

Brain Basis of Human Social Interaction: From Concepts to Brain Imaging

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Hari R, Kujala MV. Brain Basis of Human Social Interaction: From Concepts to Brain Imaging. *Physiol Rev* 89: 453–479, 2009; doi:10.1152/physrev.00041.2007.—Modern neuroimaging provides a common platform for neuroscience and related disciplines to explore the human brain, mind, and behavior. We base our review on the social shaping of the human mind and discuss various aspects of brain function related to social interaction. Despite private mental contents, people can share their understanding of the world using, beyond verbal communication, nonverbal cues such as gestures, facial expressions, and postures. The understanding of nonverbal messages is supported by the brain’s mirroring systems that are shaped by individual experience. Within the organism–environment system, tight links exist between action and perception, both within an individual and between several

individuals. Therefore, any comprehensive brain imaging study of the neuronal basis of social cognition requires appreciation of the situated and embodied nature of human cognition, motivating simultaneous monitoring of brain and bodily functions within a socially relevant environment. Because single-person studies alone cannot unravel the dynamic aspects of interpersonal interactions, it seems both necessary and beneficial to move towards “two-person neuroscience”; technological shortcomings and a limited conceptual framework have so far hampered such a leap. We conclude by discussing some major disorders of social interaction.

I. INTRODUCTION

A. Social Interaction: Background

In the African Bantu language, the word *ubuntu* means that a person becomes a person only through other people (interview of Desmond Tutu, *New Scientist*, April 2006). Neuroscientists do agree: humans and their brains and minds are shaped, and normally function, in continuous interaction with other people. Not only the physical presence but also the mental image of another person can affect the state of one's brain, behavior, and attitude. Social interaction involves communication in all its forms, such as cooperation, competition, imitation, helping, playing, informing, questioning, negotiating, bargaining, voting, and bluffing. Interaction between two individuals is strongly influenced by each person's personality, developmental history, perceptual stereotypes, social schemas, attachment style, as well as constantly varying peer pressure. In addition to the universal “basic emotions,” “social emotions” such as pride, envy, and regret modulate and drive the interaction.

Sophisticated language separates humans from all other living organisms. Consequently, studies of verbal, rather than nonverbal, communication have dominated human neuroscience. However, language is not always the best means to transfer information. For example, visuomotor imitation of finger acts is an easier way to learn knitting or other handicraft skills than following written or heard instructions.

Several brain regions have been attributed to certain socially relevant functions. For example, the superior temporal sulcus (STS) is linked to the detection of biological motion (3, 69). The medial prefrontal cortex and midline cortical structures are related to perspective taking as well as self-related processing and awareness (71, 175), the temporal pole and amygdala to social scripts, emotions, and judgments (71, 73), and the temporoparietal junction, along with medial prefrontal cortex and temporal poles, to mentalizing (71, 73). A recent meta-analysis of more than 100 fMRI studies of social cognition accordingly emphasized the role of the temporoparietal junction for mentalizing immediate goals and desires, and the medial prefrontal cortex for inferences about more enduring traits of the persons (232). Moreover, shared motor and sensory representations for self and others have been suggested to comprise several brain regions,

including the inferior frontal gyrus; these areas related to mirroring systems will be discussed in section IV.

Because of the fundamental importance of interpersonal interaction on human development and behavior, we argue that related brain mechanisms should be studied during natural social interaction rather than by monitoring snapshots of brain activity from single individuals in artificial laboratory environments. However, until the 1990s, most study paradigms in human neuroscience were highly simplified and tried to eliminate or control all variables, such as the subject's state, motivation, and attitude. This tradition, which largely turned psychology into a natural science to be practiced in laboratories using exact methods, began at the end of the 19th century. Although the simplifying approach is highly appropriate for studies of primary sensory functions, much of the fleeting, moment-to-moment information of social interaction remains beyond the reach of studies involving limited stimuli and tasks. The current challenge for brain imaging is to bring everyday human interaction, occurring in a complex natural environment between two or more subjects, into the laboratory.

Studying the brain basis of social cognition and interaction in terms of two- or multi-person neuroscience is timely worldwide, and it promises to integrate information from brain physiology, cognitive and clinical neuroscience, social psychology, emotion research, and advanced brain imaging. Even old philosophical questions, such as intersubjectivity, development of self among other persons, and empathic attunement, can be revisited. Such a multidisciplinary approach could potentially shift the focus of research from basic sensory functions in single subjects towards the brain basis of dynamic social interaction.

The scientific community now has the tools to tackle the brain basis of *ubuntu*, but the conceptual framework needs further elaboration.

B. Structure of This Review

We start our review by considering theoretical and philosophical aspects of human social interaction, emphasizing the special features of other persons as our “stimuli.” We then present a simplified schema of the human cognitive circuitry that comprises the brain, the body, and the environment (including other people). Important building blocks of this organism–environment system

(see also Ref. 122) are the action–perception loops that form the basis of an “inner world” as the result of internalization of external actions. Here, we recycle the ideas of the philosophical school of pragmatism. Furthermore, many mental functions rely on external memory surfaces, either objects or other people, that support “off-loaded” or “outsourced” cognition. Emotions and the brain’s reward systems are important in shaping the whole organism, by strengthening or suppressing certain behavioral patterns, as well as by attributing personal significances and social meanings to objects and events.

Instead of giving a full and balanced view of the extensive published literature, we develop a story that emphasizes action and interaction in shaping the mind. This approach is aimed at integrating brain-imaging data with the scattered information arising from many separate disciplines that address human mind and behavior.

An important part of social interaction is based on motor and sensory mirroring between individuals, i.e., the automated neuronal matching mechanisms between observed and self-produced actions and emotions. Similar mechanisms are likely to form the prerequisites for emotional contagion and empathy. Hence, the mirroring systems are discussed in some detail.

Besides elucidating brain mechanisms underlying the processing of realistic stimuli in everyday-like natural setups, brain imaging studies might give insight into some devastating disorders of social interaction, such as autism and schizophrenia, characterized by abnormal social attention, aberrant social meanings, or both. A better understanding of the brain mechanisms of social interaction would also be relevant for teaching, training, and therapy, as well as for understanding social conflicts and the effects of dyadic interactions during, e.g., trainee–master and patient–therapist relationships.

The reader is first advised to consult the “about brain imaging” appendix (sect. IX) that summarizes the basic principles of magnetoencephalography (MEG) and functional magnetic resonance imaging (fMRI). Both methods are widely applicable to studies of the brain basis of social interaction.

II. FRAMEWORK OF SOCIAL COGNITION AND INTERACTION

A. Social World and Humans as Stimuli

We live in a world where most of our daily environment is made or affected by other humans, either by those living now or the previous generations. Different cultures, by definition, contain qualitatively divergent traces of other people’s actions (roads, houses, and art), and it comes as no surprise that the environment shapes the developing individuals from the early beginning, including their perception and appreciation systems (170).

Other human beings differ from all other “stimuli” by their great similarity to the perceivers themselves. Thus the future actions of other persons can be predicted to some extent by means of the perceiver’s own experience of, e.g., possible movements. Humans have a strong tendency to search for agency and causal explanations for whatever events. For example, triangles, squares, and spheres moving within and out of a larger rectangle are not described as colliding or bumping into each other, but rather as chasing, following, and even teaching each other (102). Simultaneous positron emission tomography (PET) recordings have revealed activation in the STS, typically related to biological motion, and also in areas related to attribution of mental states, such as the medial prefrontal cortex and temporal poles (23).

Senses are important for social interaction. Deafness at an early age impairs mental development strongly if no gestural language is available, and early blindness affects social communication. Touch, the most intimate sense, is governed by many societal gender- and status-related norms and taboos. A part of the social touch relies on thin unmyelinated fibers; their stimulation is associated with release of oxytocin that is important for social bonding and trust (115, 142). Olfaction is known to have an important social role in many animal species, but it is poorly understood in humans, despite the flourishing perfume and deodorant industry.

B. Faces: Social Stimuli Par Excellence

Faces are essential for the development of interacting minds. One sign of the special importance of faces for human identity and recognition is the ultimate taboo of face transplantation. Faces attract the viewer’s attention, even when the viewer is asked to attend to a completely separate feature of a stimulus (74). The effective capture of gaze by faces is also evident in the eye-tracking map of Figure 1.

Already, a newborn infant prefers faces over other objects or feature assemblies, although the cortex and afferent pathways are still immature (125). At birth, the fast-conducting subcortical visual pathway, sensitive to low spatial frequencies (see Fig. 2), is already functioning and could be responsible for face recognition in newborns (for reviews, see Refs. 82, 125).

In adults, visual analysis of faces involves the fusiform gyrus, the inferior occipital gyrus, and the posterior STS (for a review, see Ref. 101). The “fusiform face area” (129) responds, 140–170 ms after stimulus onset, more strongly to faces than to any other objects (4). Nevertheless, the functional specification of the fusiform gyrus remains an issue of debate: some argue that it is a special-purpose brain area for face processing (80, 130), whereas others suggest that it is related to gaining of expertise (76,

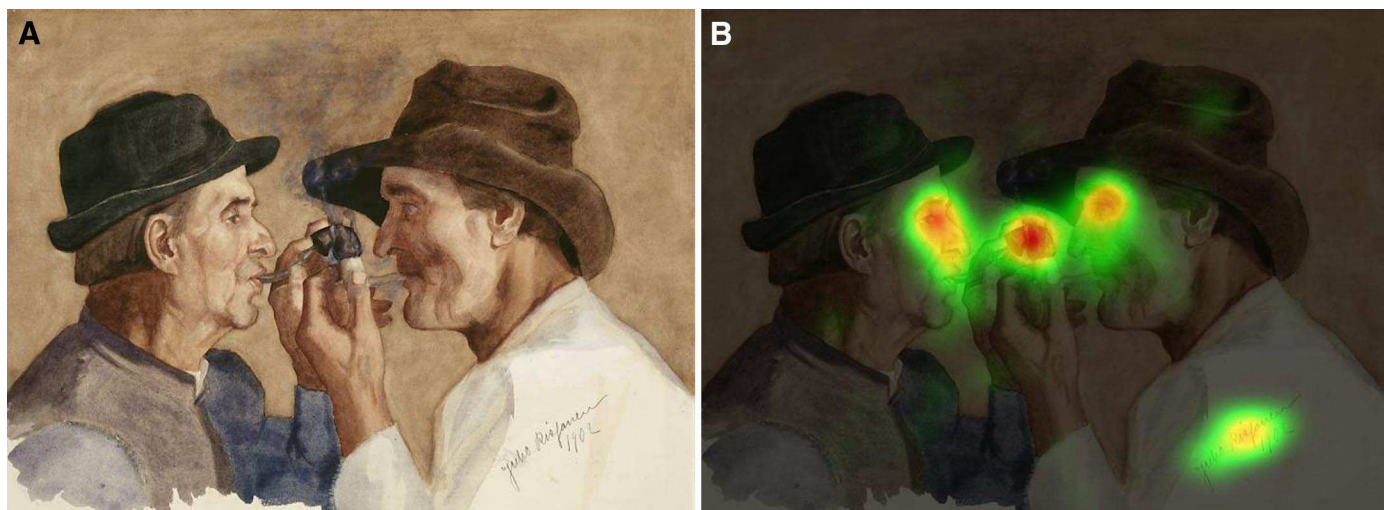


FIG. 1. *A* and *B*: gaze distribution of 20 persons on a painting (“Piipunsyöttäjät/Lighting pipes” by Juho Rissanen, 1902; copyright Ateneum Art Museum, Central Art Archives/Hannu Aaltonen, Finland). The gaze map is based on the data of 10 females and 10 males, who were allowed to view freely the image for 10 s. The eye tracking was performed with Tobii at the Laboratory of Computer and Information Science, Helsinki University of Technology. (Image courtesy to Marika Kaksonen.)

