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**Using Biomedical Technologies to Inform Economic Modeling:
Challenges and Opportunities for Improving Analysis of Environmental Policies***

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Using Biomedical Technologies to Inform Economic Modeling:

Challenges and Opportunities for Improving Analysis of Environmental Policies

Abstract: Advances in biomedical technology have irrevocably jarred open the black box of human decision making, offering social scientists the potential to validate, reject, refine and redefine the individual models of resource allocation that form the foundation of modern economics. In this paper we (1) provide a comprehensive overview of the biomedical methods that may be harnessed by economists and other social scientists to better understand the economic decision making process; (2) review research that utilizes these biomedical methods to illuminate fundamental aspects of the decision making process; and (3) summarize evidence from this literature concerning the basic tenants of neoclassical utility that are often invoked for positive welfare analysis of environmental policies. We conclude by raising questions about the future path of policy related research and the role biomedical technologies will play in defining that path.

Key Words: environmental policy, neuroeconomics, neuroscience, brain imaging, genetics, welfare economics, utility theory, biology, decision making, preferences

JEL Codes: D01, D03, D6, D87

Advances in biomedical technology have irrevocably jarred open the black box of human decision making, offering social scientists the potential to validate, reject, refine and redefine the individual models of resource allocation that form the foundation of modern economics. In this paper we review how these technological advances in measuring the human decision-making apparatus are reshaping our understanding of the models of individual choice and begin to address the implications of these findings for the analysis of environmental policies.

Economists in the 19th and early 20th century understood that human behavior was driven by complex biological and social processes that generated Benthamite feelings of pleasure and pain. Viner [113] bemoaned that “Human behavior is the product of an unstable and unrational complex of reflex actions, impulses, instincts, habits, customs, fashions and hysteria.” Despite this common view that economic behavior arose from a complex decision making process, economists were abandoned process-oriented models of economic choice because, in Jevons’ words [57], they felt “...it is impossible to measure the feelings of the human heart.”

Instead economists have treated the decision-making process as a black box that directly links fundamental, unobservable preferences to observable choices. By invoking seemingly innocuous assumptions regarding consistency of these preferences and the rationality of the decision maker, the bedrock of utility theory via revealed preference was formulated, which provided a foundation for the intricate, mathematically-sophisticated theories of economic choice that continue to dominate economic research today. While this approach has been highly successful in many circumstances, a growing body of research documents its limitations and develops behaviorally appropriate refinements [14,15,109].

Dramatic advances in technology from the fields of neurology, genetics and endocrinology may allow us to overcome Jevons’ pessimism concerning measurements of

pleasure and pain. With regard to neurology, the increasing availability, affordability and quality of neuroimaging technology allow economists to re-examine process-oriented decision-making models by mapping the neuro-physiological mechanisms of choice (see Camerer, Loewenstein and Prelec [12]). With regard to genetics, the human genome project is producing an ever-expanding set of techniques and knowledge that allow us to identify subtle genetic roles in shaping complex human behavior [76]. Finally, methods from endocrinology allow for the measurement of biomarkers of neurological activity that subsequently affect immune function and health outcomes [45]. These methodologies may open new avenues of investigation previously thought to be off-limits to economists and, through collaboration with other scientists, improve our understanding of economic decision making.

While a clearer view inside the black box of decision making will improve the descriptive quality of economic models, it raises some potentially difficult issues for positive welfare analysis. Traditional welfare analysis of environmental policy has focused on individuals' consumption and production choices as viewed through the filter of rationality, where rationality is defined by a set of axioms concerning underlying preferences, i.e., preferences exist and are complete, coherent and stable. Furthermore, those endowed with such preferences have the information, ability and motivation to enact decisions to satisfy such preferences. By exploiting such assumptions, actual or intended economic actions can be analyzed to draw inferences about the underlying structure of preferences, and these preferences can then be used to predict how policy interventions would alter the levels of surplus achieved by the affected individuals. Policy makers can use such information in cost benefit analysis or in other modes of evaluation to rank the social desirability of competing policy options.

These policy evaluation methods are only useful if the axiomatic base upon which they

are built is valid and if the techniques used to execute analyses are consistent and replicable. The validity of the assumptions underlying positive welfare analysis and related evaluation techniques have, historically, been difficult to test, though experimental methods in psychology and economics have increasingly pointed to inconsistencies in the functioning of the black box of decision making. The issues explored in this review include how biomedical techniques might inform us concerning the efficacy of hypothetical approaches in assessing underlying preference structures, the coherency of individual preferences, and the stability of individual preferences.

New biomedical techniques allow researchers to look inside this black box and begin to articulate the physiological mechanisms that generate human decisions. While this provides another and, often, unparalleled way to test key tenets of neoclassical utility theory, these techniques are not a panacea, as peeking under the lid of the black box of decision making reveals a highly intricate and interconnected network of smaller black boxes, whose interconnections and individual roles are still being explored. Even as each individual component within the black box becomes clearer to us, there remains substantial work to interpret if these physiological mechanics confirm, overlap or contradict the assumptions upon which welfare theory is built. Furthermore, if contradictions exist, economists must fully assess if welfare analysis techniques can be adapted to yield meaningful positive insights.

While we are not the first to review the influence of emerging biomedical techniques on economics [12,74,102,117], our efforts enrich and refine past work on several fronts. First, we provide a more comprehensive review of biomedical techniques currently being utilized in interdisciplinary research, including techniques from molecular genetics and endocrinology that have received little or no treatment in reviews by economists. Second, we review the literature with an eye toward deriving implications for welfare analysis and analysis of environmental

policies in particular, while other reviews have focused more broadly on the implications of biomedical techniques for economics, finance and law [12,18,56,102,117].

I. Emerging Biomedical Methods

Through the development of technologies and methods that monitor the activity of the brain and body and assess the role of genetics in shaping behavior, the biomedical field has improved our understanding of the way the mind and body execute the decision making process. This section and Table 1 provides an overview of methods that may inform the work of social scientists.

I.A. Neural Monitoring Methods

The neuron is the basic communication unit within the brain. The billions of neurons in the human brain communicate with one another via an electrochemical process. Neurons receive electrochemical signals across small gaps called synapses from other neurons, and generate electrochemical current based upon this input. If these electrical currents, when added together, surpass a threshold, an action potential is generated, whereby current travels throughout the length of the neuron and causes the release of its own electrochemical signal (usually a chemical neurotransmitter like dopamine or serotonin) into adjacent synapses that reach other neurons.

These firings transmit information between connected neurons and facilitate all the brain's functions, including decision making. The challenge of monitoring neural activity is to develop techniques that accurately measure this activity. The ideal technique would allow for perfect spatial coverage (i.e., a maximal field of view to all parts of the brain) and spatial resolution (down to the individual neuron or even to specific neuron components). The ideal technique would also provide perfect temporal resolution, i.e., to the fraction of a millisecond of activity, as neuronal activity is rapid. The ideal measurement technique would also distinguish the various activities taking place in the brain, including blood flow, chemical flows

(neurotransmitter, hormones) and electrical firings. Furthermore, the ideal technology would allow the subject to move about freely and comfortably as they might in a ‘normal’ decision making context and, of course, not threaten the subject’s health or safety. In practice no technique meets all of these ideals and each method features a mix of benefits and limitations.

1.A.1. Functional Magnetic Resonance Imaging (fMRI)

This technology has become popular among neuroscientists and neuroeconomists because it provides a non-invasive¹ means for measuring brain activity. Unlike static MR images taken in clinical settings for, say, exploring structural deficits with a bad knee or exploring the extent of a brain lesion, functional MRI provides a dynamic view of brain activity.

Brain dynamics are captured by repeatedly imaging the brain during a subject’s exposure and response to experimental stimuli. fMRI does not directly measure neuronal firing rate; rather it measures a necessary correlate. In order to fire, neurons require energy, which is delivered via blood to the region that is firing. As the energy arrives the ratio of oxygenated and deoxygenated hemoglobin changes. The MRI scanner tracks the level of oxygenated blood at positions throughout the brain by using magnetic pulses that result in detectable MR signals sensitive to blood-oxygen level. This is translated into a measurement referred to as the blood-oxygenated level dependent (BOLD) signal. Further, the brain has little ability to store energy; hence, the magnetic changes due to changes in blood flow are interpreted as changes in neural activity. While neuronal firings change by the millisecond, the blood flow necessary to support such firings is not precisely correlated to the onset of neural firings. Though our understanding of this relationship between blood flow and neuronal firings is improving, it remains imperfect. The implication is that fMRI measurements may provide a noisy proxy to the level and timing of neuronal firings (see Gore [47] for a concise overview of fMRI principles).

Compared to many technologies, fMRI is desirable because it is non-invasive, provides good spatial resolution (down to several millimeters), good temporal resolution (once every few seconds), and good spatial coverage (all brain regions can be scanned). Health or safety risks are negligible and subjects are generally open to participation as many are familiar with MRI from personal experience or common knowledge. Subjects can receive sensory stimuli of nearly any type during scanning (audio, visual, touch, taste, smell) and can respond via touchpad response.

A limitation is that subjects must remain still during scanning; movements greater than several millimeters can mean that collected data are not reliable. This limits the use of fMRI by populations with limited ability to control movement (e.g., young children). Also some subjects become claustrophobic in the scanner while some obese patients may not be able to view visual stimuli in certain types of scanners. Numerous challenges also exist in assuring high quality scans, particularly for parts of the brain near open cavities (e.g., near the sinuses), but techniques are evolving rapidly to improve the consistency and resolution of these images.

1.A.2 Positron Emission Topography (PET) Scanning

Rather than measuring variations in the components of blood, as with fMRI, PET scanning utilizes radiological tracers (e.g., H_2O^{15} , water with a radioactive oxygen isotope) that the investigator adds into the subject's blood stream (usually intravenously though sometimes via inhalation). The scanner then measures the level of radioactive emission during the tracer's decay and uses this to develop a measurement of the regional cerebral blood flow (rCBF) at various locations throughout the brain (see [119] for an overview of PET principles).

