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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

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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.

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

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 (1925) 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 of that economic behavior arose from a complex decision making process, subsequent generations of economists were driven away from process-oriented models of economic choice because, in the words of Jevons (1871), 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 (Camerer 1995, Starmer 2000, Camerer, Loewenstein and Rabin 2004).

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 2005 for a recent review). With regard to genetics, the human genome project and related work is producing an ever-expanding set of techniques and knowledge that allow us to identify subtle genetic roles in shaping complex human behavior (Leonardo and Hen 2006). Finally, methods from endocrinology allow for the measurement of biomarkers of neurological activity that subsequently affect immune function and health outcomes (Glaser et al. 1999). These emerging 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 we explore in this review include is 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. This provides a substantial improvement in our ability to test key tenets of neoclassical utility theory. While an improvement, 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 to policy makers.

While we are not the first to review the influence of emerging biomedical techniques on economics (see reviews by Zak 2004; Camerer, Loewenstein and Prelec 2005; Lee 2006; and Sanfey et al. 2006), 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 other reviews. Second, we review the literature with an eye toward deriving implications for positive welfare analysis and analysis of environmental policies in particular, while other reviews have focused more broadly on the implications of biomedical techniques for other social

sciences (e.g., law, Chorvat and McCabe 2004) or other economic fields (financial regulations, Huang 2006).

The article is composed of several sections. We begin with a detailed overview of the various biomedical methods that have or may be used by economists and other social scientists to better understand the economic decision making process. The following section introduces an overview of research that utilizes biomedical methods to illuminate fundamental aspects of the decision making process. The final section summarizes evidence from this literature concerning the basic tenants of neoclassical utility that are often invoked for positive welfare analysis. We conclude by raising questions about the future path of policy related research and the role biomedical technologies will play in defining that path.

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 great improved our understanding of the way the human mind and body operates to support and execute the decision making process. This section provides an overview of established and emerging 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 allow for the transmission of information between connected neurons and facilitate all the functions for which the brain is responsible, including decision making. The challenge of monitoring neural activity is to develop techniques and equipment that allow for accurate measurement of this activity. The ideal measurement 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 portions within the neuron). The ideal measurement 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 types of activity taking place in the brain, including blood flow, various chemical flows (neurotransmitter, hormonal) and electrical firings. Furthermore, the ideal measurement technology would allow the subject to move about freely as they might in a 'normal' decision making context and, of course, not threaten the subject's health, safety or comfort. In practice no

monitoring technique meets all of these ideals and each method features its own mix of benefits and limitations.

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

This technology has become popular among neuroscientists and neuroeconomists because it provides a non-invasive[1] means for measuring the activity of the alert brain. Unlike the static (non-functional) 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 the course of 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 is affected. The MRI scanner tracks the level of oxygenated blood at a number of positions throughout the brain by using magnetic pulses that result in detectable MRI 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 occur at the temporal resolution of a 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 the measurements generated by fMRI may provide a noisy proxy to the level and timing of neuronal firings (see Gore 2003 for a concise overview of fMRI principles).

Compared to many technologies, fMRI is desirable because it is non-invasive and 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 the technology either from personal experience or common knowledge. Subjects can receive sensory stimuli of nearly any type during scanning (audio, visual, touch, taste and smell) and can respond via limited touchpad response.

One limitation is that subjects must remain still for the duration of the 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 (certain diseases or 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] By non-invasive, we mean the surface of the subject need never be punctured.

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

Rather than measuring variations in the components of blood, like is the case 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 Zanzonico 2004 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 like that available with fMRI and, hence, limits the topics of inquiry available with PET. Furthermore, like fMRI, it requires the subject to remain almost perfectly still for the duration of scanning. An additional disadvantage of PET is that subject recruitment is more difficult: people are not as familiar with PET from clinical settings and the mention of 'needles' and 'low-level radiological injections' dampens the enthusiasm of many general population recruits. Furthermore, because of the radioactive materials involved, certain subject populations such as 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 scanning can provide a more accurate measurement of this system than fMRI, though several other technologies (discussed below) can also image activity of key neurotransmitters.

I.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. The technology features numerous electrodes that are placed at various positions on the scalp. 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 other physiological correlate such as blood. This results in tremendous temporal resolution, with the ability to trace electrical activity to the millisecond. Another advantage of EEG is that it is relatively non-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.

The chief drawback of the EEG is that it cannot measure ERPs generated by structures inside the brain's outer layer (cortex). Luckily, EEG can be used in tandem with fMRI or PET and provide localized temporal resolution unavailable from these other techniques (see de Haan and Thomas 2002 for an overview of EEG principles and its complementary use with fMRI).

I.A.4 Magnetoencephalography (MEG)

In addition to electrical currents, an active neuron also generates a change in the magnetic field around itself, 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 (see Sato, Balish and Muratore 1991 for an overview of MEG principles).

MEG still presents some 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 the spatial resolution of MEG. Like EEG, it is non-invasive, though mobility is not allowed as the scanning machine 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, which improves the comfort of the subject.

MEG subjects will usually undergo a structural MRI to provide a precise map upon which MEG output is superimposed. This lessens the time subjects are in a MRI scanner, but does not eliminate the need for other imaging interventions with the subject and requires budgeting for the use of two major pieces of biomedical equipment.

I.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 regional cerebral blood flow (rCBF) or a neurotransmitter flow. Hence, SPECT and PET share many common advantages and disadvantages (see Warwick 2004 for an overview of SPECT principles).

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 the tracers decay more slowly, they can be manufactured at central locations and transported further

distances, whereas PET tracers usually are created on-site or at a nearby central facility. This minimizes on-site staff and instrumentation costs for SPECT compared to PET, and makes SPECT easier and cheaper to implement.

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 during brain activity. 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. Also like the EEG is the fact that the fNIR measurement device is minimally intrusive and allows for as much or more mobility by the subject as an EEG. The scalp-based measurement approach does limit 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 Ferrari, Mottola and Quaresima 2004 for an overview of fNIR principles).

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 Gazzaniga, Ivry and Mangum, pg. 106, for an overview of single unit principles).

The electrode is placed just outside the membrane of a single neuron and will measure 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 (there is another animal technique called patch-clamp recording that measures electrochemical activity within the neuron, but we will not explore that here).

Spatial coverage is among the most limited, however, as information is collected for only one neuron or a small patch of neurons. Often experimental protocols require the same stimuli to be presented after repositioning 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 utilize animals in research that is meant to illuminate the human decision making process. The reliance of animal subjects is not as great as a hindrance to research as it might seem because mammalian (and particularly primate)

brain structure and function are very similar to humans. However laboratory logistical and maintenance burdens associated with animal experimentation are very high and provide a barrier to entry for such research.

I.A.8 Cyclic Voltammetry

This is another animal-only technique that mirrors the spatial coverage and resolution of single unit recording. The key difference is that in cyclic voltammetry the electrode embedded in the animal's brain measures for key chemicals (neurotransmitters such as dopamine) rather than electrical activity. As chemical activity is slightly slower than electrical activity, the temporal resolution is slightly coarser than for single unit recording (several measurements per second). Like single unit recording the lack of spatial coverage can be ameliorated by implanting recording devices in multiple locations within the brain (see Robinson et al. 2003 for an overview of principles of this technique).

I.B. Neural Manipulation Methods

This suite of techniques leverages differences in neural functioning that arises due to manipulation of neural structure or function. The differences across methods involve the technique used and whether the manipulation is naturally occurring or experimenter induced. The key idea is to 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.

I.B.1 Lesion Studies

These studies utilize human subjects that have suffered from naturally occurring brain lesions. A lesion can occur for any number of reasons, but usually eliminates permanently the activity of the neurons in a particular brain region. The location and extent of lesions are typically identified via neural imaging techniques or, in some cases, via post-mortem surgery. Lesion subjects are then matched with other subjects (normals) on the basis of age, intelligence, gender and other potentially relevant characteristics. Both groups are then exposed to the same type of stimulus (e.g., play the same decision making game) and differential responses are recorded and analyzed across groups. By systematically altering the stimulus and looking for differential responses between lesion patients and matched controls, investigators can speak to the causal roles for the brain region in which the lesion lies.

