Neuroeconomics and the Study of Addiction

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We review the key findings in the application of neuroeconomics to the study of addiction. Although there are not "bright line" boundaries between neuroeconomics and other areas of behavioral science, neuroeconomics coheres around the topic of the neural representations of "Value" (synonymous with the "decision utility" of behavioral economics). Neuroeconomics parameterizes distinct features of Valuation, going beyond the general construct of "reward sensitivity" widely used in addiction research. We argue that its modeling refinements might facilitate the identification of neural substrates that contribute to addiction. We highlight two areas of neuroeconomics that have been particularly productive. The first is research on neural correlates of delay discounting (reduced Valuation of rewards as a function of their delay). The second is work that models how Value is learned as a function of "prediction-error" signaling. Although both areas are part of the neuroeconomic program, delay discounting research grows directly out of behavioral economics, whereas prediction-error work is grounded in models of learning. We also consider efforts to apply neuroeconomics to the study of self-control and discuss challenges for this area. We argue that neuroeconomic work has the potential to generate breakthrough research in addiction science.

Key Words: Addiction, behavioral economics, delay discounting, neuroeconomics, prediction error, substance dependence

The behavior of someone with an addiction can be frustrating and perplexing. Our present goal is to consider the promise neuroeconomics holds for explaining the phenomenon of addiction. Although there is no unique feature that fully distinguishes neuroeconomics from all other approaches, the neural representation of Value is at the center of neuroeconomics (we capitalize "Value" throughout to distinguish from other senses of the word). Like the economist's central construct of "utility", Value quantifies how motivating a particular behavior or outcome is. What makes the Value of cocaine so high for the cocaine-dependent individual (at least some of the time) that all other considerations pale? Neuroeconomics investigates how brains represent, compute, store, and act upon Value. It overlaps substantially with other approaches that consider the neurobiology of Value (e.g., computational neuroscience and neuroscience of learning theory). But in its investigation of the mechanics underlying Valuation, neuroeconomics appropriates the methodological tools developed for modeling utility in economics.

Like neuroeconomics, addiction also lacks bright boundaries. People sometimes have difficulty related to their appetite for a drug or rewarding behavior. For practical reasons, a categorical operationalization might be imposed to specify when the difficulty rises to the level of pathology (e.g., that of "Substance Dependence" of the DSM-IV [1] or the proposed "Addiction and Related Disorders" of the forthcoming DSM-V [2]). But there is no established neurobiological "switch" that defines addiction.

Value is widely thought to play a central role in addiction. Dysfunctional behavior persists either because the addicted substance or activity has a very high Value or because competing alternatives have very low Value (or some combination thereof). Predating neuroeconomics, there has been longstanding interest in whether there is something abnormal about how addicts are affected by rewards. Neurobiological work has focused specifically on the mesolimbic reward pathway, emphasizing signaling of dopamine neurons projecting from the ventral tegmental area to limbic and paralimbic targets, especially the ventral striatum (3). One hypothesis is that individuals with relatively weak responses to reward "tend to be less satisfied with natural rewards and tend to abuse drugs and alcohol as a way to seek enhanced stimulation of the reward pathway" (4). This "Reward Deficiency" hypothesis exists side-by-side with the contrary hypothesis that liability to addiction is conferred by a "relatively indiscriminate and a hyper-reactive ventral striatum circuitry" (5). As recently reviewed (6), the neuroimaging data are equivocal. In part, this might be because chronic drug use or even chronic engagement in behavioral addictions such as gambling or risky sex might change the response of the individual to rewards in laboratory probes. But there are also inconsistencies among the few studies that looked at reward responsivity among individuals that do not have a significant history of substance abuse but who are at statistically high risk for developing it (7–9). These inconsistencies are part of the reason some researchers in the area lament that, as a concept, reward sensitivity "is probably too broad an idea to completely and precisely explain all of the pathophysiology underlying substance abuse" (6). Concepts borrowed from economic modeling might light a path forward, because they allow parameterization of distinct features of Valuation. These include but are not limited to methods for quantifying the response of an individual to reward as a function of its magnitude, risk, or certainty and its immediacy. Although of course it is not guaranteed, it is possible that the richer characterization of Valuation by neuroeconomics will facilitate progress in addiction science.