PET scans produce images of blood flow for all brain structures with a slightly coarser degree of spatial resolution than fMRI. Moreover, the temporal resolution of PET is quite low, as the construction of these high quality images requires averaging rCBF over minutes of

scanning. This does not allow for dynamic analysis of neural activity as with fMRI and, hence, limits the topics of inquiry available with PET. Furthermore, like fMRI, it requires the subject to remain almost perfectly still during scanning. Another PET disadvantage is that subject recruitment is more difficult: people are not as familiar with PET and the mention of ‘needles’ and ‘low-level radiological injections’ often dampens the enthusiasm of recruits. Furthermore, because of the radioactive materials involved, certain subjects (e.g., children) are excluded from participation.

One key advantage of PET is that different radiological tracers adhere to different proteins and metabolites. For example, a tracer can be chosen that binds to a single neurotransmitter, such as dopamine, which is hypothesized to serve a key role in processing rewards in the brain. If the researcher is interested in the mechanics and dynamics of a particular neurotransmitter system, PET can provide a more accurate measurement than fMRI, though several other technologies (discussed below) can also image activity of key neurotransmitters.

1.A.3 Electroencephalography of Event-Related Potentials (EEG of ERP)

EEG measures electrical activity (event-related potential or ERP) originating from neuronal firings that emanate from the surface of the brain. Electrodes are placed at various spots on the scalp, and each electrode measures ERPs, which are the summation of electrical responses generated from nearby neurons in response to a stimulus (event) provided by the researcher.

Unlike fMRI and PET, EEG measures the electrical signal generated by neural activity directly (rather than some correlate such as blood flow), which results in temporal resolution to the millisecond. EEG is often less intimidating to potential subjects and affords them considerable freedom of movement, particularly compared to fMRI and PET scans. It is also relatively cheap and portable, allowing for more observations on the same budget and the potential to take the technology ‘on the road’ if needed. Together, these attributes allow

researchers to conduct larger studies that include a more diverse subject population. A key drawback is that ERPs generated by structures inside the brain's outer layer (cortex) cannot be measured. EEG can be used in tandem with fMRI or PET and provide localized temporal resolution unavailable from these other techniques (see [27] for an overview of EEG principles).

1.A.4 Magnetoencephalography (MEG)

In addition to electrical currents, an active neuron also generates a localized change in magnetic field, and MEG measures these changes. Unlike electrical current, which forms the basis of measurement for EEG, the location of magnetic field strength changes can be located more precisely, providing even greater spatial resolution of activity for cortical regions of the brain than EEG. Furthermore, because the magnetic field change in a neuron is an instantaneous byproduct of changes in electrical current, it provides similar temporal resolution to EEG [103].

MEG has limitations with respect to spatial coverage, including limited coverage for structures deep inside the brain and for neurons that fail to run parallel to the surface of the head. However, as with EEG, computational advances are continually improving MEG's spatial resolution. Like EEG, it is non-invasive, though mobility is difficult as the scanner is stationary, and subject movement during scanning reduces measurement quality. Unlike fMRI and PET, most scanners cover only the head and allow the subject to either lie down or sit up. MEG subjects will often undergo a structural MRI to provide a precise brain map upon which MEG output is superimposed. This lessens subject time in a MRI, but does not eliminate its use and requires budgeting for the use of two major pieces of biomedical equipment.

1.A.5 Single Photon Emission Computerized Tomography (SPECT)

As with PET scanning, SPECT uses radiological tracers to measure the flow of a biological material within the brain, where the nature of the radiological tracer determines whether the scan

will measure rCBF or neurotransmitter flow. Hence, SPECT and PET share many common advantages and disadvantages (see [114] for a SPECT overview). SPECT typically features tracers that decay more slowly than PET tracers, meaning SPECT's temporal resolution is even coarser than that for PET. PET also does a better job constructing images of deeper brain structures. However, because SPECT tracers decay more slowly, they can be manufactured at central locations and transported further distances than PET tracers. This minimizes on-site staff and instrumentation costs, and often makes SPECT easier and cheaper to implement than PET.

I.A.6 Functional Near-Infrared Spectroscopy (fNIR)

By exposing the scalp to particular wavelengths of light, fNIR can record the relative ratio of oxygenated and deoxygenated blood. This imaging modality shares features with both fMRI and EEG. Like fMRI the scanning measures blood rather than neuronal electrochemical activity directly. Hence, fNIR's temporal resolution is similar to that of fMRI. Like EEG all fNIR measurement takes place at the scalp (minimally intrusive) and allows for considerable subject mobility during measurement. The scalp-based measurement approach limits coverage to the cortical (outer) brain regions and provides challenges and limitation to spatial resolution for the cortical regions covered, which limits investigation from topics that are thought to involve deeper brain structures or require precise spatial resolution (see [36] for a fNIR overview).

I.A.7 Single Unit Neuronal Recording

This highly invasive technique involves inserting an ultra-thin electrode into the brain through a hole drilled in the skull. This technique is used only with animal subjects in experimental settings due to its invasive nature. Careful placement of the electrode, often guided with imaging or other guidance techniques, allows for the procedure to be non-fatal, though some minor brain tissue damage does occur during placement (see [43], pg. 106, for an overview). The electrode is

placed just outside the membrane of a single neuron and measures the electrochemical activity of a single neuron or a small cluster of neurons adjacent to the tip of the electrode. Specifically it records the exact time of a neuronal spike. This technique features the greatest degree of spatial resolution of all techniques considered here (another animal technique called patch-clamp recording measures electrochemical activity within the neuron, but it is not explored here).

Spatial coverage is limited, however, as information is collected for only a single neuron. Often researchers will reposition the electrode several times to measure several neurons of interest, while other researchers may use multiple electrodes simultaneously. Because the electrode is collecting information about the electrical activity of the neuron, single unit recording provides temporal resolution at the sub-millisecond level.

Economists may be hesitant to use animals in research that is meant to illuminate the human decision making process. Our brain structure and function are quite similar to those of mammals (particularly primates); many insights into human decision making can be gained from animal experimentation. While results can be informative and suggestive, they can rarely provide definitive insights into human decision making. Animal laboratories are associated with extensive maintenance and management issues of their own (think weekend feedings and angry protesters) and may present a barrier to economists without collaborators in such laboratories.

A related animal-only technique that mirrors the spatial coverage and resolution of single unit recording is called *cyclic voltammetry*. In this technique the electrode embedded in the animal's brain measures key neurotransmitters rather than electrical activity [99].

I.B. Neural Manipulation Methods

These techniques leverage differences in neural functioning that arises due to intentional or incidental manipulation of neural structure or function. These methods leverage known variation

in neural structure or functioning either within subject or between closely matched subjects to identify how differences affect decision making and other cognitive tasks. Furthermore, some manipulation techniques can be used in tandem with neural monitoring techniques to provide even greater insight into the neural basis of decision making and other brain function.

1.B.1 Lesion Studies

Lesion studies use human subjects that have suffered from naturally occurring brain lesions. A lesion usually eliminates permanently the activity of the neurons in a particular brain region. The lesion's location and extent is typically identified via imaging techniques or post-mortem surgery. Lesion subjects are matched with non-affected subjects on the basis of age, intelligence, gender and other potentially relevant characteristics. Both groups are then exposed to identical stimuli (e.g., play the same decision making game); responses are recorded and analyzed across groups. By systematically altering the stimuli and looking for differential responses between lesion patients and normals, investigators infer the role of the brain region containing the lesion.

Human lesion studies face several limitations. The number of lesion patients available is limited, leading to small sample problems. Furthermore, the location and extent of lesions across subjects may vary, which leads to difficulty in interpreting the results. Also, the amount of time between the onset of the lesion and the testing could be heterogeneous. Patients with long-standing lesions may display significant plasticity and develop alternative neural circuitry in response to the lesion while those with new lesions may have not. In addition, because the timing of the on-set of a lesion is not predictable, it is rare to have within subject data (pre- and post-lesion) available. Finally, access to such patients usually occurs within a clinical setting, which greatly increases the resource commitment necessary for the investigator and limits the number of settings and locations at which such research can be conducted.

However, lesion studies have revealed key tenants of human behavior and were particularly important in the pre-fMRI era for helping researchers determine the role of various brain regions in governing human behavior (see [25] for a non-technical introduction to executive brain function that relies on lesion studies). Even today, lesion studies lead to critical insights, such as Naqvi et al.'s [88] insight that life-long smokers who suffered stroke-related injury to the insula easily stopped smoking despite numerous pre-stroke attempts to quit.

In animal studies, brain lesions can be induced by removing portions of the brain or by exposing regions to electrical current or chemical solutions (see [43], pg. 111, for an overview). Compared to human lesion studies, the treatment group is more homogeneous and analyses can leverage within-subject data (pre- and post-lesion) for better testing. Chemically induced lesions are most common as the appropriate chemical choice can provide precise control over the extent of the lesion and the type of neuronal structure that is disabled. This includes the ability to destroy only the portion of cells that, for example, carry key neurotransmitters. These studies share many of the common limitations and obstacles of animal studies previously discussed.

1.B.2 Electrical Brain Stimulation (EBS)

Electrical stimulation studies essentially reverse the direction of electrical flow discussed in single unit recording. In single unit recording, an electrode is placed near a neuron to measure nearby electrical activity. EBS reverses the process with external electrical current emitted from the electrode tip to a point within the brain. EBS shares many of the advantages and disadvantages of single unit recording. It directly influences electrical activity in the region of interest and this region can be highly localized and implemented at a very fine time scale. It is a highly invasive technique that often requires imaging or other guidance techniques such to ensure correct electrode placement. Once installed in the brain and sufficient recovery time is

allowed, animals are able to move freely and exhibit little difference in base behavior. EBS led to some seminal insights into the neural basis of reward [94] as rats implanted with electrodes would forgo food and suffer great hardship to trigger stimulation in key neural regions.