Human lesion studies face a number of limitations. First, the number of patients available for such protocol is usually quite limited, leading to small sample problems. Furthermore, the location and extent of lesions across subjects may be heterogeneous, 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 can usually occur only 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, these studies have been exceptionally fruitful in revealing key tenants of human behavior and were particularly important for sparking breakthroughs in the pre-fMRI era that helped link particular regions of the brain to gross and subtle roles of various brain regions in governing human behavior (see Damasio 1994 for a popular press introduction to executive brain function that relies on several famous lesion studies). Even today, lesion studies can lead to critical insights, such as Naqvi et al.'s (2007) insight that life-long smokers who suffered stroke-related injury to the insula easily stopped smoking despite numerous pre-stroke attempts to quit smoking.

I.B.2 Induced Lesion Studies

For animal studies, brain lesions can be induced by surgically removing key portions of the brain or by exposing brain regions to high levels of electrical current or chemical solutions. Compared to human lesion studies, this permits considerably more homogeneity in the treatment group and allows for the collection of within-subject (pre- and post-lesion) data as well as between group data, though control groups must also be subjected to a similar surgical procedure to control for possible stress-induced effects that surgery might have upon behavior. Again, animals are then subjected to decision making tasks featuring highly salient (food, drink, socializing) rewards.

Chemically induced lesions are the most common because the appropriate choice of the chemical 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. Some methods even allow for reversible or temporary lesions, which opens up the potential for pre-, post- and post-recovery data comparisons for each subject.

Limitations include the exclusive focus on the animal brain; results generated can be informative and suggestive, but can never provide definitive results for human decision making. Again, animal laboratories are associated with extensive maintenance and management issues of their own (think weekend feedings and angry protesters). Finally, even chemical lesions that remove only select functions of neurons are likely to affect numerous functions of the brain, providing only a coarse ability to identify the purpose and circuitry of the brain (see Gazzaniga, Ivry and Mangum, pg. 111, for an overview of animal lesion principles).

I.B.3 Electrical Brain Stimulation (EBS)

Electrical stimulation studies essentially reverse the direction of electrical flow discussed in the single unit recording methodology. In single unit recording, an electrode is placed near a neuron of interest to measure the electrical current generated in the vicinity of the electrode tip. Electrical stimulation reverses the process with external electrical current emitted from the electrode tip to a point of interest within the brain.

The technique 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, the animals are able to move freely and exhibit little difference in base behavior to untreated controls. This technique led to some of the seminal insights into the neural basis of reward (Olds and Milner 1954) as rats implanted with such electrodes would forgo food and suffer great hardship to trigger stimulation in key neural regions.

I.B.4. Transcranial Magnetic Stimulation (TMS)

Like electrical brain stimulation, this technique focuses on altering the electrical activity of neurons. Unlike EBS, this technique is non-invasive and is regularly used in human studies. In this method experimenters apply a device to the exterior of the head that generates a magnetic field. The magnetic field passes through the skin and skull and alters the activity of nearby (cortical) neurons. While the procedure is non-invasive and generally safe, some safety concerns persist and most protocol require a medical doctor's presence due to the possibility of subject seizure. Subjects need not stay perfectly still during the treatment, allowing for a more natural degree of mobility than during many neural scanning techniques. Compared to EBS, it provides a much coarser spatial resolution, allowing localization of the effect down to a region of only a centimeter or two. Furthermore, the degree of spillover of altered activity from one region to the next is still the subject of significant research.

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 (< 1 Hertz) will often retard neuronal firing compared to baseline while higher frequencies (> 5 Hertz) will enhance the rate of neuronal firings (Robertson, Theoret and Pascual-Leone 2003). However, the relationship between various TMS frequencies and alterations in neuronal activity can often be region specific (Knoch et al. 2005). Hence complementary use of fMRI is often suggested to validate the effect of the TMS treatment upon brain activity.

In addition to being sensitive to the frequency of TMS, brain activity also 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 this technique is only useful for the outer (cortical) regions of the brain, whereas EBS, lesion, drug and dietary interventions can affect deeper brain regions as well.

I.B.5. 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 various neurotransmitters as many drugs have been developed to either block the neural uptake of a specific neurotransmitter (antagonist) or maximize its presence and uptake into neurons (agonists). The role of a particular neurotransmitter in conducting a particular decision or function can be explored by treating the subject with a particular drug that either limits or enhances its transmission. As drug treatments are temporary, experimental designs can generate both within-subject data points (pre- and post-treatment as well as post-recovery data) and between subjects data points (preferably implementing standard double-blind designs). Furthermore, such manipulations can sometimes be used in tandem with neural monitoring techniques.

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, for example, one must monitor and ensure that subjects exposed to particular drugs have no adverse reactions or develop dependencies upon the substances involved in the study. Furthermore, the investigator and the laboratory is 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. There are invasive animal techniques, such as microiontophoresis that allow for the release of small amounts of a drug to a single point in the brain and act as the manipulative equivalent of cyclic voltammetry.

I.B.6. Dietary Manipulation

Manipulating a subject's diet can achieve some of the same results as pharmacological manipulations with respect to altering the presence of certain neurotransmitters. Specifically, this technique leverages the fact that 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 a randomly assigned portion of 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

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

include neuroimaging or biofeedback measurements). Between group and within-subject analysis (pre-, post- and post-recovery data collections are feasible) reveals the role of the neurotransmitter's presence for the tasks at hand.

The key advantage of this method compared to pharmacological interventions is that the infrastructure and regulatory burden is minimized, i.e., the investigators do not need to have access to a pharmacy, account for controlled substances, and need not worry as much about subject health and well-being. The disadvantages of this method compared to the pharmacological intervention are several. It is difficult to ensure that all subjects have fasted for an equivalent time. Furthermore, fewer neurotransmitters can be studied via dietary than pharmacological manipulation. Also, dietary methods can only ensure the depletion of a neurotransmitter while pharmacological interventions can either promote or block its uptake by neurons (see Fusar-Poli et al. 2006 for a review of dietary tryptophan depletion studies).

I.C. Biological Monitoring and Manipulation

The receipt of stimuli by the body induces not just neuronal activity, but also a related cascade of responses from the nervous and endocrine systems that impacts other systems within the body. The endocrine system, which is coordinated through the hypothalamus in the brain, secretes various hormones that travel through blood and other fluids to targeted cells throughout the body. For example, decision making scenarios might cause stress, which directs the hypothalamus in the brain to trigger actions in the endocrine and nervous systems. Stress-triggered feedback is designed to help the body respond appropriately to the 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 various personal reactions (trust, aggression, attraction) generated by such interactions. Well established measurement techniques exist for recording the many modalities of feedback generated by the body and can provide evidence of how various stimuli differentially affect neural and bodily responses. Furthermore, several techniques exist for manipulating hormone levels.

I.C.1 Endocrine System Monitoring

Measurement of hormones can provide information about how stress and social situations involved in decision making contexts manipulated by the researcher affect the biophysical response of subjects. The body synthesizes and circulates dozens of hormones, some of which also serve as neurotransmitters (e.g., oxytocin). *Epinephrine* and *norepinephrine* are hormones that are rapidly deployed by the endocrine system from storage in response to large threats and allow the body to immediately increase physical response (greater blood flow and lung function). *Cortisol* is perhaps the most well known and measured hormone in the literature involving stress response. *Adrenocorticotropic hormone* (ACTH), which stimulates the release of cortisol, is sometimes measured as well.

Outside of the stress arena, the levels of several hormones are known to be influenced by interpersonal interaction. Higher levels of *oxytocin* are thought to reduce fight/flight tendencies and instead promote interpersonal bonding. Oxytocin is generated during birth in women and during sexual orgasm in both sexes and is believed to facilitate the trust and bonding necessary for success in these settings. *Testosterone* levels, on the other hand, are commonly correlated with aggressive behavior that would undermine bonding and may influence social interactions subject to 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 Meyer et al. 2000 and Krueger, Schedlowski and Meyer 2005 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 causes fewer potential subjects to agree to participation.

