CHAPTER

33

Perspectives

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Abstract

Discovering how the brain makes decisions is one of the most exciting challenges of neurosciences that has emerged in recent years. The evolution of the field of decision neuroscience has benefited from the advance of novel technological capabilities in neurosciences, and the pace at which these capabilities have been developed has accelerated dramatically in the past decade.

Discovering how the brain makes decisions is one of the most exciting challenges of neurosciences that has emerged in recent years. The evolution of the field of decision neuroscience has benefited from the advance of novel technological capabilities in neurosciences, and the pace at which these capabilities have been developed has accelerated dramatically since 2005.

It is certainly difficult to predict what will be the most exciting developments in decision neuroscience in the future and somewhat arbitrary to organize potential perspectives along a coherent line. We have asked the contributors to this book to give us their respective perspectives for developments in their research domains. We have taken the liberty to build these perspectives based on these views and along lines outlined in a neuroscience report from the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative [1]. This BRAIN Initiative should help us develop and apply new tools and technologies to understand the brain at multiple levels. In parallel, the Human Brain Project from the EU, the Brain/MINDS Project from Japan (Brain Mapping by Integrated Neurotechnologies for Disease Studies), CanadaBrain, and a national brain project under way in China should also foster technological innovation for great discoveries that should lead to a revolution in our understanding of how the brain makes decisions, from a multilevel perspective.

IDENTIFYING FUNDAMENTAL COMPUTATIONAL PRINCIPLES: PRODUCE CONCEPTUAL FOUNDATIONS FOR UNDERSTANDING THE BIOLOGICAL BASIS OF MENTAL PROCESSES THROUGH DEVELOPMENT OF NEW THEORETICAL AND DATA ANALYSIS TOOLS

Theory and mathematical modeling are advancing our understanding of complex, nonlinear brain functions where human intuition fails. New kinds of data are accruing at increasing rates, mandating new methods of data analysis and interpretation. To enable progress in theory and data analysis, decision neuroscience will need to foster collaborations between experimentalists and researchers from physics, mathematics, engineering, and computer science.

One general approach widely used in the field of fMRI research and more recently applied to monkey electrophysiology is to use a so-called model-based approach, allowing us to identify the computations performed by a given brain region. This approach selects the best model fitting behavior among a set of models and allows us to regress brain activity with output parameters from these models. One classical model-based fMRI approach concerning learning of basic stimulus−reinforcer associations used prediction errors as regressors. Similar model-based fMRI approaches have been used to study social learning, such as learning social hierarchies based on victories and defeats in a competitive game, or modeling of strategic reasoning (see Ligneul and Dreher, Chapter 17; Palminteri and Pessiglione, Chapter 23; and Lee, Chapter 18).

One fundamental theoretical view about the brain, put forward by leading researchers such as Karl Friston

http://dx.doi.org/10.1016/B978-0-12-805308-9.00033-6

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and Rajesh Rao, is that the brain performs Bayesian computations in general, and particularly when making decisions. According to this view, decision-making and action selection are treated as an inference problem solving the problem of selecting behavioral sequences or policies. Choices are based upon beliefs about alternative policies, whereby the most likely policy minimizes the difference between attainable and desired outcomes. Policies are then selected under the prior belief that they minimize the difference (relative entropy) between a probability distribution over states that can be reached and states that agents believe they should occupy. Future developments in the field of decision neuroscience will be to test this Bayesian view of the brain in various contexts, not only for perceptual and value-based decisions but also for social decision-making. Perspectives for research include the articulation of neurocomputational definitions of value coding with a general Bayesian brain perspective. The pioneering work of Karl Friston has been developed along this line but will need to be extended to find predictable experimental validations.

