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The scylla and charybdis of neuroeconomic approaches to psychopathology

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As neuroeconomics enters its second decade, it is fair to ask whether it represents a useful confluence of two disciplines or simply a compound word with aspirations to be much more. Neuroeconomics rests upon two important assumptions, the first is the ideal rational agent model, which guides the definition of optimal decision-making and the valuations that should underlie it. The second is that neuroimaging is capable of providing insights into the neurobiology of the decision-making process. This special issue attempts to stretch the methods and metaphors of neuroeconomics toward the characterization and understanding of psychiatric disorders.

Neuroeconomics gains extra strength from three features that may help it reach beyond its beginnings – (1) its capacity to connect decision-making variables to details of neural circuits including details extracted from model animal systems, (2) its natural connection to computational theory with the best example being reinforcement learning (1,2), and (3) its connection to game theory (3).

All three areas provide support for the current effort to use neuroeconomics to forge a new understanding of certain psychopathologies (e.g. 4). One hope is that computational modeling and game theoretic structuring of behavioral probes will help leverage this effort. To be successful, these early efforts must meet at least five important criteria.

1. Does the approach produce pointers to consistent neural circuits underlying functions perturbed by mental disease?
2. Do ideas about mental disease gain extra richness from mappings on to computational models, neural structures, or functional activations in brain imaging experiments?
3. Will useful and new endophenotypes emerge from this work?
4. Is the metaphor of the rational agent helpful or limiting?

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5. Is the neural data in humans still too crude to reach up to disease or down to basic neurobiological mechanisms?

The contributions to this special issue touch on all these issues, but these are still early days and the jury is out. However, some of the most fruitful first steps appear to be in the area of neural circuits and their connection to clearly identified derangements in mental function.

Connecting to Neural circuits

Hartley and Phelps (5) in this issue provide an excellent example of how the detailed exploration of neural systems for fear conditioning can guide the understanding of how anxiety disorders could be acquired and sustained in a human and how they influence decision-making. Reaction to and learning about fearful stimuli is part of the normal behavioral repertoire of all mobile creatures; hence, neurobiologists have long been interested in fear conditioning as a model system for relating brain and behavior. Their review details the neural circuitry involved in many aspects of anxiety's influence on decision-making. This is one area where the neural structures and the logic of behavioral acquisition and extinction give much more mechanistic insight than simply studying anxiety in humans either in isolation or in brain imaging devices. Delgado and Dickerson (6) make a similar compelling case for considering multiple memory systems in the kinds of complex, real-world choices that humans routinely navigate. Similar to Hartley and Phelps (5), their contribution shows how detailed consideration of animal experiments has immediate impact on how to understand the neural basis of economic choice in humans.

Chang, Barack, and Platt escort the neural circuit analysis perspective straight into a proposal for how to use circuit-level descriptions to classify symptoms expressed in numerous psychopathologies (7). They focus on decision-making, social preference, and the valuation of time (temporal discounting) as examples. Modern genetic tools allow for the production of model organisms with specific molecular changes targeted precisely to known neural systems. One can imagine a future here where a cluster of important symptoms for some psychopathology are isolated, classified according to the information-based scheme outlined by Chang and colleagues (7), and then used to guide the production of a model organism exhibiting deficits in a contributing neural system. These possibilities are quite exciting not only because of the possible insights into basic mechanisms, but also because of the potentially fruitful interplay with clinical applications. But herein lies a gap.

What kinds of training programs can prepare a student or fellow adequately for such a vast array of theoretical and empirical approaches to problems that themselves may also require serious clinical understanding? Training programs for cognitive neuroscience, computational neuroscience, psychiatry and so on will have to evolve to meet the needs latent in such profoundly cross-disciplinary endeavors. Computational approaches to psychiatry represent one response to such challenges, but one suspects that new computational approaches alone will not be enough. Increasing the reach and resolution of non-invasive imaging of human brain function will be required in order to connect the cognitive part of neuroimaging to detailed neurobiological mechanisms.

Active social exchange as a research tool

Connecting features of mental dysfunction to animal models has been fruitful at the mechanistic level; however, some behavioral and perceptual events find such a uniquely human expression that it appears unlikely that we can simply guess which behavioral features in a model organism correspond to analogs in the human.

One approach that has arisen in recent years is to probe human mental function in active inter-personal exchange and often using probes designed around ideas from game theory. It is here that computational models have helped guide the design and interpretation of experiments (8–10; see 11 for review). King-Casas and Chiu in this issue highlight the important role of social impairments in a range of mental disorders (12). Their piece conveys a palpable tension between the excitement of gaining new mechanistic understanding in a range of important clinical maladies and the vastness of the problem ahead. One challenge for social exchange probes is that we simply do not have good models of social behavior in humans, but we need them desperately. Kishida and Montague (13) make many of the same points but point ahead to experimental settings where a subject's behavior is studied in group settings, which could serve to reveal new classes of control signals and contributing neural substrates (4,8,14). They make an argument for the pressing need to develop endophenotypes around mental function and the need to extend physical measurements in healthy and diseased human brains. As always, the presence and use of reinforcement learning models (1,2,14,15) continues to be central to such endeavors.

