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Social decision-making and the brain: a comparative perspective

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Abstract

The capacity and motivation to be social is a key component of the human adaptive behavioral repertoire. Recent research has identified social behaviors remarkably similar to our own in other animals, including empathy, consolation, cooperation and strategic deception. Moreover, neurobiological studies in humans, nonhuman primates and rodents have identified shared brain structures—the so-called "social brain"— apparently specialized to mediate such functions. Neuromodulators may regulate social interactions by "tuning" the social brain, with important implications for treating social impairments. Here we survey recent findings in social neuroscience from a comparative perspective, and conclude that the very social behaviors that make us human emerge from mechanisms shared widely with other animals as well as some that appear to be unique to humans and other primates.

The human “social brain”

Consider the following common scenario (Figure 1). You step into a busy outdoor market on a Saturday afternoon to purchase some fresh fruit from a local farmer. You are looking for a particular vendor with whom you have done business before, and whom you know is open to concede some discounts if you buy a lot of fruit. Upon arrival you notice that the vendor is in a bad mood and that his fruits are not particularly appealing. You vacillate between bargaining with him for a lower price and switching to another vendor who might be more willing to offer a better deal. But you also fear that if your preferred vendor sees you dealing with his competitor this might impair the privileged relationship you have with him. In this situation, as in many other social dilemmas, the best decision is complicated by many variables, including the unknown mental state of the persons with whom you interact or the reactions they might have towards your decision. To make an adaptive choice in this context, you must leverage the support of brain systems that identify social contexts, make inferences

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about the mental states and likely behavior of others, estimate and compare the costs and benefits of different transactions, make decisions, and learn from these interactions.

Recent research in humans, largely using blood-oxygen-level dependent (BOLD) functional magnetic resonance imaging (fMRI), has uncovered a set of brain regions reliably engaged by social decisions like the one depicted in Figure 1A. The crucial first step of identifying the social context, including recognition of agents and recall of past interactions with them, is robustly associated with activity in the medial temporal lobes and fusiform gyrus [1,2] . Next, the process of inferring the intentions of the other person based on perception of his or her current state— known as theory-of-mind or mentalizing – is known to engage the posterior superior temporal sulcus (STS), the temporal-parietal junction (TPJ), the rostral anterior cingulate cortex (rACC), and the medial prefrontal cortex (mPFC) [3-5]. Making a purchase in a market also requires computing how much you value the goods on offer—a process that reflects your personal preferences and internal state. Brain areas involved in personal valuation primarily include the ventromedial prefrontal cortex, orbitofrontal cortex, and ventral striatum [6], although other value signals have been identified in a wide array of other regions as well [7]. Current evidence suggests the same brain regions also compute the value of social factors (e.g. the value of a relationship), which need to be considered along with the value of goods in order to make a decision [8,9]. Finally, a decision needs to be taken. Several neuro-computational models of decision making have been proposed, most notably the accumulation of evidence towards a decision threshold [10,11], a process scaled by the value of available options and divisively normalized by their number [12]. The outcome of this process—namely whether it turned out better or worse than expected—provides important information one can use to update the model of the decision context, a learning process that appears to depend on the dopaminergic midbrain, striatum, ACC, and dorsolateral prefrontal cortex [13,14].

Despite this success in using functional and structural imaging to predict individual variation in social behavior, this framework remains incomplete. Spatial and temporal limitations inherent to BOLD imaging preclude understanding neural mechanisms unfolding at the cellular and molecular scale with millisecond timing. Indeed, single neurons a few microns apart can signal widely different properties both in cortex [15] and basal ganglia [16] and these responses change dynamically within the time course of a single decision [17]. Moreover, signals related to value can easily be confounded with signals related to attention and arousal [18]. Finally, practical and ethical considerations make it difficult to functionally test this model by inactivating or stimulating neuronal populations with temporal and spatial specificity in humans. These challenges make animal models of social interactions critical for developing a fully mechanistic account of human social behavior.

Deep homology in the social brain

Choosing with whom to compete, with whom to mate, and with whom to cooperate are critical decisions for many animals that strongly impact survival and reproductive success [19,20]. Selective pressure on neural circuits supporting social behavior may generate similar solutions based either on convergence in the absence of shared ancestry [21] or elaboration of traits shared by common descent [22]. Homology is defined as shared

ancestry in traits between different species. Deep homology extends the concept of homology to describe traits that are shared across a wide range of species and develop and differentiate under the control of the same genetic mechanisms [23]. An example of deep homology is the role of PAX genes in the development of eyes in vertebrates and insects; despite their differing outward appearance these organs share a common developmental pathway [23].