117, 207). The fusiform gyrus probably relates to the awareness of the presence of a face (110), and it is also activated when subjects view bodies without faces (83, 182). Nevertheless, the cortical representations of faces seem to be distributed both spatially and temporally, as are representations of many other objects.

The attractiveness of faces has a great social and commercial impact. Besides beauty and mood, the face communicates health, vividness, socioemotional features, personality, and ethnic background. Interestingly, one’s judgment of attractiveness based on the face is affected by many unconscious processes, including one’s own hormonal level (128).

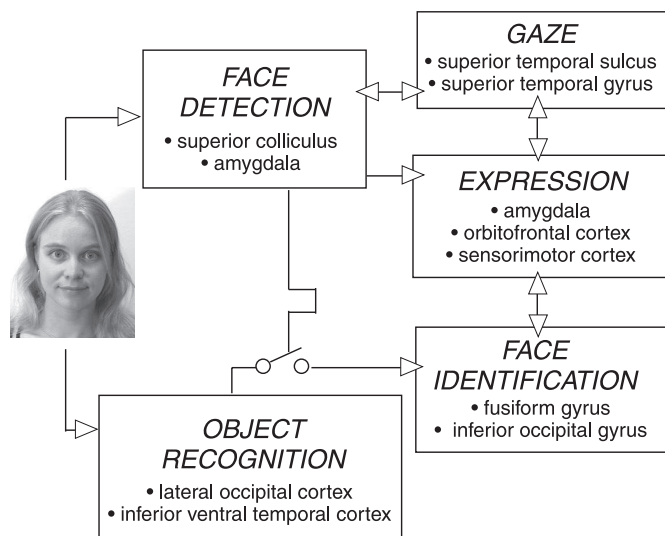


FIG. 2. A schematic presentation of brain circuits for face detection and recognition, emphasizing the subcortical route via superior colliculus and amygdala. [Redrawn from de Gelder et al. (44).]

In one recent study, subjects were asked to rate the attractiveness of faces that, they were told, belonged to their opponents in a previously played trust game (215). Persons who had behaved in a fair manner were considered more attractive than persons who had behaved in an unfair manner, although the faces were counterbalanced for fair versus unfair behavior across subjects.

In an fMRI study, the activity of the orbitofrontal cortex covaried linearly and the activity of amygdala non-linearly with judgments of facial attractiveness; the highest responses were associated with high and low attractiveness and the weakest responses with medium attractiveness (176, 246), suggesting that brain areas related to socioemotional functioning take part in attractiveness judgments. Facial attractiveness can modulate evoked responses as early as the first half second of an encounter (241).

Faces of a different color than the viewer’s own face provoke activity in the amygdala and frontal cortices, probably as a sign of concern and heightened caution (38). In fact, face familiarity affects brain processing at several levels. For example, familiar faces, in contrast to unknown faces, enhanced fMRI activity in insula, middle frontal gyrus, middle temporal, and inferior parietal areas (187), and they elicited stronger magnetoencephalographic 170-ms face-sensitive responses (140).

C. Action–Perception Loop and Formation of the “Inner World”

Humans, like all organisms, are constantly, and bidirectionally, connected to their environment, and the properties of the senses and the possible ways in which to act define the specific individual–environment relationship.

In contrast to the classical unidirectional stimulus-response approach, applied widely in, e.g., evoked response studies, humans are active participants in their interactions with the environment, searching for information and simultaneously changing the environment.

Figure 3 depicts the action-perception loops of two interacting persons. Each person influences and shapes her environment, and the environment (including other people) in turn modifies the brain of the acting person. This bidirectional influence has been largely neglected in current brain imaging, in part due to methodological limitations.

With repetition, actions become automatically associated with the expected sensory consequences (for example, pressing a piano key will be associated with a sound of a certain pitch). Consequently, it becomes possible to imagine the sensory result even before the action takes place. At this stage, the person has started to simulate the external events, predicting both perceptual and action aspects of the behavior. The emergence of the “inner world” as a consequence of behavioral and perceptual simulation means that one can have covert actions without realizing them as motor acts; moreover, percepts can be simulated without any external physical stimuli, and the consequences of the forthcoming actions can be anticipated (105).

The inner world, or the embodied mind, includes simulation of other people, their bodies, beliefs, and intentions. In this framework, even thinking is covert movement. In support of the idea of a simulated inner world, sensory-specific brain areas are activated during mental imagery (124), and visuomotor priming produces reaction-time advantage (34).

Importantly, understanding another person's actions necessitates a close action-perception link both within and between individuals. In Figure 3, two similar, interacting partners share the same environment. In this situ-

ation, the output of one individual is the input for the other individual, which will thus lead to action-perception correspondence not only within but also between individuals. Consequently, the same brain mechanisms that support one's own movements could largely be involved in the prediction of the other person's actions.

This correspondence between individuals is inevitable because the expression and the reception of a message have to be tuned to the same “wavelength”; for example, if speech (expressive) is produced at frequencies below 5 kHz, the auditory system (receptive) has to be tuned to the same frequencies for the message to be received.

Thus it becomes also understandable why, for example, the hand region of the primary somatosensory cortex (SI) is activated during observation of finger actions, and the mouth SI area is modulated when the subject sees articulation movements on a face (5, 168).

The close connection between perception and action is acknowledged by the proponents of enactive perception, who consider the content of perception to rely on the subject's sensorimotor experience. According to this viewpoint, all perception is very much like active touch where the stimuli are typically achieved via the subject's own movements (174). The strength of the environment-individual connection varies according to, e.g., the subject's age, skills, and vigilance.

Sports provide every-day examples of the importance of predicting another person's actions: in soccer, the goal-keeper has to start moving before the ball is touched, and in boxing, the reactions to visually observed movements are not enough to avoid being hit. It is necessary to anticipate the other person's actions. The gaze is often informative about such predictions: both during one's own actions and while observing others' actions, the gaze lands on the target before the hand that is reaching for the target does (62).

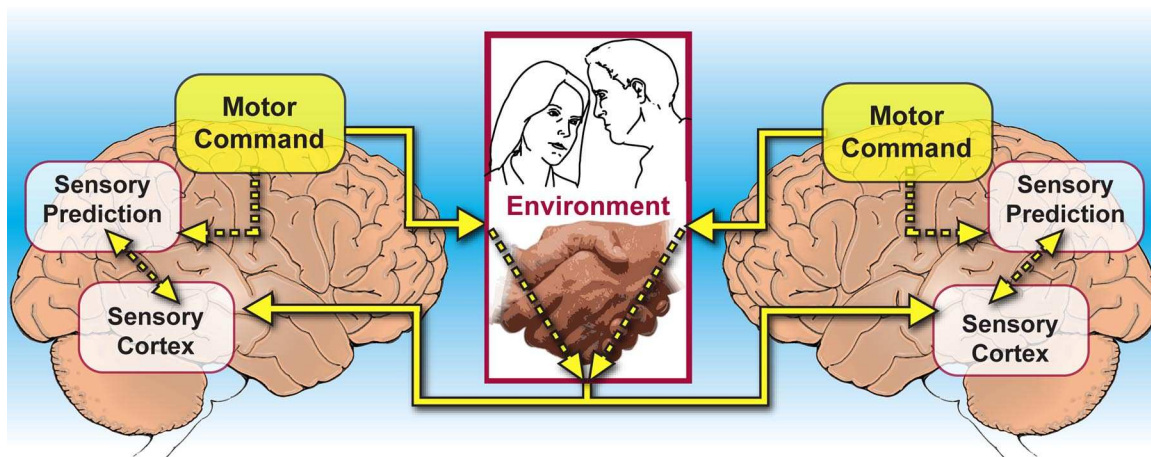


FIG. 3. A schematic presentation of the action-perception loops of two persons; both loops close via the environment.

D. Off-Loaded and Outsourced Cognition

The environment is full of cues that remind us about our past life, keep us up-to-date, and automatically trigger overlearned motor routines. The Gibsonian ecological psychology explains many cognitive functions as adaptations to the environment, assuming that action codes ("affordances") are activated and motor schemes facilitated automatically when the individual sees a graspable object that "invites" an action. Intensively used tools and objects become tightly connected to the subject's cognitive architecture: in monkeys, for example, the receptive fields of visuotactile neurons in the parietal lobe are modified during the use of tools, thereby helping the tool to be assimilated into the body schema (116).

One can argue that humans have either "off-loaded" (245) or "outsourced" large parts of their cognition to the environment. The concept of off-loading goes beyond the idea of extension of the senses and body by, e.g., radar, tools, vehicles, and weapons. It rather refers to a smart environment that contains memory surfaces that both trigger and support our actions and percepts. Some of these external cues function as real "exograms" (48) that contain information that might not be readily available in the individual's own memory.

Even more complex outsourcing, in the sense of shared work and knowledge, occurs in couples, amongst friends, and in collective work environments. Off-loading and outsourcing of thinking and cognition efficiently distribute cognitive resources, and thereby save brain-processing capacity, because a lot of important information is supported by the environment and by other persons. A demented person often turns her head to seek support from the expressions and gestures of her spouse to confirm whether she is on the right track; she has outsourced part of her memory to her spouse. Similarly, knowledge can be shared and retrieved within research teams and other collective environments. Importantly, groups of diverse problem solvers with different expertise can outperform groups of specialized, high-ability problem solvers (108). Currently, very little is known about the brain mechanisms of such group dynamics, which form the very core of social interaction, even shaping the fates of nations. The first neuroimaging study of "crowd psychology" is still awaiting realization.

III. INTERACTING MINDS

A. Intersubjectivity: From Private to Shared Experiences

Intersubjectivity refers to implicit understanding of other persons' feelings and aims and the sharing of a common world. The concept arose as a critique against

the Cartesian view of highly individual minds that were considered to be separate from the subject's own body. In contrast to the Cartesian view, bodies are quintessential for cognition and mind: the mind of a human can jump into a frog and still remain the same only in fairy tales! The body is the display stage of the mind, or "the best picture of the human soul" (Ludwig Wittgenstein, *Philosophical Investigations* 1952), often showing signs that one would like to hide from others, such as flushing of the face as a sign of embarrassment.