I.C.2. Endocrine Manipulation

These methods introduce additional amounts of a hormone or a hormone blocker into the subject's body during the course of experimental testing. These methods share many of the same opportunities and challenges as pharmacological manipulations of neural activity. While most neurotransmitter drug treatments are administered orally, some hormone manipulations involve nasal (e.g., oxytocin) or intravenous administration (see Kosfeld et al. 2005 for a recent example of this method).

I.C.3. Autonomic Nervous System Monitoring

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 (related to sweat production and also known as Galvanic skin response) and skin temperature. See Lo and Repin (2002) for a study of securities traders' responses to the ebb and flow of events during the trading day.

I.D. Genetic Methods

Genes serve as the fundamental unit of heredity in all living organisms. A gene is a unit of deoxyribonucleic acid (DNA) that carries the directions for synthesizing a specific protein or a suite of proteins. With the help of enzymes and messenger molecules (messenger ribonucleic acid or mRNA), genes direct the synthesis of proteins. Proteins, in turn, are the building blocks necessary for tissue and organ formation and function, and for the synthesis of hormones and neurotransmitters. If two individuals differ in terms of their genes, i.e., differ in their *genotype*, they may differ in terms of protein creation, in the systems that rely upon those proteins, in the functions those systems control, and,

eventually, in the organism's 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 (chemical units) – adenine (A), thymine (T), guanine (G) and cytosine (C) – that form a genetic alphabet. These bases physically form the iconic double helix. In the DNA helix A is always opposite T and C is always opposite G. The order of these bases determines the eventual function of the gene for the organism. A complete set of an organism's DNA is known as its genome, and it carries all the instructions necessary to build and maintain the organism.

The human genome is composed of about 3 billion DNA base pairs that are organized into 20,000 – 25,000 genes on 23 chromosomes. Genetic variation across the human population is small in one sense, i.e., on average two humans share 99.9 percent of the exact same DNA base pairs in their genetic map. Given there are 3 billion base pairs, however, this still allows for 3 million differences in DNA base pairs. These differences range from changes of a single base, referred to as a single nucleotide polymorphism (SNP) to more extensive changes involving multiple bases, such as variable number of tandom repeats (VNTRs). These differences allow for significant variation across individuals.

For those interested in understanding if and how genetic differences manifest, this leaves a large genotypic haystack through which to sift for the phenotypic needle of interest. Further complicating the analysis is the fact that the heterogeneous impact of some genes upon behavior does not manifest unless triggered by certain environmental stressors or chemical triggers. Such findings have fundamentally altered the perennial debate between those who assign responsibility for individual heterogeneity to nature or nurture. Indeed, the two are likely to interact leaving the nature versus nurture debate as a false dichotomy. In this section we review some of the approaches used to attack this search.

I.D.1. Phenotype-Genotype Association Studies

Association studies are a correlative exercise in which a pool of subjects is assessed according to phenotype and genotype. Phenotype can be assessed by means of surveys or responses to experimental stimuli, though most studies focus on medically defined phenotypes (e.g., disease or disorder). Genotyping takes place via a suite of chemical techniques that will not be discussed here in detail (see Kwok 2001 for an overview of methods used for SNP identification).

Genotyping usually 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, a SNP in the gene that creates the protein necessary for transporting serotonin in the brain (5-hydroxytryptamine transporter, or 5-HTT) is a logical spot to begin a search for genetic variation as many depression medications operate by altering serotonin levels. However, each gene may have many different types

of genetic variation across the population. Several criteria are often applied for selecting the genetic variations subject to investigation.

First, certain genotypes are chosen if previous research has 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 simply because it may be very difficult to enroll enough subjects with the rare genetic 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 Balding 2006 for an overview of statistical approaches used in these studies and Hardy 2002 and Comings 2003 for a discussion of the limitations of association studies).

The cost of genetic testing is decreasing rapidly and can often be handled by commercial and academic laboratories. Subjects must provide an appropriate biological specimen to the experimenter for testing. For highly targeted genetic testing subjects may only need to provide a sample of skin (usually collected by a swab from the inside of the cheek like on television police shows). For broader testing it is usually suggested to collect a blood sample, which could limit the size and representativeness of subject pool.

I.D.2. Endophenotype-Genotype Association Studies

A common criticism of association studies is that the results are often weak in terms of statistical power and size of correlation and that 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 being manifested as an observable trait, behavior or disorder. That is, even if differential protein synthesis is occurring, and it is large enough to created heterogeneous functioning of a particular system within the body, other systems may compensate, which prevents an observable manifestation. Furthermore, the phenotypic classification method may be so noisy as to miss subtle manifestations that are not fully compensated by other systems.

This has led to the development of studies that attempt to correlate genotype to endophenotypes (intermediate phenotypes, see Mattay and Goldberg 2004 for a general discussion of this approach). These are differences that are observable at the systems level, including the types of outputs described in the neural, biophysical and endocrine activity described in the previous sections. 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. Furthermore, these protocols are typically more expensive as the measurement techniques necessary to classify the endophenotype is usually more expensive than those used to classify standard phenotypes.

I.D.3. Phenotype-Genotype Linkage Studies

Genetic association studies are also marred by excessive genetic variation. That is, typically the researcher chooses a single phenotype and attempts to correlate this variation with one or more variations in genetics. However, even if the researcher searches for hundreds of candidate sources of genetic variation, there will remain potentially millions of other sources of genetic heterogeneity that exist among the subject pool that are not controlled and that may affect the quality of the analysis.

Genetic linkage studies use subject pools consisting of family members to reduce the degree of unwanted genetic variation across subjects (see Elston 2000 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 are likely to require fewer total subjects, though recruitment of those subjects becomes more difficult because multiple family members must be enrolled.

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

As we alluded in the introduction of this section, the activity of genes need not be constant throughout the life of an individual. While genes are commonly thought of a one's genetic blueprint, the more accurate analogy is that genes are a set of switches. While some genes are turned on or off as part of an organism's developmental process, the activity of other genes may be influenced by environmental stressors. Several influential studies have documented how the relationship between genetic variation and a complex phenotype only holds for subjects previously exposed to a particular stressor.

This has led researchers to emphasize the importance of monitoring and measuring subjects' exposure to key environmental influences that might influence gene expression (see Moffitt, Caspi and Rutter 2005 for an overview of this approach). For phenotypes of interest to social scientists this often includes recording a subject's historical exposure to stressful life events. This encompasses several additional challenges as some subjects are hesitant to share information about some types of stressful events (rape, prosecution, traumatic incidents). For those who are willing, it may still be difficult to recall events that may have occurred during childhood, which may be a particularly important window of time for considering environmental influences. Finally, collection, management and classification of life event data pose yet another statistical challenge during analysis.

I.D.5. Whole Genome Scans

With rapid technological advances, it is now possible to receive much more comprehensive information concerning the sources of genetic variation across the subjects in a particular pool rather than searching for variation across only a couple of well known regions of the genome. Hence, researchers can focus on identifying the phenotype or endophenotype of interest and then engage in a broad scale expedition to identify the possible correlates within the genetic map.

With billions of DNA base pairs and millions of possible sources of variation, this entails dramatic hurdles with regard to the statistical approach, especially with regard to assessing statistical significance in the presence of multiple testing and allowing for simple and subtle interactions among various sources of genetic variation. Statisticians are beginning to develop and test new algorithms for pattern recognition and wielding theory to provide more efficient approaches for assessing power and significance for results generated by such wide-scale data mining (see Carlson et al. 2004 for a review of some of these challenges and Posthuma, Cherny and Boomsma 2006 for an overview of genome-wide studies of complex behavior traits).

I.D.6. Genetic Manipulation

Many of the frustrations of genetic studies surround the use of subject populations for which there is little or no control of the genetic or environmental variation that may be related to target phenotype. By turning to animal studies, researchers can harness recent developments in bioengineering to manipulate the genetic code of research animals (usually mice, see Williams and Wagner 2000 for an overview of these techniques).

One well-known genetic manipulation technique is referred to as the 'knock-out mouse.' Such mice are created by introducing artificial segments of DNA into the appropriate gene during embryonic development. The introduction of the artificial DNA serves to disable the gene, allowing the phenotype of these mice to be compared to regular mice (perhaps siblings) that faced identical environmental stressors during development and later life.