Emerging evidence supports the hypothesis of deep homology in some of the fundamental mechanisms mediating social behavior [24]. A recent study found remarkable overlap in the expression profile of neurochemical genes across 12 brain regions involved in social decision making in 88 species of vertebrates [25]. Analysis examining the changes in gene expression patterns since the time tetrapods and ray-finned fishes shared a common ancestor about 450 million years ago identified the basolateral amygdala and the oxytocin and progesterone receptor distributions to be the most conserved through evolution (Figure 2). The authors also reported significant variability in the site of production of neuroendocrine ligands as compared to the highly conserved distribution profiles of receptors, which they propose may explain variation in the way social signals are weighed and processed, while conserving the responses to similar environmental challenges across species [25]. Despite the apparent similarities endorsing some deep homologies in the biological basis of social behavior, important behavioral differences exist between many of these species and humans [26,27].

Amongst mammals, some species of rodents engage in social behaviors shared with humans and other primates, including play and laughter [28], status-recognition and hierarchical behavior [29], rudimentary empathy [30], and adapting their social structures to environmental challenges [31]. In a remarkable recent study, neuroscientists demonstrated that prairie voles—an animal that forms strong pair-bonds between males and females—show consolation behavior towards other voles [32], a behavior typically observed in great apes [33] and other animals such as corvids, elephants and canids [34-36]. Prairie voles increased grooming of a familiar vole, but not a stranger, that had experienced an unobserved stressful event. Further, voles matched their own stress response to the stress level of their partner as indexed by increases in corticosterone and anxiety-related behaviors [32]. Together, these findings endorse previous studies suggesting some species of rodents, including mice and rats, display emotional contagion [37-39], which is thought to be a precursor for affective empathy in humans.

The neural basis of empathy appears to be partly regulated by an evolutionarily conserved peptide across some mammalian species. The neuropeptide oxytocin (OT) is robustly associated with empathy-like behaviors in small rodents [32,40-44], and some evidences suggest that this association is conserved in humans [45-48]. These findings invite the hypothesis that oxytocin shapes empathy behavior in part by acting either directly or indirectly on brain regions implicated in empathy, such as the ACC [49].

Consistent with this hypothesis, exposure to a stressed cagemate increases activity within the ACC and oxytocin antagonists infused into ACC abolish consolation behavior in the monogamous prairie voles [32]. Recent studies suggest further parallels between rodents and

humans in the interactions between empathy and the social environment. By pharmacologically blocking glucocorticoid synthesis or receptors for adrenal stress hormones, researchers have been able to reduce the level of stress experienced by mice and humans partnered with a stranger. This manipulation elicited emotional contagion between strangers, a form of empathy-like behavior typically observed only between familiar mice and not between stranger mice [50]. Notably, the authors found the same effect of social stress on empathy for pain in young human adults, suggesting an evolutionarily conserved role for stress in emotional contagion and empathy between unfamiliar individuals across species [50]. These observations invite the possibility that empathy between human strangers could be enhanced through interventions that reduce stress. It is worth noting that OT possesses anxiolytic properties in addition to its direct effects on social function [51], offering the potential for both direct and indirect modulation of empathy.

Interestingly, oxytocin binding in medial amygdala has also been reported to facilitate social recognition in rodents [52] a process that was abolished by selective application of oxytocin antagonists via disruption of synaptic plasticity [43]. The amygdala may mediate social facilitation, in part, via projections to the ventral hippocampus. In a recent study, neuroscientists optogenetically manipulated the projections from pyramidal neurons in the basolateral amygdala to the ventral hippocampus in mice performing social interaction tests [53]. Deactivation of these projections significantly increased social interactions whereas activation of the projections decreased social interactions [53]. These results indicate that social tendencies are modulated by precise departures from a resting-state level of interaction between these two brain regions.

Primate specializations in social behavior and cognition

Despite growing evidence for deep homologies in biology and social behavior across vertebrates, many of our most complex, flexible, visually-guided, and strategic social behaviors appear to be restricted to other primates [54]. For most primates, social bonds are crucial, shaping the reproductive success of males [55], females [56] and offspring [57]. Variation in social skills among human primates [58,59] and nonhuman primates [60,61] are directly related to observable variation in brain anatomy, opening the door to studying inter-individual differences in social skills. Primates' social skills are complex; individuals make concessions to maintain power [62], unite to defeat a common opponent [63], and place high value on social information [64]. Although some of these complex skills can be found in other species [65], their combination into a rich social cognitive and behavioral repertoire appears, to date, to be unique to primates.