Irrationality, Behavioral Economics, and Neuroeconomics

The intellectual underpinnings of much of neuroeconomics are found in behavioral economics. Behavioral economics emerged against the backdrop of the dominant normative approach to economic modeling known as Rational Choice Theory, which models the individual as a "rational maximizer" of her interests or "utility." Here, "rationality" is operationalized with a small set of minimum requirements that need to be satisfied for behavior to be coherent and orderly over time (10). Although this was successful for some purposes, deficiencies in many contexts motivated a breakaway group of economists and psychologists to pay special attention to irrationality to develop more descriptively accurate alternatives (11). These divergences include non-normative probability weighting (e.g., treating the difference between a chance of 0% and 1% as greater than the difference between a chance of 30% and 31%) (12), incomplete search of option space (e.g., stopping consideration of alternatives when a threshold is met rather than looking for the best option) (13), reference dependence in utility judgments (e.g., a

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willingness to drive 10 min to save $20 on $100 phone but not on a $30,000 car) (14), weighing delays nonuniformly (e.g., judging the difference between $10 now and $10 tomorrow as proportionally greater than the difference between $10 in 99 days and $10 in 100 days) (15, 16), and emotional state dependent utility (e.g., choices made only in the "heat of the moment") (17). Behavioral economics retains the modeling convention of utility functions but, unlike rational choice theory, does not assume that behavior is rational. Unlike the utility models used in traditional economics, behavioral economics disconnects descriptive models (characterizations of actual behavior) from normative models (characterizations of optimal behavior). This is sometimes made explicit by substituting the term "utility" with the term "Value" (avoiding normative baggage) as in the Prospect Theory of Kahneman and Tversky (14).

When measurement of brain function became affordable and accessible, many behavioral economists welcomed the idea of incorporating brain data into modeling, in the hope that modeling could be improved by identifying neurobiological (or functional) gears between input and output (18). Conferences were organized to push forward this project, which was called "neuroeconomics" (see Glimcher *et al.* for history [19]). In many cases, behavioral economists took up collaborations with neuroimaging researchers, seeking to identify brain correlates of behavioral economic phenomena, especially sources of irrationality (20–22). Like visual perception researchers that use illusions to gain clues as to how the visual system constructs the percept, these researchers look to divergence from rationality to gain insight into how Value is constructed. The models use behavioral economic formalizations and have been used to operationalize psychological constructs like "regret," "risk aversion," and "delay discounting." But they are potentially informed by brain data. It is worth noting that this research program is antithetical to the rational maximization approach that dominates economics (which presumes rationality) and the pioneering economists in this group faced considerable resistance. We refer to this branch of behavioral economic-based neuroeconomics as "neuro-behavioral economics" (23) and subsequently will distinguish it from neuroeconomics grounded in learning.

Delay Discounting and Addiction

Addictive behavior has many causal antecedents, and the primary psychological correlates might differ between initiation, escalation, and transition to addiction. Any of the irrationalities that are prominent in neuroeconomic work are plausible candidates for playing some part in the development and maintenance of addiction. Given space constraints, we pick one compelling case to serve as our example. "Delay discounting" is arguably the source of systematic irrationality that has been most conclusively linked to addiction. Delay discounting refers to the tendency for motivation recruited by expected events to be inversely related to their delay. If the high did not set in for weeks, but all the costs arrived immediately, drugs would not be compelling. Indeed, drug intake routes that produce more rapid psychoactive effects seem to be associated with higher addiction liability (24). If there are individual differences in delay discounting behavior, it is plausible that individuals that discount steeply will be at greater risk for addiction (15,25). Consistent with this, there have been many reports of steep delay discounting among populations with substance use disorders (26,27). Although part of this association might be based on the effects of chronic drug use (28,29), longitudinal data suggest that steep discounting predicts subsequent increases in drug use in humans (29,30) and in animal models (31).

There are, of course, rational reasons to choose more immediate rewards over delayed larger ones, including opportunity cost. But the previously mentioned minimum constraints on rationality (10) presumes that the effect of delay be a constant percentage of the reward's Utility per unit of time. Provided that it occurs at the same rate across rewards, this "exponential discounting" implies that preferences will not switch due to the mere passage of time (just as the balance in bank accounts started at different times and earning the same interest rate will never switch their order of which is larger). However, this does not match lab results of actual discounting behavior (32). Alternatively, behavioral economic theorists generally argue that actual discounting does not occur at a constant rate. For example, the difference between "now" and "in one day" is proportionally greater than the difference between 99 and 100 days. Several behavioral economic modeling alternatives have been proposed. One conceptually simple model makes "now" special by multiplying any expectancy that is not imminent by a number <1 (a fit parameter, β) (33). Discounting beyond this categorical devaluation for any delay is modeled exponentially. For a stream of consumptions (c1, c2, . .), this can be represented as:

$$V = u(C_0) + \beta \sum_{t=1}^{\infty} \delta^t u(C_t) \quad (1)$$

where u is the utility function, and parameters β and δ both serve as discount parameters, and so this model is sometimes referred to as "beta-delta" (or "β - δ") discounting. Alternatively, "hyperbolic discounting" accommodates nonconstant rate discounting without the β - δ discontinuity. According to this model, motivation is inversely proportional to delay (15,34,35). Present value for a stream of consumptions (c1, c2, . .) discounted hyperbolically can be represented as:

$$V = \sum_{t=0}^{\infty} \frac{u(C_t)}{K^* t + 1} \quad (2)$$

where V is the utility function, with higher values of the discount parameter k indicating steeper hyperbolic discounting (see Supplement 1 for consideration of attempts to reconcile seemingly irrational discounting as rational).

The nonexponential discounting functions in the preceding text imply that immediately available but inferior rewards will sometimes be chosen (15). This seems a better starting point from which to address addiction than "rational" exponential discounting. The implication of abandoning the "rational" exponential discounting is dramatic. Rather than conceiving the individual as moving through time maximizing a set of preferences, she is conceived as successive agents with conflicting preferences ("dynamic inconsistency"). Her own future self might be the obstacle to attaining her current preference, resulting in a state of limited warfare between selves over time (35). In the case of a smoker, when her nicotinic receptors are fully occupied, large utility gains from smoking are not immediately available. The expectancy of better health by not smoking might, at this time, have greater motivational force. But with metabolism of nicotine, withdrawal sets in, and the opportunity for a big reward from smoking becomes imminent (including the "negative reinforcement" gain from the alleviation of withdrawal). Here, preference reversal might occur, and the formerly less preferred act of smoking might become preferred. If the neural basis for irrational discounting was understood, it could have important implications for the science of addiction.

McClure *et al.* (21) conducted the first study pairing delay discounting with functional magnetic resonance imaging (fMRI); in their neuroeconomic study, participants made choices between

more and less immediate rewards of varying magnitudes. The analytic approach brought to these data was based on the aforementioned β - δ model, which treats the Value for something imminent (now) as discontinuous with Value given any delay. The theorists asked whether the modeling duality of β - δ (Equation 1) might correspond to an underlying duality in the neural substrates of Valuation. As they put it, "Our key hypothesis is that [β - δ] stems from the joint influence of distinct neural processes, with [β] mediated by limbic structures and [δ] by the lateral prefrontal cortex and associated structures supporting higher cognitive functions." Their results seemed to fit their prediction, with brain regions of the limbic/paralimbic network exhibiting more activity when an immediate reward was present and also more activity when the immediate reward was chosen. Following the economic model, they called these regions the β-network and contrasted it with a δ-network (lateral prefrontal and parietal cortex) that was active during choice but not especially sensitive to immediate rewards. In a follow-up report, the group used brain imaging data to develop a natural modification that removed the conceptual problematic reliance on a "zero delay" (36). In the modification, present value for a stream of consumptions (c1, c2, . .) is represented as the double-exponential discount function:

$$V = w\sum_{t=0}^{\infty} \beta^t u(C_t) + (1-w)\sum_{t=0}^{\infty} \delta^t u(C_t) \quad (3)$$

where *u* is the utility function, and discount parameters β and δ are bounded between 0 and 1, with δ closer than β to 1, and with lower values indicating steeper exponential discounting for each of the hypothesized systems, and a weighting parameter *w*, also bounded between 0 and 1, that serves to parameterize the relative contribution of the β- and δ-networks. Although discounting is exponential within each system, the aggregated result is nonexponential (37). This brought the exchange between neuroscience and economics full-circle, with potential implications for addiction—the β - δ economic model informed the analytic approach to the first neuroimaging study of discounting, and in turn, the results from a set of initial neuroimaging studies suggested a modification to the economic model.

With respect to the science of addiction, the back-and-forth described in the preceding text resulted in a highly constructive hypothesis. The idea that discounting is based on two distinct neural systems implies a candidate basis for the ambivalence and inconsistency of the addict. Perhaps the well-documented steep discounting in addicted populations is related to a relative weakness of the δ-network (38,39). And perhaps this is related to the association between chronic drug use and a weakening of prefrontal (laterally, part of the δ–network) inhibitory modulation of the limbic system (40,41). If the balance between these systems could be strongly linked to measurable neural quantities (e.g., regional metabolism, connectivity, receptor density measures) then this neuroeconomic hypothesis or one like it could dramatically advance understanding of addiction (39).