Given the incredible adaptive ability of mammals, some worried that mice that developed without a particular gene would respond in a manner that compensated for any deficiency created by the absence of a particular gene. A more recent development has created a remedy in the form of 'knock-down' mice, which are created using a technique known as gene silencing or RNA interference. In these mice the manipulation of genetic function occurs latter in life. This allows mice and a control cohort to both live a 'normal' childhood, in the sense that all genes are available and functioning normally. During adulthood, however, the knock-down mice can then have the function of this gene reduced or eliminated to provide a possibly more naturalistic view of the role of that gene in functions related to the phenotype of interest.

Other variants of genetic manipulation include adding additional copies of a certain gene thought to stimulate a certain function (transgenic mice) or making specific or targeted changes to a gene in order to bring about desired functional or regulatory changes (knock-in mice). These methods have allowed animal research to progress greatly and could be harnessed to explore phenotypes of interest to social scientists.

I.D.7. Whole Phenome Scans

The other approaches in this section begin with a phenotype of interest and then identify genetic correlates that may eventually be deemed as causal agents of the observable trait

or behavior of interest. The phenome scan turns this strategy around by instead exposing subjects to as many possible phenotype classifications as is feasible. 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 (see Jones et al. 2005), it is the one with the greatest potential involvement of social scientists. Such protocol would potentially involve significantly more time on the part of subjects, as extremely detailed knowledge of traits and behavior would be required. Indeed, some subjects may recoil at the possible intrusiveness of such questioning. Furthermore, some of the statistical challenges related to the whole genome scan, e.g., appropriate corrections for multiple testing, carry over to this context as well.

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, let this person cut in front of me, recycle or simply throw away this can?) to the monumental (do I invest in stock or bonds, 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-term and long-term costs and benefits are assigned to each action, a resulting action must be implemented, and then evaluation of the outcome associated with that action must be assessed and remembered. While seemingly manageable, this entire sequence of events must be executed while preparing for the next decision or while 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 provide some basic overview of an emerging vision of how decision making is executed in the brain, summarizing a rapidly growing body of research utilizing the various animal and human methods outlined in the previous section. This vision of the decision making process is particularly fluid at this point in time, as new data rapidly gives rise to new theoretical models, which in turn stimulates additional human and animal experimentation. Integration of the empirical and theoretical advances into a unified theory of neural decision making is beginning, but much work remains.

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

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

Examples of this vein of research are summarized by Glimcher, Dorris and Bayer (2005). They provide an overview of recent research that reveals how the monkey brain renders

decisions in several simplistic 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 measurement techniques that are not possible with human subjects but provide a degree of localized measurement precision not obtainable with human measurement techniques. This leads to many challenges in interpreting differences between animal and human experimental results, as it is difficult to assess whether the differences reflect fundamental deviations in the neural architecture and function between humans and animals or merely reflects a relative lack of spatial and temporal delineation provided by the less invasive human experimental techniques.

These primate studies provide fascinating revelations about decision making by identifying and measuring key regions of neural architecture and circuitry that lead monkeys to 'pull the trigger' on simple RUM decisions. Studies of this ilk (Hanes and Schall, 1996; Schall and Thompson, 1999; Platt and Glimcher, 1999; Dorris and Glimcher, 2004; Lee et al. 1998) use a monkey who is motivated by a primary need (thirst) to make decisions that alter the receipt of a salient reward (a pleasing fluid such as fruit juice). Monkeys cast decisions by merely altering the focus of their vision, which is tracked via invasive eye-tracking techniques. For example, a monkey would be trained to expect a particular reward after shifting its gaze from a central fixation point to a stimulus presented on the left hand side of its visual field, while looking at a stimulus presented 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 detailed summary, see Glimcher, Dorris and Bayer 2005; also, see figure 1). A key neural region called the lateral intraparietal (LIP) area generates a map analogous to the visual stimulus viewed by the monkey, only that the average neuronal firings at each spatial location within this map correspond to the relative expected value of the reward (relative expected milliliters of juice) that becomes available to the monkey if the animal shifts its gaze toward that spot.

The neuronal firing levels do not perfectly correspond to the relative expected reward because there is an inherent stochastic element to neuronal firings at each location on the map that appears to be simple biophysical noise (i.e., randomness in the firing rate). Furthermore there may exist some tendency to map 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 the relative expected utilities plus noise are physically represented by neuronal firing rates. Note that the LIP area 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 in this region.

[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.

The information from the LIP map is then passed to a region called the frontal eye fields in a manner that maintains the spatial organization of the map. In the frontal eye fields, however, the only information that is gleaned is whether the action potentials associated with a specific spatial location surpass a certain biophysical threshold. After the first location passes this threshold, the map is pruned of all other information and this location is passed to a region call the superior colliculus, which triggers the ocular motor system to shift the gaze of the animal to the location identified on the map. This shift in gaze releases the reward to the animal.

These studies provide an intriguing physical analog for many of 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 the same or 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 is the normalization process executed? This leads us to review emerging work in human imaging that details how the brain senses and evaluate various rewards.

II.B The Neurological Basis of Reward

Several key 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 (2006) call the ventral valuation network (VVN), provide similar qualitative responses to a wide array of rewards, including appealing food and drink (Zald et al. 2002), pleasant smells (O'Doherty et al. 2000), pleasing sounds (Blood and Zatorre 2001), money (Breiter et al. 2001), the provision of charitable contributions (Molls et al. 2006, Harbaugh, Mayr and Burghar 2006), the exacting of revenge (de Quervain et al. 2004), luxury cars (Erk et al. 2002), and love (Bartels and Zeki 2004).

Each region has different sensitivities during the reward process, however. For example, activity in the VMPFC appears to scale with the absolute value of delivered rewards (Knutson et al. 2001, O'Doherty et al. 2003) whereas the ventral striatum, NAc and OFC are particularly sensitive to changes in the predictability and timing of rewards (Berns et al. 2001). The OFC has been postulated to be a neural clearinghouse where relative expected utilities are associated with potentially disparate options (Montague and Berns 2002) 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 in the neuroscience community). Each of these areas is densely populated with dopamine neurons, and these neurons receive dopaminergic inputs from the ventral tagemental area (VTA) and the subtantia nigra (SN), which serve as points of origin for much of the dopamine that moves through the brain.

Dopamine is considered to play a key role in communication in this ventral valuation network. The release of dopamine in the brain makes the recipient feel good, which might be interpreted as the physiological basis for Bethamite hedonic utility or a 'rush' of pleasure. Indeed, many illegal drugs (e.g., cocaine and amphetamines) allow more dopamine to be released (technically, stops dopamine from being recaptured by neurons) and heightens this euphoric rush (hence, the generic term 'dope').

The initial hypothesis held by researchers in this field was that dopamine directly signaled reward, i.e., larger rewards released more dopamine. Such a vision of the role of this neurotransmitter would argue for a model in which dopamine becomes the physiological analog of utility, with more utility (dopamine) released as the level of goods and services are increased. Subsequent research by Schultz and colleagues over the past decade has revealed that this dopamine-reward correspondence is only partially correct and that the role of dopamine in the reward process is more subtle.

Schultz, Dayan and Montague (1997) measure the activity of dopamine releasing neurons from the VTA and SN in the brain of thirsty monkeys to reveal a more nuanced manner in which dopamine is released. During the course of the experiment, thirsty monkeys would receive a signal (bell) which would then be followed by a highly salient reward (fruit juice). During initial trials, when the monkey was learning about the relationship between the signal and the reward, the provision of the reward led to a dopamine spike (i.e., increased firing rate of dopamine releasing neurons) that was then sent to the NAc and ventral striatum. In this case the receipt of reward did correspond to a dopamine rush. However, subsequent juice deliveries of the same volume resulted in smaller and 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 much of the pleasure derived from consumption occurs in anticipation of a reward rather than the receipt of the reward.[3]

On a subsequent trial, when the volume of juice was unexpectedly increased, dopamine levels spiked not only during the cue, but also immediately following receipt of the unexpectedly large reward. After several trials where this new, higher volume of juice was administered, the post-reward dopamine levels dropped back to baseline. Finally, when juice deliveries were scaled back 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 climbed back to baseline.