Accordingly, human perception and action are situated and embodied. Because bodies are physically distinct, everybody's view of the world is unreservedly different. These differences are accentuated by differences in personal history, sensory properties, and brain characteristics, and they thereby result in private mental contents. Fortunately, however, percepts are similar enough between persons to justify generalizations and categorizations that form the basis of shared experiences. Actions as such create an intersubjective reality comprising bonding, intentions, attitudes, and meanings. Language further expands the shared world by adding name tags to objects, persons, places, conditions, and events, thereby forming a new realm of perceptible objects (30). Verbalizations, including stories and narratives, work as advanced cognitive tools that help memorization and guide, or sometimes misguide, thinking.

Intersubjective understanding is strongly affected by teaching, which aims to create similar views in the individuals of the same (sub)culture or profession. A specialist and a dilettante view the same world quite differently, and so do people with different cultural backgrounds (170). How a person perceives the world therefore depends on her social existence.

Despite the private mental contents and the social differences, brain imaging reveals considerable similarities between individuals sharing similar experiences during natural viewing conditions. In the study of Hasson et al. (98), five subjects were scanned with fMRI as they watched a 30-min segment of the same movie. Significant intersubject correlations occurred not only in the visual and auditory projection cortices, but also in association cortices as a sign of "collective ticking." The failure of some brain areas to show any synchrony across subjects during the same task agrees with many imaging studies that have demonstrated the existence of highly individual intrinsic brain networks (191).

Mutual, behavioral synchrony has been detected between infants from 2 months onward and their caretakers; a sign of what Colwyn Trevarthen calls primary intersubjectivity (see, for example, Ref. 15). The first signs of dyadic interaction occur as turn-takings when an infant is fed.

B. Self and Others: Mentalizing and Perspective Taking

“Das Du ist älter als das Ich” (“you” is older than “I”; Friedrich Nietzsche in *Also Sprach Zarathustra*, 1883–1885) suggests that the concept that refers to another person develops earlier than the concept of self. At first, a child has no sense of self; he perceives the world through the emotions, gestures, and vocalizations of other persons.

An important manifestation of the ability to distinguish between self and others is mentalizing, which refers to thinking about other people and believing that they have feelings, thoughts, beliefs, and intentions of their own. Two competing theories address the development of the “theory of mind,” i.e., the attribution of mental states to others. The “simulation theory” states that children simulate in their minds another person’s actions and intentions (41); the “theory theory” assumes that children innately develop theories about the world and other people and try to verify them in reality (29). The current brain imaging data support, at least in part, the simulation theory: nonverbal social communication appears to rely on activation of the same brain areas when the subjects are observing others’ experiences and experiencing similar situations themselves.

Mentalizing, which allows the understanding of gossip, jokes, movies, and theatre plays, is commonly said to be like “walking in the shoes of another.” However, according to Jeannerod (123), a better expression would be walking *with* the other person, which enables communication and comparison of differences between one’s own and others’ mental states. Mentalizing is connected to the ability to make both first and third person views (what I am doing and what the others are doing). Such abilities develop later in life than does, e.g., empathy (for a review, see Ref. 213), and understanding other persons’ intentions and goals still increases in old age when other cognitive abilities may decline (91).

How people see themselves and how they exist in relation to others is strongly bound to culture. In an fMRI study, the medial prefrontal cortex was activated in Chinese subjects both when they were thinking of their own personality and of the personality of their mothers, whereas in Western individuals, the same area was activated only when the subjects were thinking of themselves (247). These results agree with stronger self-appraisal tendencies in Western than Asian individuals, as have been identified by questionnaires between Canadian and Japanese individuals (198).

It has been proposed that cortical midline structures (CMS), to which the medial prefrontal cortex belongs, are socially shaped and support such aspects between self and others that are not directly related to motor coding (175; see Fig. 4). Different brain areas are related to

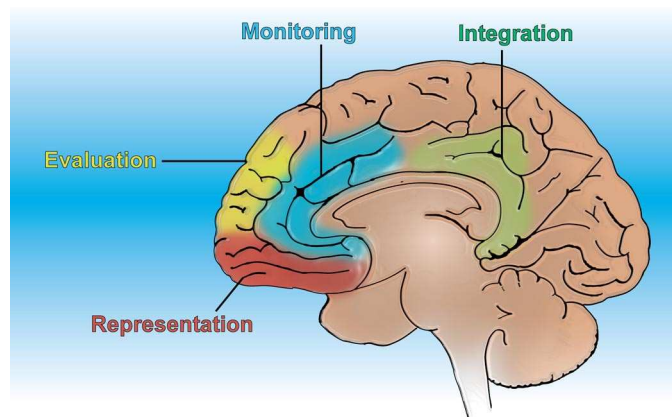


FIG. 4. Cortical midline system with the main brain areas marked with different colors. [Adapted from Northoff and Bermpohl (175).]

monitoring (anterior cingulate), evaluation (dorsomedial prefrontal cortex), representation (orbitomedial prefrontal cortex), and integration (posterior cingulate cortex) of self-referential stimuli. Interestingly, the posterior cingulate cortex and the midline frontal cortex largely correspond to the default-state network identified in brain imaging studies (66, 191) and recently attributed to social cognition (206). Accordingly, dorsomedial prefrontal cortex and medial parietal areas (in precuneus) were activated when subjects were watching social interaction between other people (113). On the other hand, the anterior paracingulate cortex was engaged when subjects were viewing other interacting subjects and tried to understand their intentions (238).

C. Attachment, Motivation, and Attachment Styles

Young individuals become attached to their caretakers. The strength of this affective bonding depends not only on the quality of care and interaction but also on hormones such as oxytocin and vasopressin (115). Besides attachment, reward and punishment systems also guide individual development: a balance between approach and withdrawal, regulated by successes and failures, affects early exploration of the environment and modulates future decisions to act.

Starting from infancy, the regularities and statistical properties of the world effectively shape brain structure and function, but with strong bias caused by the subject’s motivation and attention. Objects and ideas that one “loves” (e.g., eating, sex, drug abuse) have a high motivational salience. In the terms of Jaak Panksepp (181), motivation is based on a “seeking” system that supports curiosity, interest, and expectancy and is the *primus motor* for the individual’s energy to act. The underlying brain circuitry includes the dopaminergic mesocortical-mesolimbic pathways; dopamine is already released during anticipation of a rewarding event (208).

Attachment styles are fundamental personality traits and remain more or less the same throughout life: 1) persons with the secure attachment style are positive and confident, 2) persons with anxious attachment style are afraid of rejection in all possible situations, and 3) persons with avoidant attachment style prefer distance, do not appreciate affective signals, and rate positive pictures less positive than do other people (235). In a recent fMRI study involving a game in which the subjects received feedback on their performance, brain activation in the reward-related striatum and amygdala clearly depended on the subject's attachment style (235).

D. Gaze and Joint Attention

An important aspect of social cognition is the mutual eye gaze that connects people together and invites joint social attention in addition to providing information about the attention, interest, and intentions of the interacting persons. Already in early childhood, people start to share attention, information, and mental contents. A child is able to follow another person's gaze direction from about 3–4 mo of age onwards (for a review, see Ref. 127), and pointing gestures that elicit another person's attention start from 12 mo onwards (149). Eye gaze can be tracked by a camera similar to the one shown in Figure 8 (see the appendix). Because the fovea has the best visual acuity and is also sensitive to color, the foveated locations in a scene are sites from which visual information is sampled most intensively. Eye tracking data demonstrate that reactions to another person's actions change from reactive to proactive at the age of ~12 mo when the child already has some kind of understanding about the other person's intentions (55). At the same age, children start to use social referencing when they feel ambivalent; for example, a child who has been hurt may look at the face of the caretaker to know how to feel (220). Already preverbal 6- to 10-mo-old infants are capable of social evaluation, for example, preferring adults who help others over those who do not (90).

The direct eye gaze, the "key to the door of the infant social brain" (for a review, see Ref. 82), facilitates face recognition and cortical processing of faces as early as 4 mo of age (56, 57), and joint attention with an adult enhances the attentional processes in 9 mo olds (223).

In adults, the temporo-occipital face-sensitive evoked response, seen in both electroencephalographic (EEG) and MEG recordings and peaking at 140–170 ms, is enhanced by direct or averted gaze in contrast to closed eyes or upward gaze (225). Accordingly, the face-related PET and fMRI responses in the fusiform gyrus are modified by the perceived gaze direction (77, 180), and the posterior STS, the right parietal lobule, the right inferior temporal gyrus, and the middle temporal gyrus have been associated with processing of direct gaze (180, 243).

E. Nonverbal Communication and Unconscious Processing

During social interaction, a person is able to nonverbally transmit attitudes and feelings via gestures, actions, postures, and expressions. Since we know other persons via such motor expressions, emotion transference likely depends on motor function; in fact, it is hard to picture a human emotion that would not be communicated across individuals without motor actions. Nonverbal social interaction inevitably involves two-way emotions and mirroring. According to a recent study, expressions of fear and disgust on one's face have not evolved for social communication only. Rather, the face shape during expression of fear facilitates sensory input and the expression of disgust dampens it, implying that these emotional expressions are signs of evolutionarily significant modulations of the percepts of the environmental stimuli (224).

Visual arts, ballet, and theater rely on the assumption that another person's attitudes and intentions can be transmitted by postures and gestures without any verbalization. Similarly, the "good clinical eye" is based on successful reading of another person's postures, movements, and expressions. Abnormalities catch the attention of the observer surprisingly easily, as is evident from the "uncanny valley effect" known in the movie animation industry (165): people can follow easily cartoon characters far enough from human resemblance, e.g., Donald Duck or Shrek, whereas an animated figure that closely resembles but is not quite human (e.g., is moving in jerky steps) is disturbing and even physically revolting.

Nonverbal gestures and postures are difficult to quantify and describe. Compared with the sequentially presented auditory information in speech, the nonverbal gestures, postures, and movements contain more dense and parallel information. Humans typically carry out only one task at a time, and during dual tasks, the limits of attentional capacity are soon met (49, 195). It is possible that motor acts quickly saturate the capacity limits of conscious processing, as is evident in, e.g., imitation tasks where the goal of a movement is imitated best whereas the details of the action are copied less accurately (6).

In their elaborate review, Ferguson and Bargh (58) demonstrated that during social encounters, related social knowledge arises automatically from memory and unconsciously affects the persons' judgments and appreciation of other people, similar to the effect of priming on language comprehension. The perceived behavior also affects one's own behavior in an unconscious way. For example, people are likely to rub their face if their conversation partner does so (26).

F. Conversation and Other Face-to-Face Interactions

Face-to-face conversation as a dyadic interaction could be a good model system for future brain imaging of social interaction, especially when combined with eye tracking. For example, a patient with complete lesion of the amygdala had impaired eye contact during conversation and enhanced focus on the mouth of the speaker, probably reflecting the role of the amygdala in top-down attentional control over low-level visual cues, e.g., mouth movement (217).