Yet another perspective for future research is to extend classical reinforcement learning approaches to social decision-making (see Ligneul and Dreher, Chapter 17) and strategic reasoning (see Lee, Chapter 18). Social interactions are often repeated in a particular setting, making it possible for decision-makers to improve their strategies through experience. Therefore, the exact nature of learning algorithms utilized during iterative social decision-making and the corresponding neural substrates are important topics for psychological and neurobiological research. Previous research has shown that humans and nonhuman primates rely on a dynamic mixture of multiple learning algorithms for both social and nonsocial decision-making. For simple, model-free reinforcement learning, strategies are revised exclusively based on the observed outcomes from previously chosen actions, whereas for model-based reinforcement learning and belief learning, observed behaviors of other decision-makers and inferences about them also influence future choices. These different types of learning algorithms might be implemented in different regions of the association cortex and basal ganglia, but how the neuronal activity in each of these brain areas contributes to the specific types of computations for learning remains poorly understood. For example, how the brain can update the values for multiple actions through mental simulation is difficult to study, because the activity related to such simulation may not be tightly linked to any observable sensory and motor events. In addition, although the brain must continuously support multiple learning algorithms, how the outputs of various learning algorithms are combined and how potential conflicts between them get resolved need to be investigated further.

UNDERSTANDING THE FUNCTIONAL ORGANIZATION OF THE PREFRONTAL CORTEX AND THE NATURE OF THE COMPUTATIONS PERFORMED IN VARIOUS SUBREGIONS: VALUE-CODING COMPUTATIONS

The subdivisions of the prefrontal cortex and the computations performed by these subregions will be key to providing a mechanistic understanding of decision-making. For example, the roles of subdivisions of the medial and lateral orbitofrontal cortex will need to be specified, together with their participation in multiple modulatory loops with other important structures such as the nucleus accumbens, ventral pallidum, amygdala, and hypothalamus, as well as modulation with autonomic input from the gut (see Dagher, Chapter 32).

Similarly, functional divisions of the dorsolateral prefrontal cortex will need to be further characterized. This brain region, considered the highest level of the executive hierarchy, temporally coordinates the perception–action cycle by means of its cognitive executive functions upon the posterior cortex (see Fuster, Chapter 8). In addition, the dorsolateral prefrontal cortex has the capability of anticipating (predicting) perception, action, and outcome; this confers to that cortex the functions of planning and preadapting that are critical for effective decision-making. The ventromedial prefrontal cortex closes the perception–action cycle by collecting neural feedback from reward, monitoring of outcome, and risk assessment; it also has predictive capability of anticipated reward. All our decisions are to some degree Bayesian, based on the updating of prior hypotheses of perception, action, or outcome, whether their "database" is conscious, unconscious, or intuitive; therefore, any reasonable computational neuroscience of decision-making should include probability as an essential variable.

One key organizing concept in the field of decision neuroscience is the concept of value. Understanding the computational principles of value coding in the brain has received considerable attention from researchers to understand the neurobiological basis of decision-making. This progress has illuminated both where decision processing occurs in the brain and what information is represented in relevant neural activity. For example, neurophysiological and neuroimaging studies have identified specific brain areas

involved in option valuation and selection, including the frontal and parietal cortices, amygdala, and basal ganglia including midbrain dopamine neurons, ventral striatum, and pallidum. Neural activity in these areas has been shown to correlate with diverse decision variables relevant to choice behavior, such as reward magnitude, risk, ambiguity, and delay to reinforcement. A central principle derived from this research is that information about the idiosyncratic subjective value of choice options is represented in the neural activity of decision-related brain areas and that it is this idiosyncratic representation that appears to drive actual choice behavior. However, a critical aspect of decision-making processes (and one oddly relevant to economics and psychology) remains largely unexplored: how neural circuits represent value information. In an information-processing system, the form of information representation is a key intermediate level mediating the link between low-level implementation and high-level goals. Information coding is a particularly significant issue for biological systems, which face inherent constraints such as energetic costs and biophysical limitations. Because such constraints limit the information-coding capacity of neural systems, they require a transformation between the input (the variable to be encoded) and the output (the neural activity representing that variable) of a neural circuit. For example, the representation of the vast range of potential rewarding outcomes with the finite dynamic range of neural activity necessitates a compressive input–output computation that can have significant implications for what we choose and when we choose it.

Thus, to understand decision-related input–output functions (i.e., value coding), it will be critical for studies not simply to demonstrate correlation between neural activity and value but to quantify the precise relationships between the two. Experimental studies have begun to quantify these neural value-coding computations in brain regions such as the orbitofrontal and posterior parietal cortices. A notable finding of this initial work is that these value input–output functions are flexible and dynamic, changing in very specific ways in response to contextual influences such as the architecture of the choice set a decision-maker faces and the history of past rewards encountered by that decision-maker. Importantly, this contextual value coding is, at least in part, mediated by well-described computations such as divisive normalization that are prominent in sensory processing, an observation arguing for a general mechanism for information coding in the brain.

