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The Cognitive Neuroscience Toolkit for the Neuroeconomist: A Functional Overview

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This article provides the beginning neuroeconomist with an introductory overview to the different methods used in human neuroscience. It describes basic strengths and weaknesses of each technique, points to examples of how each technique has been used in neuroeconomic studies, and provides key tutorial references that contain more detailed information. In addition to this overview, the article presents a framework that organizes human neuroscience methods functionally, according to whether they provide tests of the *association* between brain activity and cognition or behavior, or whether they test the *necessity* or the *sufficiency* of brain activity for cognition and behavior. This framework demonstrates the utility of a multimethod research approach, because converging evidence from tests of association, necessity, and sufficiency provides the strongest inference regarding brain–behavior relationships. Set against this goal of converging evidence, human neuroscience studies in neuroeconomics currently rely far too heavily on methods that test association, most notably functional magnetic resonance imaging (MRI).

Keywords: neuroeconomics, methods, functional MRI, lesion studies, noninvasive brain stimulation

A challenge to doing research in interdisciplinary fields like neuroeconomics is becoming skilled in the sheer diversity of methods used by the different parent fields. Ideally, a neuroeconomist would have some working knowledge of the analytical tools used by choice theorists, the analytical tools used by computational modelers, experimental design in psychology and economics, statistical techniques ranging from those used in neuroimaging to those used in the analysis of behavior, and the full suite of neuroscience methods available for investigating cognition. A truly comprehensive primer on methods would have to be book-length to cover each of these topics in detail.

The goal of this review is much more modest: to provide an introductory overview of one set of items in the neuroeconomist's toolkit, the methods of cognitive neuroscience. This overview is intended for people who are new to the field and who have very little, if any, knowledge of cognitive neuroscience techniques. It is intended as a starting point for beginning students and researchers, not as the last word. Because many techniques are summarized in a small space, no one method can be covered in great detail. Rather, only the basics of each method are discussed, and interested readers are directed to key tutorial references for each technique for more detailed information. In addition to these references, beginning researchers will also want to consult one of several good methodology textbooks (e.g., Senior, Russell, & Gazzaniga, 2006; Toga & Mazziotta, 2002).

Given the constraints of space, this review is limited to only those neuroscience methods that can be used in human subjects. This excludes a great chunk of important research in neuroeconomics that uses nonhuman animals as subjects. However, this focus accords with a likely audience for this review: researchers in psychology, economics, or business who work with human subjects and are curious about incorporating neuroscience data in their research.

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In addition to introducing the techniques of cognitive neuroscience, this review also tries to answer two broad questions about methodology in neuroeconomics. First, given the plethora of neuroscience techniques available, what kind of methodological approach should research in neuroeconomics take? While several introductions to the field recommend a multimethod approach (Camerer, 2007; Camerer, Loewenstein, & Prelec, 2004; Camerer, Loewenstein, & Prelec, 2005), this overview emphasizes a particular strength of using multiple methods. Neuroscience methods differ according to the type of inference they provide concerning the relationship between brain and behavior. Broadly, methods can test the *association* between brain activity and behavior, the *necessity* of brain activity for behavior, or the *sufficiency* of brain activity for behavior. The most solid claims about brain–behavior relationships are based on converging evidence from these three kinds of tests. Neuroeconomic research programs would therefore do well to employ a combination of methods that can address questions of association, necessity, and sufficiency.

Second, given the strengths of a multimethod approach, does current research in neuroeconomics actually use this approach? Two sources of data are consulted to quantify what methods are currently being used in the field. These data suggest that, at this early stage, the field as a whole falls short of its stated goal to gather converging evidence from multiple methodologies. The vast majority of studies to date rely on tests of association, with most of these using a single technique—functional MRI (fMRI). While fMRI has several important strengths that justify its widespread use, neuroeconomic research programs would be strengthened by greater inclusion of complementary techniques that can address the inferential limitations of fMRI.

What Kind of Methodological Approach Should Research in Neuroeconomics Use?

The cognitive neuroscience toolkit is just that—a set of tools. A logical way to organize any set of tools is according to their function. This introductory overview therefore organizes human neuroscience methods functionally, according to the kinds of inferences each method provides about brain–behavior relationships. This organization differs from the canonical presentation of cognitive neuroscience methods, which emphasizes the spatial and temporal resolution of each technique (Churchland & Sejnowski, 1988). The motivation for the current framework arises from answering the question, "What kind of methodological approach should research in neuroeconomics use?" Or, in other words, "What different kinds of evidence should we gather to allow the strongest inferences about brain function?"

This discussion takes it as given that some neuroeconomists are interested in building theories about the relationship between the brain and cognition or behavior. Of course, some economists and experimental psychologists are only interested in neuroscience findings and techniques inasmuch as these can inform theories of cognition or of human economic behavior. The question of how neuroscience research can inform theories in economics and psychology is an important one, which has been extensively debated (Camerer et al., 2005; Glimcher, 2010; Gul & Pesendorfer, 2008; Harrison, 2008; McCabe, 2008). However, the methodological framework and methods overview below stress the role of each technique in elucidating brain–behavior relationships. The concluding section returns to the question of how neuroscience methods, and the knowledge of brain–behavior relationships gained through them, can inform theories in economics and psychology.

So, what different kinds of evidence combine to make the strongest inferences regarding the mappings between brain systems and cognitive functions or behaviors? To answer this question, we can examine the evidence underlying neuroscience claims that have achieved the status of broad agreement. Below, two such claims are considered. Both are routinely taught in introductory neuroscience lectures. Both were initially tested in animal models. One concerns the relationship between a specific brain region and a specific cognitive function, while the other concerns the relationship between a specific neurochemical system and a specific kind of social behavior.

As a first example, take the statement that "Area MT (or V5) subserves visual motion perception." This claim is often taught in introductory lectures on the visual system, and MT is often used as a paradigmatic example of specialization in cortical organization. What is the evidence that MT is important for motion perception?

