Blinder, P., Tsai, P.S., Kaufhold, J.P., Knutsen, P.M., Suhl, H., and Kleinfeld, D. (2013). The cortical angiome: an interconnected vascular network with noncolumnar patterns of blood flow. Nat. Neurosci. *16*, 889–897.

Chen, B.R., Kozberg, M.G., Bouchard, M.B., Shaik, M.A., and Hillman, E.M. (2014). A critical role for the vascular endothelium in functional neurovascular coupling in the brain. J. Am. Heart Assoc. *3*, e000787.

DeNofrio, D., Hoock, T.C., and Herman, I.M. (1989). Functional sorting of actin isoforms in microvascular pericytes. J. Cell Biol. *109*, 191–202.

Hall, C.N., Reynell, C., Gesslein, B., Hamilton, N.B., Mishra, A., Sutherland, B.A., O'Farrell, F.M., Buchan, A.M., Lauritzen, M., and Attwell, D. (2014). Capillary pericytes regulate cerebral blood flow in health and disease. Nature *508*, 55–60.

Hill, R.A., Tong, L., Yuan, P., Murikinati, S., Gupta, S., and Grutzendler, J. (2015). Regional blood flow in the normal and ischemic brain Is controlled by arteriolar smooth muscle cell contractility and not by capillary pericytes. Neuron *87*, 95–110.

Kornfield, T.E., and Newman, E.A. (2014). Regulation of blood flow in the retinal trilaminar vascular network. J. Neurosci. *34*, 11504–11513.

Nippert, A.R., Biesecker, K.R., and Newman, E.A. (2018). Mechanisms mediating functional hyperemia in the brain. Neuroscientist *24*, 73–83.

Rungta, R.L., Chaigneau, E., Osmanski, B.F., and Charpak, S. (2018). Vascular compartmentalization of functional hyperemia from the synapse to the pia. Neuron *99*, this issue, 362–375.

Tian, P., Teng, I.C., May, L.D., Kurz, R., Lu, K., Scadeng, M., Hillman, E.M., De Crespigny, A.J., D'Arceuil, H.E., Mandeville, J.B., et al. (2010). Cortical depth-specific microvascular dilation underlies laminar differences in blood oxygenation level-dependent functional MRI signal. Proc. Natl. Acad. Sci. USA *107*, 15246–15251.

Primate Social Communication Goes Interactive

Andreas Nieder[1],*
[1]Animal Physiology Unit, Institute of Neurobiology, University of Tübingen, Auf der Morgenstelle 28, 72076 Tübingen, Germany
*Correspondence: andreas.nieder@uni-tuebingen.de
https://doi.org/10.1016/j.neuron.2018.07.014

Social communication has traditionally been studied from the point of view of an isolated spectator not participating in social interaction. In this issue of *Neuron*, using advanced functional imaging, Shepherd and Freiwald (2018) explore the functional neuroanatomy of social communication in the brain of socially interacting nonhuman primates and discover three large-scale brain networks dedicated to the process.

Communication is the process of transmitting information from a sender to a receiver. In this definition, only the sender is active, whereas the receiver passively perceives information. In everyday social communication situations, however, the receiver reciprocates the exchange of information. We all know the greeting ritual in the morning when someone asks "How are you?" If we were not to reply, we would immediately suffocate from the attempt to communicate in a rude way. Instead, we reply "Awesome!" if we are feeling alright and are having this encounter in the United States (in Germany, we may less enthusiastically mumble "Okay"). Social communication becomes "social" and alive if we not merely observe others, but interact with them.

Although interaction is a key aspect to social communication, social cognition has traditionally been studied from a third-person stance, from the point of view of an isolated spectator that is required to merely observe others rather than participate in social interaction with them. However, this approach can only elucidate the impoverished passive, or perceiving, side of communication. It neglects the irreducible reactive side of social communication required for an involved, second-person stance that emphasizes the importance of dynamic, real-time interactions with others (Schilbach et al., 2013). Currently, it is unknown which networks in the brain may be required once a subject becomes involved in an ongoing interaction.