In addition to identifying, quantifying, and modeling these value-coding computations, two specific directions are important targets for future research. First, how are value-coding computations related to the structure and connectivity of the underlying biological circuits? One important approach to answering this question will be the examination of various circuit components, including cells with different functional roles (i.e., excitation versus inhibition), laminar locations, and connectivity patterns. New devices and techniques, such as large electrode arrays and optogenetics, will be crucial to this process. Another promising approach in this direction is a dynamical analysis of neural activity, focusing on fast-timescale (i.e., millisecond level) changes in firing rates rather than activity averaged over long windows; such dynamics can reveal key details about the functional connectivity of neural circuits and the resulting patterns of information flow. Second, how do value-coding computations affect choice behavior? Given the inherent constraints of information processing in neural circuits, biological decision-making can never reach the optimality predicted by normative models that have no real biological constraints. Quantifying the relationship between value-coding computations and choice behavior will illuminate both the constraints faced by biological choice systems and how neural computational algorithms compensate for those constraints.

DEMONSTRATING CAUSALITY: LINKING BRAIN ACTIVITY TO BEHAVIOR BY DEVELOPING AND APPLYING PRECISE INTERVENTIONAL TOOLS THAT CHANGE NEURAL CIRCUIT DYNAMICS

To enable the immense potential of circuit manipulation, a new generation of tools for optogenetics, chemogenetics, and biochemical and electromagnetic modulation should be developed for use in animals and eventually in human patients.

Since the pioneering work by Wolfram Schultz and colleagues, we have learned a great deal about the nature of dopamine responses during learning. In particular, we know that dopamine neurons signal reward-prediction error, or the difference between the reward that an animal expects and the reward it actually receives. This signal is thought to reinforce rewarding actions and suppress alternative actions, potentially through corticobasal ganglia loops defined by expression of different dopamine receptors. However, we are only at the beginning stages of understanding how dopamine neurons calculate these responses. Given the number of different possible sources of input, how do dopamine neurons converge on such similar prediction error responses? In what ways are

dopamine neurons homogeneous versus heterogeneous? Are they involved in learning from punishments as well as rewards? Furthermore, there are many unanswered questions about how dopamine release affects downstream circuits in vivo. What are the differential roles of phasic versus tonic dopamine firing in motivating learning and behavior? What is the effect of dopamine release on striatal and cortical neurons in vivo? How do striatal D1 and D2 neurons interact during behavior? What types of learning require dopamine, and what types are dopamine independent? To address these fundamental questions, newly developed molecular, genetic, and recording techniques will be critical.

By directly activating and inhibiting populations of neurons in a behavioral context, neuroscience is progressing from correlative measures to understanding of causal brain regions [transcranial magnetic stimulation (TMS), neuropsychology]. Methods such as TMS or transcranial direct current stimulation (tDCS) are thus likely (see Ruff, Chapter 19) to establish causal mechanisms for a given brain region, complementing classical neuropsychological approaches in patients with focal brain lesions (see Fellows, Chapter 22). A central challenge for a neuropsychological perspective on the role of the prefrontal cortex in value-based decision-making is to continue to dissect decision processes at the level of brain mechanisms. We have general guides to this now: clearly there are specific regions within the frontal lobes, for example, contributing in specific ways to value-based choice. However, the mechanisms that are engaged remain unclear, in part because the component processes of decision-making remain ill-defined, with likely multiple routes to decision-making in any given situation. We need to take advantage of converging methods to provide robust tests of well-specified, mechanistic models of decision-making. This of course is true for cognitive neuroscience in general, but it seems particularly true for decision neuroscience, in which, for the most part, models remain very general. Progress in the neuropsychological study of decision-making requires good behavioral measures of the constructs of interest. Although the past several years of work now better equip us in this regard, there is still much to be done. Creative approaches that go beyond button-press choices and reaction times, such as eye tracking, autonomic measures, and assessments of physical and cognitive effort, hold promise for uncovering the "microbehaviors" underlying value assessment and choice. It is also increasingly clear that we cannot take an isolationist perspective on decision-making. Decision behaviors do not emerge fully formed from some specialized "economic" module of the brain, but rather are interlinked with attention, memory, social–emotional, and action-selection processes. A better understanding of these interactions will accelerate advances, particularly as many of these related processes are much more thoroughly studied. Finally, decision neuroscience must aim to understand value-based choice broadly construed: in economic, but also political, social, and esthetic contexts. Testing the generality of explanatory models across the whole gamut of motivated behavior will, in the end, yield the most powerful insights.