Successful conversation of course requires mutual understanding. Typical conversational interactions include opening and closing addresses, interactive turn taking, as well as nonverbal cues, such as unclear utterances and pauses. Cues about the other persons' aims, attitudes, and thoughts are also derived from the tone of voice and gestures. During a single phoneme that lasts only ~100 ms, many changes take place in the speaker's articulatory system, and simultaneously, the facial gesture of the speaker can change from neutral to surprise, including lifting of the eyebrows and other related changes (184). These fleeting, moment-to-moment facial expressions emphasize certain syntactic fragments, and they form and color the meanings of a verbal message that would otherwise be ambiguous. They also ask for, and elicit, mutual responses that often remain out of the conscious perception of the listener.

During conversation, the participants focus or orient towards the other person's mind, inferring meanings, and relevancies rather than just decoding the verbal messages. The interaction involves, as probably the most important part, the recognition of the other person's affective and cognitive states. As in any perception, inferences in such situations go beyond the information given, relying on the context rather than on the stimuli only.

A large part of verbal interaction includes suggestive components: "You certainly feel exhausted after organizing that party don't you?" Hypnosis, an extreme example of suggestive interaction, reduced color-naming conflict in a stroop task with an associated decrease in the fMRI signal in ACC and visual areas (193, 194), and the suggestion to see black-and-white pictures in color resulted in activation of color-processing regions (143). In highly hypnotizable subjects, suggestions to perceive pain in a hand that was not touched by any means activated a part of the normal pain-processing circuitry (192).

These findings are accentuated examples of the powerful effects of speech on brain function. In a similar manner, psychotherapy, that is, words with transmitted contents and meanings, can modify brain circuitries and activations (78) and even change the balance of receptors for neurotransmitters (148).

IV. MOTOR MIRRORING

A. Mirror Neurons in Monkeys

Watching or interacting with another person may lead to unconscious "mirroring" of actions and intentions between the two persons. The "mirror neurons," possibly responsible for such behavior, were first reported in the monkey frontal lobe, in the ventral premotor cortex area F5 (75, 197). These monkey mirror neurons fire both when the individual performs an action and when he sees another individual performing a similar action. Therefore, they may serve as the basis for shared motor representations between the producer and the recipient of a motor-act-based message. The discovery of mirror neurons has drastically changed the traditional neurophysiological view about the motor system as a pure producer of movements.

To fire, monkey mirror neurons in area F5 require contact between the observed hand and the target object, and they only fire for goal-directed actions, whereas in humans the mirroring systems (see below) seem to have less strict constraints. Monkey inferior parietal cortex contains mirror neurons that fire differently to identical motion sequences that later result in different acts, either eating or placing; importantly, the differentiation occurs for both one's own and observed actions (64). The parietal mirror neurons seem therefore specifically suited for supporting intention reading.

As a considerable refinement of the traditional view of the motor system, anatomical tracing in monkey brain has revealed an extended, but very clearly organized, frontoparietal network comprising seven different motor areas (F1–F7), as is illustrated in Figure 5 (151). Monkey area F1 corresponds to the human primary motor cortex, and it also receives input from areas F2–F5.

Important nodes of the sensorimotor circuitry are also found in the parietal lobe, closely connected to frontal areas. The ventral intraparietal area VIP is coupled to area F4, and it controls hand and mouth movements on the basis of visual input. The anterior intraparietal area AIP, which projects to area F5, is considered to be related to affordances, the qualities of objects that are perceived as action possibilities. This AIP–F5 network forms the core of the mirror-neuron circuitry (151). F5 also receives input from parietal area PF, which itself receives input from STS.

The close relationship between action observation and action simulation finds strong support from studies of F5 mirror neurons in situations when the end part of the observed action occurs behind a screen, and the monkey only knows, but does not see, what happens there. More than half of the F5 neurons react for such occluded action (230). Auditory mirror neurons that react to sounds of

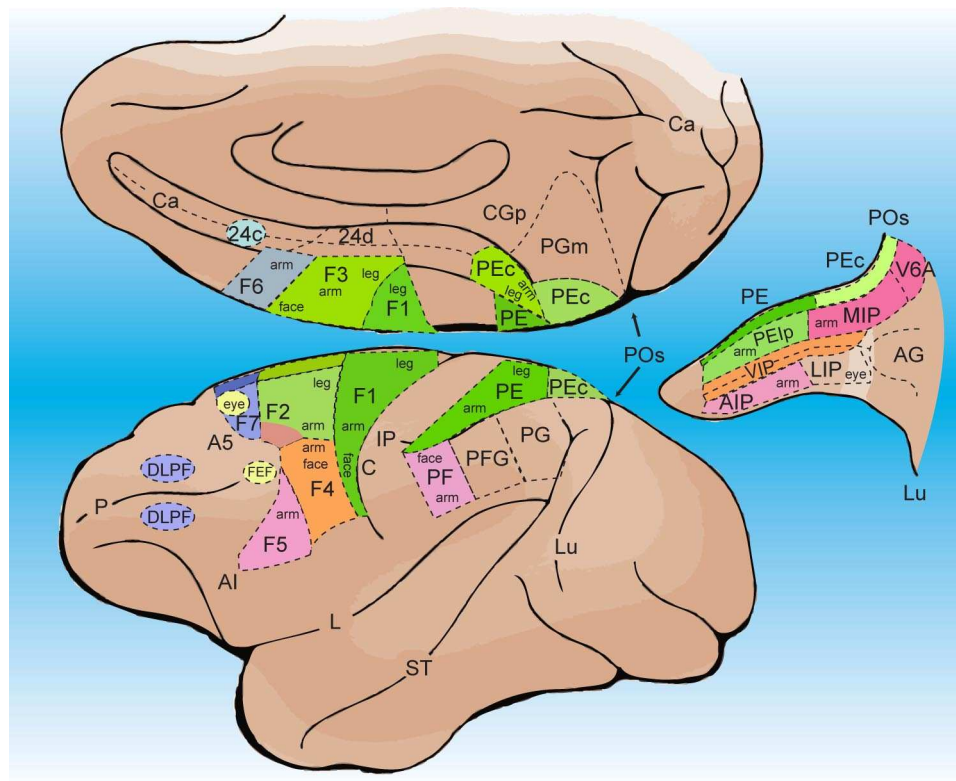


FIG. 5. Frontoparietal sensorimotor system in monkey; the interconnected frontal and parietal areas are indicated with same colors. [Adapted from Luppino and Rizzolatti (151).]

actions (that the monkey is already familiar with) have been demonstrated in the F5 region. Moreover, monkeys that heard eating actions of other monkeys, even without seeing them, increased their own eating (59), implying that action imitation can be triggered without seeing the action.

B. Human Mirror-Neuron System

When immobile humans view effortful actions (weight lifting or running) of other persons, their own respiration rate increases (179), reflecting their bodily involvement in action understanding. Certain cortical areas in humans can be attributed to the mirror-neuron system (MNS): they are activated during the subject's own motor acts and also, although weaker, while the subject observes a similar act performed by another person. Such interconnected brain areas form the human MNS, a frontoparietal sensorimotor network that is considered to support implicit understanding of other persons' actions.

1. Cortical circuitry of the MNS

The core areas of the MNS, the left inferior frontal cortex (Broca's region) and the ventral premotor cortex, likely serve as an action-perception interface (173), and thereby also as an interface between forward and inverse models that are used for motor control and

for the prediction of the sensory consequences of one's own actions; however, a similar role has been assigned to the parietal lobe (67, 111). Broca's region comprises Brodmann's cytoarchitectonic areas 44 and 45 in the left inferior frontal gyrus, and it contributes, besides the classical speech production function, to action planning, action observation, action understanding, and imitation (81, 173). Broca's region has been suggested to contain a fine-tuned functional parcellation, with the "real mirror" in the dorsal portion (163). The right-hemisphere homolog of Broca's region is less well known, but its activity often seems to accompany Broca's region, although with less intensity and somewhat longer latency, e.g., during naming and imitation tasks (171, 202).

The exact correspondence of monkey and human brain areas is still much debated. The human ventral premotor area has been suggested to be the counterpart of monkey area F4 and a part of monkey area F5 (52). On the other hand, the human Broca's region (par opercularis, corresponding to cytoarchitectonic area 44) appears to be the human counterpart of the anterior portion of monkey area F5 (52, 196).

The posterior superior temporal sulcus (STSp) and the inferior parietal lobe (IPL) contribute to the human MNS, although they do not have true mirroring properties: they are activated during observing others' movements but not during one's own actions (112, 172). IPL

accommodates motor and kinesthetic information with visual, auditory, and somatosensory inputs (196), and in monkeys it contains pure motor mirror neurons important for intention understanding (64). The STSp region responds to faces as well as to a wide variety of seen and heard actions produced by another person (3), including sounds of footsteps (200).

2. Motor cortex involvement

The primary motor cortex is downstream from Broca's region, and a part of its activity likely reflects function of Broca's region. Consequently, the viewer's primary motor cortex is activated when she just sees another person's actions, as is evident from both transcranial magnetic stimulation studies (54, 222) and from MEG recordings of the reactivity of the motor-cortex 20-Hz rhythm (20, 95). This activation is weaker than during the subject's own actions and stronger to movements seen in real life than on a video (120). Interestingly, after the motor cortex activation, the 20-Hz motor-cortex oscillations are similarly enhanced in the actor's and the viewer's brain, indicating that both the actor's and the viewer's primary motor cortex is stabilized after the movement (20; see Fig. 6). This interpretation of stabilization derives from transcranial magnetic stimulation findings associating the enhancement of the 20-Hz oscillations to cortical inhibition (27). All these results emphasize the similarities in the brain basis of performed and observed actions. However, whether the primary motor cortex contains mirror neurons, or whether it only reflects what happens upstream in Broca's region, still remains unsettled (136).

The primary motor cortex is also activated by traces of motor actions. When subjects viewed briefly presented printed and handwritten letters, their primary motor cortex was excited by the handwritten letters but not by the printed letters (150). This result agrees with embodied cognition (233).

Transcranial magnetic stimulation of the motor cortex has shown the activation of the observer's motor system to be very specific. Tongue muscles were activated while the subject was listening to "rr" which requires tongue action but not when listening to "ff," indicating phoneme-specificity in the activation of speech-related motor areas (53). Similarly, the primary somatosensory cortex was activated in a left-hemisphere-dominant manner when subjects viewed articulatory movements of a speaker (168). These results can be interpreted as reflecting the neuronal correlates of simulated sensory consequences of motor actions.

3. Context and intention

Context affects the interpretation of motor actions as well as brain activity. In an fMRI study, subjects were presented with two scenes, one displaying a tea table well prepared for a breakfast and the other with the same table but messy after the breakfast. An identical hand action towards a cup was in the first context interpreted as an intention to drink and in the latter as an intention to clean. The activity of the right frontal cortex was of different strength for observation of these similar hand actions depending on the context (114).

Usually a subject's intention is inferred from both the seen kinematics and from the context, and inferences go beyond the sensory information given. Kilner et al. (135), based on the example given by Jacob and Jeannerod (119), discussed the observation of a hand grasping a scalpel. The observer easily understands that the person's goal is to grasp the scalpel, but whether this is done with the intention to cure or to hurt cannot be disambiguated on the basis of the kinematics only. However, the contextual information will contribute: grasping of the scalpel in an operating theatre versus on a dark street results in quite different inferences about the intentions. Because decisions are probabilistic, Bayesian procedures provide useful tools for analysis of this kind of data (135).