This claim has been most systematically tested in the model system of the Rhesus macaque (*Macaca mulatta*) monkey (for a detailed review, see Newsome, 1997; Parker & Newsome, 1998). (MT is so named because of its "middle temporal" location in this animal.) Single neurons in MT fire action potentials when motion is present at a particular retinotopic location. This response is strongest when the motion is in a particular direction, and falls off as the direction of motion deviates from the "preferred" direction of that neuron. For example, an MT neuron might respond most when rightward motion is presented and least when leftward motion is presented. You can calculate how well a neuron's responses distinguish between two different directions of motion, and many neurons match or exceed the sensitivity of the animal to differences in motion direction. When discriminating between motion directions is difficult, so that the animal makes different responses to repetitions of the same stimulus, the activity of MT neurons predicts which decision the animal will make. Neurons with similar preferred directions are located next to each other in MT, and stimulating a group of MT neurons biases a monkey's perception of motion direction toward the preferred direction of those neurons. Lesions of MT impair motion perception, without affecting other aspects of visual perception.

As a second example, take the statement that "the neuropeptides oxytocin and vasopressin play a critical role in affiliative behavior." Again, students often learn this in an introductory behavioral neuroscience class. What is the evidence that oxytocin and vasopression are important for affiliative behavior?

This claim has been most systematically tested in the model systems of the prairie and montane voles (for a detailed review, see Insel & Fernald, 2004; Insel & Young, 2001). The prairie vole (*Microtus ochrogaster*) and montane vole (*Microtus montanus*) are both small rodent species found in central and western North America. Despite many similarities between the species, prairie voles and montane voles differ dramatically in mating behavior. Prairie voles form monogamous breeding pairs, with a male and female sharing parental care of their offspring. In contrast, montane voles mate promiscuously, and male montane voles are not involved in the care of their offspring. The expression of oxytocin and vasopression receptors differs dramatically in the two species. Oxytocin receptors are densely expressed in the nucleus accumbens of female prairie voles, and vasopression receptors are densely expressed in the ventral pallidum of male prairie voles. In montane voles, there is not a similar expression of oxytocin or vasopression receptors. In prairie voles, injections of oxytocin (for females) or vasopressin (for males) increase affiliative behavior toward one's mating partner. The act of mating has a similar effect on affiliative behavior in prairie voles, and injecting drugs that block oxytocin (for females) or vasopressin (for males) receptors block this effect of mating. By overexpressing the vasopressin receptor in the ventral pallidum, male montane voles can be genetically engineered to respond to vasopression in the same manner as male prairie voles do.

What can we learn from these two examples? In both cases, we see the combined use of three broad kinds of evidence (Sarter, Berntson, & Cacioppo, 1996; Silva, 2007).[1] First, there are tests of *association*. These involve observing or experimentally manipulating psychological states or behavior, simultaneously measuring neural activity, and examining the correlation between the two.[2] In probabilistic terms, tests of

[1] The framework used here borrows from Silva (2007) and Sarter, Berntson, and Cacioppo (1996). Silva's (2007) "Convergent Four" hypothesis argues that the strongest way to test a hypothesis concerning the connection between two phenomena is to gather converging evidence from theoretical work and three different kinds of experiments: *nonintervention* (here called *association*), *negative alteration* (*necessity*), and *positive alteration* (*sufficiency*). In their comment on functional imaging techniques, Sarter, Berntson, and Cacioppo (1996) distinguish between the ability of neuroimaging to test $P(\phi|\psi)$ and the ability of other techniques to test $P(\psi|\phi)$.

[2] Despite the name, tests of association can in some cases provide causal evidence (Weber & Thompson-Schill, 2010), depending on the particulars of the experiment. For example, neuroimaging experiments typically control the stimuli presented to the subjects and measure the subject's responses and brain activity. At one end of the spectrum, when examining the relationship between stimuli and brain activity, causal inference is clearly warranted. At the other, when examining the neural activity linked to different behavioral responses to the same stimuli, causal inference is clearly not warranted. Note that the causal inference provided is only ever about how changes in the environment or psychological states cause changes in brain activity, while tests of necessity and sufficiency are interested in the opposite direction of causality.

association mostly focus on the probability of a neural state (ϕ) given a psychological state (ψ), $P(\phi|\psi)$, though in some cases the analysis shifts this focus to the probability of a psychological state given a neural state, $P(\psi|\phi)$. Examples of tests of association include the correlation between neuronal activity in MT and the direction of motion perceived by the subject, and the correlation between receptor expression and mating behavior across prairie and montane voles.

Second, there are tests of *necessity*. These involve disrupting neural activity and showing that this manipulation impairs a specific behavioral or psychological function. In probabilistic terms, tests of necessity reduce the probability of a neural state and see how this changes usbthe probability of a psychological state, $P(\Delta\psi|\downarrow\phi)$.[3] Examples include the impairment in motion discrimination caused by lesions to MT and the reduction in affiliative behavior caused by oxytocin and vasopression antagonists.

Third, there are tests of *sufficiency*. These involve enhancing neural activity and showing that this manipulation results in a specific behavioral or psychological state. In probabilistic terms, tests of sufficiency increase the probability of a neural state and see how this changes the probability of a psychological state, $P(\Delta\psi|\uparrow\phi)$. Examples include the changes in motion perception induced by microstimulation of MT, and the increase in affiliative behavior induced by oxytocin and vasopression agonists.

As illustrated by the two case studies above, successful research programs in neuroscience employ a multimethod approach that combines tests of association, necessity and sufficiency. This combination provides strong evidence for the causal influence of neural states on psychological states. In tests of association, neural activity is *measured*, while in tests of necessity and sufficiency, neural activity is *manipulated*. The first kind of test establishes an important precondition for causality, that occurrences of the respective neural and psychological states are correlated. The second and third tests then test causality directly, by establishing whether the neural states are necessary and sufficient conditions for the psychological states.