Finally, causality can also be assessed using computational models, which allow researchers to assess probabilistic causality in humans. Building on theories of nonlinear dynamical systems, whole-brain computational models have been used to efficiently characterize network-level communication across distributed sets of brain areas (i.e., functional connectivity) to investigate the spatiotemporal dynamics of brain organization and complex cognitive architectures [2]. This dynamic characterization can incorporate time-dependent activity operating on varying timescales, which may capture a more complete picture of the spatiotemporal properties inherent to decision-making.

MAPS AT MULTIPLE SCALES: GENERATE CIRCUIT DIAGRAMS THAT VARY IN RESOLUTION FROM SYNAPSES TO THE WHOLE BRAIN

It is increasingly possible to map connected neurons in local circuits and distributed brain systems, enabling an understanding of the relationship between neuronal structure and function. It is now possible to envision improved technologies—faster, less expensive, scalable—for anatomic reconstruction of neural circuits at all scales, from noninvasive whole human brain imaging to dense reconstruction of synaptic inputs and outputs at the subcellular level.

For example, understanding of the circuit diagrams that underlie impulsivity, risky choice, and impulse control disorders is now possible to attain based on animal models. Impulsivity has emerged as a major dimensional construct in psychiatry with relevance to a range of disorders from addiction to attention deficit hyperactivity disorder (ADHD) and from Parkinson's disease to depression, mania, and dementia. As a heritable, disorder-associated trait, impulsivity is broadly acknowledged to affect the quality of decision-making through effects on risk sensitivity, subjective value-based judgments (e.g., temporal discounting of delayed rewards), and cognitive control mechanisms responsible for the inhibition of ongoing behavior. Several decades of research in humans and experimental animals have revealed divergent but often interacting neural circuitry

that underlies various impulsivity phenotypes, including the inability to await rewards, inability to terminate initiated behavior, preference for risky choice, or tendency to incompletely process information prior to decision-making. Yet formidable challenges lie ahead. For example, at present we lack a detailed understanding of the biological origins and neural circuitry of trait impulsivity, including environmental interactions, and how these collectively contribute to poor impulse control. Addressing this shortfall requires preclinical scientists to study predictive biomarkers and neurodevelopmental trajectories for impulsivity in much younger animals. By continuing to explore the behavioral diversity of impulsivity and adopting translational neural imaging, genomic, and objective behavioral approaches, we expect to see further advances in our understanding of trait impulsivity. This work requires a detailed dimensional analysis of impulsivity, characterized in aggregate by variation in genes, molecules, and circuits, in addition to a therapeutic focus away from brain monoaminergic systems (e.g., in the form of medication with Ritalin for ADHD) toward novel brain mechanisms and hence new neuropharmacological targets.

THE BRAIN IN ACTION: PRODUCE A DYNAMIC PICTURE OF THE FUNCTIONING BRAIN BY DEVELOPING AND APPLYING IMPROVED METHODS FOR LARGE-SCALE MONITORING OF NEURAL ACTIVITY

One important challenge in the future will be to record dynamic neuronal activity from densely sampled—and in some test cases complete—neural networks, over long periods of time, in all areas of the brain, in both mammalian systems and diverse model organisms, while making various types of decisions. There are promising opportunities both for improving existing technologies and for developing entirely new technologies for neuronal recording, including methods based on electrodes, optics, molecular genetics, and nanoscience and encompassing various facets of brain activity.