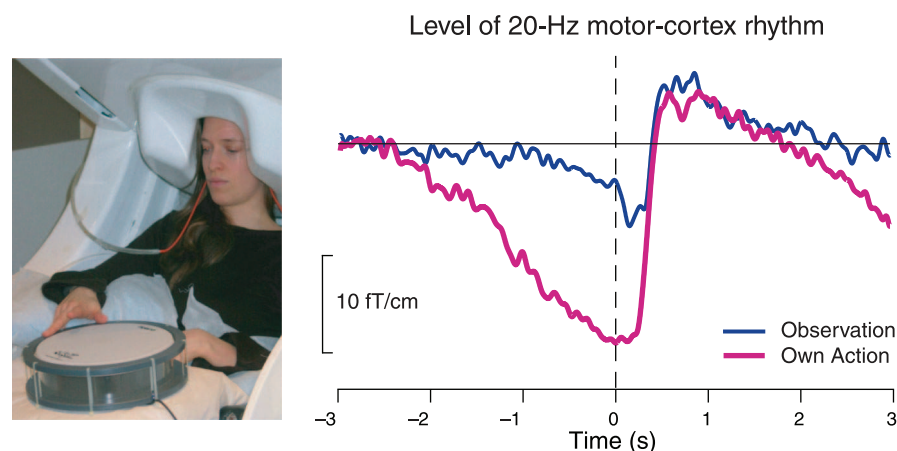


FIG. 6. Reactivity of the primary motor cortex in association with own (red) motor actions and seen (blue) motor actions, as revealed by the level of the 20-Hz motor-cortex oscillations recorded with magnetoencephalography. The finger touches the drum membrane at time 0. [Adapted from Caetano et al. (20).]

In general, people need to have their own experiences about observed actions before they can understand the actions. For example, people with Moebius syndrome, a congenital paralysis of the facial nerve, cannot make facial expressions, and some of them appear to have flattened emotions themselves; the problem is exacerbated by the difficulty other people have in evaluating the emotions behind the frozen face of the person with Moebius-syndrome (32).

C. MNS and Imitation

Imitation speeds up learning as it provides a fast track to various types of skills without the necessity of trial-and-error learning. Healthy children enjoy imitation and being imitated without requiring further rewards. In young children, vocal imitation is an essential part of learning spoken language, and later on, a child can learn by imitation many necessary motor acts, such as tying shoelaces. Furthermore, mimicry and imitation bond people effectively.

The MNS is considered necessary, although not sufficient, for imitation; in fact, monkeys with functional mirror neurons “ape” quite poorly. However, the term *imitation* has different meanings: triggering of a stereotypic motor pattern, direct copying, facilitation of motor patterns, and learning of a new motor sequence. For the latter two, mirror neurons seem necessary yet not sufficient. Several imaging studies have investigated brain activations related to imitation. For example, when novices were learning guitar playing (fingering of chords) by observing a professional guitarist, imitation and observation appeared to be supported by a similar brain circuitry (17).

Imitating a totally new action sequence is very different from a stereotypic release of motor pattern, such as, e.g., coughing when hearing a hoarse voice or contagious yawning. Everyone yawns in her own manner, without imitating detailed motor patterns, after a proper trigger, such as seeing or hearing someone yawn, or just reading about yawning. Accordingly, contagious yawning was not associated with any additional activation in Broca’s region, the core area of the MNS (188, 210).

One highly socially relevant, but puzzling and still debated, phenomenon is the imitation of facial gestures by newborn infants (160). Imitation of tongue protrusion by newborns has been reported several times, and even monkey infants are said to imitate facial gestures (60). Because the infant has never seen his own face, an automatic supramodal matching system has been proposed to transform the seen visual pattern to the infant’s own motor pattern (159). Another possibility is that neonate imitation is a sign of uninhibited enactive perception, as suggested by Kinsbourne (139), e.g., a motor-based manifestation of the omnipresent link between perception and action, where, at the maturational state of the newborn, the motor part has not yet been suppressed.

Since seeing another person’s movements activates the observers’ own motor system, it is necessary to consider why a healthy observer does not move himself during this observation. One reason is the weaker activation induced by observation versus performance of an action. Another reason stems from active inhibition of the motor action by the medial and lateral frontal lobes (14). Evidence for such inhibition comes from subjects in whom frontal-lobe lesion is associated with echopraxia, a disorder in which the subject imitates any action.

Reactions to others’ actions and movements are always multifaceted. Depending on the predetermined goal, one may imitate another (during an aerobics lesson), counteract (in karate), cooperate (while carrying a table or during a doubles game of tennis), or follow with one’s own smoothly complementing movements (during pair dance). In all these situations, the other person’s actions can affect the active observer’s motor patterns in an apparently fully automated manner. In addition, the modulation of the MNS from insula and the limbic system during social imitation bring into play the brain mechanisms of empathy (111).

Other person’s actions trigger in the viewer’s brain coordinated activation sequences. Nishitani and Hari (172) asked subjects to imitate non-namable lip forms presented in still pictures. The brain activation, recorded by MEG, showed increasingly longer latencies starting from occipital visual areas, then STS, IPL, inferior frontal gyrus, and finally the primary motor cortex; the whole sequence took ~250 ms (see Fig. 7, *left*). Such a progression of activity could be related to visual recognition that starts by visual analysis and ends, via feed-forward connections, by recognition (and understanding) of the actions.

The proposed MNS circuitry in Figure 7 (*right*) resembles the experimental activation sequence of Figure 7 (*left*) but assumes the processing to be hierarchical, with reciprocal feedback connections between at least F5, PF, and STS. Consequently, and in line with Bayesian modeling of brain function (68) that incorporates prior information (the context), the activation sequence is modeled in terms of predictive coding (68, 135), by assuming that neuronal processing at each stage both generates predictions of the input reaching the next phase and is sensitive to the prediction error resulting from lower-level computations. The prediction error (the difference between the real and predicted data) is then minimized. This proposed model of human MNS function still requires further experimental support.

D. Shaping of the MNS

Although developmental studies of the mirror-neuron system are few, and the associated brain mechanisms are still unknown, the MNS is known to be shaped by experience. At birth, the coarse connections between sensory

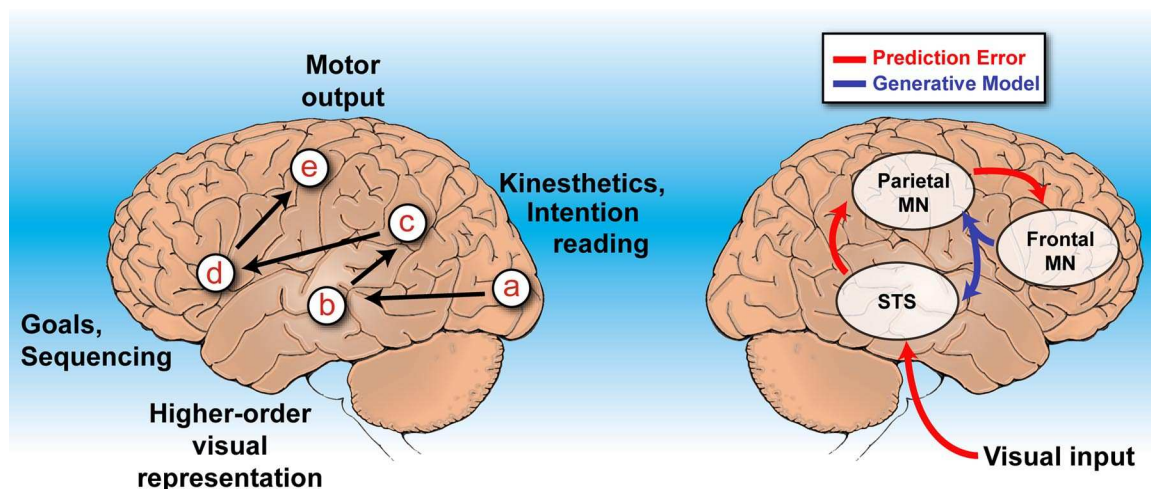


FIG. 7. Circuitry of the human mirror-neuron system as revealed by MEG recordings of Nishitani and Hari (172) and the possible functions supported by the nodes of the circuitry. On the *right*, the corresponding predictive-coding circuitry proposed by Kilner et al. (135). Similar systems likely exist in both hemispheres.

and motor brain systems are ready. During development and practice (e.g., in expert dancers), these connections are fine-tuned. In adults, the strength of MNS activation depends on the viewer's own experience of the observed action, as in, for example, the use of chopsticks (121). Similarly, the better a person can do an action, the better she is in simulating others performing similar actions (141). In expert dancers, complex motor patterns arise de novo within 5 wk and then resonate, as indicated by fMRI imaging, with observed or mentally simulated action sequences (36).

But do these findings really reflect motor expertise or could they be due to visual expertise, since the motor expert has also seen the action very frequently? An elegant imaging study differentiated between motor and visual expertise in professional ballet dancers (21), relying on the gender specificity of a part of ballet actions. During rehearsals both females and males become visual experts for both types of movements, although they perform only the half of them devoted to their own gender. The brain activation patterns strongly supported the motor expertise hypothesis: the activation was stronger to movements related to the dancer's own sex (21). The results further support the statement that humans understand others via their own kinesthetic faculties.

Some action or posture reading, if not strictly mirroring, seems to extend beyond species. For example, both predators and prey benefit from reading each other's motor intentions in anticipating the other's next move. Intriguingly, domestic dogs utilize humans' bodily gestures better than wolves raised in similar surroundings, showing a remarkable case of across-species communication (234). However, observation of species-specific communication actions trigger differences at brain level: viewing humans speak activated the premo-

tor MNS areas, whereas viewing monkeys lip-smacking or dogs barking did not (16). Thus mirroring seems to take place in the context of the viewer's own motor repertoire, although observed actions of other species activate the precentral brain areas.

V. EMOTIONS IN SOCIAL CONTEXT

A. Biological and Social Emotions

Humans and other mammals share the basic system for what Panksepp (181) calls e-motions to refer to their evolutionary survival value. Seven basic emotions (happiness, sadness, fear, surprise, anger, contempt, and disgust) exist in all human cultures. Social or moral emotions, such as pride, guilt, shame, or embarrassment, differ from the basic emotions in their external triggers (87), and both the perception and expression of social emotions differ culturally between individualistic and collectivistic nations (50).

Emotions form the omnipresent background for behavior and attitudes, and they serve as the primus motor of social interaction (65). A person lacking emotional responsiveness makes irrational decisions, as is evident from the behavior of patients suffering from frontal-lobe lesions (e.g., Ref. 39).