In this issue of *Neuron*, Shepherd and Freiwald (2018) set out to tackle this question and explored social communication networks in the brain of interacting rhesus monkeys. Using functional magnetic resonance imaging (fMRI), they measured regional blood flow in the brains of rhesus monkeys that watched video clips of other rhesus monkeys inside a scanner (Shepherd and Freiwald, 2018). The videos displayed the real moving faces of conspecifics in two different social contexts: the first context simulated a third-person context in which the monkey in the video was looking away from the subject (averted-gaze context). This provided Shepherd and Freiwald (2018) to explore the neural processes in the subject as a detached spectator that simply observes the faces of a conspecific from a third-person stance. In the second context, the monkey in the video was looking and grimacing straight at the subject (direct gaze context) (Figure 1). This condition prompted the subject to make face and mouth movements directed at the conspecific in the video. The most common facial movement exhibited by the subject was "lipsmacking," an affiliative and affective signal often observed during face-to-face social interactions in advanced nonhuman primates. Because the subject reciprocated social signals and thus attempted to interact with the monkey in the video clip, this second context sufficed a second-person context. This condition opened a window into deciphering the brain's networks engaged in involved and reactive social
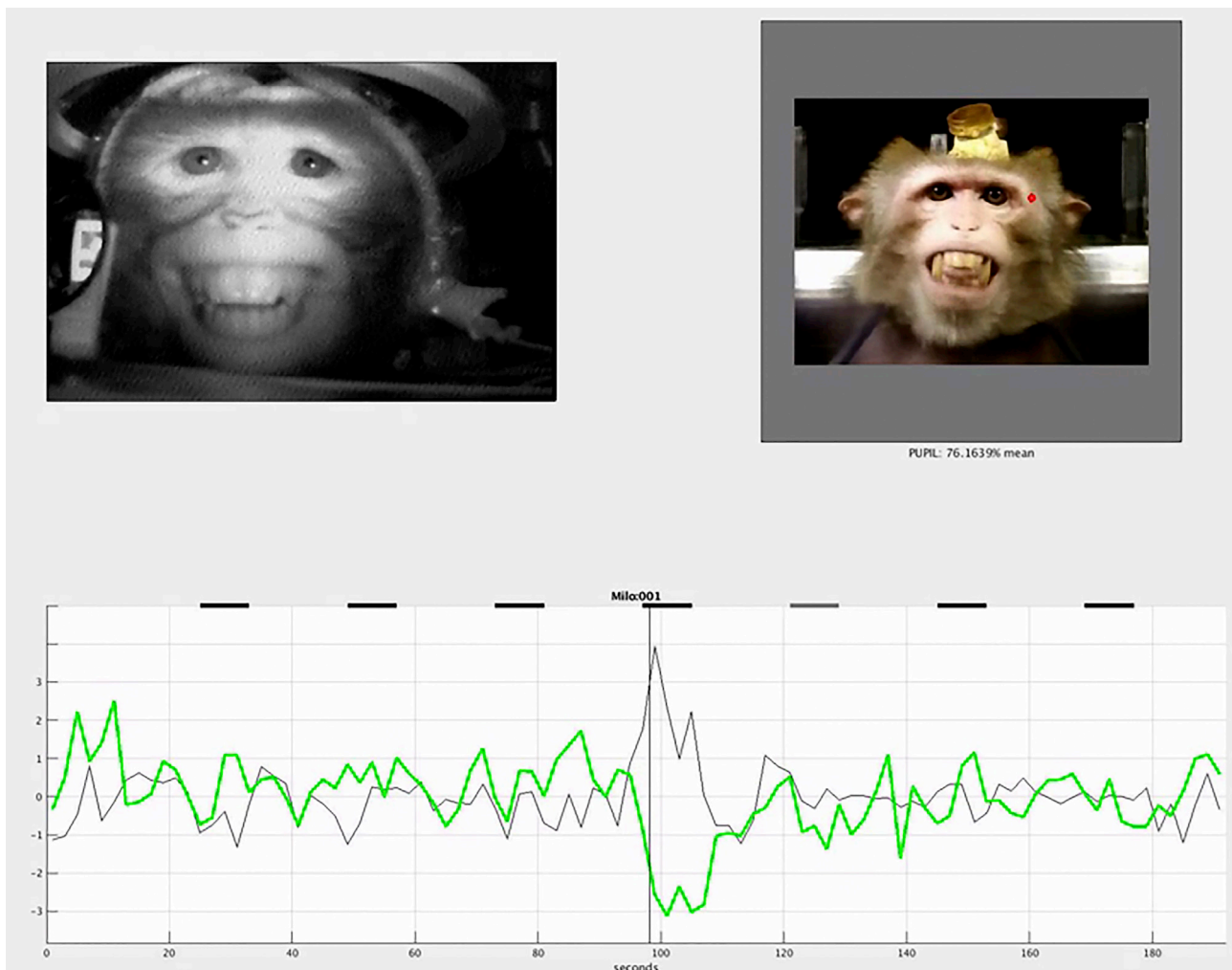
Figure 1. fMRI in Socially Interacting Rhesus Macaques
Adapted from a scene in Video S1 by Shepherd and Freiwald, 2018.
Top: in this scene, the facial expressions and movements shown by the monkey in the color video clip (top right) were directed straight at the scanned subject monkey (top left) to create a second-person context.
Bottom: the black graph represents the automatically detected facial movements elicited from the subject. The green graph shows the single-trial fMRI response in the facial representation of primary motor cortex (M1) temporally correlated with the movie (the vertical black bar in the center represents the time point of the interactive scene depicted above) and the subject's facial movements. M1 is activated during orofacial interaction (fMRI signal decrease indicates increased neural activity).

