

(which is true of most microbiome studies to date), they would not have been able to determine whether the bacterial taxa decreased or increased in absolute abundance. The increase of *Pseudomonads* under herbivory they observed was found to be associated with decreased relative abundances of all other taxa in the same sample. Normalization using host DNA allowed them to observe that several taxa, as well as the total bacteria, increased in absolute abundance [5]. This demonstrates how adding a quantitative analysis to the marker-gene sequencing data can move us towards better estimates of bacterial densities within hosts, and it was essential in reaching biologically relevant conclusions. This practice is increasingly advised for microbial community studies in general, and the authors [5] provide a straightforward method that can readily

be applied in future plant-microbiome studies.

REFERENCES

1. Thaler, J.S., Fidantsef, A.L., Duffey, S.S., and Bostock, R.M. (1999). Trade-offs in plant defense against pathogens and herbivores: a field demonstration of chemical elicitors of induced resistance. *J. Chem. Ecol.* 25, 1597–1609.
2. Haney, C.H., Wiesmann, C.L., Shapiro, L.R., Melnyk, R.A., O'Sullivan, L.R., Khorasani, S., Xiao, L., Han, J., Bush, J., Carrillo, J., *et al.* (2018). Rhizosphere-associated *Pseudomonas* induce systemic resistance to herbivores at the cost of susceptibility to bacterial pathogens. *Mol. Ecol.* 27, 1833–1847.
3. Wilkinson, S.W., Magerøy, M.H., López Sánchez, A., Smith, L.M., Furci, L., Cotton, T.E.A., Krokene, P., and Ton, J. (2019). Surviving in a hostile world: plant strategies to resist pests and diseases. *Annu. Rev. Phytopathol.* 57, 505–529.
4. Berendsen, R.L., Pieterse, C.M., and Bakker, P.A. (2012). The rhizosphere microbiome and plant health. *Trends Plant Sci.* 17, 478–486.
5. Humphrey, P.T., and Whiteman, N.K. (2020). Insect herbivory reshapes a native leaf microbiome. *Nat. Ecol. Evol.* 4, 221–229.
6. Kembel, S.W., O'Connor, T.K., Arnold, H.K., Hubbell, S.P., Wright, S.J., and Green, J.L. (2014). Relationships between phyllosphere bacterial communities and plant functional traits in a neotropical forest. *Proc. Natl. Acad. Sci. USA* 111, 13715–13720.
7. Bäckhed, F., Fraser, C.M., Ringel, Y., Sanders, M.E., Sartor, R.B., Sherman, P.M., Versalovic, J., Young, V., and Finlay, B.B. (2012). Defining a healthy human gut microbiome: current concepts, future directions, and clinical applications. *Cell Host Microbe* 12, 611–622.
8. Chung, S.H., Rosa, C., Scully, E.D., Peiffer, M., Tooker, J.F., Hoover, K., Luthe, D.S., and Felton, G.W. (2013). Herbivore exploits orally secreted bacteria to suppress plant defenses. *Proc. Natl. Acad. Sci. USA* 110, 15728–15733.
9. Hökeberg, M., Gerhardson, B., and Johnsson, L. (1997). Biological control of cereal seed-borne diseases by seed bacterization with greenhouse-selected bacteria. *Eur. J. Plant Pathol.* 103, 25–33.

Brain Mapping: Understanding the Ins and Outs of Brain Regions

Bradford Z. Mahon^{1,2}

¹Department of Psychology, Carnegie Mellon University, Neuroscience Institute, 5000 Forbes Avenue, Pittsburgh, PA 15213, USA

²Department of Neurosurgery, University of Rochester Medical Center, 601 Elmwood Avenue, Rochester, NY 14642, USA

Correspondence: bmahon@andrew.cmu.edu

<https://doi.org/10.1016/j.cub.2020.03.061>

A recent study in which primary motor cortex activity was imaged with sub-laminar resolution has found that, while overt motor actions led to activity in both superficial and deep cortical layers, motor imagery engaged only superficial layers.