More recent evidence bearing on the β-δ system competition hypothesis has been mixed. There is reasonably consistent evidence that the functioning of the lateral prefrontal cortex during intertemporal decision-making biases choice toward later but larger alternatives (42–46). However, other evidence does not support the full model. Most notably, Kable and Glimcher (47) carried out an intertemporal choice study and observed that activation within the network McClure *et al.* identified as "β-regions" was not differentially sensitive to immediacy but rather tracked overall value. Subsequent studies have also not been consistent with the idea that the striatum tracks Value in a way that is hypersensitive to immediacy (42,43,48) (at least not during decision-making [49]). It would be going too far to conclude from the more recent data that a β-δ system duality does not exist—delay discounting tasks are tedious and might be ill-suited to capture competition between hot and cool systems as envisioned (17,50). Moreover, fMRI is only sensitive to differences of a particular spatial and temporal scale. But at the moment, the evidence weighs against the aforementioned dual system competition account of delay discounting task performance, as currently observable with fMRI.

Learning, Neuroeconomics, and Pathologically High Valuation

The second track of neuroeconomic research relevant to addiction is more rooted in the study of learning than in behavioral economics (51). The high Valuation of an addicted substance emerges through learning—nobody starts life with compelling motivations to take drugs. But behavioral economic research largely ignores learning. By contrast, learning is a central topic within neuroscience, and the neuroscience of learning is a large and successful research program. Indeed the neuroscience of learning long predates the term "neuroeconomics." However, because of the key role played by the construct of Value (52–55), some reinforcement learning models are partly associated with neuroeconomics (51). We refer to this work as "learning–neuroeconomics," to distinguish it from neuroeconomics grounded in behavioral economics.

A reinforcement learning model is a mathematical formulation designed to capture features of learning. An environment is defined, and the model attempts to learn the Value of each of a small set of "states." In such an environment, each state is associated with some reward or punishment. This can be formalized as

$$\delta = r_t + \gamma V(s_{t+1}) - V(s_t) \quad (4)$$

where $V(s_t)$ is the estimated value for state s_t and $0 < \gamma < 1$ is a discounting factor indicating the effects of delay for one time-unit in observing the next state, s_{t+1}. The model observes s_t and receives r_t as its outcome. So, the estimated value for s_t after this observation can be r_t (the immediate outcome) plus the value of the following state (s_{t+1}). By contrast, the estimated value for s_t before this observation is $V(s_t)$. So, in fact, prediction error is the difference between the estimated value for s_t after observing its outcome, $r_t + V(s_{t+1})$, and the estimated value before this observation, $V(s_t)$. The estimated value is updated with this prediction error:

$$V(s_t) \leftarrow V(s_t) + \alpha\delta \quad (5)$$

where α is the learning rate, which indicates the speed of learning. This simple reinforcement model "learns" the Values of states with prediction error computed on each trial. After enough time, when the estimations of state Values of the model approaches the realized Values, the prediction error approaches zero.

What can the reinforcement learning model reveal about addiction? As with temporal discounting, the most obvious potential path is one in which the parameterizations within the model can be linked to neurobiological or neurophysiological measurements. For reinforcement learning, experimental evidence points to phasic activity of dopamine neurons as a plausible substrate for encoding prediction error (56–61). This might be particularly relevant to addiction, because the acute increase in dopamine activity within the mesolimbic reward pathway is associated with the abuse liability of psychoactive substances (62). It is reasonable, therefore, to expect that reinforcement learning models might inform hypotheses to explain addiction as a learning phenomenon. The first such hypothesis was suggested by Redish (63). In his framework, the direct

neuropharmacological effect of abused drugs on striatal dopamine partly mimics the dopamine activity that encodes "prediction error." Unlike bona fide prediction error, this faux prediction error signal does not decline as the reward becomes predictable, because it is caused exogenously by the psychoactive drug. As a result, the Value associated with the drug increases without bound (64).

The Redish model, of course, does not account for all relevant data. In its original form, it does not account for the dysregulation in addicts related to rewards outside their addiction, such as sexually evocative stimuli (65) and money (66). Nor does it account for dramatic individual differences in developing addiction, given similar histories of use (67). Nor does it account for addiction to behaviors that do not exogenously stimulate dopaminergic functioning. Several alternative reinforcement learning models have been proposed (68–70), in some cases retaining the core principle of the original Redish model. For a discussion of these alternatives, see Supplement 1. Systematic "overvaluation" due to faux prediction error, if a neurobiologically real phenonmenon, is likely just one among several sources of vulnerability to addiction (71).