communication. Both of these social contexts were contrasted with a nonsocial control condition, in which the scrambled and unrecognizable faces of monkeys were shown in the video.

By comparing and contrasting fMRI activity to different contexts, Shepherd and Freiwald (2018) isolated three distinct brain networks with different locations and functions: networks for social perception, social context representation, and facial motor output. The first network for social perception processes faces of another monkey during the

non-interactive averted-gaze context. Not surprisingly, the well-known face patches in the temporal and prefrontal cortices containing neurons that selectively respond to faces among the regions became activated (Freiwald et al., 2016). In addition, regions in the intraparietal sulcus associated with shifts of attention and gaze, but also the anterior cingulate sulcus in the medial bank of the frontal lobe, were activated, as well as thalamic and amygdalar nuclei, the latter being associated with emotional processing. While these regions showed

increased fRMI activity during social perception, other brain areas, such as prefrontal areas and large parts of the insular, motor, and cingulate cortices, showed reduced activity.

The results discovered in the second network specific to the interactive second-person social contexts, in which the subject became engaged in social communication (mainly without orofacial movements), proved to be even more interesting. In the cortex, a region in the rostral aspect of the medial wall of the frontal lobe occupying four brain areas

was much more strongly activated by the second-person context (direct-gazing faces) than by the third-person context (averted-gazing faces). These four areas were the medial prefrontal cortex (mPFC), the dorsomedial prefrontal cortex (dmPFC), and the rostral aspects of the gyrus (ACCg) and the sulcus of the anterior cingulate cortex (ACCs). In the brainstem, the periaqueductal gray was specifically activated. This implies that social context, irrespective of instigator and point of view, appears to be represented in a spatially confined brain circuit.