The combination of existing techniques using multimodal neuroimaging approaches in both nonhuman and human primates is also likely to bring insights into how the brain makes decisions. For example, the combination of intracranial EEG (iEEG) recordings in patients with epilepsy (whether with single cells or macroelectrodes) and fMRI, or single/multiple-cell recordings combined simultaneously with fMRI in monkeys, should bring a better understanding of the precise temporal dynamics at the systems level. Similarly, the new PET–fMRI scanners, which allow us to map simultaneously both radiotracers and to acquire blood oxygen level-dependent (BOLD) responses during decision-making tasks, should bring exciting new findings to the community. Converging approaches using the same paradigms with different imaging modalities (e.g., EEG or MEG) and fMRI, together with physiological measures (e.g., pupil dilation, heart beat, etc.) should allow us to specify the dynamics of decisions together with a broader view at the neurophysiological level.

Another interesting perspective from our field comes from the observation that the social environment shapes neural structures and processes, and vice versa. In Chapter 28, Fernald gave a few examples of these interrelationships using genetics and social behavior in animals. Social animals interact with others and their environment to survive and reproduce if possible. To do this, animals acquire, evaluate, and translate information about their social and physical situation into decisions about what to do next. The information gathered and the resulting decisions can profoundly alter both the behavior and the physiology of an animal. These choices in the brain are both produced by and result in a diverse array of cellular and molecular actions. The challenge is to discover where decisions are made and, in particular, what information is used to guide specific choices. With new genetic techniques, animal studies directed at understanding how the brain decides are not restricted to a limited number of "model organisms" but any animal with an interesting decision-making behavior.

THE ANALYSIS OF CIRCUITS OF INTERACTING NEURONS

The circuits of interacting neurons are particularly rich in research opportunities, with potential for revolutionary advances. This area of research represents a real knowledge gap. We can now study the brain at very high resolution by examining individual genes, molecules, synapses and neurons, or we can study large brain areas at low resolution with whole-brain imaging. The challenge remaining is what lies in between—the thousands and millions of neurons that constitute functional circuits.

One example is to understand the essential circuitry that mediates the neural bases of goal-directed action. Bradfield and Balleine point that current research in neuroscience is predominantly technique driven and, as a consequence, it can be a challenge to maintain the balance between doing what is expedient and asking questions that are worth answering. Not all recently developed techniques are equally useful in studying complex psychological capacities, something that is particularly true of studies investigating goal-

directed action in animals. In such experiments the events to which the nervous system is exposed are predominantly under the animal's control rather than the experimenters', meaning, therefore, that, because the initiating and terminating conditions for actions are fluid, the dynamics of the neural processes that mediate both acquisition and subsequent performance can be very complex. The challenge for the future is to bring this complexity under control. To the extent that is achieved it may become possible to address one of the most important open questions: it is still not known with any precision what learning rules mediate the acquisition of goal-directed actions. Establishing the essential circuitry supporting this learning process should help in that regard but there are important behavioral constraints to bear in mind. For example, different learning processes appear to be engaged at different rates by different schedules of reward: ratio schedules generate more consistent goal-directed learning and higher rates of performance than interval schedules even when parameters are selected that match rates of reward delivery or interresponse times. Whether such distinctions can be captured in associative or computational terms is still an open question. A number of researchers have recently claimed that goal-directed learning is best captured, computationally, by model-based reinforcement learning, using which a model of the environment is constructed to ensure that action selection maximizes long-run future reward. However, the performance of goal-directed actions respects the causal value of an action with respect to its specific outcome, and causal value does not necessarily coincide with reward maximization. Indeed, considerable evidence suggests that animals prefer causal actions to both equally rewarding noncausal actions and to performing no actions at all. Establishing the essential circuitry that mediates goal-directed action and the computational processes implemented in that circuit that make such actions possible is one of the most important research problems and most difficult challenges for future research.

DEVELOP INNOVATIVE TECHNOLOGIES AND SIMULTANEOUS MEASURES TO UNDERSTAND HOW THE BRAIN MAKES DECISIONS

Consenting humans who are undergoing diagnostic brain monitoring or receiving neurotechnology for clinical applications provide an extraordinary opportunity for scientific research. This setting enables research on human brain function, the mechanisms of human brain disorders, the effect of therapy, and the value of diagnostics. Seizing this opportunity requires closely integrated research teams performing according to the highest ethical standards of clinical care and research. New mechanisms are needed to maximize the collection of this priceless information and ensure that it benefits both patients and science.