According to brain imaging results, basic and social emotions involve partly different neuronal circuitries. Recognizing basic emotions, such as fear, from facial or bodily expressions is associated with activity of the amygdala and other limbic areas (for reviews, see Refs. 1, 2, 43), whereas moral emotions are more associated with activation of the medial orbitofrontal cortex, temporal pole, and STS (22, 162). The social emotion of regret, "feeling responsible for the negative outcome of one's

own choice," is mediated through the medial orbitofrontal region, and it also involves activation of areas related to biological emotions, for example, the anterior cingulate cortex, hippocampus, and amygdala (33). As an indication of cultural differences, Japanese and Western subjects displayed different brain activation when observing fearful faces (166).

According to Halgren et al. (88), the amygdala is activated as early as 120 ms after presentation of neutral faces. The amygdala has a modulatory effect on a wide range of brain areas, including STS, primary visual cortex, fusiform face area, orbitofrontal cortex, and the anterior cingulate cortex; the effects are (predominantly) ipsilateral so that, e.g., right-sided amygdala lesions result in diminished modulation of the right fusiform face area (237). Furthermore, the amygdala is considered important in attaching value to stimuli (70). Amygdala activation is stronger for faces with low than high spatial frequencies; instead, the fusiform face area prefers high spatial frequencies, suggesting that emotional features can be recognized in the low spatial frequencies of an image (236; see also Fig. 2).

B. Emotion Contagion: Mimicry and Synchrony

When a newborn infant starts to cry in a ward, other babies join in as a sign of emotional contagion. In older children and in adults, emotional contagion relies, at least in part, on unconscious postural and expressional mimicry (for reviews, see Refs. 25, 100). Children become aggressive towards their peers after observing angry adults (37), and parents' diastolic blood pressure and skin conductance change in reaction to their newborn's emotions (155). Moreover, people often unconsciously synchronize their rhythms and movements with their interaction companions: mothers and infants move synchronously in various ways, and so do friends and lovers (100). In fact, joint movements seem to be closely linked with rapport, being "on the same wavelength" with someone (11, 227).

Perception of emotion seems to include neural mechanisms that would generate similar emotions in the observer (190), allowing the observer to share the emotional state of another individual. Emotion contagion is considered a precursor of empathy, which provides information on the mental states of other people as well as the motivation for cooperative behavior and communication (for reviews, see Refs. 46, 190).

In one fMRI study, happy, sad, and neutral facial expressions of emotion were shown while subjects curled their lips upwards, downwards, or remained motionless (244). Congruent faces contrasted with incongruent faces elicited faster reactions in the subjects' facial expressions and enhanced activation in hippocampus, amygdala, and

parahippocampal region, thereby suggesting emotional contagion to be intertwined in the experience of the emotion itself. Also, the overlapping activations of anterior insula in observed and felt disgust (of odors) suggest the same (242). Emotional faces trigger stronger brain activity when they are presented dynamically rather than as static images; the changes are seen both in the observer's face muscles and in the visual motion area MT/V5, premotor cortex, amygdala, and STSp (138, 147, 204).

C. Feeling Another Person's Touch and Pain

The observer's own primary and secondary somatosensory areas are involved during observation of another person who is experiencing touch or pain, or is performing hand or mouth actions. Such evidence derives from MEG (5, 199) and scalp evoked potential (18) recordings, as well as from fMRI studies (12, 134).

When subjects see another person receive painful stimuli, or merely a cue that such a possibility will arise, their own affective pain circuitry may be activated, including the anterior cingulate cortex and the anterior insula (AI) (e.g., Refs. 13, 118, 167, 212, 214, 215). These findings support the existence of partially shared neuronal networks for directly experienced and observed pain. This proposition is strengthened by findings that the activation strength of the AI in the viewer's brain is related to the perceived pain intensity the viewer observes in another (201), similar to what happens during direct pain (where experienced pain intensity correlates with insula activation strength) (31). Furthermore, the AI activity correlated with behavioral empathy measures when subjects witnessed pain experienced by a loved one (214), or when they observed the face of a person in pain (201). A relationship between empathy and AI activation is also suggested by the finding that in adolescents with conduct disorder, the insular volume correlates with empathy score (221).

In a study by Singer et al. (215), subjects first played a game with a fair and an unfair partner and saw the game partner receive painful stimuli. In female observers, the AI activation was dampened in response to unfair compared with fair persons, and in males, the AI activation disappeared totally, as if men did not care about the physical punishment of unfair players.

It has also been suggested that social pain, the feeling of being excluded, shares part of the pain affective circuitry (for reviews, see Refs. 51, 153). While viewing a ball-tossing game, participants showed increased fMRI activation in dorsal ACC when they were excluded from the game; activation of the area also correlated with the subjects' social distress. However, ACC, as an interface between limbic and neocortical functions, has been related to many different functions (35). Thus the activa-

tions of the ACC, as well as the activations of the visceromotor anterior insula, are extremely vulnerable to erroneous reverse inferences that aim to implicate the involvement of these areas in a specific cognitive function on the basis of the observed brain activations. Many AI and ACC activations can in fact be related to stress and the related changes in the activity of the autonomic nervous system.

On the down side of understanding other persons' suffering is the strenuous coping required from nurses and clinicians who have to develop a defensive shield towards the negative emotions or seen pain to maintain their own health (see, e.g., Ref. 131). Nursing can be especially stressful for empathic persons, and experienced clinicians have learned to regulate their empathic responses for the suffering of their patients (28).

VI. STUDIES OF REAL-TIME INTERACTION

A. Bringing Everyday Life Into the Laboratory

To bring everyday social experiences into the imaging laboratory, we need to monitor the brain activations and bodily functions of dynamically interacting subjects during rapidly changing situations. The challenges for such studies include development of more natural stimuli and setups, the importance of which is emphasized by, e.g., the findings that dynamical expressions activate amygdala more intensively than still pictures (147). Accordingly, new analysis tools are needed to follow rapidly changing activation patterns and to identify neuronal circuits related to the tasks. For example, reverse correlation techniques seem useful in addressing links between brain activation and events in the environment of natural stimuli, such as a movie (98), and independent component analysis is a promising method for identifying brain networks reacting to certain stimuli (10, 156).

The aforementioned study of Singer et al. (215) is a beautiful example of bringing daily life into the imaging laboratory: the subjects were made to like or dislike others before brain scanning by involving them in a game, in which part of the opponents (real actors) were instructed to behave in an unfair manner. Similar approaches could be applied in future studies in natural settings.

B. Scanning Two Persons at the Same Time

Given the great importance of dyadic interaction in human behavior, it is important to study brain functions of two interacting subjects at the same time. Such approaches have, however, considerable methodological challenges. It is especially problematic to decide which

brain signatures should be monitored during social interaction and what the relevant measures and time scales would be. Moreover, the brain signals should be complemented by measures of the autonomic nervous system. Autonomic activity, although quintessential for the dynamic interaction between the heart and the brain, has been very rarely monitored during brain imaging beyond studies specifically related to processing of emotional stimuli or visceral awareness. Changes in heart rate and respiration can, however, also occur during motor preparation and motor imagery (63, 185), and the strength of brain EEG rhythms and fMRI signals can covary with heart rate (45). Moreover, autonomic measures could become synchronized during social interaction, as has been shown to occur for respiration during conversation (157). Reflecting the subject's "visceral connection" to the world and to other people, autonomic measures could thereby unravel bodily states that are not evident in overt behavior but are still closely connected to the subject's mental contents and thus helpful for a more holistic understanding of the subject's behavior.

Facial expressions, serving as important social cues, can change dramatically within 100 ms, i.e., during a single phoneme (184). Such fleeting microexpressions color the verbal message and may strongly affect the result of face-to-face communication, learning of skills during a master-apprentice relationship, and the success of a therapy session. Temporal synchrony within tens or hundreds of milliseconds seems to be a strong unifying requirement in all social communication: for example, emotional mimicry involves synchronous reactions, expressions, and postures between individuals (100). To be able to track any of these phenomena, the recording methods used for studies of real-time social interaction should provide temporal resolution on the order of 10–20 ms.

Some important information about the time courses of different brain areas in natural settings derives from studies of self-regulation of brain activity during real-time fMRI. For example, Weiskopf and co-workers (239, 240) used fMRI for neurofeedback, letting subjects freely try to generate brain activations that could be used to manipulate, e.g., a cursor to play ping-pong in the scanner. This approach, similar to operant conditioning, aimed at training subjects to control their own brain activity, wherever it might be generated. Regarding the specificity of the modulated brain activity, this procedure differs drastically from common brain-computer interfaces, where the input typically comes from the motor cortex, either invasively (see, e.g., Ref. 229) or noninvasively. However, the approach of Weiskopf and co-workers (239, 240) should make the training easier, because the subject has more possibilities to modulate the brain activity. In the EEG community, neurofeedback has been previously used to modulate, e.g., the level of alpha and mu rhythms, either

for relaxation or for trying to reduce the appearance of epileptic discharges (218, 219).

To assess the feasibility of recording brain activity simultaneously from two interacting persons, Montague et al. (164) recorded fMRI from two persons located in different scanners situated over 1,000 miles apart and connected via internet. This “hyperscanning” with fMRI demonstrated the technical feasibility of the approach, but the study involved considerable time lags between the stimuli and responses. Therefore, electrophysiological techniques are preferable, since they operate on time scales dictated by natural dyadic interaction. However, the key question in interactional studies is to find out which brain signals should be recorded and monitored during interaction. External stimuli typically evoke such small electrophysiological responses that they can only be reliably detected, without averaging, from limited brain areas. Measuring brain rhythms is not ideal either, since the rhythms are modulated by external stimuli in very subject-specific ways and rather slowly, on the scale of tens or hundreds of milliseconds. Such sluggishness is likely too slow for following rapid changes in interpersonal interaction. Many technical and methodological challenges, therefore, are still waiting for solutions.

Tognoli et al. (228) used a dual EEG device to study the dynamics of coordination between two people. The subject pairs were executing self-paced finger movements either independently or while watching the other person's movements. During the visual condition, it was possible to synchronize the movements of both people. When their movements were in synchrony, whether in phase or antiphase, the centroparietal 10- to 11-Hz activity was enhanced. Although this finding is promising for future studies with more interactional conditions, such as conversation with turn taking, the study unfortunately did not provide accurate temporal information of the two persons' brain signals, because the final results were pooled over longer epochs.

Also, Babiloni et al. (7) recently recorded EEG from four persons involved in a cooperative card game where a pair of participants played against the other pair. Depending on whether a person acted as the first or the second player of the pair, the brain rhythms were different in strength and distribution. The authors innovatively also introduced and computed “hyperconnectivity,” the connectivity between two players' brains. However, it was unfortunate that the final results were pooled over longer epochs, and again, no information was obtained about the brain signatures supporting the moment-to-moment interactions. It is possible that the best solutions in future brain imaging of human interaction will be based on decoding techniques, analogous to those used in fMRI to determine brain correlates of natural stimuli (133).

Although many aspects of social interaction can be studied in settings where only one person is in the scan-

ner at a time, the situated and embodied nature of human cognition, requiring monitoring of brain, body, and environment (with the other person) at the same time, definitely deserves more attention. The subject's “visceral connection” to the world could unravel bodily states that are not directly evident in overt behavior or in brain activity. Accurate analysis of the subject's social environment is also important because of the off-loading and outsourcing of some cognition to the environment.