Like humans, monkeys take into account the well-being of others when they make decisions. When interacting with friends, for example, rhesus monkeys work to avoid delivery of an unpleasant air puff to their partner and work to deliver a reward instead [66]. This sensitivity decreased proportionally with social distance between the two monkeys as measured in their home environment, and was correlated with the amount of mutual gaze and mutual eye blinking observed between partners [66]. In a similar experiment, researchers trained rhesus macaques to play a modified version of the classic dictator game while recording from single neurons in the basolateral amygdala [67]. They identified neurons that signaled the

value of rewards for both self and for a social partner when dictators made overt decisions to give or withhold reward but not when the computer made the decisions, suggesting an active role for these neurons in social decision making. The authors further showed that unilateral infusion of oxytocin into the basolateral amygdala increased prosocial behavior but equivalent injections into the dorsolateral prefrontal cortex did not [67]. Effective oxytocin-induced enhancement in prosocial behavior was accompanied by increases in attention to the partner as well.

In addition to sensitivity to the welfare of others, monkeys and apes, like humans, also make inferences about the mental states of others. Gaze following is an important developmental and evolutionary precursor to theory of mind [68,69], the process of inferring the mental state of another individual. Both chimpanzees and rhesus macaques follow the gaze of others to obtain information about hidden objects and events [70]. As in humans, gaze following by rhesus macaques involves both overt gaze shifts and covert changes in the allocation of attention [71]. Gaze following also appears to follow a similar developmental time course in monkeys and humans. Primatologists tracked the gaze of 481 rhesus macaques ranging from infancy to old age and found that gaze following arises in infancy, peaks in the juvenile period, and declines with normal aging [72]. Notably, this developmental trajectory goes awry in disorders like autism which are defined in part by social impairments [73]. Electrophysiological studies in monkeys have identified neurons in the amygdala [74] and the posterior superior temporal sulcus [75] that detect and track the gaze of others. Moreover, neurons in the lateral intraparietal cortex, an area implicated in orienting and attention, “mirror” the gaze of other monkeys [76].

Mentalizing in nonhuman primates appears to go beyond mere gaze following. Chimpanzees, marmosets, tamarins, and rhesus monkeys, to name just a few species, all show evidence for at least a rudimentary capacity to make inferences about another individual’s mental state and can use that information, for example, to motivate cooperation [77-79]. Recent evidence even suggests that great apes can infer false beliefs that a peer might hold, as well as anticipate errors that are consequent of this false belief [80]. In a remarkable recent intracranial recording study, neurophysiologists investigated the neural correlates of intention inference in macaques. The authors trained rhesus monkeys to play an iterated prisoner’s dilemma game while recording neuronal activity via a multielectrode array in the dorsal anterior cingulate cortex (dACC) of one player. Monkeys decided between defecting for a small certain reward or choosing to cooperate and receive a larger uncertain reward [81]. The authors identified some neurons selective for the monkey’s own choice, some selective for the partner’s choice, and a third subgroup of neurons selective for the *predicted* choice of the partner monkey. Neurons selective for the predicted intentions of others might contribute to the computations necessary for strategic social behavior. The authors tested this idea by using microstimulation to disrupt normal patterns of neuronal activity in dACC, which impaired cooperation [81]. This deficit was specific to cooperative interactions but did not impair the capacity to retaliate following defection by the partner, or to engage in zero-sum behavior in which there was no possibility of mutual benefit. These findings strongly implicate the dACC in computations necessary for strategic cooperation, and echo findings by Chang and colleagues that neurons in dACC and gyral ACC, as well as

orbitofrontal cortex, carry signals associated with prosocial decisions made by rhesus monkeys playing a dictator game [82].