These experiments led to several important insights. First dopamine release is synonymous with reward receipt only for short-term unexpected changes in delivered rewards. More generally dopamine does not encode 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

[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."

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 such a 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 authors develop a formal model referred to as a temporal difference (TD) model of reward learning:

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 with a given level of reward, as represented by dopamine release, is transient, with any amount provided quickly leading to the same level of dopamine release. Temporal difference 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 (Abler et al. 2006, Berns et al. 2001, Knutson et al. 2001, O'Doherty et al. 2003 and 2004).

One limitation of these experiments is the subject's inactive role, i.e., passively receiving signals and rewards delivered by the experimenter. 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 the activity shifts to another region within the striatum (the dorsal striatum or caudate), which is connected to the necessary motor pathways that can engage to trigger choice (Elliott et al. 2004). 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 (Rosenstein and Barto 2004), in which one system is chiefly involved in evaluating possible rewards while another system engages to act upon this information.

Other neural structures that are intimately 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 fear and other aversive stimuli (Rosen and Donley 2006), 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.

[4] Congruent with Carl Sandburg's insight, "Nearly all the best things that come to me in life have been unexpected, unplanned by me."

The most recent development in this literature is the creation of increasingly detailed neural processing models that articulate the roles of various neural substrates in each portion of the decision making process. These models generate predictions that then guide subsequent imaging experiments.

For example, Daw et al. (2005) describes a model where simple TD learning executed by dopamine neurons in the striatal regions competes against more statistically sophisticated learning models executed in frontal regions. For potentially rewarding actions involving more complex sensory inputs (and, hence, more data rich environments), the model predicts that the simpler TD model may be preferred, which can lead to habit formation, i.e., the same actions are continued even when the value of the reward associated with a particular action (or cue associated with delivery of a reward) is diminished. For many events, particularly events where the chain of causality from action to reward was more direct (and computation less costly), the more statistically sophisticated learning system was the system dominantly called upon for the purposes of learning. 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 multiple decision systems (Schneider and Shiffrin 1977). This literature postulates the existence of two general types of processing undertaken within the brain. Autonomous processes are fast, cognitively efficient, and can be executed 'in the background' while many other items are being processed. Often these processes generate highly domain specific actions for common decisions that arise. Controlled processes are slower, are more cognitively taxing and are more likely to be engaged when circumstances are novel. These different types of systems may be preferential for helping guide 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, i.e., decision makers often face an optimal search problem. 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 like that of Cohen et al. (2005), Daw et al. (2005), Haruno and Kawato (2006), which postulate different evaluative loops with competing strengths and weaknesses, have served as the neural basis for several recent behavioral economic models that focus on self-control issues (Berhheim and Rangel 2004, Fudenberg and Levine 2006, O'Donoghue and Loewenstein 2004, Benhabib and Bisin 2004).[5] Pathologies such as addiction appear to undermine the ability of the brain to allocate or distribute decisions to various evaluative loops and give rise to apparently sub-optimal choices, though the classification of these choices as sub-optimal is in itself a matter of

[5] However, as Glimcher, Dorris and Bayer (2005) 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.

discussion for economists providing normative and positive analysis of policies meant to address such issues (Bernheim and Rangel 2004, 2005).

While much of the focus of this review and the literature centers on neural mechanisms featuring dopamine-based 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 (2005) formulate a model in which acetylcholine provides a signal of riskiness with a given decision context 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 for predicting future reward. The role of these neurotransmitters may be to force the system to switch among the various evaluative loops, to rely upon more external (sensory) cues or to allow for greater memory formation in response to new, external information, which might be necessary to override encoded information about past contexts. McClure, Gilzenrat and Cohen (2005) postulate the dopamine works with norepinepherine to help a muli-loop system effectively shift between exploitative to exploratory circuitry.

Other neurotransmitters also play critical roles in various portions of the decision making process. For example, experiments with rats suggest that repression of serotonin function can lead to decisions in which future rewards are discounted more heavily (Denk et al. 2005).[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 (Kosfeld et al. 2005).

III. Neoclassical Pillars Through the Lens of Biomedical Methods

Clearly evolutionary pressures shaped the current form and function of the brain. However, evolutionary pressures only drive selection to the point of ensuring reproduction and survival of offspring, and the neural apparatus designed to ensure reproductive success may feature only partial overlap with the apparatus that economists envision to execute neoclassical utility maximization. In this section we review results of some provocative studies that cause us to reconsider several of the bedrock assumptions of neoclassical utility theory critical to the execution of positive 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 the nature of preferences themselves.

[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 (Daw and Doya 2006).

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 key themes. First, can the stated preferences of individual, elicited via 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 in which the individual only engages in part of the decision making process (anticipation and decision stages) without experiencing any change in the level of reward received. Second, in the case of revealed preferences, does the hedonic representation of a possible consequence during the decision process systematically differ from the hedonic experience received when that consequence occurs? 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 new light on this long-standing question. If the pattern of neural activation engendered by a hypothetical question is indistinguishable from that engendered by a question with consequences, 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 key differences could arise between hypothetical and consequential decisions, as critical parts of the neural process involve using dopamine to update expectations based upon previously received rewards. While the question of 'hypothetical bias' has not yet been explicitly addressed using the techniques described herein, several studies exist which may shed light on the types of inferences we may be able to eventually draw.

Knutson et al. (2001) scan subjects in an fMRI while they completed a task that featured a sequence of visual stimuli. Subjects see a colored square, then a cross-hairs image, 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 task the subject receives one dollar if a button is pushed while the white square is displayed (rewarded trial); the reward of one dollar is announced during the outcome phase. In the other version of the trial, subjects are asked to push the button during the white square even though they are aware that no financial reward is provided (unrewarded). The key difference is that one set of trials the action has financial consequences, while the other trials the consequence is only the resolution of curiosity (did I press the button in time?).

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

The difference in neural activation between rewarded and unrewarded trials was significant in several regions during both the early (anticipation) and outcome phases of the trial. The differences during anticipation were particularly stark, as fourteen distinct regions showed statistically different levels of activation across the ventral valuation network 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. (2001) perform a fMRI study featuring a task similar to Knutson et al. (2001), though imaging results for the anticipation and outcome phases are not analyzed separately. The results in Elliot et al. (2001) 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 valuation exercises. For example, a typical dichotomous choice valuation task requires significant cognitive effort to evaluate if the proposed scenario is preferred before the subject activates a motor response (marking the survey or hitting the response button), 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 in a timely fashion. Despite the differences from valuation tasks, the results give an initial suggestion that unrewarded tasks engender a different neural decision and evaluation processes 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. (2001) task also features some 'cheap talk' elements, which have proven fruitful in reducing hypothetical bias in experimental settings, in that during the unrewarded task subjects are asked to respond 'as rapidly as possible.' It would be straight forward to alter an fMRI task to test the efficacy of cheap talk interventions as well.

It is interesting to note that 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 responses to open-ended questions 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 do not bode well for calibrating open ended responses. Discrete choice formats, on the other hand, require normalization of these 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

In order to make a choice among alternatives, one must engage in the process of expectation, i.e., one must imagine and anticipate the results that each choice might generate. The crucial question then 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 quite differently in the brain than is reward receipt, even if there is no uncertainty concerning reward provision. Many of these elements are obvious from our previous 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 initially expected (say, following a reliable cue). Indeed human imaging works confirms that neural activation during reward expectation is distinct from reward receipt.

For example, Knutson et al. (2001) find that different regions respond to the anticipation and experience of monetary rewards. Consistent with simple temporal difference 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 with the actual 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 increased BOLD signal when the subject is given the reward. Other studies have also found this dissociation between regions processing the anticipation and the receipt of rewards (see O'Doherty 2004 for a nice 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).

Keeping in line with the temporal difference reward learning 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 be received in a manner that activates these dopamine rich regions. 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 (Kahneman 2000) that formulate separate anticipated and experienced utility functions.