Clinical endpoints as starting points

This special issue also presents a more traditional starting point of beginning with a known disorder (like addiction or depression), but then using a different perspective (neuroeconomics) to re-define elements of these problems or to provide new hypotheses about their neural substrates.

Monterosso et al. (16) make a case for neuroeconomics approaches providing new breakthroughs in the area of addiction. They focus on the way that humans value the near-term and medium-term future (delay discounting) and on prediction-error signaling; an area defined exclusively by computational models and their connection to neural substrates.

Ernst reviews how goal-directed and reward-related processing can map many of the symptoms in depression to hypotheses about malfunctioning neural substrates (17). The details in this piece reveal the dependence of the various proposals either on direct elements of computational models or on qualitatively features associated with the models (1,2). Sonuga-Barke and Fairchild make a similarly strong case for understanding important features of Attention-Deficit Hyperactivity Disorder by re-conceptualizing them as issues related to personal agency and the parts of this agency that malfunction in ADHD (18). Their piece is provocative in suggesting that the current medical model in this domain is fundamentally misleading, and that an economic agency model can go some distance to a better understanding of how to characterize ADHD.

Challenges to a way forward

The importance of computational modeling is one theme apparent throughout all the contributions to this special issue; however, these models are still quite simple and in many cases require a significant number of *ad hoc* choices to make them work. We must remain vigilant and skeptical about facile interpretations of such efforts because of the complex environments in which human minds now operate.

The second challenge is development and its interaction with contributing genetic substrates. Developmental insults combined with genetically-prescribed sensitivities provide one important source of malfunctioning mentation later in life.

The third challenge is scope. Decision-making and the valuations that underlie it do not exhaust the range of functions required to have healthy cognition. A broadening of issues addressed and approaches used is warranted.

The fourth challenge is the crudeness in space and time of non-invasive neuroimaging and modeling. The problems with high density EEG are well known. The two main limitations with functional magnetic resonance imaging are its crude spatial and temporal scales and a remaining gap in our understanding of all the detailed signal sources that contribute to the measurement. Our understanding of this signal space will need to improve vastly before neural activations can be considered mechanisms in the same way neurobiology at the cellular level identifies and tracks mechanisms.

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References

1. Dayan P, Daw ND. Decision theory, reinforcement learning, and the brain. *Cogn Affect Behav Neurosci.* 2008; 8(4):429–453. [PubMed: 19033240]
2. Rangel A, Camerer CF, Montague PR. A framework for studying the neurobiology of value-based decision-making. *Nature Reviews Neuroscience.* 2008; 9:545–556.
3. Camerer CF, Fehr E. When does “economic man” dominate social behavior? *Science.* 2006; 311:47–52. [PubMed: 16400140]
4. Kishida KT, King-Casas B, Montague PR. Neuroeconomic approaches to mental disorders. *Neuron.* 2010; 67(4):543–554. [PubMed: 20797532]
5. Hartley CA, Phelps EA. Anxiety and decision-making. (*Biol Psych.* 2012 In press.
6. Delgado MR, Dickerson KC. Reward-related learning via multiple memory systems. *Biol Psych.* 2012 In press.
7. Chang SWC, Barack DL, Platt ML. Mechanistic classification of neural circuit dysfunctions: insights from neuroeconomics research in animals. (*Biol Psych.* 2012 In press.
8. Ray D, King-Casas B, Montague PR, Dayan P. Bayesian Model of Behaviour in Economic Games. *Advances in Neural Information Processing Systems (NIPS).* 2008; 21:1345–1353.
9. Hampton AN, Bossaerts P, O’Doherty JP. Neural correlates of mentalizing-related computations during strategic interactions in humans. *PNAS (USA).* 2008; 105(18):6741–6746. [PubMed: 18427116]

10. Yoshida W, Dolan RJ, Friston KJ. Game theory of mind. *PLoS Computational Biology*. 2008; 4(10):1371/journal.pcbi.1000254
11. Behrens TEJ, Hunt LT, Rushworth MFS. The computation of social behaviour. *Science*. 2009; 329:1160–1164. [PubMed: 19478175]
12. King-Casas B, Chiu PH. Interpersonal decision neuroscience: understanding social behavior in psychiatric illness through multi-player economic games. (. *Biol Psych*. 2012 In press.
13. Kishida KT, Montague PR. Imaging models of valuation during social interaction in humans. (. *Biol Psych*. 2012 In press.
14. Maia T, Frank MJ. From reinforcement learning models to psychiatric and neurological disorders. *Nat Neurosci*. 2011; 14(2):154–162. [PubMed: 21270784]
15. Montague PR, Dolan RJ, Friston K, Dayan P. Computational Psychiatry. *Trends in Cog Sci*. 2012; 16(1):72–80.
16. Monterosso J, Piray P, Luo S. Neuroeconomics and the study of addiction. (. *Biol Psych*. 2012 In press.
17. Ernst M. The usefulness of neuroeconomics for the study of depression across adolescence into adulthood. (. *Biol Psych*. 2012 In press.
18. Sonuga-Barke EJS, Fairchild G. Neuroeconomics of Attention Deficit/Hyperactivity Disorder: Differential influences of medial, dorsal and ventral prefrontal brain networks on sub-optimal decision-making? (. *Biol Psych*. 2012 In press.