Another noteworthy aspect of primate social behavior is our tendency to make strategic decisions based on perceived long-term societal implications. For example, experimental psychologists [83] applied transcranial direct current stimulation (tDCS) over the right lateral prefrontal cortex to human participants playing an economic game and found that anodal stimulation (thought to increase neural excitability [84,85]) led to an increase in norm-compliant behavior when social punishment threats were present and a decrease in norm-compliant behavior when these threats were absent. Despite these changes in behavior, stimulation did not change how participants perceived the fairness of these exchanges or what they expected for not complying with the social norm. In another study, researchers asked human participants to make blameworthiness and punishment judgements [86]. Based on a model of social norm enforcement [87], the authors hypothesized that the dorsolateral prefrontal cortex (DLPFC) acts as "node" that receives and integrates harm and blameworthiness signals when individuals decide whether or not to mete out punishment. As predicted, they found that repetitive transcranial magnetic stimulation (rTMS) over both right and left DLPFC evoked a departure from normal punishment behavior without affecting judgements of blameworthiness, implicating the role of DLPFC in norm enforcement. Though we believe testing this hypothesis using a non-social control condition would have further strengthened these results, these studies have taken a step forward in highlighting the neural circuits regulating complex social decisions in primates.

Translational applications

Ultimately, furthering our basic understanding of the social brain will provide new targets and opportunities to treat humans suffering from social impairments. Research across several species of mammals has identified a highly conserved social modulator in the neuropeptide oxytocin, provoking a recent surge of excitement about its therapeutic potential (Figure 3)[88]. Numerous studies have found that intranasal administration (IN-OT) of oxytocin enhances a range of complex social cognitive processes in both healthy humans and patients [45,89,90]. A recent meta-analysis of human IN-OT studies found that oxytocin increases recognition of facial expressions of emotions (Cohen's $d = .21$) and increases trust towards members of one's group (Cohen's $d = .43$) [91]. Another meta-analysis examined the effects of IN-OT on autism spectrum disorder, schizophrenia and social anxiety, and reported a combined effect size of $d = .32$ on a variety of outcome measures important for social interactions including social anxiety and emotion recognition [92]. Encouraging findings like these have inspired a large number of clinical trials to document the efficacy of oxytocin for improving social functions in psychiatric populations. According to the U.S. National Institutes of Health (NIH), there are currently 39 active clinical trials studying the effects of oxytocin on social cognition in patients, 13 of which in children with ASD (ClinicalTrials.gov, 2016). In the vast majority of these trials, oxytocin is administered using a nasal spray. Many parents, patients and clinicians eagerly await the results of these clinical trials.

Despite this optimism, experts have raised a number of concerns about the validity of results emerging from oxytocin studies in humans [47,93-97]. For example, a team of oxytocin researchers [97] conducted a meta-analysis of all meta-analyses examining the effects of oxytocin on cognitive and behavioral variables in humans. They found that the average effect size was $d = .28$, or a quarter of a standard deviation difference between oxytocin and control groups. Given such a small effect size of oxytocin, sample sizes of over 300 participants would be required to detect its effects reliably, meaning, with a statistical power equal or above 80%. Yet, the average sample size in these studies is under 50 participants, making it highly unlikely that any given study would detect a true effect of oxytocin (12-16% chance of finding a true effect given these small sample sizes) [97]. In this light, it is puzzling that 88% of published studies report a significant effect of oxytocin in humans [97]. With such small sample sizes, methodologically sound studies should fail to detect effects of oxytocin more than 80% of the time for statistical reasons alone. Therefore, either the vast majority of oxytocin studies ever conducted in humans were never published (i.e. file-drawer effect) [98], or the majority of published studies have hidden methodological issues that undermine their conclusions [99,100]. Large-scale, multi-center studies with appropriate statistical power are urgently needed to resolve this important issue [101].

A second concern is the penetration of oxytocin to the central nervous system when administered intranasally in humans [94]. Oxytocin is a large peptide that does not cross the blood brain barrier readily [102]. Oxytocin and other drugs delivered through the nose are thought to be translocated to the brain via the olfactory and trigeminal nerves [103] which lie deep within the nasal cavity and sinuses. It remains unclear precisely how effectively oxytocin can reach receptors in the brain when administered by nasal spray, as done in human trials [95], compared with other modes of delivery such as aerosolization. Recent studies in rhesus macaques found that intranasal spray of oxytocin does not lead to detectable increase of the peptide in the cerebrospinal fluid (CSF), casting doubts on the results of human studies using this route of administration [104]. Neurobiologists showed that using a pediatric nebulizer to deliver aerosolized oxytocin [105] instead of a nasal spray significantly increased CSF levels in two monkeys. Subsequently, an independent group of researchers replicated the findings from the latter study using a larger sample size (8 monkeys; 4 oxytocin, 4 Placebo) and a within-subject design for baseline comparison [104]. These encouraging results invite the possibility that some of the variability in findings across studies of oxytocin administration in humans might reflect differences in the success of intranasal delivery.