Holland and Gallagher (2004) note that both the amygdala and OFC are engaged in developing the expectations against which delivered rewards are compared during the learning process 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 relationship between particular cues and eventual rewards, with the OFC later codifying the learned relationship. When the environment changes, such that a particular cue is no longer associated with a given reward, it is the amygdala that again signals this change first, with the OFC merely 'unlearning' the old relationship after disassociation of the old cue

and reward, waiting for the amygdala to figure out the new relationship before codifying the new relationship that emerges. It is the learned association in the OFC, however, that is relied upon most heavily for helping guide decision making, as this region may need to retain several sets of cue-reward associations so that it can compare of the relative value of competing actions based on past learning to trigger 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 Kahneman and Sugden 2005 for a discussion of this very question and Kahneman and Krueger 2006 for a related discussion)? This goes beyond simple distinctions of stated versus revealed preferences, for many purchases involve expending money to first buy an item with the actual utility received from its use coming much later. Indeed, in most cases it is the consumer's expectations concerning the eventual utility that prompts the expenditure, not the actual utility experienced at the point of consumption.

If there is a fundamental systematic bias between these two that result in decisions that, in retrospect, people find suboptimal, what is the role of policy? In some instances, such as addiction (Bernheim and Rangel 2004, 2005), 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 (Camerer et al. 2003).

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 level or the quantity of goods and services. This is a seemingly innocuous assumption, particularly given the static nature of many textbook examples of economic decision making. With the popularization of Kahneman and Tversky's (1979) work on prospect theory, which in part 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 (Sugden 2003; Koszegi and Rabin 2006).

Neoclassical utility functions are often quite 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 slowly expanding utility functions to accommodate insights drawn from key research in cognitive psychology that suggests that the absolute rewards received by an individual must be interpreted in context. This context can come from many sources, including the individual's: past (self referential, giving rise to differential treatment of losses and gains and baseline effects), peers or other reference groups (peer referential, giving rise to fashions and '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 overview of dopamine learning models readily paves the way for this context, as the degree of expectation of a reward can alter the brain regions that process its receipt. Breiter et al. (2001) demonstrate how the context of an absolute reward is crucial to the nature of neural responses generated in response to its receipt. Building off theoretical work of Mellers et al. (1997), they hypothesize that the same absolute reward (in their case the receipt of no financial reward, $0) will generate different neural responses when this reward level is the best possible outcome ($0, -$1.50, -$6) than when it is the worst possible outcome ($10, $2.50, $0).

The authors found two brain regions – the NAc and sublenticular extended amygdala (a region near the NAc and amygdala) – that revealed greater relative activation when receiving $0 was the best of all possible outcomes than when it was the worst possible outcome. 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. (2005) also reveal that counterfactual information can affect the neural processes involved in evaluating a particular outcome 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 other (unselected) gamble, providing the subject with counterfactual data. The authors 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 the authors show that the OFC is much more active when counterfactual data is given to the subject, with the level of OFC activation scaling linearly with the level of relief or regret. That is, OFC would drop below baseline levels of activity if the subject's choice turned out better than the unselected gamble (relief) and rise above baseline if the unselected gamble turned out better than the selected gamble (regret). The ACC and hippocampus revealed similar sensitivities to the counterfactual data.

When subjects suffer a 'regretful' outcome in a particular trial, it appears to influence neural activity during subsequent decision. During the choice cast immediately following a regretful outcome, several additional regions display activity that is not otherwise present. These regions include the DLPFC, which is widely implicated in behavior necessary to control impulsive choices. As more and more regretful outcomes are accumulated by a subject, the OFC becomes increasingly active during the decision process as does the amygdala, which is known to communicate the emotional valence of

of stimuli, particularly aversive stimuli. Ursu and Carter (2005) and Windmann et al. (2006) also find related evidence of how context affects reward processing and decisions.

These findings provide a solid neurological basis for the expanding volume of work that documents framing effects in choice settings. This common knowledge has clearly worked its way into political communications as well with parties wisely expressing outcomes in the frame of reference most beneficial to their political cause. It poses some difficult questions for both 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 not be relevant in future circumstances.

III.C. Malleable Preferences

Mainstream neoclassical economics has primarily treated preferences as complete, fixed and static; in the words of Hobbes, "…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." ([1651] 1949, p. 100). Such an assumption provides great convenience during welfare analyses, for there exists a stable set of preferences that are sovereign to the consumer and against which gains and losses can consistently be measured.

Any proposed changes to policy will yield predictable changes in surplus that can be used to assess the desirability of the proposed change and, given the cardinal nature of the measures generated and given some aggregation rule across individuals, one may even 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 possible policy interventions could shape preferences.

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

Persuasive communication is at the heart of many strategic initiatives generated in both the private and public sector. While many initiatives may serve to better inform people about available options so that choices better reflect current preferences, many others focus on persuading individuals to alter existing preferences. Branding provides an excellent example of persuasive campaigns. Brands and their associated images are key strategic elements of many business plans, and through sustained advertising and promotional campaigns, brand imagery has pervaded our culture.

McClure et al. (2004) document the role of product branding 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 the subjects were not informed which brand was being delivered (blind), while in other scans the delivery of one type of cola was always preceded by the presentation of the brand's logo (branded).

When tasted without brand identification outside of the fMRI, subjects' choices between Coke and Pepsi were equally split and not significantly correlated with previously stated brand preferences. However, the brand they chose in the blind taste test did generate a larger BOLD signal in the ventromedial prefrontal cortex (VMPFC) during the fMRI portion of the protocol. The VMPFC is a region known for registering gustatory rewards. The two brands engendered no differences in activity in other brain regions so long as the scanned subjects were blind to cola's brand identity.

Once brands were identified, several interesting results emerge. In a standard (non-scanning) taste test, subjects systematically preferred 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 once again 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 essential 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 deliveries produced no difference in the VMPFC. That is, a subject's neural response in the VMPFC was the same whether labeled or unlabeled cola was delivered. This is not terribly 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 dorsal lateral prefrontal cortex (DLPFC) recorded greater activation for the branded than the unbranded delivery of Coke. Both these 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 this as one stark manifestation of a preference shift. The neural evaluative process and subsequent choice of product were clearly altered by the presentation of brand image. It would appear that the accumulated brand development spending by Coke was effective in altering the manner in which a simple appetitive reward was processed by the brain, at least for the sample of subjects involved in the McClure et al. (2004) study. When brand information was absent, subjects generated neural responses in one region (VMPFC) that correlated with brand-blinded choices, while the revelation of the iconography associated with the more popular brand activated a separate circuit also consistent with the actual choice.

This finding spawns many questions, such as what are the neural mechanisms at work 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? Also, are there other manifestations of preference change that lead to different neural patterns? For example, could commercial communications lead to a direct change in the reward

[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).

level measured in the VMPFC? 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

With the development of the human genome project and the concomitant technical improvements available to assay individual genetic differences, there has been 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. (2002) correlate a serotonin polymorphism with heterogeneity in impulse control.

Other examples include work by David E. Comings and several sets of colleagues who have correlated polymorphisms for genes associated with several neurotransmitters with pathological gambling (Comings et al. 2001); several dimensions of personality including novelty seeking, harm avoidance, reward dependence and cooperativeness (Comings et al. 2000a); and several complex behavioral disorders including attention deficit hyperactivity disorder, oppositional defiance disorder and conduct disorder (Comings et al. 2000b). While the Comings studies (and a raft of other similar studies, see Munafo et al. 2003 for a review) have suggested some intriguing linkages between genes and behavior with potential import for economic behavior, this vein of literature has been marked by highly inconsistent results, with many initial findings failing to be replicated by subsequent studies (Munafo et al. 2003).

This lead some researchers to begin to investigate if the lack of replication was driven, in part, by failure to control for key environmental factors that might affect gene expression, i.e., control for how factors such as stressful life events or early developmental stressors might have switched on or off key outputs of a particular genetic variant (recall the purpose of a gene is to help create a protein, which can affect the level of neurotransmitters available within the brain). While the concept of environmentally mitigated genetic impacts on phenotype is not new (Leonardo and Hen 2006), the number of studies that test for gene-environment interactions has only recently begun to increase.

