Ray Dolan

The body in the brain

In J. M. Coetzee's novel *Elizabeth Costello*, the protagonist, fictional author Elizabeth Costello, delivers a prize lecture entitled "The Lives of Animals." Costello contrasts reason, exemplified by the Descartian credo *Cogito Ergo Sum*, with what she describes as

> fullness, embodiedness, the sensation of being – not a consciousness of yourself as a kind of ghostly reasoning machine thinking thoughts, but on the contrary the sensation – a heavily affective sensation – of being a body with limbs that have extension in space, of being alive to the world. This fullness contrasts starkly with Descartes' key state, which has an empty feel to it: the feel of a pea rattling around in a shell.

Here, Costello radically asserts that consciousness is multilayered – and that a fundamental layer is 'embodiedness,' the representation of our body in our brains. She later points out that embodiedness provides a sentient bridge between human consciousness and that of animals.

In making the seemingly paradoxical claim that bodily and mental states are intimately conjoined, Coetzee, via his fictional alter ego, raises a provocative question, one that a neuroscientific analysis, let alone a definition, of consciousness has yet to address. His account of consciousness echoes a similar challenge William Golding made in *The Inheritors*, which extensively documents the mental lives of Neanderthals – where thought and felt experience, engendered by perturbed bodily states, are indistinguishable.

I cannot claim to rise completely to the challenge of explaining the continuities between representations of the corporeal self and the conscious self. Nonetheless, I will approach it, starting by accepting the general premise, articulated most eloquently by Antonio Damasio, that the brain's representations of bodily states are fundamental to our ongoing mental experience.[1] As Damasio stated, "*We only know that we feel an emo-*

Ray Dolan is a professor at and director of the Wellcome Department of Imaging Neuroscience in London, England. The author of numerous articles in cognitive neuroscience, he is also the recipient of the Alexander von Humboldt international research award.

1 Antonio Damasio, *Descartes' Error* (New York: G. P. Putnam, 1994).

tion when we sense that emotion is sensed as happening in our organism."[2] In this essay, I will address what we currently know about how our brains generate and, in turn, remap one component of bodily states, specifically those mediated by the autonomic nervous system. My choice of the autonomic system reflects not only my own scientific interest but also the fact that the autonomic nervous system provides the most dynamic mapping between the body and brain and vice versa.

Homeostatic regulation is fundamental to the physiological organization of complex organisms. Examples of homeostatic control include body temperature, acid (pH), and salt regulation. All physiological systems operate within narrow constraints that must be continuously maintained to ensure the viability of an organism. In turn, any perturbation in bodily state, such as altered cardiovascular status, invokes a need for homeostatic control. This homeostatic control is largely accomplished via multiple feedback loops that include contributions from specialized vestibular, proprioceptive, and pain afferent signals. Information from these diverse systems is integrated within higher brain centers to provide an ongoing, continually updated image of the state of the body in the brain.

The importance of maintaining the internal milieu has been a central organizing principle in physiology since the time of Claude Bernard (1813 – 1878), who noted,

> So far from the higher animal being indifferent to the external world, it is on the contrary in a precise and informed relation with it, in such a way that its equilibrium results from a continuous and delicate compensation, established as by the most sensitive of balances.

Among the body's homeostatic systems, the autonomic nervous system is the most flexible and dynamic. Output signals to the body, generated in the brain's central autonomic effector sites, give the body a continuously updated picture of the motivational state of the brain. In turn, afferent signals from the body provide the brain with an updated representation of the current state of the body. In concert, these regulatory signals integrate bodily states with short- and long-term motivational needs, which depend on the current and anticipated future environments. My prime focus is to account for how such autonomic bodily states, which reflect a dynamic signaling between body and brain, are generated and, in turn, remapped within the brain.

Anatomically and functionally there are two segregated components to the autonomic nervous system: the sympathetic and parasympathetic subdivisions. Among its key functions sympathetic activity facilitates motor action, increasing cardiac output and reducing blood supply to the gut. In contrast, parasympathetic activity promotes more recuperative functions such as reducing heart rate, lowering blood pressure, and slowing gut motility. Consequently, bodily states associated with survival behaviors (e.g., the fight-or-flight response) are characterized by increased sympathetic activity and, in most instances, decreased parasympathetic activity. It is also notable that many autonomic responses, which tend to be outside one's conscious control (for example, sweating, piloerection, and vasomotor change such as blushing), contribute to the emotional expression and subtle

2 Antonio Damasio, *The Feeling of What Happens* (New York: Harcourt Brace, 1999).

social signaling that guide human interaction.