What Neuroscience Methods Provide Which Kinds of Inference?

This methodological framework—distinguishing between tests of association, necessity and sufficiency—provides a way to functionally organize the methods of human neuroscience (Tables 1 and 2). Table 1 uses this framework to categorize methods that link regional neural activity to mental function. Table 2 similarly categorizes methods that link neurochemical systems to mental function. The following sections provide a brief description of each technique listed in Tables 1 and 2, organized by the categories used in these tables. For each technique, tutorial references dedicated to that technique are listed, which the interested reader should consult for additional information.

Methods for Linking Regional Neural Activity to Mental Function

Tests of Association Between Regional Neural Activity and Mental Function

fMRI. fMRI is the most widely used method in neuroeconomics, and in cognitive neuroscience more generally (for more information on fMRI, see Bandettini, 2009a, 2009b; Huettel, Song, & McCarthy, 2004; Jezzard, Matthews, & Smith, 2001). Like all MRI, fMRI involves measurements made with an MRI scanner. MRI scanners have a large static magnetic field. For a typical research scanner with a field strength of 3 Tesla, the field is 60,000 times the strength of the Earth's gravity. Signals based on the properties of nuclear magnetic resonance are then measured by making small, local modulations in the strength of this field. In fMRI, the dominant source of these signals comes from protons in water molecules. Different kinds of MR images have different *contrasts*—that is, they are sensitive to different properties of the measured tissue. The kind of contrast used in most fMRI is referred to as

[3] Technically, the probabilistic framework is not concerned with causality, and it does not matter whether the change in neural state is because of an experimental manipulation or is simply observed. The only distinction is between $P(\phi|\psi)$ and $P(\psi|\phi)$, so $P(\psi|\phi)$, $P(\Delta\psi|\downarrow\phi)$, and $P(\Delta\psi|\uparrow\phi)$ are formally the same. The important point to emphasize is that tests of association are often of $P(\phi|\psi)$, while tests of necessity and sufficiency are of $P(\psi|\phi)$.

Table 1
Functional Overview of Human Neuroscience Methods, Part 1: Methods That Link Regional Neural Activity to Mental Processes

Type of test	Method linking regional neural activity to mental function	Example(s) using this method
Tests of association	Functional MRI	Kable & Glimcher (2007); Plassmann et al. (2007), and Tom et al. (2007) demonstrated utility-like value signals during human choice, consistent with those posited in decision theory.
	Positron emission tomography ([^{15}O] water, etc.)	de Quervain et al. (2004) showed that increased dorsal striatal activity was associated with the willingness to incur costs to punish defectors in an economic exchange.
	Electroencephalography	Yeung & Sanfey (2004) demonstrated that the valence and magnitude of outcomes had differential effects on ERP responses.
	Magnetoencephalography	Ambler, Braeutigam, Stins, Rose, & Swithenby (2004) recorded magnetic activity during simulated shopping.
	Near-infrared spectroscopy	Luu & Chau (2009) decoded subjective preferences from hemodynamic activity in prefrontal cortex.
	Anatomical imaging	Bjork, Momenan, & Hommer (2009) found that increased volume of dorsolateral prefrontal cortex was associated with reduced discounting of delayed rewards.
	Invasive recordings	Zaghloul et al. (2009) demonstrated that human substantia nigra neurons respond to unexpected outcomes, similar to dopaminergic responses in other species.
Tests of necessity	Lesion studies	Bechara et al. (1997) documented decision making deficits in patients with ventromedial prefrontal damage; Fellows & Farah (2007) observed that similar damage led to more intransitive preferences.
	Transcranial magnetic stimulation	Figner et al. (2010) found that disruption of left lateral prefrontal cortex resulted in increased impatience on an intertemporal choice task.
	Transcranial direct current stimulation (cathodal)	Knoch et al. (2008) demonstrated that disruption of right lateral prefrontal cortex led to increased acceptance of unfair offers in the Ultimatum Game.
Tests of sufficiency	Transcranial direct current stimulation (anodal)	Fregni et al. (2008) showed that stimulation of lateral prefrontal cortex reduced craving in smokers.

$T2^*$ contrast ("T-2-star," so named in comparison to T1 or T2 contrast, both of which are used in anatomical imaging). $T2^*$ is sensitive to, among other things, the oxygenation level of the blood. This is because deoxygenated hemoglobin has magnetic properties, and therefore causes local susceptibility effects that decrease $T2^*$ contrast. Oxygenated hemoglobin does not have magnetic properties. Because local increases in neural activity are associated with increases in cerebral blood flow, and these increases in blood flow are associated with increases in blood oxygenation, local increases in neural activity are associated with increases in the fMRI signal. This fMRI signal is commonly referred to as the blood oxygenation level dependent, or BOLD, signal.

BOLD fMRI has several advantages that make it a preferred technique in human neuroscience. Although many methods measure correlates of neural activity noninvasively in humans, fMRI provides the best combination of spatiotemporal resolution and anatomical coverage. Functional MRI provides a simultaneous measurement of neural activity across almost the entire brain, including subcortical regions (the exceptions being a few regions hampered by technical signal-dropout artifacts, such as orbitofrontal cortex and the temporal pole: Ojemann et al., 1997; Weiskopf, Hutton, Josephs, & Deichmann, 2006). This whole-brain coverage is achieved at a high spatial resolution (typically 3 mm) and at a good temporal resolution (typically a measurement every 2 s). On the

Table 2
Functional Overview of Human Neuroscience Methods, Part 2: Methods That Link Neurochemical Systems to Mental Processes