Examples include linking hormones and BOLD response during behavioral tasks (see Hermans and Fernandez, Chapter 30, and Lefbvre and Sirigu, Chapter 31). Another related example concerns the effects of acute stress on decision-making, which are just beginning to be understood. Such stress-induced shift from "reflective" to "reflexive" behavior may map two distinct large-scale neural systems. This mapping is based on a vast body of animal findings of effects of stress-related neuromodulators within individual brain regions. It is essential that this cross-species inference is corroborated in humans. There is, however, a paucity of human pharmacological work detailing region-specific effects and time-dependent effects of catecholamines such as dopamine and norepinephrine. In particular, we highlight the lack of human work on stress-induced dopamine release, which to our knowledge is limited to one seminal paper showing increased dopamine release using PET. Understanding the specific roles of dopamine and norepinephrine in the central response to stressors will be critical to developing an understanding not only of immediate effects on decision-making processes, but also of the specific vulnerabilities that occur in response to acute stress in the realm of psychopathology. Regarding corticosteroids, a fruitful road for further exploration will be to specify the role of corticosteroids in limiting or terminating the acute response to stressors and promoting "reflective" types of decision-making to enhance long-term adaptation. In particular, this role of corticosteroids has not been explored fully in relation to stress-related psychopathology. In investigating this, it will be important to distinguish the roles of baseline shifts and phasic responses to stressors. One particularly promising avenue is to further explore the potential of corticosteroids in enhancing various forms of extinction-based therapy. Another large gap in our knowledge is how rapid and comprehensive shifts in neural activity are generated across large-scale neural systems. We highlighted the potential contribution of stress-related neuromodulators to this process, but these probably have downstream effects on the balance between excitatory and inhibitory neurotransmitters, which remain poorly understood. Finally, the combination of basic neuroscience work with network-level analyses using functional neuroimaging in humans has yielded important new insights about the architecture of human cognition and its regulation at various levels of stress and arousal. One important future challenge is to translate these network-level findings back to basic neuroscience, in

which these network-level effects can be studied in much more spatiotemporal detail using, for instance, in vivo electrophysiological recordings and optogenetic manipulations.

ADVANCING HUMAN DECISION NEUROSCIENCE: UNDERSTANDING NEUROLOGICAL/PSYCHIATRIC DISORDERS AND TREATING BRAIN DISEASES

Clinical developments coming from the field of decision neuroscience and reward processing are vast and likely to bring new promises. For example, in Parkinson's disease, the main current treatment is the dopamine precursor drug, L-dopa, but its efficacy decreases over time while severe side effects increase. Understanding the brain's motor circuits and decisional system with deep brain stimulation, which can restore motor circuit function in patients with Parkinson's disease for up to several years, may also help to understand how we form a decision. Which factors specifically involve the inhibitory cortical network interacting with subthalamic nucleus (STN) function in the decision-making process? Is it the decision conflict per se or other factors such as choice difficulty, appetitive/aversive valence of the choices, or information integration that influence STN activity and adjustment of response thresholds? Changing dynamically the response threshold might be a universal function in decision conflict or might be task specific. Therefore it has to be shown if different neuronal circuits/mechanisms are involved, for example, adopting risk-taking strategies or acting under time pressure along the line of an accuracy–speed trade-off. In a clinical perspective the exact electrode position in relation to changes in inhibitory control should give us further insights into the exact fiber tracts that are involved in the adjustment of response threshold. High-frequency stimulation has a negative impact on decision threshold. In analogy it should be clarified if low-frequency stimulation improves the decision-making process, reflecting the other side. Similar research concerning deep brain stimulation of various areas into brain circuits for mood and emotion have the potential to advance psychiatry in similar ways.

As noted previously, reinforcement learning combined with model-based fMRI has proven a valuable tool to reveal the brain regions computing prediction errors during learning stimulus–reward/punishment associations. It is now possible to use such tool to understand various neurological and psychiatric diseases, such as schizophrenia. Critically, this perspective links clinical observations to a vibrant and rapidly developing cognitive neuroscience field. More complex and sophisticated models of reinforcement learning are beginning to demonstrate the importance of adaptations in key parameters such as prediction error and learning rate. By explicitly studying this adaptivity and how it may be perturbed in mental illness, we are likely to develop an ever-richer explanatory link between key symptoms of mental illness and alterations in brain, behavior, and cognition. Progress in refining our understanding in this regard could ultimately pave the way for the introduction of precision medicine (scientifically based, individually tailored treatment) interventions in psychiatry.