Autonomic output is continuously adjusted to reflect our physical, cognitive, and motivational needs with respect to our environment. This adjustment entails homeostatic control, which, in turn, requires feedback from the body to the brain's central effector-control mechanisms. Central homeostatic autonomic control is supported primarily by a functional organization of deep brain nuclei within structures such as the hypothalamus, pons, and medulla. Posterior and lateral hypothalamic nuclei influence sympathetic function via brain-stem centers such as the tegmentum; raphé nuclei; periaqueductal grey; and paraventricular, parabrachial, and medial reticular nuclei. Meanwhile, the anterior hypothalamus influences parasympathetic efferent responses via medullary nuclei such as the nucleus ambiguus and dorsal motor nucleus of the vagus, Edinger-Westphal nucleus, and salivatory nucleus. Regions such as the central nucleus of the amygdala, as well as the bed nucleus of the stria terminalis and locus coeruleus, also contribute to autonomic control, as they project directly to brain-stem autonomic nuclei and sympathetic cell bodies in the spinal cord. At the level of the brain stem, afferent feedback of visceral information is represented in the nucleus of the solitary tract and in hypothalamic nuclei that lie in close proximity to these efferent autonomic centers.

The default mode for autonomic control of bodily states is autoregulatory. But higher brain centers supporting cognitive functions, such as memory and mental imagery, also modulate lower autoregulatory autonomic control centers. One can gather this from introspective observation alone. For example, recollecting a threatening event from the past can induce changes in respiration, skin conductance, and heart rate despite the absence of any overt change in the demands upon our bodies. The influence of higher centers is also evident in anatomical and physiological observations, whereby stimulation of distinct cortical and subcortical regions can evoke autonomic responses. These areas of stimulation include the insula (implicated in somatic and visceral representations), the motor cortex, the neostriatum and cerebellum (involved in initiation and control of limb movements), the amygdala and hippocampus (involved in emotion perception, threat responses, and episodic memory), and the anterior cingulate and ventromedial prefrontal cortices (implicated in attention, motivation, and decision making). Thus, there appears to be an obligatory yoking of autonomic regulatory control in lower brain regions to functions mediated by higher brain centers.

A contemporary approach to understanding the relationship between bodily and brain states involves using brain-scanning techniques, such as functional magnetic resonance imaging (fMRI), to measure brain activity noninvasively, close to real time. By scanning the brains of subjects performing specific mental or physical tasks that alter cardiovascular autonomic responses (e.g., increases in heart rate and blood pressure), it is now possible to correlate indices of altered bodily states with corresponding states of the brain.

In one of the first investigations of higher cortical control of autonomic function, my colleagues and I adopted this approach. First, we tested for brain activity common to performance of effortful mental and physical tasks. Our principal observation was the correlation of activity in the anterior cingulate

cortex and the pons with increased cardiovascular output.[3] This finding indicated that in addition to classical autoregulatory sites, such as the pons, higher cortical regions implicated in cognitive control, such as the anterior cingulate cortex, are important for integrating volitional behavior (the sustained effort of doing the tasks) with peripheral states of cardiovascular arousal.

Extending this approach, we then determined whether specific cortical regions contribute to influences on bodily states mediated by the actions of either the sympathetic or parasympathetic system. Again, we scanned subjects while they performed motor and cognitive tasks to induce variability in heart rate. Measures of heart-rate variability (HRV) were then derived from R-wave intervals of the recorded electrocardiogram (ECG), utilizing a power-spectral analysis of R-R interbeat intervals. This type of analysis provides a means for distinguishing parasympathetic from sympathetic nervous control: 'high-frequency' spectral power (0.15 – 0.50 Hz) reflects parasympathetic nervous control, whereas 'low-frequency' spectral power (0.05 – 0.15 Hz) reflects sympathetic control.