1.B.3. Transcranial Magnetic Stimulation (TMS)

Like electrical brain stimulation, this technique focuses on altering the electrical activity of neurons. Unlike EBS, TMS is non-invasive and is used with humans. Experimenters attach a device to the subject's head that generates a magnetic field that alters the activity of nearby (cortical) neurons. While non-invasive and generally safe, most protocols require a medical doctor's presence due to the possibility of seizure. Subjects are mobile during the treatment than during MRI and PET scans. Compared to EBS, TMS provides coarser spatial resolution, allowing localization of the effect down to a region of a centimeter or two.

Unlike EBS, which clearly enhances increases electrical activity near the neurons of interest, the relationship between neural activity and TMS is still under investigation, with an initial consensus that low frequency TMS often retards neuronal firing compared to baseline while higher frequencies enhance the firing rate [98]. However, the relationship between TMS frequency and alterations in neuronal activity can be region specific [65]. Hence complementary use of fMRI is often suggested to validate the effect of the TMS treatment upon brain activity. Furthermore, the brain responds differently to altered TMS timing (number and length of TMS exposures) and intensity. The effects of TMS also dissipate rapidly (within minutes), meaning the window of opportunity for conducting behavioral tests of subjects is limited. Another limitation is that TMS is only useful for the outer (cortical) regions of the brain, whereas EBS and lesion interventions can affect deeper brain regions as well.

1.B.4. Pharmacological Manipulation

Many drugs affect how the brain functions and, hence, lend themselves for use in human and animal experimentation. Pharmacological interventions are particularly useful for examining the role of neurotransmitters as many drugs block the neural uptake of a specific neurotransmitter (antagonist) or maximize its presence and uptake into neurons (agonists). By treating subjects with a neurotransmitter antagonist or agonist, the role of that neurotransmitter during decision making can be explored. As drug treatments are temporary, experimental designs can generate both within-subject data points (pre-treatment, post-treatment and post-recovery) and between subjects data points. Furthermore, such manipulations can be used with brain imaging.

Implementing pharmacological interventions requires that investigators surpass even greater scrutiny with respect to subject care, particularly when administering controlled substances. While subject follow up is minimal after most fMRI studies, researchers must monitor and ensure that subjects have no adverse reactions to the drug used in the study. Furthermore, the investigator and laboratory are exposed to greater administrative and legal burdens because they may need to acquire, store and administer controlled substances. A further limitation of pharmacological manipulations is that there often have poor spatial resolution, as diffusion of a drug and its effects are difficult to control once ingested, injected or inhaled. Invasive animal techniques, such as microiontophoresis, do allow for the release of small amounts of a drug to a single point in the brain.

I.B.5. Dietary Manipulation

Manipulating a subject's diet can achieve also alter the presence of certain neurotransmitters like drug manipulations. Some neurotransmitters are synthesized using only a limited number of essential amino acids (e.g., serotonin is synthesized only from tryptophan). If these amino acids are absent from the diet, the body is unable to produce that neurotransmitter. This differs from

the effects caused by drug interventions in which the volume of neurotransmitter is unchanged but its level of uptake by neurons is controlled by the drug. In practice human or animal subjects are made to fast for a period (usually overnight for humans) after which randomly chosen subjects are fed meals lacking the amino acids necessary for the synthesis of the neurotransmitter of interest. All other subjects are fed a similar tasting meal with these amino acids. Both groups are exposed to the same experimental stimulus and responses recorded (this could also include neuroimaging or biofeedback measurements). Between group and within-subject analysis can reveal the role of the neurotransmitter's presence for the tasks at hand.

The key advantage of this method compared to drug studies is that the infrastructure and regulatory burden is minimized. The disadvantages of this method compared to drug studies several. It is difficult to ensure that all subjects have fasted for an equivalent time. Furthermore, fewer neurotransmitters can be studied via dietary than drug manipulation. Also, dietary methods can only ensure the depletion of a neurotransmitter while drugs can either promote or block its uptake by neurons (see [40] for a review of dietary tryptophan depletion studies).

I.C. Biological Monitoring and Manipulation

The body's receipt of stimuli induces not just neuronal activity, but also a related cascade of responses from the nervous and endocrine systems that impacts the entire body. The endocrine system, which is coordinated by the hypothalamus in the brain, secretes hormones that travel through blood and other fluids to cells throughout the body. For example, decision making scenarios might cause stress, which directs the hypothalamus to trigger actions in the endocrine and nervous systems. Stress-triggered feedback helps the body respond to stress, i.e., to survive the source of the stress, often via a fight or flight response.

Economic interactions often involve interpersonal contact (bargaining, exchange), which

can trigger hormonal secretions associated with the reaction to that contact (trust, aggression, attraction). Measurement of hormones can provide information about how stress and social interactions involved in decision making can affect biophysical response. The body synthesizes and circulates dozens of hormones, some of which also serve as neurotransmitters (e.g., oxytocin). *Epinephrine* and *norepinephrine* are hormones that rapidly deploy in response to fundamental threats and allow the body to respond quickly (greater blood flow and lung function). *Cortisol*, which is associated with stress, and *adrenocorticotrophic hormone*, which stimulates the release of cortisol, can be measured as well.

Outside of the arena of stress, the levels of several other hormones are influenced by interpersonal interaction. Higher levels of *oxytocin* are thought to reduce fight/flight tendencies and promote interpersonal bonding. Oxytocin, which is generated during birth in women and during sexual orgasm in both sexes, is believed to facilitate the trust and bonding necessary for success in such settings. Alternatively, *testosterone* levels are often correlated with aggressive behavior that undermines bonding and may influence social interactions during conflict, though the direction of causation between aggression and *testosterone* is still an open topic.

Cortisol levels can be accurately assayed from a subject's saliva, which allows for a non-invasive collection technique that few potential subjects find objectionable (see [72,83] for cortisol studies featuring gamblers). High quality measurement of many hormones, however, requires the collection of blood, which entails considerably more resources for collection (e.g., nurses) and may repel potential subjects. As in drug studies, hormone levels can be manipulated by introducing additional amounts of a hormone or a hormone blocker into a subject's body during an experiment. These methods share many of the same opportunities and challenges as drug studies. While most neurotransmitter drug treatments are administered orally, some

hormone manipulations involve nasal administration [70].

Hormone secretion and other responses coordinated by the hypothalamus through the central nervous system will result in measurable changes in body function. These include changes in heart function (measured via an electrocardiogram), respiration, blood pressure, pulse rate, pupil dilation, eye blink rate, skin conductance response and skin temperature. See Lo and Repin [77] for a study of securities traders' responses to events during the trading day.

I.D. Genetic Methods

Genes are the fundamental unit of heredity in all organisms. A gene is a unit of DNA that carries directions for synthesizing a specific protein or proteins. With the help of enzymes and mRNA, genes direct the synthesis of proteins. Proteins, in turn, are the building blocks for tissues and organs, and for the synthesis of hormones and neurotransmitters. If two individuals have different genes, i.e., differ in their *genotype*, they may differ in protein creation, in the systems that rely upon those proteins, in the functions those systems control, and, eventually, in observable traits or behavior (*phenotype*). Scientists have become increasingly interested in understanding how genotype may affect complex behavioral phenotypes, including personality differences, complex psychological conditions, and decision making tendencies.

Each DNA strand consists of four nucleotides bases – adenine (A), thymine (T), guanine (G) and cytosine (C) – that form a genetic alphabet. These bases physically form the iconic double helix. The order of these bases determines the gene's eventual function. A complete set of an organism's DNA is known as its genome, which carries all instructions needed to build and maintain the organism. The human genome has about 3 billion DNA base pairs organized into 20,000 – 25,000 genes on 23 chromosomes. Genetic variation across humans is small in one sense, i.e., two humans share about 99.9 percent of the same DNA base pairs in their genetic

map. Given there are 3 billion base pairs, however, this still allows for 3 million differences. These differences range from changes of a single base, referred to as a single nucleotide polymorphism (SNP) to more extensive changes involving multiple bases. These differences allow for significant variation across individuals. Understanding how genetic differences manifest presents significant analytical challenges. Further complicating the analysis is the fact that the impact of some genetic variation upon behavior does not manifest unless triggered by environmental triggers. Such findings have fundamentally altered the perennial ‘nature versus nurture’ debate – the two interact leaving nature versus nurture as a false dichotomy. In this section we review some of the approaches used in genetic studies of behavior.

1.D.1. Phenotype-Genotype Association Studies

Association studies correlate subjects’ phenotype and genotype. Phenotype can be assessed by surveys or responses during experiments, though most studies use medically defined phenotypes (a disease or disorder). Genotyping takes place via a suite of chemical techniques (see [73] for one overview). Genotyping involves identifying common variations in genes known to impact the production of proteins with a connection to a system of interest. For example, when the phenotype is depression, it is logical to look for variation in the gene that creates the protein necessary for transporting serotonin in the brain because many depression medications work because they alter the brain’s serotonin levels.

Several criteria are often applied for selecting the genetic variations subject to investigation. First, certain genotypes are chosen if previous research identified associations between that genotype and related phenotypes. Second, other genetic variations in the same gene may be also explored. Furthermore, it is common to focus on genetic variation that is common across a population rather than the rare variation because it is difficult to enroll enough subjects

with a rare variant. For more complex phenotypes, researchers will often cast a broader net and search for multiple variations in several genes. This leads to statistical difficulties, however, as adjustments necessary to account for multiple hypotheses testing often yield very low statistical power, even for large sample populations (see [2] for an overview of relevant statistical approaches and [20, 50] for a discussion of the limitations of association studies).

The cost of genetic testing is decreasing and can be handled by many commercial and academic laboratories. Subjects must provide an appropriate biological specimen to the experimenter for testing. This can consist of a skin sample (e.g., a swab from inside the cheek like on television police shows) or a blood sample, which requires medical staff support.