Similarly, understanding the neuronal bases of negative motivational behavior including avoidance will be crucial points to elucidate aversive behavior related to psychiatric disorders such as anxiety. Nonhuman primate models would be essential for preclinical study. It would be required to find a neuronal circuit for aversive behavior and observation of its abnormal state. These processes would pave the way to understanding psychiatric disorders and developing treatments.

One example comes from the field of anxiety disorders. Research on psychiatric disorders has increasingly focused on broad biological and psychological mechanisms that can confer risk for psychopathology generally speaking, with specific manifestations of disorders influenced by environmental factors experienced at different developmental time points. A huge challenge currently faced by the field is delineating what these key domains of functioning are that may confer such broad risk when disrupted, and how these disruptions are neurobiologically characterized, all to better understand who may develop these conditions and treat or ideally prevent clinical anxiety. In the search for these broad underlying mechanisms of anxiety disorders, the research domain of decision-making has been largely ignored, with most human neuroimaging studies focusing instead on the passive elicitation of fear or anxiety. While phenomenologically valid, this approach falls short in demonstrating the adaptive or maladaptive behavioral consequences of anxiety, including the choices one makes between potentially rewarding and punishing outcomes. Along with emerging investigations of value-based decision-making in anxiety and its disorders, extant data that do not explicitly probe decision-making processes provide evidence for disruptions to neurobiological mechanisms throughout the decision-making process. Future research that systematically explores alterations to specific aspects of the decision-making process and associated changes in brain function or structure, and links these changes with symptoms of anxiety and associated psychopathology, has the potential to advance our

ability to diagnose, treat, and prevent the emergence of anxiety disorders.

Our understanding of brain mechanisms underlying decision-making is also likely to bring new knowledge to the understanding of drug and behavioral addictions. For example, gambling serves as a real-world example of risky decision-making and an activity that becomes excessive for some people. Chapter 27 by Clark explores what we currently know about decision-making and its underlying brain basis in gambling, with a focus on gambling disorder, the first recognized behavioral addiction in the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition. Despite long-standing discussion in behavioral economics as to why people play such games, given their negative expected value, it is only recently that researchers have begun to investigate phenomena like loss aversion and the illusion of control in groups of participants separated in terms of gambling involvement.

CONCLUSIONS

Collectively, the chapters from this book, *Decision Neuroscience*, illustrate that: (1) theories and experiments in neuroscience are helping to illuminate the mechanisms underlying decisions; (2) much remains to be done regarding complex decisions; (3) social decision neuroscience offers a special challenge of addressing more complex problems that depend on predicting the intentions of others; (4) the social environment shapes neural structures and processes, and vice versa; and (5) new experimental methods (optogenetics) or noninvasive causal methods (e.g., TMS, tDCS) will help researchers to decipher the necessary brain regions engaged in specific processes when making different types of decisions.

To conclude, this book opens up three main perspectives:

1. *Pursue human studies and nonhuman models in parallel*. The goal is to understand the human brain, but many methods and ideas are developed first in animal models, both vertebrate and invertebrate. Experiments should take advantage of the unique strengths of diverse species and experimental systems. The research on animals has been and will remain crucial to determining the neural basis of the underlying mechanisms of decision-making.
2. *Cross boundaries in interdisciplinary collaborations*. No single researcher or discovery will solve the brain's mysteries. The most exciting approaches will bridge fields, linking experiments to theories, biology to engineering, tool development to experimental application, human neuroscience to nonhuman models in innovative ways.
3. *Integrate spatial and temporal scales*. A unified view of the brain will cross spatial and temporal levels, recognizing that the nervous system consists of interacting molecules, cells, and circuits across the entire body, and important functions can occur in milliseconds or minutes, or take a lifetime.

The most important perspective of the field of decision neuroscience will be a comprehensive, mechanistic understanding of how the brain makes decisions that emerges from synergistic applications of new technologies and conceptual structures.

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