From this study, we inferred that there are distinct cortical inputs into sympathetic and parasympathetic control of bodily arousal. An increase in the low-frequency sympathetic component of the ECG was associated with increased anterior cingulate, somatomotor, and insula cortex activity. Of particular interest was the connection between anterior cingulate cortex activity and influences expressed through the autonomic nervous system's sympathetic axis.[4] Increases in the parasympathetic component, on the other hand, were expressed in the anterior temporal cortex and deep brain structures, in particular, the basal ganglia.

Altered cardiovascular state is one index of bodily arousal resulting from increased autonomic drive; electrodermal activity (EDA), or enhanced electrical conductance of the skin with increased sweat secretion, is another. EDA is generated via the sympathetic system, and, unlike cardiovascular reactivity, its expression is not confounded by concurrent parasympathetic influences.

To determine how central brain states contribute to the generation of EDA, we designed a gambling task in which we presented subjects with a playing card (with a face value between one and ten) and then had them guess if the value of the successive card would be higher or lower.[5] We then rewarded a correct decision by giving the subject money and punished a wrong decision by taking the subject's money. Each time, we waited eight seconds to reveal the second card; during this delay subjects exhibited an anticipatory state of autonomic arousal that reflected the degree of uncertainty in the outcome. If the first card had a face value of five, there was maximal uncertainty; if its value was one or ten, there was no uncertainty.

3 H. D. Critchley et al., "Cerebral Correlates of Autonomic Cardiovascular Arousal: A Functional Neuroimaging Investigation in Humans," *Journal of Physiology* (*Lond*) 523 (1) (2000): 259 – 270.

4 H. D. Critchley et al., "Human Cingulate Cortex and Autonomic Control: Converging Neuroimaging and Clinical Evidence," *Brain* 126 (2003): 2139 – 2152.

5 H. D. Critchley, R. Elliott, C. J. Mathias, and R. J. Dolan, "Neural Activity Relating to Generation and Representation of Galvanic Skin Conductance Responses: A Functional Magnetic Resonance Imaging Study," *Journal of Neuroscience* 20 (2000): 3033 – 3040.

Using this game, we could explore which brain regions corresponded to a sympathetic state of arousal (as indexed by enhanced EDA) during the process of appraising each decision's risk value. Activity in the anterior cingulate and dorsolateral prefrontal cortices correlated with the degree of anticipatory EDA response, while both risk and arousal modulated activity in the anterior cingulate and insula cortex. These results led us to infer that these regions mediate between a cognitive state of risk and uncertainty and an associated bodily state of increased sympathetic arousal.

Although EDA changes automatically in response to the environment, subjects can be taught to exert control over their autonomic responses with biofeedback techniques. Using EDA as an index of sympathetic arousal, we trained subjects to perform a biofeedback relaxation task. In this study, we presented subjects with a 'thermometer' measuring their level of EDA arousal. By scanning these subjects as they reduced their EDA, we showed that this decrease in EDA correlated with increased activity in the anterior cingulate cortex, inferior parietal cortex, and globus pallidus. We then concluded that these regions contributed to intentional influences on sympathetically mediated bodily states.

In this study, exteroceptive information, as provided by the 'thermometer,' enabled biofeedback control of autonomic states. But what happens if this form of feedback is inaccurate or noisy? In such situations subjects can still accomplish the task by ignoring the exteroceptive signal and focusing instead on their own interoceptive state (for example, their state of cardiovascular arousal). In a follow-up experiment we used a similar biofeedback relaxation task but scrambled the accuracy (by adding random 'noise') or the sensitivity (by scalar adjustments of feedback) of the visual index of electrodermal arousal (EDA). These manipulations, as expected, only enhanced the subjects' reliance on their own interoceptive states.

Performance of biofeedback relaxation tasks activated the anterior cingulate, insula, thalamus, hypothalamus, and brain stem, as well as the somatosensory cortex and the dorsolateral prefrontal cortex. Both accuracy and sensitivity of feedback influenced activity within the anterior insula in particular. Thus, the perceptual qualities (sensitivity) of the feedback could increase the already enhanced insula response to noise in the feedback signal. These findings led us to surmise that activity in the anterior cingulate cortex mediates an intentional drive to decrease sympathetic activity, whereas the insula supports *sensory* integration of interoceptive and exteroceptive information, reflecting the current bodily state of autonomic arousal.[6]

The experimental approach described so far relies exclusively on studies conducted with healthy subjects. Homeostasis is crucially dependent on feedback signals. Once something perturbs the body, afferent-feedback circuits provide the brain with a representation of the body's altered state (or a metarepresentation, meaning a representation that indexes a disturbance in homeostasis). But where are these states mapped in the brain? This question should garner wide interest in view of Damasio's suggestion that feedback representations of visceral and somatomotor activity give not only emotional color to ongoing experience

6 H. D. Critchley et al., "Volitional Control of Autonomic Arousal: A Functional Magnetic Resonance Study," *Neuroimage* 16 (2002): 909–919.

but also support a bedrock representation of 'the self.'