Type of test	Method linking regional neural activity to mental function	Example(s) using this method
Tests of association	Positron emission tomography ([^{11}C] raclopride, etc.)	Zald et al. (2004) showed that variable rewards were associated with increased dopamine transmission in the striatum; Cools et al. (2009) found that individuals exhibiting greater dopamine synthesis were better at reversal learning.
	Genetics	Frank, Moustafa, Haughey, Curran, & Hutchison (2007) observed a triple dissociation between the effects of three different dopaminergic genes on reinforcement learning.
Tests of necessity	Pharmacology (antagonists)	Rogers, Lancaster, Wakeley, & Bhagwagar (2004) showed that beta-adrenergic blockade reduced the impact of losses during risky decision making; Pessiglione, Seymour, Flandin, Dolan, & Frith (2006) showed that dopaminergic blockade impaired learning from gains.
	Neurotransmitter depletion	Crockett, Clark, Tabibnia, Lieberman, & Robbins (2008) found that serotonin depletion increased rejection of unfair offers in the Ultimatum game.
Tests of sufficiency	Pharmacology (agonists)	Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr (2005) demonstrated that administration of oxytocin increased trust during economic exchange; Pessiglione et al. (2006) demonstrated that dopaminergic stimulation improved learning from gains.
	Neurotransmitter loading	Schweighofer et al. (2008) tested the effect of serotonin loading and depletion on reward discounting.

practical side, many institutions have MRI scanners and the technical expertise necessary to run them, and several good software options for analyzing fMRI data are freely available, which lowers the practical barriers to starting an fMRI research project.

The basic analysis of fMRI data involves comparing BOLD activity under two different conditions, with this statistical comparison usually being performed independently at each spatial location. By designing the right set of comparisons between stimuli or tasks, one can ask questions about where regional brain activity is associated with different mental functions.

Because fMRI has good spatiotemporal resolution and the possibility for many repeated trials, more sophisticated experimental designs and analyses are also possible. Parametric designs look for BOLD activity that changes with parametric variations in stimuli or task variables, rather than categorical changes, which can strengthen inferences regarding the causes of neural activity (Aguirre & D'Esposito, 1999; Buchel, Wise, Mummery, Poline, & Friston, 1996). Model-based fMRI (O'Doherty, Hampton, & Kim, 2007) builds on parametric designs, by testing for activity that is correlated with parametrically varying hidden variables that are estimated in a statistical model of the subject's task behavior. Both parametric and model-based fMRI designs identify not just *where* neural activity changes, but also *how* activity in these regions changes with experimental variables. Adaptation and repetition suppression designs (Grill-Spector & Malach, 2001; Henson & Rugg, 2003; Weigelt, Muckli, & Kohler, 2008) capitalize on the finding that repeated stimuli are associated with reduced BOLD activity, using this effect to ask what stimuli are treated as the same in a given neural population. Multivariate techniques such as pattern classification (Haynes & Rees, 2006; Norman, Polyn, Detre, & Haxby, 2006) ask how the spatial pattern of neural activity changes under different conditions. Both adaptation and pattern classification techniques tap into neural coding at the subvoxel level, and by testing what stimuli a region can distinguish between and which it cannot distinguish, these techniques show how information is encoded in that region. Finally, other

statistical techniques have been used to test for interactions ("functional" or "effective" connectivity) between different brain regions, using the correlations or coherences between time-series, and how those interactions change with experimental manipulations (Friston, 1994; Friston et al., 1997; McIntosh, Bookstein, Haxby, & Grady, 1996; Sun, Miller, & D'Esposito, 2004). All of these designs and analyses go beyond localization, or a simple mapping of the regional brain activity associated with specific stimuli or tasks, to ask more detailed and textured questions about how brain activity is related to mental activity.

Functional MRI does have both theoretical and practical limitations. Perhaps the most important theoretical limitation is the source of the fMRI signal. The BOLD signal reflects mass activity across the more than one million neurons in a voxel, and may be more closely linked to changes in synaptic conductances than neuronal spiking (Logothetis, 2008; Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001). This means that the signal cannot easily distinguish bottom-up versus top-down signals or neuromodulatory versus other inputs (Logothetis, 2008). The BOLD signal does not provide information about neural dynamics that occur at a fast time scale, and may be insensitive to other neural dynamics as well. Practically, the requirement of being in an MRI scanner constrains the kind of experiments that are possible. For example, experiments that require any head movement or large body movements are not possible. There are also restrictions on the kinds of subjects that can be tested. Subjects who are contraindicated for MRI (e.g., have metal in their body) or those who cannot lie motionless in a relatively small space (e.g., young children, claustrophobics) cannot be tested. Functional MRI is also more expensive than behavioral testing or several of the other techniques discussed below.

Positron emission tomography (PET). PET predates fMRI as a technique for noninvasively mapping changes in cerebral blood flow (for more information on PET, see Raichle, 1998). In PET, a radioactive tracer is injected into the blood stream. For measurements of cerebral blood flow, [^{15}O] water is used. The decay of this tracer in the brain is then measured. This radioactive decay involves the creation of positrons, and these positrons are quickly annihilated when they react with nearby electrons, thereby creating two photons that leave the point of annihilation in exactly opposite directions. PET scanners are designed to detect the coincident arrival of these photon pairs. The location of their origin, and thus the point of radioactive decay, can then be estimated from these measurements. In the case of [^{15}O] water, differences in the amount of radioactive decay across regions indicate differences in cerebral blood flow.

With the development of fMRI, the use of PET in cognitive neuroscience has waned. Functional MRI offers several advantages over PET. Functional MRI does not involve radioactivity, which restricts the number of measurements you can make in a given subject. Functional MRI also offers better spatial (3 mm vs. 1 cm) and temporal (2 s vs. 1 min) resolution. A typical PET study involves 1 to 2 measurements per subject per condition, with each measurement reflecting neural activity averaged over one minute. This restriction limits the kind of designs that can be used in PET compared to fMRI; for example, "event-related" designs are not possible with PET. In addition, fMRI is less expensive and more widely available than PET.