Adding to the complexity of the translational impact of oxytocin therapy, a recent study found that the distribution of oxytocin receptors is much more restricted than vasopressin receptors in macaques, and is mainly limited to deep structures of the diencephalon and brainstem, including the nucleus basalis of Meynert and the superior colliculus as well as amygdala [106]. Unfortunately, observations of increased oxytocin levels in the CSF or blood plasma following nasal administration does not guarantee that exogenous oxytocin reaches its target receptors in the deep nuclei of the brainstem, nor that it does so in sufficient concentrations to trigger a positive behavioral effect [93]. Noteworthy is the fact that oxytocin is also produced outside the brain in the heart, testes, uterus, gastrointestinal tract, and several other structures [107], which can bias plasma measurements of oxytocin in

social experiments [108]. A better way to activate central oxytocin receptors might be to stimulate endogenous pituitary oxytocin release using a pharmacological agent rather than exogenously administer it through intranasal route [109].

Despite the efforts of many research groups to develop oxytocin-based treatments for social impairments in clinical populations, there remain serious doubts whether and how IN-OT administration can stimulate pro-social behaviors in humans. Whereas the literature in rodents and other small mammals is uncontroversial [32,40-44], much more research is needed to uncover the neural mechanisms by which oxytocin affects the primate brain. Due to both neuroanatomical and behavioral similarities to humans, nonhuman primates are an excellent model to assess the efficacy and safety of chronic oxytocin administration [110,111] as well as deepen our understanding of the mechanisms mediating the effects of oxytocin in the human brain—knowledge that will help us design improved and potentially personalized treatments for individuals with disorders in which social function is impaired.

Concluding remarks

Social neuroscience is still in its infancy. Despite this early stage, groundwork has been laid for a basic framework in which different brain areas and circuits contribute selectively to the perception, recognition, selection, and recall of socially-relevant information. Insights from research conducted in various species, including humans, has highlighted significant convergence in the neuroanatomy and neurophysiology of these brain circuits, as well as the underlying genetics that shape neural structure and function, which encourages further comparative research. Importantly, new gene-editing technologies, such as CRISPR [112], may soon allow study of primate-specific social behaviors by harnessing the power of molecular genetics – an investigative tool heretofore limited to rodents, worms and flies – with potentially far-reaching translational implications [113,114]. Based on the foregoing, we advocate a collaborative, comparative approach, in which social neuroscientists continue to integrate insights from humans with complementary insights from animals, to understand what is in essence the foundation of human society and its potential for harmony or discord, with hopes for the benefit of all.

Box 1

Genes and social behavior in primates

Genetic influences play an important role in modulating the activity of brain areas involved in social cognition. For example, inter-individual variability in social phenotype can be traced back to polymorphisms in the oxytocin and vasopressin receptor gene and/or promoter region [115,116]. Moreover, the sensitivity to exogenous administration of oxytocin seems to be modulated by similar genetic factors [117], which has important implications for future personalized treatment approaches. More molecular genetic research is needed to identify novel genetic variations that can explain both normal and abnormal inter-individual variations in sociobehavioral phenotype.

Recently, nonhuman primates have emerged as potential models for unraveling the genetics of individual variation in complex social behavior. Capitalizing on naturally-

occurring behavioral and genomic variation, researchers studied the inter-individual interactions of a large colony of free-ranging macaques and mapped their social network ties based on grooming, an important affiliative behavior that serves to build and maintain bonds between individuals [118]. The authors found that social network position—that is, how many friends and allies each individual had—was not only heritable but linked to polymorphisms in two genes that regulate serotonin function, which have been implicated in depression, addiction, and autism in humans [118]. Since social network position itself cannot be heritable, these findings imply that aspects of social temperament and social skill useful in building connections with others have a genetic basis, which holds the potential of clear translational value for understanding the biological bases of human disorders attended by social impairments. This study and others [119] endorse the potential power of exploiting naturally-occurring variation in genomics and social behavior to understand and develop new treatments for human social pathology. While using this approach, however, researchers will have to be careful about potential epigenetic effects on the expression of those genes, including the oxytocin receptorgene, and their associated sociobehavioral phenotype [120].