I.D.2. Endophenotype-Genotype Association Studies

Association studies are often criticized because the correlative results often provide weak statistical power and the results are often difficult to replicate. This is not surprising given that there are many ways in which underlying genetic differences can be ‘smoothed out’ prior to manifesting as an observable trait, behavior or disorder. That is, even if differential protein synthesis occurs, and it creates heterogeneous functioning of one system, other systems may compensate, thus preventing an observable difference. Furthermore, the phenotypic classification method, e.g., surveys, may miss any remaining differences. This has led to the development of studies that attempt to correlate genotype to *endophenotypes* [80]. These are differences in systems-level functioning, e.g., differences in neural activation or cortisol secretion. Such studies generally require smaller subject populations because additional sources of noise, i.e., going from the systems to organism level of observation, are removed.

I.D.3. Phenotype-Genotype Linkage Studies

Genetic association studies suffer from excessive genetic variation. That is, typically the

researcher chooses a single phenotype and attempts to correlate this variation with one or more genetic variations. However, even if the researcher searches for hundreds of candidate sources of genetic variation, there remain potentially millions of other sources of genetic heterogeneity that exist among the subject pool that are not controlled and that may affect phenotype. Genetic linkage studies use subject pools consisting of family members to reduce the degree of unwanted genetic variation across subjects (see [34] for an overview of linkage approaches and comparisons to association studies). The trick, of course, is to find family members that have enough variation in the phenotype and candidate genes of interest. Compared to simple association studies, linkage studies require fewer total subjects, though recruitment of those subjects becomes more difficult because multiple family members must be enrolled.

1.D.4. Genotype-Phenotype Associations Mitigated by Environmental Factors

The activity of genes need not be constant throughout life. While genes are commonly perceived as a genetic blueprint, the more accurate analogy is the gene as a switch. While some genes are turned on or off by internal triggers as part of an organism's developmental process, other genes may be triggered by environmental stressors. Several studies show how the relationship between genotype and a complex phenotype only holds for subjects exposed to such stressors [e.g., 17].

This has led researchers to emphasize the importance of measuring subjects' exposure to environmental influences that can influence gene expression (see [84] for an overview). For some phenotypes this often includes recording a subject's exposure to stressful life events. This encompasses several additional challenges as some subjects will not share information about certain stressful events (e.g., rape). Others may have difficulty recalling events that occurred during childhood, which is a particularly influential time for many environmental influences.

1.D.5. Whole Genome and Phenome Scans

With rapid technological advances, it is now possible to receive more comprehensive information concerning the sources of genetic variation across a subject pool rather than searching for variation across only a couple of well known polymorphisms. Hence, researchers can focus on identifying the phenotype of interest and then engage in a broad scale expedition to identify correlates within the genetic map. With billions of DNA base pairs and millions of sources of variation, this entails dramatic statistical hurdles, especially with regard to assessing statistical significance across multiple tests and allowing for simple and subtle interactions among sources of genetic variation. Statisticians are testing new pattern recognition algorithms and wielding theory to provide more efficient approaches for assessing power and significance for such wide-scale data mining (see [16] for a review of statistical challenges and [96] for an overview of genome-wide studies of complex behavioral traits).

One can also reverse the strategy and instead conduct a whole phenome scan [58]. A subject is exposed to as many phenotype classifications as possible. Subsequently the variation in one or more genes is then correlated against multiple phenotypic classifications. While this is the newest genetics-based methodology to be proposed, it is the one with the greatest potential involvement of social scientists. Such protocol may involve more subject time, as detailed knowledge of traits and behavior are required.

II. Biomedical Insights into the Human Decision Making Process

Life is a perpetual sequence of choices ranging from the mundane (should I push the snooze button?) to the monumental (do I marry this person, choose a particular cancer treatment?). Decision making is a multifaceted process involving sensory capture, information processing, and motor control. Possible actions must be defined; short- and long-term costs and benefits must be assigned to each action; a choice must be rendered and implemented; and the outcome

must be assessed and remembered. While seemingly manageable, this entire sequence of events must be executed as several other decisions are simultaneously deliberated, giving rise to demand for scarce biological and neural resources for executing each choice process.

In this section we overview an emerging vision of how decision making is executed in the brain, summarizing a rapidly growing body of research using animal and human methods previously outlined. This vision of the decision making process is fluid at this point in time, as new data rapidly gives rise to new models, which in turn stimulates additional experimentation.

II.A. A Bottom-Up View of Economic Decision Making: RUM in the LIP

One approach to understanding economic behavior from a neurological perspective is to focus on a very simple decision, e.g., choosing one option from a limited choice set akin to a random utility maximization (RUM) problem, and to fully articulate the neural circuitry engaged during decision making. Once a neurologically articulate understanding of the simple decision is gained, one can build from this foundation to understand more complex economic decisions.

Glimcher, Dorris and Bayer [46] review research that reveals how the monkey brain renders decisions in several simple economic contexts. Bottom-up researchers rely heavily upon animal models and have made great progress by studying non-human primates. The monkey brain is remarkably similar in structure and function to the human brain and allows for invasive techniques that provide localized measurement precision not obtainable with techniques used with humans. This leads to challenges in interpreting differences between animal and human results: do differences reflect basic deviations in neural structure and function or differences in the spatial and temporal delineation afforded by animal versus human measurement techniques?

These primate studies provide fascinating revelations about decision making by identifying and measuring key regions of neural circuitry that lead monkeys to ‘pull the trigger’

on simple RUM decisions. Studies of this ilk [30,49,75,95,104] use a monkey who is motivated by a primary need (thirst) to make decisions that alter the receipt of a salient reward (water or juice). Monkeys cast decisions by altering the focus of their vision, which is tracked by special equipment. For example, a monkey is trained to expect a reward after shifting its gaze from a central point to a stimulus presented on the left hand side of its visual field, while looking at a stimulus on the right-hand side may result in no reward.² The final part of these experiments is the installation of single-neuron recording devices (see section I) in the regions of interest.

What has emerged from these studies is a model of the neurobiological underpinnings of discrete choice (for a more detail, see [46] and figure 1). A region called the lateral intraparietal (LIP) area generates a map analogous to the visual stimulus viewed by the monkey, only that the neuronal firings at each spatial location on this map correspond to the relative expected value of the reward (relative expected milliliters of fluid) the monkey associates with that spot.

The neuronal firing levels do not correspond perfectly to the relative expected reward because there is a stochastic element to neuronal firings at each location that appears to be simple biophysical noise (i.e., randomness in firing rates). Furthermore the map may be a monotonic transformation of relative expected value, i.e., a relative expected utility, though more work is needed to distinguish if the observed curvature in these mappings is robust. Hence the LIP generates a normalized representation of a RUM model where relative expected utility plus noise are represented by neuronal firing rates. Note that the LIP encodes *relative* expected utility of rewards rather than absolute values. Experiments where the absolute reward levels are increased but the relative reward levels are maintained yield virtually identical mappings.

The information from the LIP map is passed to a region called the frontal eye fields (FEF) in a manner that maintains the map's spatial organization. The FEF, however, only gleans

whether the action potentials associated with a specific location surpass a certain biophysical threshold. After one location passes this threshold, the map is pruned of all other information and this location is passed to the superior colliculus, which triggers the ocular motor system to shift the animal's gaze to the location identified on the map.

These studies provide an intriguing physical analog for the quantities that enter a simple RUM model and detail the neurological mechanism that identifies the option to be chosen. Glimcher and colleagues go so far as to define these firing levels in the LIP as physiological expected utility. However, several questions remain, such as: Does this region serve the same function in humans? Do other regions first generate similar maps and send the information in tact to the LIP? Do other regions first encode absolute levels of expected utility and, if so, where and how does normalization occur? This leads us to review emerging work in human imaging that details how the brain senses and evaluate reward.

II.B The Neurological Basis of Reward

Several neural regions are regularly implicated by human studies of reward prediction and evaluation, including the ventral striatum (or putamen), nucleus accumbens (NAc), orbitofrontal cortex (OFC) and ventromedial prefrontal cortex (VMPFC, see figure 2). These regions, which Montague, King-Casas and Cohen [86] call the ventral valuation network (VVN), provide similar qualitative responses to many rewards, including food and drink [118], pleasant smells [93], pleasing sounds [8], money [10], the exacting of revenge [28], and luxury cars [35].

Each region has different sensitivities during the reward process, however. For example, activity in the VMPFC appears to scale with the absolute reward value [68,90] whereas the ventral striatum, NAc and OFC are particularly sensitive to the predictability and timing of rewards [6]. The OFC is thought to be a neural clearinghouse where relative expected utilities

are associated with potentially disparate options [85] for the purpose of comparison and action, which would lead it to take on a role similar to the LIP in monkeys (though such a consensus has not been reached among neuroscientists). Each of these areas is densely populated with dopamine neurons, and these neurons receive input from the ventral tegmental area (VTA) and the substantia nigra (SN), which serve as the origin for much of the brain's dopamine flows.

Dopamine plays a key communication role in the VVN. The release of dopamine makes the recipient feel good, which might be interpreted as the physiological basis for Benthamite hedonic utility or a 'rush' of pleasure. Indeed, many illegal drugs (e.g., cocaine and amphetamines) stop dopamine from being recaptured by neurons and heighten this euphoric rush (hence, the generic term 'dope').

Researchers initially thought that dopamine directly signaled reward, i.e., larger rewards released more dopamine. If this were the case, dopamine would become the physiological analog of utility, with more utility (dopamine) released as the level of goods and services increased. Subsequent research over the past decade revealed that this dopamine-reward correspondence is only partially correct and that the role of dopamine is more subtle. For example, Schultz, Dayan and Montague [107] measure the activity of dopamine releasing neurons in the VTA and SN of thirsty monkeys. During the experiment, thirsty monkeys would receive a signal (bell) which would then be followed by fruit juice. During initial trials, when the monkey was learning the link between signal and reward, the provision of the reward led to a dopamine spike (increased firing rate of dopamine releasing neurons) that sent dopamine to the NAc and ventral striatum. In this case the reward's receipt corresponded to a dopamine rush.