There is still a role for PET, however. In particular, PET can measure blood flow in absolute terms (mL/g/min), while BOLD fMRI only provides a relative measure. Absolute measures of blood flow permit comparisons across subjects, across sessions, and across brain regions. PET can also measure quantities other than blood flow. For example, other tracers can be used to measure cerebral metabolism (Fox & Raichle, 1986), or, as discussed below, different components of specific neurotransmitter systems (Zald et al., 2004).

Electroencephalography (EEG). Aside from lesion studies, EEG is one of the oldest human neuroscience techniques (for more information on this technique, see Handy, 2005; Luck, 2005). In EEG, electrodes are placed on the scalp to measure electrical changes that result from brain activity. All neuronal signaling is electrochemical, and electrical signals within neurons are accompanied by simultaneous extracellular changes. These electrical signals can propagate through the brain and skull and be detected on the scalp. The size of these signals at the scalp is very small, 10 to 100 μV, an order of magnitude smaller than at their source.

Classically in EEG studies, the time-locked responses to many repetitions of a stimulus are averaged. The spatial and temporal profile of this average response, called the event-related potential or ERP, is then investigated. More recent statistical techniques have focused on decomposing the ERP so that varying responses on single trials can be investigated (Debener, Ullsperger, Siegel, & Engel, 2006). In addition to the ERP, EEG can also be used to measure changes in oscillatory activity that accompany task performance.

One of the advantages of EEG is great temporal resolution (<1 ms). This allows investigations of the timing and evolution of neural activity at the timescale at which cognition occurs. It also permits studies of neural signals that occur at a very fast time scale, such as synchronized or oscillatory activity. Another advantage is that EEG is less expensive and more widely available than fMRI. The EEG setup also places fewer constraints on experimental design (e.g., no loud noises or restricting subjects' movement) and can be altered to be portable, so that measurements could be taken outside of a laboratory.

An important disadvantage of EEG is that it cannot spatially localize activity in the manner that fMRI or PET can. This is because of the "inverse problem" (Michel et al., 2004). EEG measures electric potentials at the scalp, and the question of what configuration of brain sources could have led to the observed data is an ill-posed problem—an infinite number of different configurations are possible in principle. Thus, calculating an inverse solution is only possible by making certain assumptions, and the validity of this inverse solution is complicated to test. Recent efforts have focused on developing new statistical techniques for calculating the inverse solution, developing new hardware such as dense electrode nets that help further constrain this solution, and conditionalizing the solution on other data such as fMRI activations (Michel et al., 2004).

Magnetoencephalography (MEG). MEG measures fluctuations in the magnetic field at the scalp that are caused by changes in neural activity (for more information on MEG, see Lounasmaa, Hamalainen, Hari, & Salmelin, 1996). The source of this signal is similar to that of EEG signals. Neuromagnetic fields have a strength of 50 to 500 fT, which is many orders of magnitude smaller than the Earth's magnetic field (0.5 mT) or fluctuations because of noise in the environment (1 nT–1 μT). Detecting neuromagnetic signals therefore requires very sensitive detectors called SQUIDs (superconducting quantum interference devices), as well as sophisticated noise cancellation techniques. In a typical MEG setup, a fixed helmet containing more than 100 detectors is placed on top of the subject's head.

The advantages and disadvantages of MEG can be compared to those of EEG. Like EEG, MEG provides great temporal resolution (<1 ms), but poor spatial resolution. Solutions to the inverse problem in MEG are somewhat more reliable and accurate, because the magnetic permeability of the head is more uniform than its electrical conductivity, which greatly simplifies the calculation of the MEG signal pattern produced by a given neural current source (Lounasmaa et al., 1996). On the downside, MEG equipment is much more expensive than that used for EEG. MEG equipment is also not portable.

Near-infrared spectroscopy (NIRS). NIRS (for more information on NIRS, see Gratton & Fabiani, 2001; Hoshi, 2005) is another noninvasive imaging method that can be used in humans. NIRS uses a light source and detector to measure the absorption and scatter of near-infrared light by the skull and underlying tissue. In its most widely used form, NIRS detects changes in absorption due to changes in oxygenated and deoxygenated hemoglobin, and therefore is sensitive to the same kind of hemodynamic signals measured by BOLD fMRI. There are also reports that NIRS can be sensitive to faster signals arising because of changes in scatter associated with neuronal firing (Gratton & Fabiani, 2001), but these signals are much weaker than the hemodynamic signals that are typically assessed (Obrig & Villringer, 2003).

Despite measuring a similar signal, NIRS provides much poorer spatial localization than fMRI, and is restricted to measuring the dorsal cortical surface directly underneath the skull. Recent technical developments are aimed at improving spatial localization, by using different types of measurement (time- or frequency-resolved in addition to continuous wave) or by using imaging techniques that combine multiple sources and detectors (Hoshi, 2005; Obrig & Villringer, 2003). NIRS does have some advantages relative to fMRI, including much higher

temporal resolution, as well as specific measurements of both oxygenated and deoxygenated hemoglobin. One of the biggest advantages of NIRS is that the measurement devices are portable, unobtrusive and lower-cost. NIRS can therefore be used in populations that cannot easily be scanned, such as infants and young children, claustrophobics and others contraindicated for fMRI, and specific patient populations. It is also possible to construct wearable NIRS systems that allow measurements while subjects move around (Hoshi, 2005).

Anatomical imaging. The above methods all test for dynamic changes in regional neural activity associated with the engagement of particular mental functions. There are also techniques for testing for static differences in brain anatomy associated with differences in mental function. These techniques test for associations across (rather than within) subjects, using an individual differences approach. The relevant individual differences might be in the structure (e.g., size, cortical thickness, or gray/white matter composition) of brain regions as measured with anatomical MRI (Ashburner & Friston, 2000) or in the structure of white matter tracts as measured with diffusion-tensor imaging (DTI; Johansen-Berg & Rushworth, 2009; Mori & Zhang, 2006).