A seminal gene-environment study by Caspi et al. (2003) analyzes the genetic correlation between a key polymorphism in genes affect serotonin function and recent episodes of depression for a large cohort of subjects in their mid-20's. 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 subjects' neurological responses to basic rewards are strongly affected. For example, Rand (2004) estimates that employers lose more than $51 billion per year due to absenteeism and reduced productivity.

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

relationship between major life events and depression. Furthermore, only subjects that had never previously reported a depressive episode were considered, which drastically limits the possibility of reverse causality.

This path-breaking study is important for several reasons. First, it documents how elements of the macroeconomic situation can feed back into individual preferences. Unemployment and financial stressors, which are potentially tied to the aggregate economic situation, can affect to outcomes such as depression that can shift preferences and impact the supply and effectiveness of labor. One can truly see how economic depressions received this moniker and postulate feedback mechanisms that may recast business cycle dynamics. In the general scientific literature, this study and others have slowly led to a de-emphasis of 'nature versus nurture' thinking and an emerging vision of 'nature via nurture.'

The Caspi et al. (2003) study has inspired a growing number of replication studies (Grabe et al. 2004; Kendler et al. 2005; and Gillespie et al. 2005) and related studies that test for find environmentally mitigated correlations between genetics and other behavioral and personality outcomes (conduct disorder, Foley et al. 2004; behavioral inhibition, Fox et al. 2005; childhood depression, Kaufman et al. 2006; novelty seeking, Keltikangas-Jarvinen et al. 2004).[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. Considerable work exists to understand the implications of this work for policy evaluation, however.

III.C.3. Therapeutic Methods of Changing Preferences

The multi-loop decision-making models discussed in the previous section posit possible competition between striatal and frontal brain regions where striatal circuits rely upon dopamine to quickly code rewards relative to expectations while the frontal regions integrate information from the striatal and other regions, and may engage in more sophisticated cognitive processes that conduct more statistically rigorous analysis of possible decisions and rewards. This suggests that therapeutic interventions, such as drugs, physical stimulation or behavioral practices, may exist that could affect the relative output of certain regions or tip the balance of inputs during decision making in a manner that alters subsequent choice.

Knoch et al. (2006a) conduct an experiment utilizing TMS that reveals one tantalizing example of such an intervention. The investigators had three groups of subjects play a simple game in which they must choose between a pair of gambles where one gamble

[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. (2003) study involving older subjects revealed no significant interaction between the genetic and environmental aspects of depression (Gillespie et al. 2005). 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.

involves relatively greater risk (higher reward with lower probability). 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 the TMS over the right DLPFC, which is densely connected and co-activates with the adjacent areas in the orbitofrontal cortex (OFC), chose risky options with greater frequency than those in the other two groups (who took risky decisions with statistically similar frequency to one another). Thus, it would appear that TMS, when applied to the right DLPFC, has the ability to shift risk preferences for a brief period following the treatment.

The right region of the OFC has been previously implicated as a key region for controlling impulsive behavior (Garavan et al. 1999). It opens the door to understanding how manipulations of this region could alter decision making behavior. The authors speculate that alternative frequencies applied during TMS could lead to alternative neuronal firing patterns and, hence, alternative behavioral responses, and cite evidence from their previous work that correlates various TMS frequencies with a spectrum of behavioral responses (Knoch, Bruegger and Regard, 2005).

While Knoch et al. (2006a) report increased risk taking due to their intervention, other authors have identified interventions that cause the opposite affect. Rahman et al. (2006) work with a group of subjects that suffer from a form of dementia known to affect the orbitofrontal cortex, which causes them to take more risky decisions than age-matched healthy controls. The investigators use a double-blind within-subject design and find that the administration of Ritalin (methylphenidate) reduced the tendency of these patients to take risky bets. Ritalin consumption has been shown to increase neural flows of dopamine, whose presence is important for reward error signaling and associated 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. Several salient examples arise in the context of social interactions during economic exchange. Knoch et al (2006b) replicate the experimental design from Knoch et al. (2006a) 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 either accept or reject the first mover's proposal. Acceptance leads to the distribution of the money between the two parties according to the offer and rejection leads to no payment for either party. The neoclassically rational response by the second mover is to accept any 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 by second movers.

Knoch et al. (2006b) apply TMS to the second mover prior to the accept/reject decision. Furthermore, in half the trials, the first mover's offer is the result of volitional choice of the first mover (human), while for the remaining trials the offer is randomly generated by a computer (computer); in each case the second mover is aware of the process by which the offer is generated. This subtlety in design allows the investigators to isolate the role of interpersonal emotional interaction in the second-mover's response (reciprocity) from

the role of a second mover's preference for more equal distributions of payments (pure concerns for equity).

As in Knoch et al. (2006a), TMS to the right DLPFC evoked significantly different choices, with this group being more likely to accept the smallest offers (offers of 25% of the available pot of money) 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 and accept the smaller level of payout was affected. Furthermore, the three groups were no different in their propensity to reject the same offer if it were generated by a computer rather than by the first mover. This solidifies that the interpretation that manipulating the right DLPFC via TMS affects how the subjects were processing the interpersonal emotive content of the offer rather than affecting purely distributional preferences. The investigators suggest that the disruption in the right DLPFC hinders integration of information from areas of the brain the 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. (2005) 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 in a double-blind experimental design.

The trust game involves a first mover (investor) and a randomly-matched second mover (trustee), who each receive identical monetary endowments. The investor may send some portion of the endowment to the trustee, which is tripled by the experimenter before being physically delivered to the trustee; both parties are aware that transferred funds are tripled. The trustee, upon observing the transfer, may chose to send any portion of the accumulated funds (endowment and transfer) back to the investor, though there is no multiplication of this 'back-transfer.' The game involves risk for the investor, as a transfer increases the total payments received across both players, but may not result in an increase in the investor's payout, particularly if the trustee behaves selfishly.

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 probabilities and payments faced by the investor 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 had an effect on subject's tolerance for any kind of 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 game, suggesting that oxytocin administration

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

shifted preferences in that interpersonal risk aversion (Bohnet and Zeckhauser 2004 call this betrayal aversion) was reduced. 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. (2004) study in which brand revelation produced clear 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 at his or her disposal that is freely supplied by the government. There are no competing colas or other close substitutes available. Each person consumes the maximum feasible amount of cola each day 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 that are no short-term productivity boosts associated with its consumption (assume its caffeine free).

Now consider a proposal that would spend a billion dollars to create a logo and expansive advertising campaign for this cola, complete with fun toe-tapping jingles and commercials that associate drinking the cola with attractive people and good times. 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 should be 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 of the McClure et al. (2004) study, 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 simple example, we assume all consumers are already fully informed.

Governments regularly 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 if there

exists a coherent approach to evaluation that allows for the ranking of potential policies given that policies are aimed at preference change.

Sugden (2005) proposes that, when preferences are incoherent in that different framing may arise in the implementation of a policy than was used to estimate the preferences used to analyze the policy, an analyst might be wise to rely upon estimates of the surplus that will manifest during the long-run implementation of the policy. While not arguing with the logic of such an approach, this approach may not be desirable if preference change itself is one of the policies under consideration.

Let us return to our example of generic cola. Suppose the government now considers ending its provision of generic cola and banning its use. It estimates that the lost surplus associated with such a ban is $1 billion per year while the cost of provision is merely $800 million. Clearly such a ban would not pass a cost-benefit test. Now suppose the government could conduct an aversion campaign that would cause most people to dislike the drink. Such a campaign would cost $250 million and would drive the surplus lost from such a ban down to $100 million. The $250 million for the aversion campaign plus the $100 million in lost surplus are now less that the $800 million spent delivering the generic 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 post-implementation position.

IV. The Future of Environmental Policy Analysis

While still in its infancy, at least in application to 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 positive welfare analysis as a tool for policy decisions.

It is our view that we are approaching a three-pronged fork in the road. The first path ignores the voluminous 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. Although taking such a path is attractive, it is potentially unfulfilling and dangerous.