The goal of cognitive neuroscience is to explain behavior in neural terms. In the service of that goal, the past several decades have seen new tools and analytic techniques support ever more detailed maps of human brain structure and function. One of the most widely used techniques, blood-oxygen-level-dependent (BOLD) functional magnetic resonance imaging (fMRI), has relatively high spatial resolution in the setting of whole brain coverage, but is notoriously limited by low temporal resolution. On the other hand, methods that measure extra-

cranial electrical potentials — magnetoencephalography (MEG) and electroencephalography (EEG) — have millisecond temporal resolution but, because of their limited spatial resolution, cannot resolve functional activity associated with temporally overlapping inputs and outputs in a brain region. As they report in this issue of *Current Biology*, Persichetti *et al.* [1] have broken the impasse by using a functional MRI method with the sensitivity to distinguish superficial laminar activity, associated with afferent inputs, from deep laminar

activity, associated with efferent outputs [2]. This technique, vascular space occupancy (VASO), is based on measuring cerebral blood volume, and has higher contrast-to-noise at high spatial resolution than conventional BOLD fMRI [1,2].

Persichetti *et al.* [1] scanned healthy adult subjects who performed either an overt hand action with their left hand (finger tapping) or imagined doing so. Functional imaging focused on the primary motor representation of the left hand. The authors report two core

findings: first, while overt motor actions led to activity in both superficial and deep layers, motor imagery engaged only superficial layers; and second, overt motor actions that followed either imagined or overt actions led to repetition suppression in superficial layers but repetition enhancement in deep layers.

As Persichetti *et al.* [1] discuss, it has long been known that motor imagery can improve performance, and that there is spatial overlap in activity elicited in the primary motor cortex by imagined and actual movements (for references see [1]). Those observations had been argued to support the inference that the same *processes* involved in actual movement are engaged by imagined movement. Note, though, the evidentiary gap between demonstrations of ‘neural overlap’ and the inference of overlapping processes [3,4] — that evidentiary gap is what is bridged by the new research by Persichetti *et al.* [1]. More broadly, their contribution highlights how prior demonstrations of ‘neural overlap’, as implemented using conventional BOLD fMRI at the level of ‘brain regions’, merely define the problem that needs to be solved.

It would be difficult to overstate how consequential the new study by Persichetti *et al.* [1] could be as a demonstration of how to revisit long-standing theoretical questions. This is because, with VASO, ‘brain region’ is replaced with cortical lamina. But the breakthrough is not just the increase in spatial resolution: spatial resolution does not, in and of itself, increase the explanatory efficacy of a brain map [5,6]. The breakthrough is the demonstration of how to leverage the isomorphisms between, on the one hand, superficial layer activity and inputs to motor cortex, and on the other hand, deep layer activity and motor cortex outputs. This has implications far beyond motor imagery, as there are a number of hotly debated issues across the cognitive neurosciences that turn on how to interpret the role of motor activity in tasks that do not require overt motor actions.

A prominent example is the role of motor systems in action recognition. It is well established that motor and motor-relevant structures are activated during action observation. This has been observed in the domains of hand actions

[7], speech processing [8], and whole body movements [9]. There is ‘neural overlap’ between the systems involved in action production and those involved in action recognition. Such observations of ‘neural overlap’ have led to a resurgence of interest in ‘motor theories’ of action recognition [10]. The core of such theories is a claim about *process overlap*: namely, that recognition involves running production processes to ‘simulate’ the perceived input. As has been noted by a number of authors [4,11,12], it is not obvious that one can infer process overlap from neural overlap. Even more problematic for such inferences, lesions to motor areas (with concomitant motor impairments) are not necessarily associated with action recognition deficits (see for example [13,14]). Those lesion data place a hard limit on how richly we may interpret observations of neural overlap to inform theories of process overlap. Formulated as a question: if motor systems are not necessary for action recognition, then why are they activated? Perhaps the answer will lie in a deeper understanding of *how* they are activated — the dynamics of interactions and information exchange among motor areas and systems that provide inputs to and modulate responses in the motor system.