A complementary approach is to engineer primates with genetic variants implicated in human disorders characterized by social impairment. In a remarkable achievement, scientists used a lentivirus to deliver the human Methyl-CpG binding protein 2 (MeCP2) variant—which causes Rett syndrome in humans—to long-tailed macaque (*Macaca fascicularis*) embryos which resulted in expression of the variant MeCP2 in the brains of infant monkeys [121]. The transgenic monkeys showed an autistic phenotype including repetitive behavior and reduced social interactions with peers. Previous attempts to model MeCP2-induced Rett syndrome in mice induced repetitive behavior but failed to replicate concomitant social impairment. Importantly, the MeCP2 variant and attendant phenotype were also expressed in offspring of the transgenic parents, permitting breeding of these animals for subsequent studies of the neural mechanisms leading to MeCP2 Rett syndrome. These findings strongly support the use of genetic engineering techniques to generate and study primate models of psychiatric conditions that are poorly recapitulated in standard small animal models like mice and rats.

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Glossary Box

Blood-oxygen-level dependent imaging

A non-invasive functional neuroimaging method that maps the flow of deoxygenated hemoglobin molecules in small blood vessels across the brain. This hemodynamic response is associated with single neuron spiking and dendritic potentials averaged over large volumes of tissue (voxels) each containing hundreds of thousands of cells often with different physiological properties.

Oxytocin
A brain peptide produced and released by the hypothalamus with receptors located both inside and outside the central nervous system in mammals. Oxytocin is important for social bonding, maternal behavior, aggression, and territoriality in small mammals. Evidences suggest that these roles might be conserved to some degree in monkeys and humans.

Gaze following
Social behavior in which an animal infers the object of attention of another individual by looking at her eyes. Gaze following is observed in numerous species of mammals and seems to indicates interest in the mental state of others. It is impaired in autism spectrum disorder patients.

Electrophysiology
Single-cell electrophysiology refers to a neural recording technique whereby high-impedance electrodes are lowered into the brain to monitor the voltage fluctuations either inside or outside neurons. Using electrical amplification, filtering and thresholding, the action potentials of neurons can be recorded with sub-millisecond time resolution.

Prisoner's dilemma game
Economic game in which two individuals choose between options with outcomes crucially dependent on the unknown intention of the other to cooperate or not. In this game, mutual cooperation provides the highest payoff for both partners over repeated iterations of the game, but most people defect in order to avoid the risk that their partner will fail to cooperate.

Zero-sum game
A family of economic games in which the gains of one participant are exactly counterbalanced by the losses of the other participant. Example zero-sum games are competitive sports such as tennis. When playing doubles in tennis, however, a player engages in a non-zero-sum game with his teammate.

Muscimol
A potent, selective agonist for the $GABA_A$ receptor. The receptor is naturally activated by the brain's principal inhibitory transmitter, GABA. When directly injected into the brain, muscimol disrupts neural activity over a volume of several cubic millimetres of tissue, permitting causal brain-behavior relationships to be established.

Optogenetics
Neural manipulation technique which involves the use of light to activate or deactivate groups of neurons with high temporal and spatial resolution. These neurons are rendered sensitive to light of a specific wavelength by genetically engineered viral vectors carrying genes coding for light-sensitive ion channels called opsins.

Dictator game
An economic game in which one participant, called the dictator, is given an amount of goods which she needs to split between herself and another participant. The dictator can choose to allocate any amount to the other participant, including giving nothing, and the other cannot

have any impact on her decision. Human participants rarely comply with theoretical predictions of total selfishness, showing an aversion to unfairness.

Transcranial direct current stimulation

A neurostimulation technique which uses a constant, low-current stimulator consisting of an anodal and cathodal electrode placed on the scalp of subjects to modulate large brain regions of interest. Cathodal stimulation is thought to slightly depolarize neuronal populations, thus increasing their likelihood of firing, while anodal stimulation is thought to hyperpolarize neurons' membrane.

Statistical power

The statistical power of a study refers to its capacity to detect a significant effect of the independent variable under study, assuming that this variable's effect truly exists in reality. The power of a study depends on the sample size, the size of the true effect, and the scatter of the data. To be properly powered, a study needs to have at least 80% chance of detecting the effect, assuming it exists.

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Trends box

Evidences converging from several animal models of social interactions offer an unprecedented view at the brain areas and networks involved in social cognition.

Experimental manipulation of social brain networks in human and non-human animals offer new causal insights that go beyond mere correlation between brain and social behavior.

Neuropeptides such as oxytocin offer great promise as a modulator of social behavior in humans. Experts, however, ask for cautious interpretation of the literature in humans and request more research in non-human primates.

Behavioral and neurobiological investigations of social behavior across species is beginning to reveal much more continuity between humans and other animals than ever before imagined.