Invasive recordings. In addition to the above noninvasive techniques, there are also rare opportunities to measure neural activity more directly in the human brain (for more information on invasive recordings, see Engel, Moll, Fried, & Ojemann, 2005). These opportunities are only available in specific patient populations where invasive neural recordings are already being performed as part of a clinical treatment. Examples include patients with Parkinson's disease undergoing surgery to implant a deep brain stimulator, and patients with epilepsy undergoing invasive monitoring and surgery to detect and remove epileptic tissue. In such patients, neural recordings might occur acutely during surgery or more chronically (over days) as part of monitoring. Obviously, because any research study is secondary to the patient's treatment, these studies have many practical limitations. Also, by definition, the subjects in these studies all have some kind of brain pathology, which could limit generalizability of the data. Nevertheless, these studies provide a rare source of data from the human brain that is comparable to that obtained in nonhuman animal models.

Multiple neurophysiological methods are used in these studies. During surgery, recordings are usually performed with a single (or small number) of electrodes. Presurgical monitoring can be performed with grids of multiple large electrodes (3–4 mm) placed on the cortical surface, a technique referred to as electrocorticography (ECoG; Miller et al., 2007), or with depth electrodes that penetrate deep into the brain, a technique referred to as stereotactic-EEG (SEEG; Lachaux, Rudrauf, & Kahane, 2003). Both of these techniques can record oscillatory activity, at a greatly increased spatial precision and signal-to-noise compared to noninvasive EEG/ERP. Depth electrodes can also record multiunit activity and can be adapted to include microwire extensions for recording single-unit activity or probes for measuring neurotransmitter concentrations.

Tests of the Necessity and Sufficiency of Brain Regions for Mental Function

Lesion studies. Perhaps the oldest technique in human neuroscience is the neuropsychological approach, which examines how damage to the brain results in the breakdown of mental function (for more information on lesion studies, see Kolb & Whishaw, 2009; Rorden & Karnath, 2004; Shallice, 1988). This was the method of inquiry in the classic studies of Paul Broca and Carl Wernicke, and reports of striking dissociations after brain damage date back to the ancients (Benton, 1991).

Modern experiments might study brain damage arising from many different sources. Stroke (ischemic or hemorrhagic) is most often studied, because it results in a relatively focal lesion. Other sources of focal lesions include neurosurgery (i.e., tumor removal, temporal lobe resection, corpus callosotomy) and penetrating head injury (Phineas Gage being a prominent historical example). Anoxia can cause more diffuse but still localizable damage. Degenerative diseases that cause more diffuse damage, such as frontotemporal dementia or Alzheimer's disease, have also been studied (Grossman et al., 2010). Investigators have also studied Parkinson's disease to examine the effects of degeneration of the dopaminergic system (Rutledge et

al., 2009; Shohamy, Myers, Grossman, Sage, & Gluck, 2005).

Often, the neuropsychological approach has not been used for brain mapping at all, but rather as a tool for dissecting the structure of the mind. In the tradition of cognitive neuropsychology (Shallice, 1988), for example, the focus is on how a case illuminates the organization of mental functions, rather than where the brain is damaged. Central to cognitive neuropsychology is the search for dissociations. A single dissociation occurs when an individual with brain damage exhibits a deficit in one task while performing at normal levels in all others. Such dissociations are informative, but alone could be explained by tasks being differentially sensitive to brain damage. A double dissociation occurs when one individual exhibits a deficit on Task A but not Task B, while a second individual exhibits the opposite, a deficit on Task B but not Task A. Double dissociations cannot be explained by differential task sensitivity, and therefore suggest that the two tasks depend on partially isolable mental processes.

Of course, the neuropsychological approach can also be used to address the question of what brain structures are necessary for a particular mental function. Especially with the advent of modern imaging techniques, neuropsychological studies have increasingly turned in this direction. One approach is to perform group studies, where subjects are grouped according to the location of their lesion, and the performance of different groups is compared (e.g., Bechara, Damasio, Tranel, & Damasio, 1997; Fellows & Farah, 2007; Hsu, Bhatt, Adolphs, Tranel, & Camerer, 2005). An alternative is to group subjects by their performance, and to compare the overlap of lesions in subjects with and without deficits (e.g., Adolphs, Damasio, Tranel, Cooper, & Damasio, 2000; Tranel, Damasio, & Damasio, 1997). A potential drawback to both of these methods is that they involve a binary classification of the brain or behavioral data that overlooks any heterogeneity in lesion location or performance (i.e., a subject is either in or out of a particular lesion group, a subject either does or does not have a deficit). Methods such as voxel-lesion symptom mapping (VLSM) overcome these drawbacks by treating both the brain and behavioral data as continuous measures (Kimberg, Coslett, & Schwartz, 2007; Rorden, Karnath, & Bonilha, 2007).

The strength of lesion studies is the ability to perform tests of necessity in humans, to examine whether loss of a brain region leads to loss of function. One aspect of lesion studies that could limit inference is that the damage is not under experimental control, so it is possible that the behavior in question is related to the person's premorbid personality or medical condition rather than to the brain damage. In many cases, this is not a plausible interpretation, but there are some examples—for one, an experimenter observing a deficit after temporal lobe resection for epilepsy might worry whether the deficit was caused by the epilepsy rather than the resection. Such concerns can be addressed by constructing the appropriate comparison groups to rule out potential confounds. Other issues that limit inference in lesion studies are: (a) cortical reorganization during recovery from stroke, so that intact regions could be compensating for damaged ones in chronic patients; (b) great variability across subjects, which can make it difficult to relate structure-to-function with precision; and (c) the often severe nature of the damage, which can make it difficult to examine the more subtle functions of a brain region. Finally, on the practical side, conducting large-scale lesion studies requires an infrastructure for the recruitment, retention and testing of subjects that, although probably less expensive than neuroimaging, is less widely available (Fellows, Stark, Berg, & Chatterjee, 2008).