Patients with discrete lesions to efferent or afferent limbs of these control loops can, in theory, provide a means to investigate the dynamics of autonomic regulation and, indeed, the wider influence of bodily responses on emotion and cognition. But the neurological literature lacks any clear lesion that effectively compromises feedback for autonomic states. Even a patient with a high spinal cord lesion that impairs most forms of somatic sensory feedback still has intact autonomic feedback through the vagus nerve.

So, instead, my colleagues and I have studied patients with pure autonomic failure (PAF), an acquired syndrome that results in degeneration of the peripheral autonomic system.[7] This syndrome affects postganglionic sympathetic and parasympathetic neurons in the absence of a central neurological pathology. Patients with this disorder no longer generate peripheral autonomic responses to stress, supplying a unique glimpse into how autonomically generated bodily states are remapped in the brain.

We reasoned that the primary difference in brain activity between PAF and control subjects performing identical stress tasks would be an absence of afferent feedback from the body. Initially, we observed increased activity in the pons in PAF subjects, across effortful and effortless cognitive and physical tasks, which is consistent with the idea that this region is responsible for continuous autoregulatory, autonomic control. The absence of afferent regulatory feedback in PAF subjects accounts for their enhanced level of activity in this region. In addition, PAF patients demonstrated reduced activity in the insula and primary somatosensory cortices across all tasks, indicating the involvement of these areas in a metarepresentation of altered bodily states.

Of particular interest was identifying the brain areas in which PAF patients and controls exhibited differences during physically and mentally taxing tasks (accompanied by autonomic arousal in controls), but not during effortless tasks. Significantly greater anterior cingulate activity was evident in PAF patients, who generated no cardiovascular arousal, compared to matched healthy controls. This finding is consistent with the idea that the anterior cingulate is responsible for context-specific autonomic modulation of bodily states to meet ongoing behavioral demands. In healthy subjects, context-specific autonomic responses provide a negative feedback signal to regulate the efferent sympathetic drive. Without such feedback, PAF subjects do not experience a decrease in anterior cingulate cortex activity.

In a similar experiment, we exposed both PAF patients and control subjects to a threat stimulus (a face paired with a shock), inducing bodily changes associated with fear. Again, we could determine how the absence of afferent information from the body alters brain activity. While PAF patients can perceive a threat and generate a central output signal from the brain, they lacked activity in the insula cortex, pointing again to the insula as providing the map of interoceptive states of autonomic arousal.[8]

7 H. D. Critchley, C. J. Mathias, and R. J. Dolan, "Neuroanatomical Basis for First- and Second-Order Representations of Bodily States," *Nature Neuroscience* 4 (2001): 207 – 212.

8 H. D. Critchley, C. J. Mathias, and R. J. Dolan, "Fear Conditioning in Humans: The Influence of Awareness and Autonomic Arousal on Functional Neuroanatomy," *Neuron* 33 (2002): 653 – 663.

Many of our neuroimaging investigations implicated regions such as the anterior cingulate and insula cortices in autonomic control, particularly in the contextual generation and representation of states of bodily arousal, respectively. Thus, lesions affecting these regions should generate abnormal autonomic responses during volitional behavior. First, we studied three patients who had acquired damage to the anterior cingulate cortex. During the performance of effortful tasks all three patients demonstrated an absence of adaptive cardiovascular responses.[9] The patients' heart-rate variability (HRV) supplied additional evidence of an association between anterior cingulate function and control of autonomic-induced change in bodily states. Power-spectral analysis of their HRV revealed abnormalities primarily in sympathetic power, consistent with our prior conjecture that the anterior cingulate cortex provides an interface between cognitive effort and generation of sympathetic bodily arousal. Indeed, these observations strikingly support our theory that the anterior cingulate cortex is involved in integrating higher states of cognition, as required during volitional behaviors, and autonomic states of bodily arousal.