A similar situation is framed by research on motor system activity during conceptual processing — such observations have been argued to support ‘embodied’ views of concept representation. The core idea of the ‘embodied cognition’ hypothesis is that conceptual representations are constituted, at least in part, by information that is in a motor format [15]. For instance, reading the word ‘kick’ activates the foot area of motor cortex, while reading the word ‘kiss’ activates the mouth area [16] (but see [17]). The embodied cognition hypothesis argues that the reason why the foot area of motor cortex is activated when reading the word ‘kick’ is because the first-person motor simulation of ‘kicking’ instantiates, online, the meaning of the word ‘kick.’ The evidentiary basis for embodied cognition thus boils down to the same (assumed) equivalence between ‘neural overlap’ and ‘process overlap’ [18]. And again, lesion data present a direct challenge to the core claim of embodied cognition: motor

deficits after lesions to motor areas are not necessarily associated with conceptual impairments [13]. This in turn frames the same question: if motor regions are not necessary for concept representation, then why are they active during conceptual processing? *How* does the ‘foot’ part of the motor system come to be selectively activated when a subject reads the word ‘foot’ (if the printed stimulus has not already been semantically interpreted)?

The common denominator across the domains briefly reviewed above is how to interpret observations of neural overlap. In this regard, the Persichetti *et al.* [1] contribution frames a much larger issue: a brain map is relevant to an explanation of behavior in the measure to which the map’s labels pick out computational content and processes that make up an explanatory account of behavior [5,6]. BOLD fMRI maps are not the solution that cognitive neuroscience seeks — the reason is that they do not obviously constrain inferences about process. Persichetti *et al.* [1] offer a demonstration of how to functionally *label* brain maps of motor cortex in a way that elucidates a process-based explanation. Testing hypotheses about *how* motor systems are activated in tasks that do not involve overt motor action advances mechanistic understanding of how the brain works, and moves us closer to the goal of explaining behavior in neural terms. For instance, a prior study by Lingnau *et al.* [19] found that repetition suppression effects in motor areas do not transfer from executed actions to observed actions — contrary to a core prediction of ‘motor theory’ type interpretations of motor cortex activity during action observation. The Persichetti *et al.* [1] findings may suggest that the lack of repetition suppression reported by Lingnau *et al.* [19] might be the result of BOLD summing over repetition suppression (superficial layers) and repetition enhancement effects (deep layers).

A distinction drawn by Simon [20] in a different context is relevant here: that between state and process descriptions of a complex system. A *state description* of the brain would specify which functions are located where and which parts of the brain are connected one to the other. The observation that primary motor cortex is active during imagined motor

movements, action observation, and processing of action verbs amounts to a state description. Such demonstrations of ‘neural overlap’ merely frame the problem that needs to be answered: they are a ‘state description of the solution’ [20]. As such, they leave us with *two* things that need to be explained: the original behavioral phenomenon — for example, why imagining motor movements leads to performance improvements — and the neural correlates of that behavior (motor imagery involves activity of motor cortex). By contrast, a *process description* of the brain would account for *how* a given phenomenon is generated; it is a ‘recipe’, as it were, for producing the phenomenon in question [20]. Generally speaking, computational and cognitive theories offer process descriptions (always set against architectural assumptions that subsume a state description of the system). The breakthrough of Persichetti *et al.* [1] is to show how it may be possible to bring together, within a common data form and using non-invasive methods, a state description of the human brain with a process description of the human brain.