Transcranial magnetic stimulation (TMS). TMS is based on Faraday's principle of electromagnetic induction (for more information on TMS, see Pascual-Leone, Walsh, & Rothwell, 2000; Walsh & Cowey, 2000). A rapidly fluxing magnetic field is induced by running an electrical current through the closed loop of the TMS coil. This magnetic field traverses the scalp and skull, and induces an electrical current in the underlying neural tissue. A typical setup uses a figure-eight shaped coil that induces a magnetic field of $\sim$2 T. The depth and width of the cortical area stimulated depends on the characteristics of the coil and its placement, but a rough estimate is that the cortical area stimulated is $\sim$3 cm^2 at a depth of $<$2 cm. TMS therefore has a relatively focal spatial effect, but can only be used to affect the dorsal cortical surface (although specialized coils that can reach deeper tissues are being developed; Wagner, Valero-Cabre, & Pascual-Leone, 2007). In

a typical setup, a stereotaxic system is used to track the location of the subject's head and the TMS coil, and in conjunction with an anatomical scan of the subject's brain, to guide the precise placement of the TMS coil with respect to cortical landmarks.

The electric current induced in neural tissue by TMS is strong enough to cause neural firing. A single-pulse of TMS therefore disrupts neural processing by inducing a burst of nonspecific neural firing, which is then terminated by cortical inhibition (Siebner et al., 2009). Because the timecourse of this effect is ~200 ms, single-pulse TMS has relatively good temporal specificity. Single-pulse TMS can therefore be used to test the temporal window within which disruption of cortical processing has an effect on behavior (Pascual-Leone et al., 2000; Walsh & Cowey, 2000).

Repeated pulses of TMS (rTMS) can also be administered. Here it is critical that users remain within the established safety guidelines, because adverse effects of rTMS have been reported outside this range (Wassermann, 1998). Short (<1 s), high frequency bursts can be used if a temporal effect slightly longer than a single pulse is desired. Alternatively, longer trains (~10 min) of pulses can be administered. In this case, rTMS results in a prolonged (15 min −1 h) modulation of cortical excitability. Depending on the intensity and frequency of stimulation, this modulation can either enhance or suppress cortical activity, although most studies use low-frequency (<1 Hz) parameters that result in suppression of cortical activity.

Transcranial direct current stimulation (tDCS). Like TMS, tDCS is a method for noninvasive brain stimulation (for more information on tDCS, see Been, Ngo, Miller, & Fitzgerald, 2007; Wagner et al., 2007). Typically, a constant current (<2 mA) is applied to the scalp through patch electrodes (25–35 cm^2 area) for a time period of up to 20 minutes. Depending on whether the anode or cathode is placed over the cortical region of interest, tDCS either increases (anodal tDCS) or decreases (cathodal tDCS) neuronal excitability in a region of the cortical surface beneath the electrode. These effects can persist for 15 min to 1 h after stimulation. In cognitive studies, a behavioral task is performed either during or directly after tDCS, and the effects of stimulation on behavior are examined. Sham stimulation, where the current is ramped up and immediately back down rather than applied continuously, can be used as a control condition.

The precise neuronal effects of TMS and tDCS likely differ, so they should not be considered interchangeable techniques. Nevertheless, it is useful to compare the benefits and drawbacks of the two methods. Similar to TMS, tDCS enables reversible activation and inactivation studies in humans and is restricted to studies of the dorsal cortical surface directly below the skull. In comparison to TMS, the equipment for tDCS is less expensive, more portable, and more easily scalable to study a group of subjects at the same time. In addition, no adverse effects of tDCS have been reported, beyond minor headaches or itching beneath the electrode. TMS, however, permits greater spatial and temporal control of stimulation, because it can be applied in single pulses and directed to more localized cortical regions.

Methods for Linking Neurochemical Systems to Mental Function

Tests of Association Between Neurochemical Systems and Mental Function

PET. As discussed above, PET can be used to obtain measures of regional cerebral blood flow or metabolism. PET can also be used to probe the function of neurotransmitter systems, using radioactive tracers that bind specific neutrotransmitter receptors, transporters or enzymes. For example, [^{11}C] raclopride has been used to measure dopamine D2/D3 receptors (Zald et al., 2004), while [^{18}F] fluorodopa has been used to measure dopamine synthesis (Cools et al., 2009). The main limitation on what neurochemical processes can be studied is in the development of appropriate radioactive ligands.

One way to employ these kinds of PET scans is to look for associations *between subjects*. For example, individual differences in dopamine synthesis in the striatum have been related to differences in reversal learning (Cools et al., 2009). Another way to employ these kinds of PET scans is to look for associations *within subjects*, across different tasks. For example, [^{11}C] raclopride has been used to measure changes in dopamine release under different

task conditions, by assuming that neurotransmitter released endogenously competes with the radioactive tracer (Zald et al., 2004; although see Egerton et al., 2009, for several important caveats to this technique).

Genetics. Many techniques are now available for linking genetic differences (genotypes) to differences in behavior or brain function (phenotypes). Because most cognitive neuroscience studies incorporating genetics have focused on polymorphisms affecting one or more neurotransmitter systems, genetics is labeled here as a method for linking neurochemical systems to mental function. It is important to remember, however, that this is only a small portion of the possible genetic differences that could be studied.