VII. DISORDERS OF SOCIAL INTERACTION

Deficits in social interaction occurring in many psychiatric illnesses, e.g., autism and schizophrenia, are devastating both for the patients and to the people around them. Brain imaging in experimental setups of social interactions might improve understanding of the neuronal underpinnings of such disorders.

A. Autism

Autism is a spectrum of neurodevelopmental disorders with a strong genetic component; the prevalence estimates range from the typically cited 0.2–0.6% (154) to over 0.9% if subtle impairments of social interaction are included (estimates provided by the United Kingdom National Autism Society). For reasons not yet fully uncovered, autism is more common among males than females, with a ratio of 3:1 (72). Autistic persons seem uninterested in social interaction, have difficulties in joint attention, and are unable to attribute mental states to self and others.

The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) lists several diagnostic criteria for autistic disorders. The first class deals with qualitative impairments in reciprocal social interaction, such as the use of eye gaze or facial expression. The second class concerns qualitative impairments in communication, such as social imitative play, and the third class includes restricted, repetitive, and stereotyped patterns of behavior and interests, such as distress over changes in small, nonfunctional details of the environment. The diagnosis of autism requires that these developmental abnormalities have been present during the first 3 years of life. Infants can be prescreened for autism diagnosis around 18 mo of age, when they already fail to orient to social stimuli and have difficulties in understanding make-believe play (9, 42).

Healthy infants show more interest in faces than in any other single object category (126). Both autistic and normally developing children can use another person's gaze direction as a cue for attention orienting, but the heightened skin conductance responses of autistic children during observation of faces with direct gaze suggests

that autistic children feel unpleasant when they are objects of attention (145, 146). Accordingly, eye-gaze tracking data demonstrate that autistic persons avoid looking at faces when possible (183, 216) and thereby gain less practice in reading faces than do healthy people. Autistic children may show abnormal activation for faces in the fusiform area (for reviews, see, e.g., Refs. 79, 203); however, some studies have reported fusiform face responses in autistic subjects, associated with hypoactivation of other face processing regions, such as STS and inferior frontal cortex (84, 85). Furthermore, faces with direct versus averted gaze evoked slightly different MEG responses in autistic and normally developing children (144).

Highly functioning autistic subjects suffering from Asperger's syndrome seem to lack the natural preference for imitating others' actions in a mirror-image fashion when facing the other (6); rather, they imitate complex action patterns on the basis of visual cues, without being able to place themselves in the perspective of the other person. In MEG recordings, highly functioning autistic adults had delayed and dampened activation in the inferior frontal gyrus, with more prominent abnormalities in the right than the left hemisphere (171). Such delays could result from sluggish processing in the inferior frontal cortex, reflecting abnormal connectivity between the inferior parietal lobe and the inferior frontal cortex; this view agrees with findings that autistic persons cannot predict the next steps in action sequences (24). Similarly, in an fMRI study, the activity in the frontal cortex was dampened in autistic children, and the decreased activation covaried with the children's scores on emphatic scales (40). Taken together, these findings suggest a disorder either in the frontal or parietofrontal part of the MNS. A recent voxel-based morphometry study strengthens this view by showing that autistic subjects have anatomical abnormalities in brain areas belonging to the MNS (86).

Despite these MNS deficits, it is improper to reduce autism to "broken mirrors"; autism as a multifaceted syndrome has many expressions and causes. One core problem is the lack of motivation to engage in social interaction, perhaps due to inadequate maturation and function of the subcortical pathways, resulting in diminished rewards and pleasure value for faces (127). According to another hypothesis, the connections between the brain areas involved in theory-of-mind system are weaker (72). Yet another hypothesis considers autism as an extreme of the normal male cognitive profile (8) that can involve several of the above problems.

B. Schizophrenia

Schizophrenia comprises a wide spectrum of disorders, stemming from a complex interplay of genetic and

developmental factors, often after traumatic precipitation. Part of the cognitive disturbances in schizophrenia is due to the subjects' considerable context independence, leading to performance that is better than in healthy subjects in some decision tasks, where the context is misleading (158). However, in true social situations, the schizophrenic subjects make erroneous interpretations about other person's intentions and easily end up with problems of social interaction. On the other hand, a social deafferentation hypothesis proposes that withdrawal from social interaction leads to spurious social meanings that become associated with hallucinations and delusions (106).

Aberrant salience in psychosis is informative about the emergence of meanings. Dopamine release out of synchrony with sensory events could contribute to the creation of inappropriate salience, thereby accentuating meanings to minor events in the environment (132). When antipsychotic drugs dampen the salience, the person pays less attention to the minor details that previously seemed so meaningful and significant, feels less distress, and gradually becomes less disturbed by delusions as a result of a more normal interaction with the environment (132). The essential effect of the environment is evident from the culture-dependent changes in the contents of delusions over centuries.

Psychotic patients may have difficulties in distinguishing actions of self and others. In an MEG study of 11 schizophrenic patients and their unaffected twins, the reactivity of the motor cortex was weaker in the schizophrenic subject than in his/her twin; however, no additional MNS disorder was observed (211). These findings suggest a disorder in motor cognition, in the way actions are planned, organized, perceived, and understood (123), rather than in the MNS proper.

C. Rehabilitation of Disorders of Social Interaction

The possibility of training social emotions is a highly interesting and topical question. The existence of sensitivity periods in social interaction, similar to the critical periods of sensory systems, is currently unknown, although highly likely. Enhanced speech, with formants accentuated and format transitions slowed down, has been successfully used to train dyslexic children to perceive speech better (161). One may imagine that an analogous procedure, with enhanced facial expressions or with enhanced saliency of facial features, might be used to capture attention to faces in children insensitive to social cues. In autistic children, repeatable imitation sessions enhance social behavior, such as eye contact, smiling, touching, and reciprocal play (61). More recently, the mental expertise of Buddhist monks in cultivating posi-

tive emotions has been suggested to change brain circuits associated with empathy (152).

Oxytocin improves a person's ability to infer mental states from social cues in the eye region (47), and, interestingly, some preliminary experiments have already been made to show that oxytocin administration can be beneficial for treatment of autistic persons; after oxytocin treatment, adult autistic subjects improved in comprehension of affective speech (107).

VIII. CONCLUSIONS

Human beings are social by nature and live in continuous interaction with each other and the external world. Therefore, human brain functions should be studied bearing these social underpinnings in mind. To converge data from brain imaging and social sciences, we have emphasized the organism–environment system as well as the importance of the body for acting, emotions, and communications. Within this framework, the omnipresent action–perception loops lead to the creation of an inner world, the embodied mind, which strongly relies on the interaction with the environment. The mind, with its many levels, is socially shaped and reconstructed dynamically by moment-to-moment interactions. Furthermore, a large part of human cognition is off-loaded or outsourced to the environment, a phenomenon that should be investigated in future brain-imaging studies.

Despite the private contents of individual minds, humans are able to share their understanding of the world and maintain common representations, such as art and narratives. An important part of this intersubjectivity is supported by highly automated motor and sensory mirroring systems that enable people to live with others, even if not exactly understanding how it feels to be the other person. Similar basic mirroring mechanisms likely form the prerequisites for motor imitation, emotional contagion, and even empathy.

Although a unified theory of the mind seems too lofty a dream, current brain imaging is converging neuroscience with various disciplines interested in human social cognition and interaction. All these views and skills are necessary to improve our understanding of the determinants of human social interaction. In the future, the understanding of the human mind can be further deepened by moving from one-person neuroscience towards two- and multi-person neuroscience, both conceptually and experimentally.

IX. APPENDIX: ABOUT HUMAN BRAIN IMAGING

With modern brain imaging methods, brain function can be studied accurately both in time and in space.

Positron emission tomography, PET, which uses radioactive ligands to trace different substances, was important in the early days of brain imaging to study human cognitive function. It has now largely been replaced by functional magnetic resonance imaging, fMRI, but remains invaluable in the receptor mapping of various patient groups. However, both PET and fMRI are limited by the sluggishness of hemodynamics and metabolism. Electroencephalography (EEG) and magnetoencephalography (MEG) allow noninvasive measurements of brain activity at a millisecond time scale, and they thereby complement information provided by fMRI, which has excellent millimeter-range spatial resolution. With EEG and MEG, the time courses of processes underlying percepts, movements, and speech can be studied with high precision.

Brain imaging takes us beyond anatomy to scrutinize brain function. However, rigorous behavioral studies are needed to accompany imaging experiments. A combination of different techniques can provide reliable information about the sites and timings of various macroscopic brain events. Requirements for movement limitation currently restrict possible brain imaging experiments of social interaction, but new movement correction algorithms are emerging.

Additional useful methods include eye tracking (103), which provides information about the subject's target of attention. Measures of autonomic function, for example, the skin conductance response or heart-rate variability, can serve as signs of arousal and emotional load.

A. Temporal Scales of Cognition

The time scales for stimuli and brain processes relevant for perception, cognition, and action span from <1 ms to hundreds of milliseconds, and short-term and long-term memory operate on time scales from seconds to even years. Recent fMRI studies suggest a hierarchy for temporal processing windows in the scale ranging from seconds to tens of seconds (99). However, previous electrophysiological studies addressing the effects of inter-stimulus interval (231) on evoked responses suggest that even subsecond time scales are relevant for assessing temporal hierarchies. Awareness can lag the onset of physical stimuli by 100–400 ms (92), and in some conditions, another person's actions are predicted 100–150 ms beforehand (20, 62, 137). Many perceptual and cognitive functions, such as multisensory integration, backward masking, sensory memory, and attentional blink, take place within 50–500 ms. Based on only 20- to 30-ms viewing, humans are able to categorize complex biological stimuli, for example, determining whether a natural scene contains an animal or not, and the cortical evoked response indicates that categorization is completed

within 150–200 ms (226). Clinical assessment requires temporal accuracy down to the millisecond scale, resolving events even earlier than the earliest cortical or subcortical responses.

B. MEG in a Nutshell

MEG is useful in the study of brain function whenever millisecond-scale temporal resolution is required (89, 93, 94, 96). Neuronal currents produce weak magnetic fields that, when arising in concert in tens of thousands of neurons, are detectable outside the head with sensitive SQUID (superconducting quantum interference device) sensors. The signals are considered to reflect mainly postsynaptic, rather than axonal, currents (89, 94). The SQUIDS are kept immersed in liquid helium, 4 degrees above absolute zero, and the helium-containing dewar, a well-insulated vessel, is brought close to the subject's head (see Fig. 8). Modern neuromagnetometers, containing hundreds of SQUIDS arranged in a helmet-shaped array to cover the whole scalp, are currently used in ~140 laboratories worldwide.

The most likely activation areas in the brain are deduced from the measured MEG patterns by solving the “inverse problem,” that is, by determining the neuronal generators of the measured signals. The solutions are either discrete current dipoles that serve as pointlike idealizations of local currents, or distributed current patterns.