Neuroeconomics and Self-Control

Neuroeconomic approaches are generating new research with the potential to advance understanding of addiction (72–74). By parameterizing factors relevant in Valuation, they provide richer characterizations than concepts like "reward sensitivity." These models may inform the search for genetic and neurobiological factors relevant to the disorder. Reinforcement learning work might shed light on the development of high Valuation that accompanies addiction, and more behavioral economic-based neuroeconomics might shed light on the nature of the Valuation of less-immediate expectancies. Neither of these, however, addresses the role played by effortful self-control, which we highlight as an important emergent direction of neuroeconomics.

There has been a wave of experimental work on self-control in social psychology, where it is predominantly conceived as a limited capacity that functions like a muscle (75,76), although there are great limitations to this conception (77,78). Within systems-level neuroscience research, a common approach relies on simple model tasks taxing behavioral inhibition that are easily paired with neuroimaging (e.g., Stop-Signal, Go/No-Go, Stroop). Their usefulness as a model of self-control over an addiction is uncertain (79). Unlike an error on any one of these tasks, "slips" or "relapses" generally require temporally extended goal-directed behavior. A lapse might look like a mistake in hindsight, but unlike errors on the Stroop Task, it is not a mistake that is reliably corrected when the individual is allowed to deliberate. Still, there is some support for the predictive validity of these model tasks (80,81).

Neuroeconomic approaches to self-control focus on Value; how is Value affected by self-control? A study by Hare *et al.* (82) conveys the spirit of neuroeconomic work on this question. Participants in their study made choices, simultaneously with fMRI, about whether to eat particular foods that varied on ratings of tastiness and healthiness. It was hypothesized that these dimensions would both impact Valuation but would do so through different neurobiological pathways. Their results did not suggest that Value-tracking (particularly within the medial orbitofrontal cortex [83]) was dissociated from choice during self-control but instead that the medial orbitofrontal cortex Value signaling during self-control was mediated (indirectly) by dorsolateral prefrontal cortex signaling. This work, informed by economic modeling, potentially advances understanding of self-control, with obvious implications for addiction.

But the preceding text describes only a first step. Self-control efforts affect contingencies in a way that is difficult to bring under experimental control. Consider the smoker that "resolves" to quit (part of the everyday conception of self-control). Such resolutions are often insufficient but are not wholly powerless and arguably contribute to most successful cessation from smoking and other addictions. How do they affect Value? Suppose our individual is offered a cigarette after her resolution. How are the contingencies that she now faces any different than they were before the resolution? Outwardly, they appear unchanged. Any cigarette still entails some very small increased risk of heart and lung disease and the like. But the resolution presumably can make "this cigarette" more costly in some way. Smoking it entails a new cost—the cost of failing on the resolution (84). At least it does some of the time. Other times, the resolution might be forgotten or perhaps just rejected. What determines how this process unfolds?

Several related proposals have been advanced to explain the phenomenon described in the preceding text (15,35,85–88). Central to each is the notion that the same person that has a high Value for one cigarette (relative to what can be expected if she turns it down) might have a low Value for the overall behavioral pattern of "being a smoker." The competition between a "just this one" construal of choices versus more expansive or "global" construal (e.g., to be a smoker or a nonsmoker) has implications for addictive behaviors. How can the techniques of neuroeconomics be applied to investigate this process as a contributor to Value? One challenge is that of experimentally controlling the processes that people engage in spontaneously when they make resolutions and then later are affected by them. This is especially difficult, given that current signal-to-noise for fMRI requires repetition of any behavior of interest. At least in part, the problem will likely be lessened by technological improvements and experimental innovation. But a second challenge concerns the internal feedback that resolution-making entails between Value and expected future behavior (89). The expectations of our smoker about her future behavior affect the Value of the current cigarette, and the Value of that current cigarette affects expectation about future behavior. This internal feedback makes the process chaotic (89,90). Its investigation might require alternative modeling tools, especially tools from game theory. As with neuroeconomic approaches to delay discounting and learning, the primary advance will come when neuroeconomics can offer better parameterizations of self-control behavior. Because of the dynamics and internal-feedback of self-control phenomena, this is a harder problem than those discussed earlier, and capturing it reasonably well will require a different class of models. It is encouraging that the topic is attracting great attention from theoretical economists, some of whom are explicitly pursuing a neuroeconomic agenda (91–95). If neuroeconomics can develop models of Valuation that capture the dynamics of self-control, it will have contributed something extraordinary to the understanding of addiction.

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