However, subsequent juice deliveries of the same volume resulted in smaller dopamine spikes, until dopamine levels observed during the receipt of the juice returned to a baseline level.

Dopamine levels would spike immediately following the cue, however, suggesting that the pleasure derived from consumption occurs in a reward's anticipation rather than in its receipt.³

On a subsequent trial, when the volume of juice was unexpectedly increased, dopamine levels spiked during the cue *and* immediately following receipt of the unexpectedly large reward. After several trials at this new, higher volume of juice, the post-reward dopamine levels dropped back to baseline. Finally, when juice deliveries were reduced to the original level, post-reward dopamine levels dropped below baseline. After several additional trials with the original juice delivery volumes, post-reward dopamine release levels returned to baseline.

These experiments led to several key insights. First dopamine release is synonymous with reward receipt only for short-term unexpected changes in reward. More generally dopamine encodes not the absolute value of a reward but rather its value *relative to what is expected*. In short, the most dopamine was delivered during unexpected rewards, while the dopamine from expected rewards quickly diminishes back to baseline.⁴ Second, in stable, predictable rewarding scenarios, dopamine spikes upon the receipt of reliable cues of subsequent rewards rather than upon the receipt of the reward itself. Schultz and colleagues postulate that this mechanism serves a crucial role in learning, where increased reward stimulates the pleasurable dopamine release while the diminution a particular reward stymies dopamine release. These insights led the authors develop the temporal difference (TD) model of reward learning:

$$\text{Dopamine neuron firing rate}_t = \varepsilon_t = \alpha(\text{Reward}_t - \varepsilon_{t-1}),$$

where ε_t is the reward prediction error in period t and $\alpha > 0$. In short the TD model simply states that satisfaction (dopamine release) with a given level of reward is transient, with any amount provided quickly leading to the same level of dopamine release. TD models are now a common cornerstone of many decision making models, and rightfully so as the results of human imaging

studies involving reward delivery regularly adhere these predictions [1,6,68,91,92]. One limitation of these experiments is the subject's inactive role, i.e., passively receiving signals and rewards. The focus of the model is learning, and learning is most critical in situations when the subject must guide subsequent actions toward greater rewards, which suggests that TD models may only be part of the reward processing picture.

When action is required to trigger reward delivery, different neural circuitry becomes involved and activity shifts to another striatal region (the dorsal striatum or caudate), which is connected to motor pathways that can trigger choice [33]. In such cases the temporal difference view of learning about reward becomes only one part of a larger system that assesses reward and motivates behavior. This has led to the development of 'critic-actor' models [101], in which one system evaluates possible rewards while another system acts upon the information.

Other neural structures that are intertwined with the VVN include the amygdala, anterior cingulate cortex (ACC), and dorsolateral prefrontal cortex (DLPFC). Each region has been implicated in different aspects of the decision process. The amygdala helps assess the value of emotive inputs, particularly aversive stimuli like fear [100], and passes relevant information to the NAc. The ACC is thought to help identify and evaluate errors made during the decision making process and to serve as a region in which conflicts between competing actions are deliberated. The DLPFC has been identified as an executive region necessary for goal maintenance and the inhibition of impulsive behavior.

Increasingly detailed neural processing models that articulate the roles of various neural substrates in each portion of the decision making process are now emerging. These models generate predictions that guide subsequent experiments. For example, Daw et al. [26] develops a model where TD learning executed by striatal dopamine neurons competes against more

statistically sophisticated learning models executed in frontal regions. For potentially rewarding actions involving more complex sensory inputs, the model predicts that the simpler TD model may be preferred, which can lead to habit formation, i.e., the same actions are repeated even after the value of the reward associated with a particular action is diminished. For events where the chain of causality from action to reward was more direct (and computation less costly), the more statistically sophisticated frontal learning system was used. Because these systems utilize more data, they respond rapidly to changes in the value of rewards, i.e., habit formation is less likely.

These models tap into a deeper theme in the psychology and cognitive neuroscience literature – that of multiple evaluative loops and decision systems [105]. This literature postulates that two general types of processing are undertaken within the brain. Autonomous processes are fast, cognitively efficient, and can be executed ‘in the background’ while other items process. Often these processes generate highly domain specific actions for common decisions that arise. Controlled processes are slower, more cognitively taxing and more likely to engage for novel circumstances. These contrasting systems may help organize the so-called exploit versus explore decision. That is, decision makers perpetually face a tension between exploiting a current rewarding situation and exploring other possibly rewarding situations. In noisy environments the fitness of the decision maker will be improved if it can identify and evaluate novel situations that might be worthy of exploration.

Such multi-loop neural models [19,26,52], which postulate evaluative loops with different strengths and weaknesses, have served as the neural basis for recent behavioral economic models that focus on self-control issues [3,39].⁵ Pathologies such as addiction appear to undermine the brain’s ability to allocate decisions to various evaluative loops and give rise to apparently sub-optimal choices, though the classification of these choices as sub-optimal is itself

a matter of discussion and contention among economists [3,4].

While the focus of this review and the literature centers on dopamine-based neural communication, there is also evidence that other neurotransmitters such as serotonin, acetylcholine, norepinephrine and oxytocin may play important roles in neural theories of choice. For example Yu and Dayan [116] formulate a model in which acetylcholine provides a signal of riskiness while norepinephrine provides a signal of uncertainty, i.e., spiking when the broader context of decision making begins to shift and prior probabilities of reward may be irrelevant. The role of these neurotransmitters may be to force the system to switch among the various evaluative loops, to rely upon sensory cues or to allow for greater memory formation in response to new information. McClure, Gilzenrat and Cohen [81] postulate that dopamine works with norepinephrine to help a multi-loop system effectively shift between exploitative and exploratory circuitry. Other neurotransmitters also play critical roles in the decision making process. For example, experiments with rats suggest that repression of serotonin can lead to decisions in which future rewards are discounted more heavily [29].⁶ Oxytocin is critical in processing stimuli involving a social dimension, particularly facilitating interpersonal decisions that require some degree of trust on the part of the decision maker [70].

III. Neoclassical Pillars Through the Lens of Biomedical Methods

Evolutionary pressures clearly shaped the human brain's current form and function. However, such pressures only drive selection to the point of ensuring production and survival of offspring, and not necessarily the execution of neoclassical utility maximization. In this section we review some provocative studies that cause us to reconsider several assumptions of neoclassical utility theory critical to the conduct of welfare analysis. Implications for decision modeling that arise from this selected review range from questions of validity of techniques for evaluating policies to

fundamental questions about the foundational assumptions of decision making, including preference coherence and stability. We begin with a set of questions that arise in applied policy analysis then move on to more fundamental questions about preferences themselves.

III.A. Differences between Rewards Expected and Rewards Received

Evaluation of new policy requires predictions of behavior beyond the scope of observability. In this section we explore two themes. First, can an individual's stated preferences, elicited in a hypothetical scenario, provide meaningful information upon which to evaluate policy? This issue holds a special place in the environmental economics literature as the use of contingent valuation has sparked a robust debate concerning the efficacy of methods in which individual responses hold no consequences, i.e., situations where the individual only engages in part of the decision making process (anticipation and decision) without experiencing any change in reward level. Second, for revealed preferences, does the hedonic representation of a possible consequence during evaluation systematically differ from the hedonic experience of reward? This section explores the basis for differences in anticipated versus experienced utility.

III.A.1 Hypothetical Bias and Consequentiality

The key question is this: can hypothetical responses reliably predict actual responses? Neural imaging can shed additional light on this question. If neural activation observed during a hypothetical question is indistinguishable from that during a binding question, one may feel more confident in the efficacy of hypothetical questions. Given our review of the process by which learning and action take place in the brain, one might imagine differences between hypothetical and consequential decisions, as critical parts of the neural process use dopamine to update expectations based upon previously received rewards.

While 'hypothetical bias' has not been explicitly addressed using biomedical techniques,

several studies may be informative. Knutson et al. [68] perform fMRI while subjects complete a task featuring a sequence of visual stimuli. Subjects see a colored square, then a cross-hairs, followed by the brief display (160 to 260 milliseconds) of a white square, during which subjects are to press a button.⁷ Subjects then learn if the button was pushed in time (outcome phase).

The researchers compared neural activation during two versions of this task. In one subjects receive one dollar if a button is pushed while the white square is displayed (rewarded trial); the reward is announced during the outcome phase. In the other version, subjects are asked to perform the same task even though they are aware that no financial reward is available (unrewarded). So, in one version the action has financial consequences, while in the other the consequence is only the resolution of curiosity (did I press the button in time?).

The difference in neural activation between rewarded and unrewarded trials was significant in several regions during both the anticipation and outcome phases of the trial. The differences during anticipation were particularly stark – statistically different levels of activation were observed in 14 regions across the VVN and other related structures, including the NAc, the dorsal and ventral striatum, the mesial prefrontal cortex, and the amygdala. The feedback phase produced differences in four regions, including the ventral striatum and the OFC. Elliot et al. [31] perform a study featuring a task similar to [68]. Their results provide similar qualitative results; neural activity in several regions is significantly different between rewarded and unrewarded trials including areas in the ventral striatum and amygdala.

The tasks from the above two studies are not a perfect analog to tasks presented during contingent valuation exercises. For example, a dichotomous choice valuation task requires significant cognitive effort to evaluate if the proposed scenario is preferred before the subject physically responds (marks the survey), while in the fMRI tasks the subject faces no real choice

(pressing the button is preferred to not pressing the button) and the focus is on executing the correct motor response. Despite the differences from valuation tasks, the fMRI results suggest that unrewarded tasks engender a different neural process than rewarded tasks.

