VMb is complicated by a nomenclature discrepancy— it is often called VPMpc, which falsely implies that it belongs to the exteroceptive somatosensory pathway to sensorimotor cortex. However, VMb in

monkeys projects primarily to the fundus of the superior insular sulcus,[49] where it is continuous anteriorly with the VMpo projections.[19] Furthermore, this distinction is also validated by the topographical gradients of the interoceptive (VMb + VMpo: antero-posterior) and exteroceptive (VPM + VPL: medio-lateral) representations, which are orthogonal, both in the thalamus and in the cortex of monkeys and humans.[4,48,50]

Second, the existence of VMpo has been explicitly denied by a leading expert on the thalamus, E. G. Jones, who claims that lamina I projects widely in somatosensory thalamus, that "the Craig group has relocated" VMpo to accommodate criticism, and that I have never demonstrated topography in this pathway.[51,52] His objections are widely cited by clinicians, who can't see VMpo in current MR images (e.g., Ref. 53). However, to my mind, these objections are opaque, because (1) the anterograde tracer injections reported by Graziano and Jones[51] were imprecise and involved most of the dorsal horn, which will certainly produce widespread labeling; (2) our cytoarchitectonic descriptions of VMpo have not changed;[48,54,55] and (3) I clearly documented topography.[48] Unfortunately, Graziano and Jones[51] denoted VMb as VMpo, apparently because the monoclonal antibodies they used did not reveal the calbindin 28 kD content of lamina I terminals that we have documented with polyclonal antibodies (suggesting hidden epitopes). This point is illustrated in Figure 2. My colleagues and I published documentation that a commercially available polyclonal antiserum: (1) demonstrates calbindin immunoreactivity in approximately three fourths of lamina I spinothalamic neurons; (2) reveals the loose bundle of their ascending fibers in the lateral funiculus (historically equivalent to the "lateral spinothalamic tract"); (3) identifies their dense terminal bursts in VMpo, both in monkeys and in humans; and (4) colocalizes with anterogradely transported labeling in their terminations in VMpo following precise injections in lamina I.[48,54,56] Whereas Jones implies that these observations are fictitious, the raw material has been witnessed by my collaborators and by several visitors to my laboratory; in addition, these observations have now been verified by others.[57,58] Indeed, the location of VMpo in the human thalamus that we identified using calbindin labeling fits very well with published microelectrode recordings in awake human
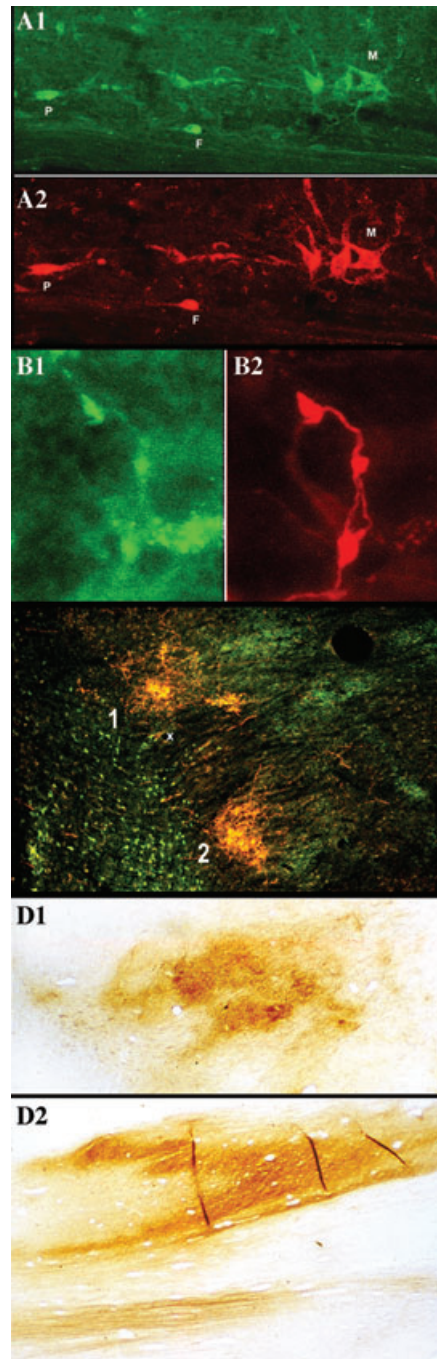


**Figure 2.** A composite of images from prior studies demonstrating the calbindin immunoreactivity of lamina I STT cells (A), their terminals in VMpo (B), the overlap of their anterogradely labeled terminations (red) with the calbindin-labeled terminal bursts (green; C), and the calbindin-labeled bursts in human VMpo and in the superficial dorsal horn and the lateral funiculus of human upper cervical spinal cord (D). Reformatted from Craig *et al.*[56] (A, D) and Craig[48] (B, C).

patients,[54,59] and the anteroposterior topography of lamina I projections to VMpo and of VMpo projections to the dorsal posterior insula provides the best explanation for a growing number of functional imaging findings (e.g., Refs. 21, 50, 60–63).