The possibility that the insula cortex is the primary substrate for a second-order mapping of bodily states led us to believe that this region mediates conscious awareness of bodily states – or, more precisely, feeling states – an idea also central to Damasio's account of feeling states.[10] Feeling is the subjective, private, or experiential component of emotion. In the present context, feeling refers to *the responses of our sense organs and internal milieu, including visceral states, to the environment, and the consequential responses within central mechanisms that monitor induced internal change*. To address the question of whether visceral awareness is associated with enhanced activity in this cortical region, we studied a group of interoceptively aware subjects.

The critical experimental hurdle here was creating a reliable index of visceral awareness. It turns out that a heartbeat-detection task can test sensitivity to visceral states. In this task, subjects must indicate the timing of their own heartbeat. The subjects are played back a signal, visual or auditory, triggered by their own heartbeats – with or without an experimentally manipulated lag. The subjects must then determine whether or not the feedback signal is synchronous with their interoceptively monitored heartbeat. Approximately half the population is good at detecting their heartbeats; interestingly, these subjects are also more emotionally aware and expressive.

Our study showed that enhanced attention to one's visceral state was associated with increased activity in a number of brain regions, in particular, the somatosensory and insula cortices.[11] Furthermore, detecting the desynchronization between the feedback signal and one's own heartbeat, a manipulation that places greater demands on interoceptive awareness, involved increased activity in the right insula. This finding converged with recent neuroanatomical discoveries indicating this region's importance to awareness of one's feelings. In particular, results showing that this region receives a dedicated lam-

9 Critchley et al., "Human Cingulate Cortex and Autonomic Control."

10 Damasio, *The Feeling of What Happens*.

11 H. D. Critchley et al., "Neural Systems Supporting Interoceptive Awareness," *Nature Neuroscience* 7 (2004): 189 – 195.

ina-1 spinothalamic input that converges with vagal inputs (a major source of visceral feedback) in the right anterior insula, and neuroanatomical evidence revealing that this region has a distinct laminar architecture found only in humans and higher primates, are in keeping with this interpretation of our neuroimaging findings.[12]

A question arising from these findings, though, is the degree to which neural mechanisms that mediate awareness of one's own bodily state contribute to awareness of the bodily states of others. Such awareness is at the core of the psychological attribute of empathy, and, arguably, this attribute underpins a human disposition to altruism and compassion. The suggestion here is that our ability to empathize with others relies on neuronal systems that underlie a higher-order representation of our own bodily and emotional states.

We addressed this very question in a study in which subjects received either a highly painful or not painful stimulus, and then viewed a loved one receive a painful stimulus. The intriguing result was that the emotional component of pain evoked when a subject actually received a painful stimulus was also triggered when the subject witnessed a loved one receive the same pain.[13] The regions of shared activation, for pain to self and to others, involved anterior cingulate and insula cortices – areas that I have suggested mediate the generation of sympathetic autonomic output and the afferent mapping of autonomically generated perturbation in bodily states.

Human neuropsychology has traditionally embraced a dualist model of brain and body. The fact that virtually all cognitive states are, to a greater or lesser degree, yoked to bodily states means that our conventional ideas of a fundamental division between the mental and the corporeal are in need of revision. What we apprehend in the realm of the senses is represented by images and concepts that facilitate representation in memory and awareness. What we sense from our bodies is, for the most part, only recognized as a vague background state, a current of feeling within our ongoing mental life, that is largely without symbolic mediation and conceptual form. However, this absence of conceptual form arguably provides the basis for the felt immediacy of experience, and a subjective consciousness, that emerges out of a dynamic mapping between brain and body.

12 J. Allman, A. Hakeem, and K. Watson, "Two Phylogenetic Specializations in the Human Brain," *Neuroscientist* 8 (2002): 335 – 346; A. D. Craig, "Human Feelings: Why Are Some More Aware Than Others?" *Trends in Cognitive Science* 8 (2004): 239 – 241.

13 T. Singer et al., "Empathy for Pain Involves the Affective But Not Sensory Components of Pain," *Science* 303 (2004): 1157 – 1162.