Several modifications to the task to make it mirror common valuation tasks could provide a more direct test for potential differences in neural engagement engendered by hypothetical and consequential instruments and if various elicitation formats (open-ended versus discrete choice) affect the degree of differentiation in neural activity between hypothetical and consequential tasks. Note that the Knutson et al. [68] task also features some ‘cheap talk’ elements, which have proven fruitful in reducing hypothetical bias in experimental settings, where the subjects are asked to respond ‘as rapidly as possible’ during unrewarded tasks. It would be straight forward to alter an fMRI task to test the efficacy of cheap talk interventions.

Most fMRI tasks require a discrete choice while, to the best of the authors’ knowledge, no fMRI work has featured tasks in which open ended quantities are chosen by respondents. Our intuition is that open-ended responses more directly reflect raw utility estimates, which are thought to be generated in the NAc and ventral striatum. Hence, the vast differences observed in striatal and NAc activity between hypothetical and consequential formats may not bode well for calibrating open-ended responses. Discrete choice formats, on the other hand, require normalization of raw, option-specific utilities into relative utility terms. If the lack of reward salience uniformly shifts these raw physiological utility measurements, the ordinal information may still be retained, particularly if neural activation in the areas where this normalization process occurs (e.g., the OFC) is similar between hypothetical and consequential questions.

III.A.2 Anticipated versus Experienced Utility

To make a choice among alternatives, one must generate expectations, i.e., one must imagine and

anticipate the results of each option. The crucial question arises – is anticipation of a potential reward processed in a manner that is identical or consistent with the experience of receiving the reward? Several fMRI studies suggest that reward expectation is processed differently than is reward receipt, even if there is no uncertainty concerning reward provision. Many of these elements are obvious from the discussion of dopamine learning models in the previous section, where the dopamine flow associated with rewards shift from the time the reward is received to the time when a reward is expected (say, following a reliable cue). Human imaging research confirms that neural activation during reward expectation is distinct from reward receipt.

For example, Knutson et al. [68] find that different regions respond to the anticipation and experience of monetary rewards. Consistent with simple TD models of dopamine learning, they find the ventral striatum and NAc activate in a monotonic fashion with the size of the anticipated reward but do not respond to the receipt of the reward. Dissociated from this circuit is another circuit in the medial prefrontal cortex (MPFC), which is insensitive to anticipation of gains but showed increased BOLD signal when the subject is given the reward. Other studies also find a dissociation between regions processing reward anticipation and receipt (see [92] for a review) and point to several other regions often activated during anticipation (the amygdala and the orbitofrontal cortex, which also receive substantial inputs from the dopamine system).

In line with the TD models, one vision is that expectation itself rapidly diminishes the ability for the receipt of reward to activate these dopamine rich areas and instead moves the accounting for such reward receipts to regions that are unable to generate such euphoric rushes of dopamine. Hence, only unexpected rewards may activate dopamine releasing neurons. The very act of forming expectations and anticipating reward may, through rapid habituation, alter the region that processes the receipt of reward and open the door to a difference in neural

processing for reward anticipation and receipt. This is in line with recent theories [61] that formulate separate anticipated and experienced utility functions.

Holland and Gallagher [55] note that both the amygdala and OFC are engaged when the brain develops the expectations against which delivered rewards are compared and, hence, indirectly impact the dopaminergic flows following reward receipt. These authors note that it is the amygdala that dominates with regard to expectation formation in the early stages of learning about the link between cues and eventual rewards, with the OFC later codifying this link. When the environment changes, such that a cue is no longer linked to a reward, it is the amygdala that first signals this change. The OFC merely ‘unlearns’ the old relationship and waits for the amygdala to figure out the new relationship before codifying it. It is the codified association in the OFC, however, that guides most decision making. This region retains several sets of cue-reward links for rapid comparison purposes during the events leading up to a final decision.

This lack of unified neural processing between expectation and experience has fundamental consequences for welfare analysis. For example, if we believe in a hedonic utility measurement, and wish to use this as the basis for policy making, do we base this measurement on the utility expected or actually experienced (see [60] for a discussion of this very question and [59] for related discussion)? This goes beyond simple distinctions of stated versus revealed preferences, for often we pay for an item before using it. Indeed, it is often the expectation of utility that prompts expenditure, not the actual utility experienced at the point of consumption.

If there is systematic bias between the expectation and experience of reward such that people find choices suboptimal in hindsight, what is the role of policy? In some instances, such as addiction [3,4,5], this deviation between expected and experienced utility may become pathological, with consumers spending vast resources to try to override a system of consumption

where a cue (e.g., the sight of another person lighting a cigarette) triggers a vastly inflated expectation of utility that is never experienced. Research that documents such systematic differences between expected and experienced utility naturally leads the discussion to topics that are uncomfortable for some economists, such as the possible role of paternalistic policies [11].

III.B. Context Dependent Utility

A key assumption of utility theory is that the arguments of a utility function are measured in absolute terms, i.e., income or the quantity of goods. This is a seemingly innocuous assumption, particularly given the static nature of textbook examples of economic decision making. With the popularization of prospect theory, which posits that human judgment is influenced by outcomes relative to logical reference points such as initial endowments (gains versus losses), more recent work has further developed models that formalize reference-dependent utility theories [71,110].

Neoclassical utility functions are Spartan – the individual receives income, goods and services that neatly translate into a level of utility according to the given functional form. Behavioral economists are expanding utility functions to allow absolute rewards to be interpreted in context. This context can come from many sources, including the individual's: past reward (self referential, giving rise to distinct treatment of losses and gains and baseline effects), peers or other reference groups (peer referential, 'keeping up with the Jones'), unexplored alternatives (counterfactual referential, giving rise to 'what if' evaluations), and most likely outcomes (expectation referential, giving rise to unappreciated gains that fail to meet expectations).

The dopamine learning models pave the way for this context, as the expectation of reward can alter the brain regions that process its receipt. Breiter et al. [10] demonstrate how the context of an absolute reward is crucial to the nature of neural responses during reward receipt. Building from theoretical work by Mellers et al. [82], they hypothesize that the same absolute

reward (the receipt of no financial reward, \$0) will generate different neural responses when this reward is the best possible outcome (\$0, -\$1.50, -\$6) than when it is the worst (\$10, \$2.50, \$0). The authors find two regions – the NAc and sublenticular extended amygdala (a region near the NAc and amygdala) – reveal greater relative activation when receiving \$0 was the best outcome than when it was the worst. The authors suggest this is congruent with the subject treating \$0 as a gain in the former case and a loss in the latter case, though they caution that this interpretation may only hold for extreme cases because the results from a case in which the receipt of \$0 was a middling alternative did not result in an intermediate level of relative activation.

Coricelli et al. [24] also find that counterfactual information affects the neural processes involved in outcome evaluation as well as the neural processes engaged to cast subsequent decisions. In their fMRI task subjects observe a pair of gambles, choose the preferred gamble, see the preferred gamble's resolution and receive notification that their payment has been adjusted accordingly. In some trials subjects also observe the outcome of the unselected gamble, providing the subject with counterfactual data. They show that the revelation of counterfactual data, while not altering the subject's financial reward, does alter how the resolution of the selected gamble is processed by the brain and how brain activity adjusts in subsequent decisions. Specifically they show that the OFC is more active when counterfactual data is provided, with the level of OFC activation scaling linearly with the level of relief or regret. That is, OFC activity drops below baseline if the subject's choice turns out better than the unselected gamble (relief) and rises above baseline if the unselected gamble turns out better than the selected gamble (regret). The ACC and hippocampus reveal similar sensitivities to counterfactual data.

When subjects suffer a 'regretful' outcome in a particular trial, it influences neural activity during the subsequent decision. During the choice following a regretful outcome,

several additional regions display activity including the DLPFC, which is implicated in behavior necessary to control impulsive choices. As more regretful outcomes are accumulated, the OFC becomes increasingly active as does the amygdala, which is known to communicate the emotional valence of stimuli. Ursu and Carter [112] and Windmann et al. [115] find similar evidence concerning the role of such context during reward processing and decision making.

These findings provide a neurological basis for the expanding volume of work on framing effects. It creates some difficult questions for posing hypothetical questions that might be used to evaluate policy alternatives, as a particular frame must be chosen, and for interpreting the relevance of revealed preference data if the past decisions leading to the collected data were cast in a frame that might differ from future circumstances.

III.C. Malleable Preferences

Economics has primarily treated preferences as complete, fixed and static. In the words of Hobbes [54, pg. 100], “...consider men as if but even now sprung out of the earth, and suddenly (like mushrooms), come to full maturity, without any kind of engagement with each other.” This assumption provides great convenience for welfare analyses, as there exists a stable set of sovereign preferences against which gains and losses can consistently be measured. Any proposed policy changes will yield predictable surplus changes that can be used to assess the desirability of the proposed change and rank competing proposals. If policy alternatives were to purposefully shift preferences, however, the basis for neoclassical welfare analysis becomes murky. In this section we review several studies that explore how policy may shape preferences.

III.C.1. The Role of Advertising and Promotion

Persuasive communication lies at the heart of many strategic initiatives in the private and public sectors. While some initiatives strictly inform people of available options so that choices better

reflect current preferences, many initiatives persuade individuals to alter their preferences. Branding is a prime example of persuasive campaigns. Brands are key elements of many business plans, and through promotional campaigns, brand imagery has pervaded our culture.

McClure et al. [81] explore the role of brands in the processing of primary rewards. In their famous reworking of the “Pepsi Challenge” the authors gather fMRI images as subjects taste Pepsi and Coke. In some scans, subjects were not informed which brand was being delivered (blind), while in other scans the delivery of one cola was always preceded by the presentation of the brand’s logo (branded). During blind taste tests outside of the scanner, subjects’ choices between Coke and Pepsi were equally split and were not significantly correlated with previously stated brand preferences. However, the brand chosen in the blind taste test did generate a larger BOLD signal in the VMPFC during fMRI scanning. The VMPFC is a region known for registering gustatory rewards. The two colas engendered no differences in activity in other brain regions so long as the scanned subjects were blind to the brand identity.