Outstanding questions box

1. How does oxytocin modulate social behavior in the primate brain? What are the neurophysiological and cellular-level mechanisms that lead to these effects? What brain regions are causally involved in this oxytocin-mediated modulation and which ones are modulated only indirectly via other connected areas?
2. Does intranasal-oxytocin administration really have a beneficial effect in human clinical populations? If so, how does oxytocin reach deep brain receptors using this administration technique? Would stimulating endogenous oxytocin release be a better strategy for clinical applications? How safe is a life-long oxytocin treatment? What are the secondary effects of this systemic administration?
3. Can the CRISPR gene-editing technology be used in rodents and non-human primates to generate other novel models of psychiatric and neurological disorders? Will these primate models be produced at an affordable price so they can become part of common research methods in neuroscience labs?
4. What other animals could be used to model and study human social cognition? What makes a good model of social interaction and what makes a bad one? To what extent can biological homologies be ascertained when comparing the social behavior of humans and other animals? How can we rule out the possibility that biological analogies, rather than homologies, explain similar social behaviors between two species?
5. Are hemodynamic responses in brain regions measured using BOLD imaging composed of different neuronal sub-populations that play different roles during social decision making? If so, how should we interpret a change in BOLD signal in these heterogeneous areas? Can we resolve this issue by using single-cell neurophysiology in non-human animals?
6. How can the non-social and social functions attributed to some well-studied structures such as the amygdala coexist in the same area? Are different neuronal subpopulations within the same area responsible for such social and non-social signals? Is the same circuitry responsible for both functions, performing the same computation regardless of the social nature of the stimuli?
7. How useful is the notion of a “social brain”? Are there really brain regions or cell populations that are exclusively involved in social computations and not other tasks? Is it more parsimonious to assume that brain areas apply the same computation regardless of whether the input information is of social or non-social origin? Can differences in other factors (say, task difficulty or environmental complexity) between social and non-social paradigms explaining differential activation in “social brain” areas?

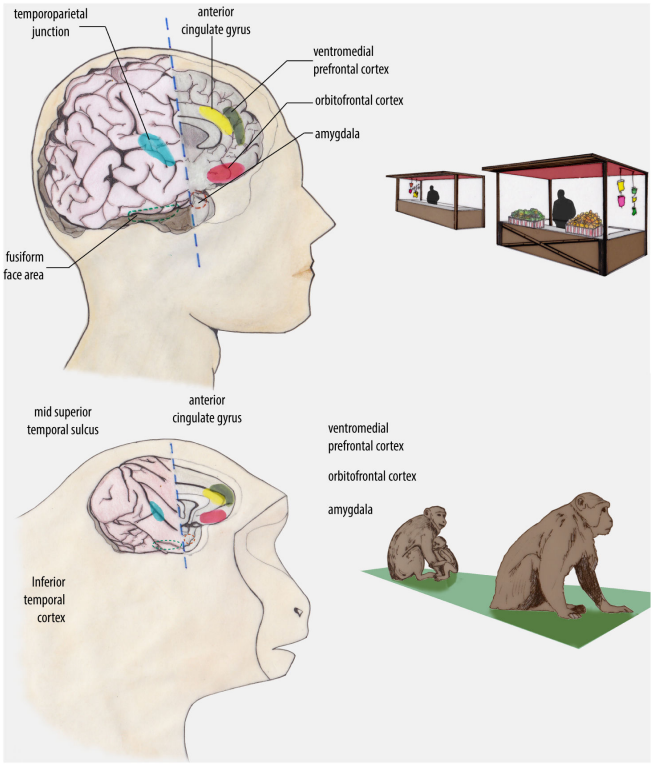

Figure 1.

Social dilemmas and the primate brain. When faced with a social dilemma such as choosing whom to deal with at the food market, several brain areas process social information to guide the decision (Up). These social dilemmas are also part of the life of other species, such as monkeys living in large groups (Down). Whether to cooperate with another male or to help caring for the offspring of a female member of the group might have different payoffs on the short and long term that are hard to predict. Homologous brain areas responsible for social cognition can be studied in animal models to understand both function and dysfunction in the human brain.

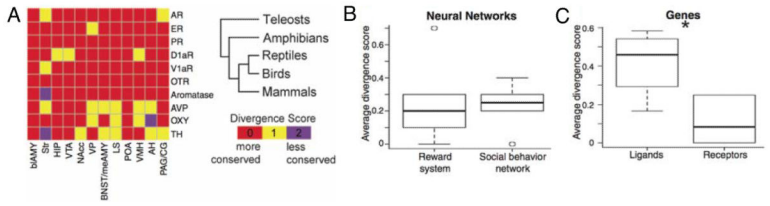

Figure 2.