In its simplest form, neoclassical policy analysis is an outcome based approach. Early modelers could not view the intricate and messy details of the decision process. Rather they had to rely on what people told them and observations of the individual's actual behavior. Observed patterns of behavior were then used to derive models of decision

making consistent with the 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 analysis framework based on how we think people make decisions. This is not to criticize the neoclassical foundations of policy analysis but rather make an appeal for a broader understanding of the decision process now that technology and science allow it. Once we accept the need for a broader understanding of decision making with a foundation in modern decision science, we are left with a choice between two equally challenging paths of future research.

One path leads down the path of abandonment and reinvention of neoclassical decision theory. Researchers choosing the path of abandonment 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 an overly pessimistic view. 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 extends the path of neoclassic thinking to accommodate bumps in the road. While slightly 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 (2004, 2005) 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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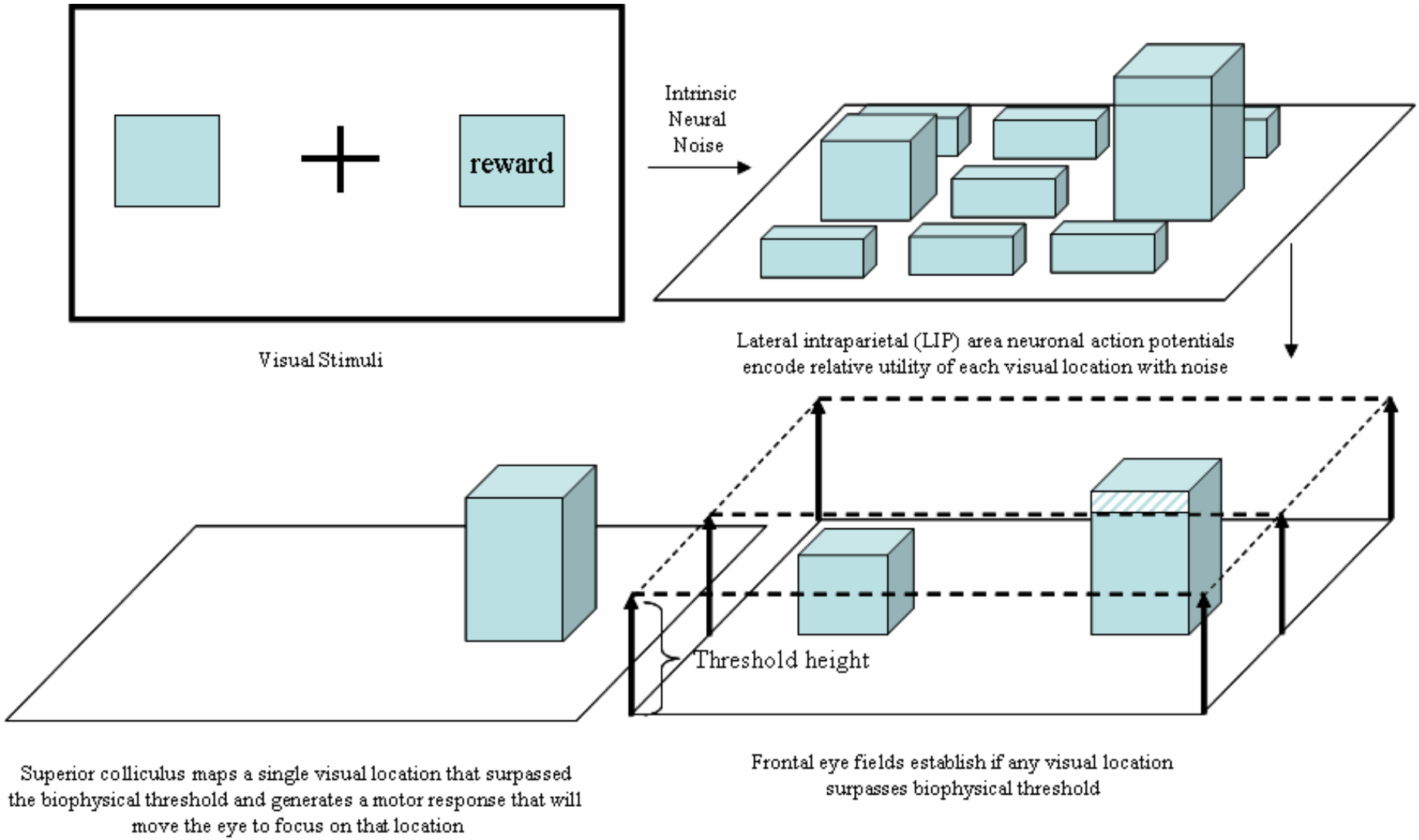

Figure 1. Flow of neural processing for a discrete choice task as executed by a monkey. Adapted from Glimcher, Dorris and Bayer (2005)

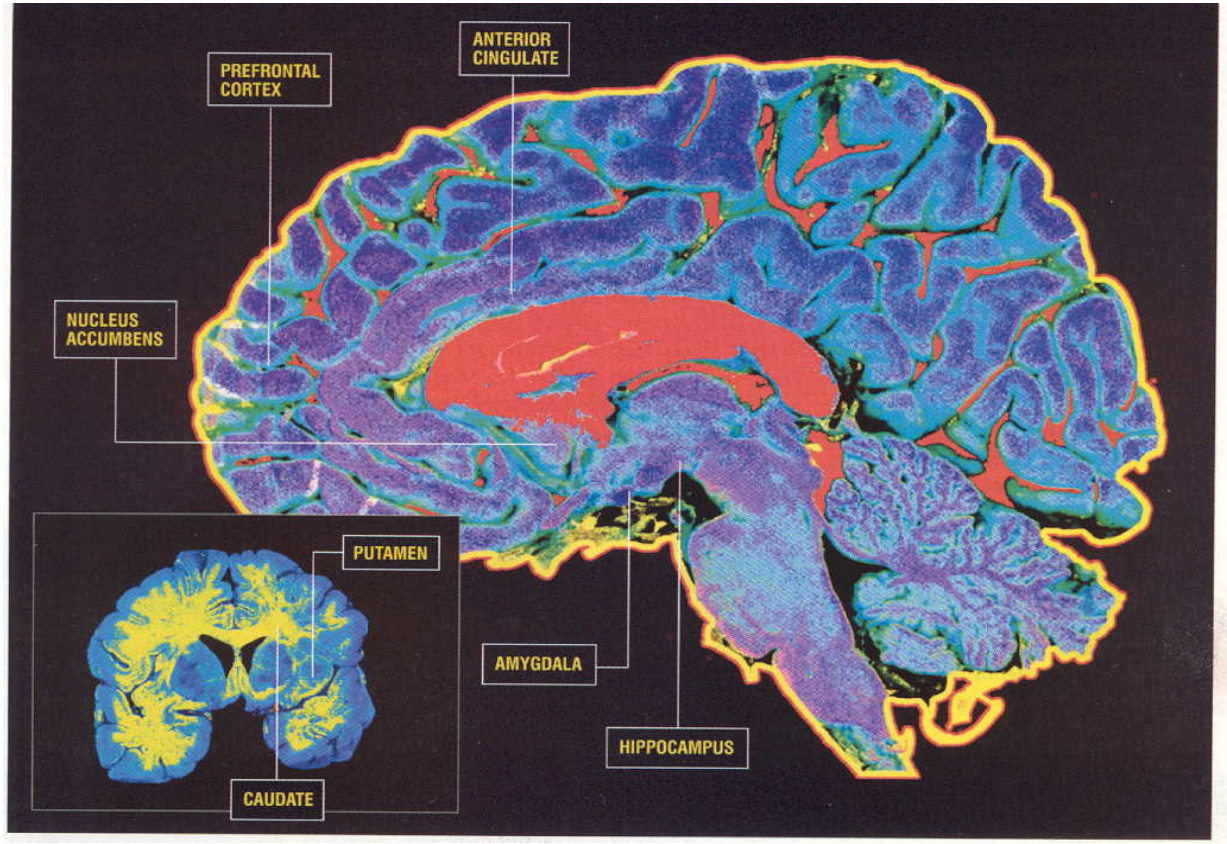

Figure 2. Side (saggital) view of a brain cross section detailing key regions of interest in many reward-related studies. Inset picture: front (coronal) cross section of two key regions of the striatum, dorsal (caudate) and ventral (putamen). Source: Camerer, Loewenstein and Prelec (2004)