Once brands were identified, several interesting results emerge. In a standard (non-scanning) taste test, subjects systematically prefer Coke to an unlabeled alternative, which subjects were told could be either Pepsi or Coke, but was always Coke. However, when the same taste test was given for Pepsi, subjects did not systematically prefer Pepsi to an unlabeled alternative, where subjects were also told the alternative was either Coke or Pepsi but, in reality, was always Pepsi. Hence, the subject pool regularly preferred labeled Coke to unlabeled Coke, but were essentially indifferent between labeled and unlabeled Pepsi.⁸

When these taste tests were repeated during scanning, the differences in BOLD response between the labeled and unlabeled cola produced no difference in the VMPFC. That is, neural response in the VMPFC was the same whether labeled or unlabeled cola was delivered. This is

not surprising given there was no change in the chemical composition of the liquid delivered. However, statistically significant differences in BOLD response for labeled and unlabeled Coke (but not Pepsi) were observed in other brain regions. Specifically, several locations in the hippocampus and one region in the DLPFC recorded greater activation for the branded than the unbranded Coke. Both regions have been previously associated with emotion-related behavioral change. The hippocampus has also been implicated in the recall of emotion-based memories.

We interpret these results as a preference shift. The neural evaluative process and subsequent choice of product were clearly altered by branding. It would appear that Coke's branding efforts were effective in altering the manner in which a simple appetitive reward was processed by the brain, at least for the subjects involved in this study. When brand information was absent, subjects generated neural responses in one region (VMPFC) that correlated with brand-blinded choices, while the revelation of Coke's brand image activated a separate circuit in a manner consistent with actual choice. This finding spawns many questions. What are the neural mechanisms that integrate the additional input from the hippocampus and DLPFC with the unchanged input from the VMPFC to change the preference ordering between the two brands? Are there other manifestations of preference change that lead to different neural patterns? For example, could commercial communications lead to a change in VMPFC activity? This finding also spawns some fundamental questions concerning welfare analysis, which we articulate and discuss at the close of this section.

III.C.2. Genetics, Environmental Factors, and Preference Change

The human genome project and its concomitant technical improvements in assaying individual genetic differences have created an explosion of studies focused on linking genotypes to higher-order phenotypes such as personality types and behavioral disorders. For example, several

promising studies have linked polymorphisms in genes known to affect the functioning of key neurotransmitters to psychometrically defined personality dimensions related to risk aversion, e.g., Bjork et al. [7] correlate a serotonin polymorphism with heterogeneity in impulse control. Other examples include work by David E. Comings and several sets of colleagues who correlate polymorphisms in genes associated with several neurotransmitters with: pathological gambling [23]; several dimensions of personality [22]; and several complex behavioral disorders [21]. While Comings and others (see [87] for a review) have suggested some intriguing linkages between genes and behavior with import for economic behavior, this literature has been marked by inconsistent results, with many initial findings failing to be replicated [87].

This led researchers to investigate if the lack of replication was due, in part, to a failure to control for environmental factors affecting gene expression. While the concept of environmentally mitigated genetic impacts on phenotype is not new [76], the number of studies that test for gene-environment interactions has only recently increased. A seminal gene-environment study by Caspi et al. [17] analyzes genetic correlation between a polymorphism in genes affecting serotonin function and recent episodes of depression for a large cohort of subjects. Depression, while a clinically defined medical disorder, can also be thought of as a shift in preferences for a wide array of consumption goods and leisure, as a subject's neurological response to basic rewards is strongly affected. For example the Rand Corporation [97] estimates that employers lose more than \$51 billion per year due to employee depression.

Caspi and colleagues found an increased likelihood of a major depressive episode after enduring one or more major life stressors (related to employment, financial, housing, health or relationship issues) during the past five years for the 69 percent of subjects with one genetic variant. The other subjects revealed no relationship between major life events and depression.

This path-breaking study is important for several reasons. First, it documents how elements of the macroeconomic situation can impact individual preferences. Unemployment and financial stressors, which are potentially tied to the aggregate economic situation, can lead to outcomes such as depression that can shift preferences and impact the supply and effectiveness of labor. One can see how economic depressions received this moniker and postulate feedback mechanisms that may recast the modeling of business cycle dynamics.

The Caspi et al. [17] study has inspired a growing number of replication studies [44,48,64] and related studies that test for environmentally mitigated correlations between genetics and other behavioral and personality outcomes (conduct disorder, [37]; behavioral inhibition, [38]; childhood depression, [62]; novelty seeking, [63]).⁹ These studies suggest that potentially large segments of the population are genetically predisposed to preference shifts that may be triggered by the outcomes of the policy process.

III.C.3. Therapeutic Methods of Changing Preferences

The multi-loop decision-making models discussed in section II.B posit competition between striatal and frontal brain regions where striatal circuits use dopamine to quickly code rewards relative to expectations while the frontal regions integrate information from striatal and other regions, and may engage in more sophisticated evaluation. Therapeutic interventions, such as drugs or physical stimulation, could affect the relative output of certain neural regions or tip the balance of inputs during decision making in a manner that alters subsequent choice.

Knoch et al. [66] use TMS to reveal one tantalizing example of such an intervention. The investigators had three groups play a simple game in which the subject chooses between a pair of gambles where one gamble involves a higher reward with lower probability of winning. Prior to playing the game, one group receives low-frequency TMS to the right DLPFC, one group

receives the same treatment to the left DLPFC, while the third group receives a placebo treatment over the right DLPFC. Subjects receiving TMS over the right DLPFC, which is densely connected and co-activates with the adjacent areas in the orbitofrontal cortex (OFC), choose riskier options with greater frequency than the other two groups. Thus, it would appear that TMS, when applied to the right DLPFC, can shift risk preferences temporarily.

The right region of the OFC has been implicated in the control of impulsive behavior [42]. It opens the door to understanding how manipulation of this region could alter decision making behavior. The authors speculate that alternative TMS frequencies may lead to alternative neuronal firing patterns and, hence, alternative behavioral responses, and cite evidence from previous work that correlates TMS frequency with a spectrum of behavioral responses [65].

While Knoch et al. [66] report increased risk taking due to TMS, others have identified interventions that cause the opposite affect. Rahman et al. (2006) work with subjects that have a type of dementia known to affect the OFC, which causes them to take more risky decisions than age-matched healthy controls. The investigators find that the administration of Ritalin (methylphenidate) reduced the tendency of the dementia patients to take risky bets. Ritalin consumption has been shown to increase neural dopamine flows, which is important for reward error signaling and learning that requires feedback between frontal and striatal brain regions.

Risk-taking behavior is not the only arena in which preferences can be altered via therapeutic manipulations. Knoch et al. [67] replicate the experimental design from [66] only they replace the game involving gambles with an ultimatum game. The ultimatum game involves a first-mover, who proposes a division of a fixed amount of money, and a second mover, who can accept or reject the first mover's proposal. Acceptance leads to distribution of the money according to the first-movers offer, while rejection leads to no payment for either

party. The neoclassically rational response by the second mover is to accept any non-negative offer, though a broad range of experimental data suggests that offers distributing less than 25 percent of the money to the second mover are regularly rejected.

Knoch et al. [67] apply TMS to the second mover prior to the accept/reject decision. Furthermore, in half the trials, the first mover's offer is the choice of a human first mover, while for the remaining trials the offer is randomly generated by a computer. In each case the second mover knows whether a human or a computer made the offer. This design element allows the investigators to determine whether the second-mover's response is motivated by interpersonal considerations or by a mere concern of payment equity.

As in [66] TMS to the right DLPFC evoked significantly different choices, with this group being more likely to accept the smallest, 'least fair' offers and to spend less time contemplating unfair offers. Interestingly, all groups rated the fairness of such offers equally, suggesting that while beliefs about the fairness of such offers were not different across the treatment groups, the propensity to reject unfair offers was affected. Furthermore, the three groups were no different in their propensity to reject the same offer if it were generated by a computer. This solidifies that the interpretation that manipulating the right DLPFC via TMS affects how the subjects process the interpersonal emotive content of the offer. The investigators suggest that the disruption in the right DLPFC hinders integration of information from areas of the brain that generate input concerning the emotional, interpersonal aspects of the situation, which allows pure self interest to then dominate the decision making process, though further investigation will be needed to solidify such an interpretation.

Kosfeld et al. [70] also manipulate preferences in social economic exchange through the nasal administration of a key neurotransmitter, oxytocin.¹⁰ Prior to participating in a trust game

or in a risky investment game, subjects are nasally administered either oxytocin or a placebo. The trust game involves a first mover (investor) and a randomly-matched second mover (trustee), who each receives identical monetary endowments. The investor may send to the trustee some portion of the endowment, which is tripled by the experimenter before being given to the trustee; both parties know that transferred funds are tripled. After receiving the transfer, the trustee may send any portion of the accumulated funds back to the investor, though there is no multiplication of this ‘back-transfer.’ The investor faces a risk if he transfers funds because the trustee may behave selfishly and return nothing to the investor.

The risk game played by the remaining subjects was constructed such that the subject faced the same opportunity to transfer money from an endowment into a risky investment, where the odds of losing the investment or receiving a payout mirrored the investor’s probabilities and payments in the trust game. However, whether an investment resulted in a return or a loss was driven by a non-human random process. Hence, the investigators could disentangle whether oxytocin may have affected the subject’s tolerance for any risk or only interpersonal risk.

The authors find that investors receiving oxytocin transferred significantly more to the trustee than did the placebo group, though the oxytocin and placebo groups invested the same in the generic risky investment. This suggests that oxytocin shifted interpersonal risk aversion (Bohnet and Zeckhauser [9] call this betrayal aversion). Aside from its functional importance during child birth and nursing, oxytocin receptors are located in brain regions associated with social behavior, including those regularly engaged during the formation of normal social attachments and affiliations. Given these results, it appears that the ability to trust others in economic exchange may be counted as a context in which oxytocin plays a role.