REFERENCES

- Persichetti, A.S., Avery, J.A., Huber, L., Merriam, E.P., and Martin, A. (2020). Layer-specific contributions to imagined and executed hand movements in human primary motor cortex. *Curr. Biol.* 30, 1721–1725.
- Huber, L., Handwerker, D.A., Jangraw, D.C., Chen, G., Hall, A., Stuber, C., Gonzalez-Castillo, J., Ivanov, D., Marrett, S., Guidi, M., *et al.* (2017). High-resolution CBV-fMRI allows mapping of laminar activity and connectivity of cortical input and output in human M1. *Neuron* 96, 1253–1263.e7.
- Poldrack, R.A. (2011). Inferring mental states from neuroimaging data: from reverse inference to large-scale decoding. *Neuron* 72, 692–697.
- Martin, A. (2016). GRAPES-Grounding representations in action, perception, and emotion systems: How object properties and categories are represented in the human brain. *Psychon. Bull.* 23, 979–990.
- Krakauer, J.W., Ghazanfar, A.A., Gomez-Marín, A., MacIver, M.A., and Poeppel, D. (2017). Neuroscience needs behavior: correcting a reductionist bias. *Neuron* 93, 480–490.
- Poeppel, D. (2012). The maps problem and the mapping problem: two challenges for a cognitive neuroscience of speech and language. *Cogn. Neuropsychol.* 29, 34–55.
- Rizzolatti, G., and Craighero, L. (2004). The mirror-neuron system. *Annu. Rev. Neurosci.* 27, 169–192.
- Meister, I., Wilson, C., Deblieck, A., Wu, A., and Iacoboni, M. (2007). The essential role of premotor cortex in speech perception. *Curr. Biol.* 17, 1692–1696.
- Calvo-Merino, B., Grezes, J., Glaser, D.E., Passingham, R.E., and Haggard, P. (2006). Seeing or doing? Influence of visual and motor familiarity in action observation. *Curr Biol* 16, 1905–1910.
- Liberman, A., Cooper, F., Shankweiler, D., and Studdert-Kennedy, M. (1967). Perception of the speech code. *Psychol. Rev.* 74, 431–461.
- Caramazza, A., Anzellotti, S., Strnad, L., and Lingnau, A. (2014). Embodied cognition and mirror neurons: a critical assessment. *Annu. Rev. Neurosci.* 37, 1–15.
- Hickok, G. (2009). Eight problems for the mirror neuron theory of action understanding in monkeys and humans. *J. Cogn. Neurosci.* 21, 1229–1243.
- Mahon, B.Z., and Caramazza, A. (2005). The orchestration of the sensory-motor systems: Clues from Neuropsychology. *Cogn. Neuropsychol.* 22, 480–494.
- Rogalsky, C., Love, T., Driscoll, D., Anderson, S., and Hickok, G. (2011). Are mirror neurons the basis of speech perception? Evidence from five cases with damage to the purported human mirror system. *Neurocase* 17, 178–187.
- Allport, D. (1985). Distributed memory, modular subsystems and dysphasia. In *Current Perspectives in Dysphasia*, S.P.N.R. Epstein, ed. (Edinburgh, UK: Churchill Livingstone), pp. 32–60.
- Pulvermüller, F. (2013). Semantic embodiment, disembodiment or misembodiment? In search of meaning in modules and neuron circuits. *Brain Lang* 127, 86–103.
- Postle, N., McMahon, K.L., Ashton, R., Meredith, M., and de Zubicaray, G.I. (2008). Action word meaning representations in cytoarchitectonically defined primary and premotor cortices. *Neuroimage* 43, 634–644.
- Mahon, B.Z. (2015). The burden of embodied cognition. *Can. J. Exp. Psychol.* 69, 172–178.
- Lingnau, A., Gesierich, B., and Caramazza, A. (2009). Asymmetric fMRI adaptation reveals no evidence for mirror neurons in humans. *Proc. Natl. Acad. Sci. USA* 106, 9925–9930.
- Simon, H. (1962). The Architecture of Complexity. *Proc. Am. Phil. Soc.* 106, 467–482.