Single-cell data from interacting nonhuman primates support these fMRI findings. In monkeys monitoring each other's actions for adaptive behavioral planning, Yoshida et al. (2011) showed that the medial prefrontal cortex contains groups of neurons that selectively encode one's own actions or the other's actions. In humans, moreover, neuronal activity changes in the medial aspects of the prefrontal cortex are frequently related to social cognition, such as processing affective information or inferring mental states of others ("mentalizing"). Together, these findings suggest that the mPFC is involved in self-other differentiation during interactive social communication.

Knowledge about social context as provided by this interactive (second-person) social network constitutes a prerequisite for social signal production. Signal production was represented in the third facial movement network, which encoded facial movements and expressions (Figure 1). This distributed but spatially-specific facial motor control system included lateral cortical areas, such as the primary motor cortex (M1), the ventrolateral premotor cortex (vlPMC), and part of the insula. In addition, a suite of medial motor areas was activated, most prominently, the supplementary motor cortex (SMA/M2) and two cingulate motor areas (CMAs), the rostral (CMAr/M3) and caudal (CMAc/M4) CMAs. The CMAs have anatomical connectivity to other cortical motor areas, such the brainstem and the spinal cord, but they are also reciprocally connected with the dorsolateral prefrontal cortex of the executive control system (Morecraft and Tanji, 2009). While the CMAc/M4 regulates motor functions, the CMAr/M3

is involved in executive control of broad aspects of behavior, including generation of motor intention, behavioral selection, behavioral monitoring, and monitoring of behavioral outcomes. Shepherd and Freiwald (2018) also found that non-communicative (drinking and ingestion movements) versus communicative (lip-smacks and facial expressions) motor acts engaged the facial motor network differently. Across the integrated facial control system, medial motor areas (M2 and CMAs) were relatively more active for communicative signals, whereas lateral regions (M1 and lateral PMC) were relatively more active for non-communicative facial movements.

While facial expressions are clear visual communicative signals, lipsmacking has gained special interest among cognitive neuroscientists as a putative precursor for the evolution of speech and language in the human lineage. One of the two main hypotheses that aims to explain language evolution is the "gestural theory." It assumes that our ancestors primarily used gestures to communicate purposefully, from which spoken language emerged later in evolution as the ability to control vocalizations increased. Lip-smacking can be seen to support the gestural theory because it is a communicative gesture that already exploits the primate orofacial apparatus used for human speech. Functional imaging in humans seems to support this idea: lip reading (the observation of human silent speech) activates Broca's area, more precisely *pars opercularis* (Brodmann area BA 44) of the left inferior frontal gyrus, and the observation of monkey lipsmacking activates the same region bilaterally (Gallese, 2007). As a putative evolutionary precursor of this finding, a special class of "mirror neurons" in monkeys seems to signal the observation of communicative facial actions. Mirror neurons in the ventral premotor cortex (BA 6, posterior to BA 44 of Broca's area) discharge both when a monkey performs specific motor actions and when it observes another individual performing a similar action. When a human experimenter performs lipsmacking in front of the recorded monkey, a small proportion of mouth-related mirror neurons, termed "communicative mirror neurons," in the vlPMC discharge (Gallese, 2007).

Consistent with this observation, the vlPMC was also strongly activated during facial movements in this study by Shepherd and Freiwald (2018). However, vlPMC activation was primarily detected during non-social face movements, whereas medial motor areas preferentially signaled lipsmacking and facial expressions. This differentiation between non-social and social signals in the facial motor network, together with a disparity in anatomical locations between the ventral premotor cortex (BA 6) in monkeys and Broca's area (BA 44) in humans, indicates an explanatory gap when interpreting lipsmacks as gestural precursors for the origin of language.

In contrast to the gestural theory, the competing "vocal theory' proposes that language evolved from simpler forms of primate vocal communication. The theory asserts that vocal communication signals would readily have supported linguistic faculties as soon as humans expressed language by means of speech. Also within this framework, lipsmacking in nonhuman primates, although entirely silent, is discussed as an evolutionary precursor of speech (Ghazanfar and Takahashi, 2014). This is because the production of lipsmacking in macaque monkeys is similar to the production of orofacial rhythms during speech.