III.C.4. Malleable Preferences and Welfare Analysis

The findings in the previous three subsections spawn some intriguing questions concerning policy analysis. Focusing particularly on the McClure et al. [81] study in which brand revelation produced alterations in choice and neural processing, let us conduct a simple thought experiment. Assume a world where every person has an unlimited supply of generic cola that is freely supplied by government. There are no competing colas or other close substitutes. Each person consumes the maximum feasible amount of cola and the cola that goes unused is freely disposed. Each person is fully familiar with its taste and its nutritional properties. Furthermore, everyone knows that there are no long-term benefits or costs associated with its consumption and there are no short-term productivity boosts associated with its consumption (assume it is caffeine free).

Now consider a proposal that spends a billion dollars to create a logo and expansive advertising campaign for this cola, complete with toe-tapping jingles and commercials that associate drinking the cola with attractive people. No person will drink more cola because of this – everyone is already drinking as much as is possible. How would a traditional cost-benefit analysis rate such a policy? The math is straightforward – the policy creates \$1 billion in costs and yields no benefits. However, if the promotional campaign is as effective as the Coke campaigns were for the subjects in [81], it is clear that some type of surplus is being created.

This hypothetical policy proposal is particularly troubling because it specifically seeks to alter preferences. By the assumptions of neoclassical theory, preferences are stable, hence any policy aimed at changing them would be ineffective. If consumers merely lacked information concerning product attributes and that information was costly, the problem would be tractable by neoclassical standards, as there exists latent surplus that is created when information is provided that allows uninformed consumers to fully assess products against fixed preferences and alter decisions accordingly. However, in our example, we assume consumers are fully informed.

Governments engage in programs aimed to influence public opinion and preference, though it is unclear how such programs would be evaluated in a neoclassical cost-benefit paradigm. Surely the loss experienced by a population from, say, restricting the availability of a particular good (e.g., beach access) will be lessened if accompanied by campaigns that reduce the preference for these goods. The question becomes whether there exists a coherent approach to evaluation that ranks potential policies given that policies try to change preferences.

Sugden [111] proposes that, when preferences are incoherent, e.g., different decision frames could lead to different policy conclusions, the analyst should rely upon the results generated from data created by the decision frame that will manifest during the long-run implementation of the policy. While not arguing with this logic, such a recommendation may not be desirable if preference change itself is one of the policies under consideration.

Let us return to our generic cola example. Suppose the government considers ending its provision of generic cola and banning its use. It estimates that the lost surplus associated with a ban is \$1 billion per year while cola provision costs \$800 million. Clearly the ban would not pass a cost-benefit test. Now suppose the government conducts a \$250 million aversion campaign that causes people to dislike cola and drives the surplus lost from a ban to \$100 million. The \$250 million for the aversion campaign plus the \$100 million in lost surplus are now less than the \$800 million spent delivering cola. While an outright ban of the cola could not pass a cost benefit test, a ban coupled with an aversion campaign can if the value of consumer surplus is measured at the post-implementation position.

IV. The Future of Environmental Policy Analysis

While still in its infancy, at least in the study of economic decision making, the use of biomedical technologies has irrevocably and perhaps irreparably shaken the foundations of

positive welfare analysis. The early stages of our understanding of the decision process as viewed through the lens of neurologists prevent us from making decisive conclusions about the future of environmental policy analysis. Rather this discussion should be viewed as a wake-up call for environmental decision makers and analysts. In light of the future transparency (or at least translucency) of the decision process afforded by ever improving technologies, fundamental questions arise about the future of welfare analysis as a tool for policy decisions.

It is our view that we approach a three-pronged fork in the road. The first path ignores the growing set of biomedical results on decision processes (of which only a fraction are described herein) and stubbornly maintains the current course. In other words, the neoclassical model is correct and welfare analysis based on the neoclassical decision model is not only defensible but correct. Such a path is attractive, though potentially unfulfilling and dangerous. In its simplest form, neoclassical policy analysis is an outcome based approach. Early modelers could not view the intricate details of the decision process. Rather they relied on what people said and did. Observed behavior was then used to derive models of decision making consistent with observed outcomes. These reduced-form decision-making models provide the foundation for prediction and evaluation of new policies that are beyond the scope of observable behavior.

Technological restrictions prevented an in-depth understanding of the actual decision process leading to observed behaviors and in the end leaves us with an analytical framework based on how we think people make decisions. This is not to criticize the neoclassical foundations of policy analysis, but rather to appeal for a broader understanding of the decision process now that technology allows it. Once we accept the need for a broader understanding of decision making with foundations in modern decision science, we are left with a choice between two equally challenging paths of future research.

One path abandons and reinvents neoclassical decision theory. Researchers may think: If neurological findings reject the basic assumptions of neoclassical preference theory, then neurological preference theory is invalid and all techniques based on such assumptions are invalid. The implications of such thinking are troubling. Rejection of neoclassical decision theory means either developing new schools of thought for decision modeling, or abandoning the pretense of behavioral modeling in favor of process based approaches to policy design. While philosophically defensible, we feel this is overly pessimistic. Adherents to such thinking will make reference to strict interpretation of the scientific method: If the underlying assumptions are proven invalid, the entire theory and all consequent testable hypotheses must be rejected.

The final path continues to extend neoclassic thinking to accommodate bumps in the road. While more optimistic in its outlook, such a path still presents a daunting task. The first steps down this path are underway. Within the broad scope of neoclassical preferences, teams of interdisciplinary researchers have begun to provide a rich set of models for thinking about the complex decision processes being uncovered. Although these models are at times simplistic, at times case specific and, as of yet, do not yield universal frameworks for policy analysis, the extension of existing models for welfare analysis keeps the focus on the evaluation of potential outcomes. We view Bernheim and Rangel's neurologically inspired models of addiction and subsequent analysis of policy options [3,4,5] to be exemplars of such an approach.

In contrast to Robert Frost's two roads diverging, the three possible future paths for environmental policy analysis are not equally attractive in foresight—although in hindsight, the path chosen may indeed make all the difference. While we, as a discipline, are not in a position to determine the correct path just yet, the rapidly accelerating volume of results flowing from the biomedical-social science interface will soon force us to choose a path.

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Notes

¹ By non-invasive, we mean the surface of the subject need never be punctured.

² The eye-gaze choice mechanism is preferred because the motor system driving eye movements is independent of the more general motor system and vastly simpler to understand and track.

³ In the words of Arthur Schopenhauer, “A man’s delight in looking forward to and hoping for some particular satisfaction is a part of the pleasure flowing out of it, enjoyed in advance.”

⁴ Congruent with Carl Sandburg’s insight, “Nearly all the best things that come to me in life have been unexpected, unplanned by me.”

⁵ However, as Glimcher, Dorris and Bayer [46] caution, it is not accurate to depict the human decision making process as involving distinct, independent systems where the more rapid and simplistic evaluation loops are labeled as ‘primitive,’ ‘irrational,’ or ‘emotive’ because there is ample interaction among the systems.

⁶ However, progress in more precisely refining the role of serotonin in theories of choice has been hindered because, unlike for dopamine, the measurement of serotonin neuron activity faces greater technical difficulties [26].

⁷ Highly motivated and trained subjects do not always press the button in time, particularly for the shortest display lengths of the white square.

⁸ This finding essentially reverses the “Pepsi, no Coke” stance emphatically maintained by Pete Dionasopolis (John Belushi), the owner/operator of the Olympia Café (Saturday Night Live, circa 1977).

⁹ One issue that is still unclear is whether such interactions are relevant for all age groups or only younger age groups, as most of the studies revealing significant interactions use subjects under the age of 30. In fact, a replication of the Caspi et al. [17] study involving older subjects revealed no significant interaction between the genetic and environmental aspects of depression [44]. This may suggest a greater influence of stressful life events on the behavioral outcomes of younger populations, though more research is needed to solidify such a conclusion.

¹⁰ Oxytocin is also commonly referred to as a neuropeptide, which is a class of neurotransmitters.

Figure 1. Flow of neural processing for a discrete choice task as executed by a monkey.
 Adapted from Glimcher, Dorris and Bayer (2005)

Figure 2. Side (sagittal) view of a brain cross section detailing key regions of interest in many reward-related studies. Inset picture: front (coronal) cross section of two key regions of the striatum, dorsal (caudate) and ventral (putamen). Source: Camerer, Loewenstein and Prelec (2004)

Table 1. Summary of Neural Monitoring and Manipulation Methods

Method	Maximum Spatial Resolution	Maximum Temporal Resolution	Limitations
Functional Magnetic Resonance Imaging (fMRI)	Mm	second	(a) Quality images difficult to obtain near cavities (b) measures blood response (c) restricts subject movement
Positron Emission Topography (PET)	several mm	minutes	(a) measures blood response (b) restricts subject movement
Electroencephalography of Event-related Potentials (EEG of ERP)	several cm	millisecond	(a) no coverage of interior brain structures
Magnetoencephalography (MEG)	Cm	millisecond	(a) no coverage of interior brain structures (b) restricts subject movement
Single Photon Emission Computerized Tomography (SPECT)	Cm	minutes	(a) measures neurotransmitter response (b) restricts subject movement
Functional Near-Infrared Spectroscopy (fNIR)	several cm	second	(a) measures blood response (b) no coverage of interior brain structures
Single Unit Neuronal Recording	several μm	millisecond	(a) animals only (b) only collects information at several sites
Cyclic Voltammetry	several μm	second	(a) animals only (b) only collects information at several sites
Human lesion studies	Cm	years	(a) no experimenter control
Animal lesion studies	several mm	days	(a) animals only
Drug manipulations	Cm	hours	
Dietary manipulations	several cm	hours	(a) Can only diminish level of a neurotransmitter
Electrical Brain Stimulation (EBS)	several μm	millisecond	(a) animals only (b) stimulates activity at only a few sites
Transcranial Magnetic Stimulation (TMS)	several cm	minutes	(a) no coverage of interior brain structures