### The "pain pathway"

The concept that a distinct and separate pathway for nociceptive-specific lamina I neurons underlies pain sensation has been directly challenged by several prominent investigators who believe that spinal lamina V ("wide dynamic range") neurons are "necessary and sufficient" for pain,[64–66] despite mounting evidence to the contrary.[67–69] Their contention was recently decisively refuted by evidence that such lamina V neurons convey Group II muscle afferent activity, accordingly respond tonically to limb position, and project directly onto ventral horn motorneurons and other skeletal motor-related sites; thus, they are an integral component of the motor system.[70–72] Recent functional imaging results on a key topic of disagreement (temporal "windup;" see Ref. 73) from these investigators in fact demonstrate cortical activation which corroborates the role of lamina I spino-thalamo-cortical projections, although none of my work is cited.[74] Nevertheless, in light of the role of the lamina I pathway in homeostasis, I believe it would be inappropriate to call it simply a "pain pathway".[75]

### Gustatory cortex

Confusion regarding the identification of interoceptive cortex in humans was caused by the initial localization of primary gustatory cortex in humans to the anterior end of the insula, which was thought to be consistent with its location in the monkey.[30] That confusion was rectified by the recognition that it is situated in the mid-insula of humans, where it is contiguous with the region activated by lamina I,[3,20] and thus is part of a coherent primary interoceptive cortical region. This recognition was compelled in part by growing evidence that the anterior insula of humans is activated by emotional and cognitive aspects of all tasks in functional imaging experiments, reflecting capacities that monkeys do not have.

### Awareness and the insula

The concept that the anterior insula provides a fundamental basis for human self-awareness was recently questioned by a group of neurologists, based on their studies of a unique patient ("Roger;" see Ref. 76). They claimed that Roger has "virtually complete bilateral insula and anterior cingulate damage" due to encephalitis, but that he still passes many intelligence tests and a test for interoceptive (heartbeat) awareness (after infusion of isoproterenol). A separate report,[77] however, provided MRI evidence revealing that portions of the left anterior insula and anterior cingulate remain intact in Roger's brain, as well as behavioral evidence indicating that these remnants are functional. Specifically, Roger is "jocose" (i.e., pathologically happy) and trusts everyone, he greatly appreciates music, and he shows no signs of aphasia or speech apraxia; all of these are significant indicators of a functional left anterior insula.[78–80] Roger's symptoms, in fact, fit very well with those demonstrated by anesthesia of the right forebrain during the Wada test in patients with an intact left forebrain,[81] and they contrast starkly with those of patients with frontotemporal dementia (FTD), who have degenerate insular and cingulate cortices and demonstrable loss of self-awareness and self-conscious emotion.[82,83] By contrast, Roger's inability to perform the standard heartbeat perception test for interoceptive awareness (i.e., without any drugs) fits with the complete loss of the right anterior insula, which is selectively associated with this task.[84]

### Forebrain emotional asymmetry

The concept of forebrain emotional asymmetry based on the homeostatic model of awareness mentioned above[2] fits with psychophysiological evidence for forebrain affective asymmetry that has accumulated over the past 25 years.[85] This psychophysiological evidence had been opposed by several vocal antagonists on methodological grounds, but the same investigators recently published their acknowledgement of the validity of these data.[86] Nevertheless, this concept of forebrain emotional asymmetry does not match the widely taught idea that the left brain is analytical and the right brain is emotional, which emerged from the split-brain research on patients in whom the corpus callosum was sectioned, for which Roger Sperry received the Nobel Prize in 1981. A collaborator in the split-brain work, Michael Gazzaniga, is now a prominent leader in cognitive neuroscience, and he asserts that the left-brain interpreter is "the glue that creates our sense of being" (p. 301, Ref. 87). By contrast, the homeostatic forebrain asymmetry model

suggests that the human capacity for speech evolved in the left hemisphere because of its role in parasympathetic function; the vagus nerve became associated with vocalization eons ago.[88] It is noteworthy also that Sperry explicitly stated that "emotional processes appear to exert a general unifying influence" in the split-brain patients he studied.[89] Since it is likely that the left and right anterior insulae are interconnected by way of the anterior commissure, which was rarely (if ever) sectioned in the split-brain patients studied by Sperry and colleagues, this field is still an open research frontier.

### The self and the ACC

Lastly, there are several prominent neuroscientists who do not yet appreciate the evidence supporting the concept that the anterior insula and the anterior cingulate together form a core control network that guides all mental activity and behavior in adult humans (for references, see Ref. 4). In the homeostatic model I proposed, the insula underpins feelings and awareness and the cingulate underpins motivations and behavior, and both are normally coactive. By contrast, some authors recommend that the so-called default network represents the self—that is a set of cortical regions which deactivate when subjects become engaged in a task (including particularly the posteromedial cingulate). Those authors ignore virtually all of the evidence I have summarized (e.g., Refs. 90, 91). Others assert that the medial prefrontal cortex, and especially the anterior cingulate, substantializes the self; interestingly, the insula often displays activity in their studies that is less prominent than the activity in the cingulate, but it is ignored (e.g., Refs. 92–94). Finally, the concept that the earliest emergence of "phenomenal" or "core" consciousness lies in the brainstem (e.g., PAG) also has prominent adherents (e.g., Refs. 24, 95), but the evidence I have reviewed indicating that the bilateral anterior insulae underpin *all* human feelings certainly argues otherwise.

## Conclusion

The homeostatic view of integration in the insula, based on a functional anatomical perspective, provides a plausible model for human awareness that fits well with available evidence. The central role of the optimization of energy utilization as an evolutionary pressure can explain the pattern of organization of insular integration and its significance for human behavior. This model faces challenges that need further analysis, but it has striking explanatory power, for example, for the perceptual moment, for the emergence of music, for the opponent interaction between positive and negative emotion, and for the convergence of enormous numbers of functional imaging studies. This model makes testable predictions regarding subjective time perception, music appreciation, emotional balance, cardiorespiratory control, and so on, in patients in whom the anterior commissure has been sectioned, the right or left insula has been removed, or patients with FTD. I look forward to studies that will address such exciting features as the frame rate of the cinemascopic progression, the role of the von Economo neurons, or the interactions between the anterior insula and the anterior cingulate.

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## Conflicts of interest

The author declares no conflicts of interest.

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