Maybe even more important than motor skills, such as generating and maintaining the correct vocal rhythm, in the investigation of social communication are cognitive pre-adaptations. One such critical precursor for the development of a flexible speech and language system is the volitional control of vocal utterances. Interestingly, juvenile rhesus macaques are capable of controlling vocal production in a goal-directed way, and recent electrophysiological studies (Gavrilov et al., 2017) investigated the neuronal correlates of this behavior in brain areas that overlap with the social and motor networks described by Shepherd and Freiwald (2018). These recordings showed that neurons in the ventrolateral prefrontal cortex (BA 44 and 45; the monkey homolog of Broca's area) and CMAr/M3 participate in monkey volitional call initiation, albeit with different roles. While pre-vocal activity in vlPFC is tightly linked to volitional call onset and encodes the decision to produce volitional calls, pre-vocal activity

in downstream CMAr/M3 onset activity was not indicative of call timing and can best be interpreted as a motivational preparatory signal (Gavrilov et al., 2017). These and a variety of other data were conceptually summarized in a "dual network model" that posits a volitional articulation motor network originating in the prefrontal cortex (including Broca's area) that cognitively controls vocal output of a phylogenetically conserved primary vocal motor network situated in subcortical structures (Hage and Nieder, 2016). Of course, the monkey vocal system in isolation can also only explain certain aspects of language origin.

Perhaps, lipsmacking, as a prime example showing how facial gestures and vocalizations are intimately entwined, forces us to rethink the radical ideas about language evolution. Even though both the gesture theory and the vocal theory have traditionally been discussed as

being incompatible, they may portray a more complete picture of language origin when combined into a multi-modal theory (Masataka, 2008). After all, human language continues to utilize mutually informative gestures and vocalizations. The new study by Shepherd and Freiwald (2018) forces us to take a fresh look from the perspective of whole-brain functional neuroanatomy when pondering about the evolution of social communicative systems in primates.

REFERENCES

Freiwald, W., Duchaine, B., and Yovel, G. (2016). Face processing systems: from neurons to real-world social perception. Annu. Rev. Neurosci. 39, 325–346.

Gallese, V. (2007). Before and below 'theory of mind': embodied simulation and the neural correlates of social cognition. Philos. Trans. R. Soc. Lond. B. Biol. Sci. 362, 659–669.

Gavrilov, N., Hage, S.R., and Nieder, A. (2017). Functional specialization of the primate frontal lobe during cognitive control of vocalizations. Cell Rep. 21, 2393–2406.

Ghazanfar, A.A., and Takahashi, D.Y. (2014). The evolution of speech: vision, rhythm, cooperation. Trends Cogn. Sci. 18, 543–553.

Hage, S.R., and Nieder, A. (2016). Dual neural network model for the evolution of speech and language. Trends Neurosci. 39, 813–829.

Masataka, N. (2008). The Origins of Language. Unraveling Evolutionary Forces (Springer).

Morecraft, R.J., and Tanji, J. (2009). Cingulofrontal interactions and the cingulate motor areas. In Cingulate Neurobiology and Disease, B.A. Vogt, ed. (Oxford University Press).

Schilbach, L., Timmermans, B., Reddy, V., Costall, A., Bente, G., Schlicht, T., and Vogeley, K. (2013). Toward a second-person neuroscience. Behav. Brain Sci. 36, 393–414.

Shepherd, S.V., and Freiwald, W.A. (2018). Functional Networks for Social Communication in the Macaque Monkey. Neuron 99, this issue, 413–420.

Yoshida, K., Saito, N., Iriki, A., and Isoda, M. (2011). Representation of others' action by neurons in monkey medial frontal cortex. Curr. Biol. 21, 249–253.