Compared with EEG, the MEG signals are less distorted due to the transparency of the skull and other

extracerebral tissues to magnetic fields; hence, the active brain sites can be pinpointed in a more straightforward and reliable manner. EEG signals measure voltage differences (that is, electric potentials) between two electrodes, each of which can affect the EEG signals. In comparison, the signal measured with an MEG sensor reflects brain activity without bias from other sensors. The practical advantages of MEG over EEG first became evident in the identification of several neuronal sources of several evoked responses and of spontaneous brain rhythms used in clinical assessment and basic research (for a review, see Ref. 93).

A sphere is a good volume conductor model for the brain and is widely applied in modeling the neuronal sources of the measured MEG signals. Computationally more demanding realistic head models can also be used. In an ideal sphere, only currents that are tangential to the surface (or tangential components of tilted currents) will produce a magnetic field outside the sphere, whereas the magnetic field produced by any other current will be limited to the inside of the sphere due to symmetry reasons. Because of the anatomical organization of the cerebral cortex, the main signals picked up by MEG therefore arise from fissural cortices, where especially the apical dendrites of pyramidal cells are tangential with respect to the skull surface. Combined electrophysiological and magnetic recordings from guinea pig hippocampal slices also implicate pyramidal cells as the main sources of the MEG signals (178).

In the apical dendrites of pyramidal cells, currents flow in different directions, leading to considerable can-



FIG. 8. MEG recording with a helmet-shaped neuromagnetometer. An infrared camera for simultaneous eye tracking can be seen in front of the subject. The *inset* on the right shows the 306-channel sensor array, normally located within the device immersed in liquid helium. (Courtesy of Veikko Jousmäki and Mika Seppä, Brain Research Unit, Helsinki University of Technology.)

cellation at the macroscopic level relevant for MEG recordings. Perhaps only 1%, or even less, of the net effect is seen; however, this fraction still serves as a good indicator of local signaling. It is also important to note that even tiny subpopulations of neurons acting in concert can explain the major part of the total signal; for example, among 10^7 oscillatory elements (approximately equivalent to the number of pyramidal cells in a 1-cm^2 patch of cortex), 1% of synchronous elements would explain over 96% of the total signal (97).

C. Basics of fMRI

fMRI (for a comprehensive textbook, see Ref. 109) is the most widely used brain imaging method to study human brain function, including social cognition. The fast spread of fMRI has been promoted by the large number of magnets (in year 2008, $\sim 30,000$) for clinical magnetic resonance imaging (MRI); most of these magnets are also suitable for fMRI.

Conventional MRI and fMRI rely on quantum-mechanical properties of the hydrogen nucleus, the proton. Each proton, with its spin, can be considered as a small (magnetic) top. In the same way that a top rotates around the earth's gravitational field, a proton precesses about an external magnetic field. The precession frequency depends linearly on the strength of the magnetic field: the stronger the field, the faster the precession. At 3 T, the protons precess at ~ 128 MHz.

When a subject is put into a strong magnetic field (typically 1.5–3 T, sometimes 7 T, or even more), a pro-

portion of the protons (about 5–6 parts per million) align in the direction of the external magnetic field (Fig. 9), since aligning along the anti-parallel direction is energetically more costly. This population imbalance creates a small net magnetization in the direction of the external magnetic field.

Protons can be excited by applying a brief, external magnetic field that pulsates at the protons' precession ("resonance") frequency and is orthogonal to the steady magnetic field. As the protons return to the original (equilibrium) state, they send out signals at the same radiofrequency. The relaxation times T_1 and T_2 characterize the time taken for the protons to return to the original position and lose synchrony with respect to neighboring protons. Because the relaxation times depend on the protons' environment in the tissue and on the local magnetic field, it is possible to form an image that depends on tissue properties.

fMRI can be recorded by measuring blood oxygenation level-dependent (BOLD) signals, first discovered by Ogawa et al. in 1990 (177). Neuronal activation leads to increased blood flow in the activated areas and even in the neighboring region, whereas the oxygen consumption does not increase to the same extent. The result is a decrease in the absolute amount of deoxygenated venous blood in the activated brain area. Deoxyhemoglobin is paramagnetic, causing a small magnetic disturbance in the surrounding tissue; no such disturbance is elicited by the oxyhemoglobin, which is diamagnetic. Thus protons close to red blood cells that contain deoxyhemoglobin will experience a different magnetic field than other pro-

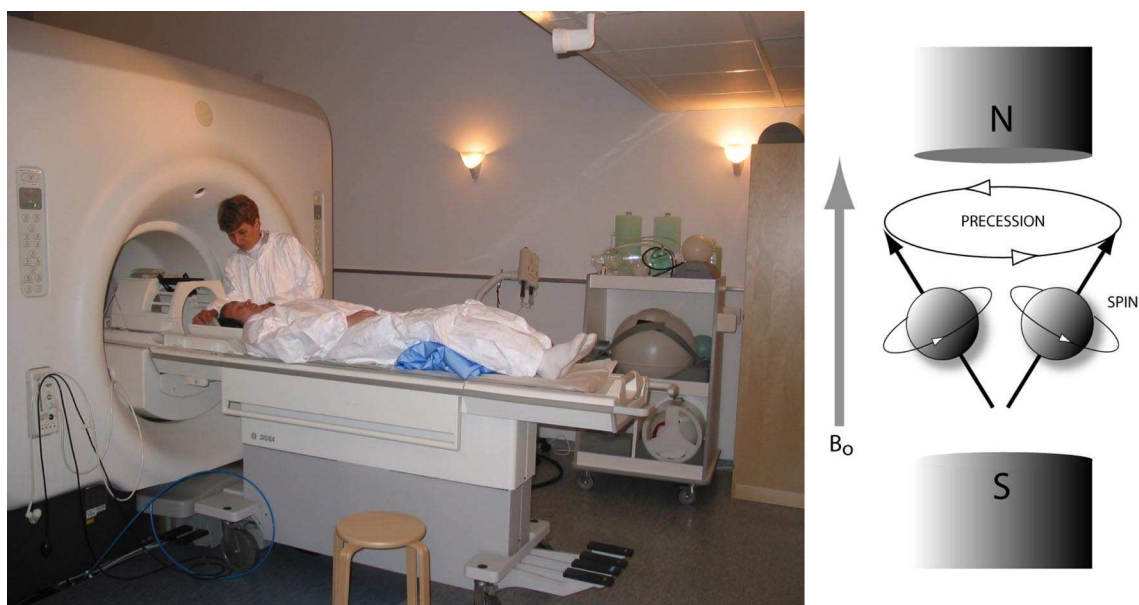


FIG. 9. *Left*: a 3-tesla magnetic resonance imaging device, with the subject just going into the magnet. (Courtesy of the Advanced Magnetic Imaging Centre, Helsinki University of Technology.) *Right*: protons precessing in a strong magnetic field.

tons, and the resulting changes in the precession frequency will affect the amplitude of the measured MR signal. During neuronal activation, the disturbance caused by paramagnetic deoxyhemoglobin typically decreases, giving rise to a positive BOLD signal.

D. Evoked Versus Spontaneous Activity

For a long time, functional brain imaging has focused on recording brain responses to various external stimuli, applied under reproducible, experimentally controlled conditions, with the assumption that the brain is basically a reflexive system. Another approach that has recently received much attention in the PET and fMRI literature is the study of “resting-state networks,” i.e., the brain’s intrinsic activity (66, 191). In electrophysiology, on the other hand, the development has occurred in reverse order: the early studies (and clinical applications) of EEG were based on examination of the spontaneous (“background”) activity (169), and studies of evoked responses became feasible only with the advent of computers that allowed signal averaging.

The distinction between resting (intrinsic) and evoked (extrinsic) neural networks is conceptually important because some of the changes observed in brain imaging studies may just reflect task-related changes in the intrinsic activity; in that case, it would be quintessential to know the level and distribution of the resting-state activity. The extrinsic networks are assumed to behave in a rather similar manner across subjects, reacting to external stimuli, whereas every individual’s intrinsic, resting-state networks have their own specific temporal patterns. Recently, some overlap has been shown between the brain regions typically involved in the resting-state networks and social cognitive processes (206).

E. Pitfalls of Brain Imaging

Neuroimaging can identify brain areas and networks activated in a certain situation and provide insight into the relationship between brain signals and behavior. It is important to find out how specific the measured brain activation is to the experimental setup; here “activation” refers to any measured signal that results from excitation or inhibition taking place in thousands of neurons at the same time (19).

Possible inferences that can be made on the basis of brain imaging data have been discussed extensively (e.g., Ref. 205). Reverse inferences (189) attempt to identify the underlying cognitive functions on the basis of the observed brain activation pattern. Since an active spot in the brain-imaging map does not mean that the area is specific to the studied function, clear hypotheses and specificity analyses are essential. On the other hand, forward infer-

ences (104) try to distinguish between at least two possible mechanisms in a similar manner as in neuropsychological double-dissociation tasks. The forward inferences could be used to find out whether two tasks rely on identical brain circuitries but with different activation strengths, or whether the tasks have totally different neuronal bases.

Studies of humans have a clear advantage over animal recordings because humans can report on the causes of their actions, feelings, and decisions. Still, the questionnaires given may rely on poorly controllable factors, such as insight, motivation, and the subject’s honesty, and subjects typically tend to answer in a more socially desirable way than could be presumed from their actions. Nevertheless, behavioral data strengthen the inferences from brain imaging and give directions for the interpretation of the imaging data.

Inferences from brain imaging are stronger when they are based on a group of subjects or patients rather than single individuals. However, combining individual data into a common brain space requires normalization that may affect the findings. For example, a wider interindividual anatomical difference in one hemisphere versus the other may lead to the disappearance of statistically significant group-level activation. Moreover, spatial smoothing, which is often necessary for combining data from individual subjects, may spread the activation so that it becomes difficult to probe, e.g., convergent activation from different senses (209). Because fMRI data are typically presented as thresholded statistical maps, the visualized extent of activation can be illusory because of its strong dependence on the signal-to-noise ratio. Putting more emphasis on the comparison of signal intensities would largely remediate this problem.

With predefined regions of interests (ROIs), based on previous literature and specific hypotheses, the analysis can efficiently focus on interesting brain regions, as is done in invasive electrophysiology. On the down side, the ROI-based approach may miss unexpected but scientifically important activation sites in novel experiment setups. Covariances computed between brain regions bring information about large-scale neuronal networks, but causalities are difficult to resolve by means of current analysis methods. One should also avoid mereological errors in which the properties of the whole are assigned to its parts; for example, brain areas do not decide, think, or perceive, whereas humans do.

The activation “blobs” in statistical fMRI maps reflect the concerted action of a large number of neurons, as do current dipoles in MEG. With improving resolution, the activations may appear more scattered because of parcelation of the underlying brain function. The amygdala, for example, comprises several nuclei (186) that support different subprocesses, and distinguishing between them

would improve interpretations in situation where the same brain area seems to be activated in apparently controversial conditions.

In skillful hands, brain imaging is a most valuable tool for studying the neuronal underpinnings of cognitive activity.

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