Conservation of neurochemical genes regulating social behavior across vertebrate lineages. (A) Genetic divergence score for each gene (rows) in each brain region (columns) across a parsimonious model of vertebrate phylogeny (top-right). Red squares indicate a divergence score of 0, meaning that this gene has been highly conserved over the past 450 million years of evolution. Purple squares indicate a score of 2, meaning that this less conserved gene has undergone at least 2 changes over the same period. (B) The average divergence score for each brain region within either the mesolimbic reward system (VP, Str, LS, BNST/meAMY, VTA, HIP, NAcc, blAMY) or the social behavior network (VWH, BNST/meAMY, AH, LS, PAG, POA) indicate that both systems evolved at the same slow rate over the course of vertebrate evolution. (C) Averaging the divergence score for each neurochemical gene across brain regions reveals that the sites of ligand production are more evolutionary flexible than where their receptors are expressed. Regions: AH, anterior hypothalamus; BNST/meAMY, bed nucleus of the stria terminalis/medial amygdala; HIP, hippocampus; LS, lateral septum; NAcc, nucleus accumbens; PAG, periaqueductal gray/central gray; VMH, ventromedial hypothalamus; VP, ventral pallidum; VTA, ventral tegmental area; POA, preoptic area; Str, striatum; blAMY, basolateral amygdala. Genes : AR, androgen receptor; ER, estrogen receptor; PR, progesterone receptor ; D1aR, dopamine D1 receptor; V1aR, vasopressin 1a receptor; OTR, oxytocin receptor; AVP, arginine vasopressin; OXY, oxytocin; TH, tyrosine hydroxylase. Adapted from [25], with permission from *Science*.

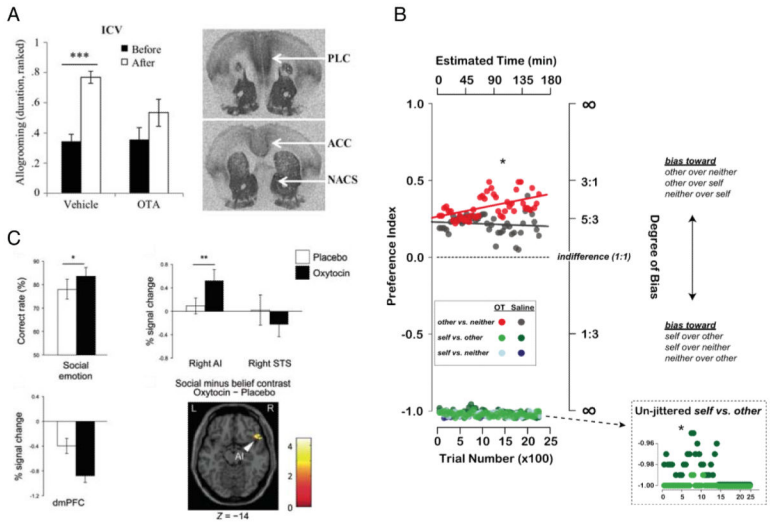

Figure 3.

Phylogenetically conserved effects of oxytocin on prosociality in the rodent, monkey, and human. (A) The prairie vole naturally exhibits prosocial consolation behavior towards a peer who underwent a stressful event (white bars), but not if an oxytocin antagonist is administered intracerebrally before the consolation test (OTA). Autoradiographs (right) shows distribution of oxytocin receptors in the prairie vole's ACC, nuclear accumbens (NACS), and paralimbic cortex (PLC). (B) The rhesus macaque exhibits an increased preference towards rewarding a peer vs. rewarding no-one following intranasal administration of oxytocin (OT) via a pediatric nebulizer (red dots vs. grey dots). (C) The human autistic child shows a slightly better aptitude at identifying social emotions in conspecifics following intranasal administration of oxytocin using a nasal spray. This behavioral increased is paralleled by an increase in BOLD activity in the right anterior insula of autistic patients, but not in the dorsomedial prefrontal cortex (dmPFC), nor the right superior temporal sulcus (STS), which are abnormal at baseline in this sample. Panel (A), (B), and (C) reprinted from [32], [105], and [90] with permission from, *Science*, *PNAS*, and *Brain*, respectively.