Most cognitive neuroscience studies have used a *candidate gene* approach, in which a small number of preidentified genetic polymorphisms are tested (for more information on this approach, see Green et al., 2008). Some widely studied polymorphisms are in genes that code for neurotransmitter receptors (e.g., the D2 or D4 dopamine receptors, the A2-adrenergic receptor), neurotransmitter transporters (e.g., the dopamine, norepinephrine, serotonin or acetylcholine transporters), enzymes involved in neurotransmitter synthesis (e.g., dopamine beta-hydroxylase, tryptophan hydroxylase), enzymes involved in the breakdown of neurotransmitters (e.g., catechol-O-methyltransferase, monamine oxidase), and proteins involved in neurotransmitter receptor signaling cascades (e.g., DARPP32 protein). Usually, but not always, there is already molecular biological evidence that the genetic difference studied results in changes in the function of the associated protein (i.e., the protein is more or less efficient or is expressed to a greater or lesser degree). In these studies, genetic material is obtained from saliva or blood samples, and each subject's genotype for the candidate gene is determined. Then behavioral performance (or neural activity) is correlated with genotype. Because genotype is not manipulated by the experimenter, these should be considered tests of association. These are also *between subjects* rather than *within subject* associations.

Although most published studies in cognitive neuroscience have used the candidate gene approach, the most recent and advanced genetic technologies allow for much larger studies. These range from using gene chips to examine hundreds of polymorphisms at a time, to performing *genome-wide association studies* (Manolio, 2010). In the latter case, the entire genome is scanned for loci associated with a particular phenotype. These larger-scale studies require a greater infrastructure of people and technology.

There are several complexities to keep in mind regarding genetic studies (Green et al., 2008). Most (if not all) behaviors are affected by many genes (*polygenicity*), so the effect of any one gene on the phenotype of interest is likely to be very small. Also, a given polymorphism is likely to have effects on multiple phenotypes (*pleiotropy*). Furthermore, there could be interactions between different polymorphisms, including interactions between different polymorphisms within the same gene. Finally, these genetic differences are present throughout the life span, so they may exert effects through developmental or compensatory changes, and interactions between the gene and the environment are likely to play an important role.

Tests of Necessity and Sufficiency of Neurochemical Systems for Mental Function

Pharmacology. Pharmacological interventions can be used to test the necessity and sufficiency of neurochemical systems for mental processes (for more information on this approach, see Robbins & Arnsten, 2009). These studies involve administering a drug that blocks (an antagonist) or stimulates (an agonist) a particular kind of neurotransmitter receptor, and comparing behavioral performance on and off the drug.

A main limiting factor to these studies is the existence of a drug that modulates the system of interest and can be safely administered to drug-naïve subjects. Another practical limitation is the possible need for a physician's oversight. Theoretical interpretation of these studies should take into account that: (a) drugs act at many locations in the brain (and body) simultaneously, and these effects may interact, (b) most drugs are not perfectly specific and can have effects at multiple sites (e.g., multiple receptor subtypes), and (c) the same drug can have different and sometimes opposing effects at different doses.

In addition to manipulating neurotransmitter systems pharmacologically, there are also methods for increasing or decreasing the basal levels of serotonin and dopamine/norepinephrine (Mendelsohn, Riedel, & Sambeth, 2009; Silber & Schmitt, 2010). These methods involve dietary manipulations that overload or deplete tryptophan (the metabolic precursor of serotonin), or that overload or deplete phenyalanine and tyrosine (the metabolic precursors of dopamine and norepinpehrine).

Methods That Monitor Peripheral Nervous System Activity

So far, this review has focused on methods that link mental functions to regional brain activity or to the action of diffuse neurochemical systems. Several other methods in the neuroeconomist's toolkit do not fit into these two categories, but can be broadly characterized as measurements of peripheral nervous system activity. This includes indirect indices of autonomic (sympathetic/parasympathetic) activity, such as measurements of heart rate, blood pressure, respiration rate, pupil diameter, and galvanic skin response. These measurements have shown associations with arousal, learning, and decision making (Satterthwaite et al., 2007), and are also particularly useful in studies of emotion (Olsson & Phelps, 2007). Other measures, such as eye tracking or facial electromyography (EMG), index peripheral somatomotor activity. Eye tracking can provide information about attention and information processing (Krajbich, Armel, & Rangel, 2010), while facial EMG can indicate the presence of different emotions (Halberstadt, Winkielman, Niedenthal, & Dalle, 2009). All of these techniques can provide important data for neuroeconomic studies.

Combining Methods

The functional organization of this methods overview stresses how different methods provide different kinds of inference, and therefore highlights what can be gained by studying the same decision paradigm with multiple different methods. Many of these gains occur even when the different methods are used in separate studies. In some cases, though, the simultaneous use of two different methods enables one to ask novel questions that could not be answered with one technique alone or with the two techniques used at separate times.

Some good examples involve the simultaneous combination of fMRI with another method. Simultaneous EEG and fMRI allows one to look for BOLD activity that varies on a trial-by-trial basis with the amplitude or timing of an event-related potential, providing a stronger way to link data from the two methods (Debener et al., 2006). Simultaneous TMS and fMRI can map the functional interactions between brain regions, by testing how brain regions distant from the target respond to TMS pulses, or by testing how distant regions compensate during task performance when the targeted region is depressed (Siebner et al., 2009). Combining fMRI with genetics can identify intermediate phenotypes—neural responses that vary with genotype and that might prove more reliable than behavioral phenotypes (Canli & Lesch, 2007; Green et al., 2008; Hariri, Drabant, & Weinberger, 2006). Combining fMRI with pharmacology can allow one to better pinpoint the location of any pharmacological effects (Leslie & James, 2000; Shah & Marsden, 2004). Finally, peripheral measures can be combined with fMRI to study the central correlates of peripheral effects (Gray et al., 2009).

Is Research in Neureconomics Using a Multimethod Approach?

A natural follow-up question to this overview of cognitive neuroscience techniques is, "Which methods are most neuroeconomists using?" Furthermore, given that the strongest inferences regarding brain-behavior relationships require converging evidence from tests of association, necessity and sufficiency, does research in neuroeconomics actually employ this approach? This is an important question in assessing neuroeconomics at this early stage of the field's development. Most introductions to the field stress the benefits of employing multiple methodologies (Camerer, 2007; Camerer et al., 2004; Camerer et al., 2005). Furthermore, proponents of neuroeconomics point to this multimethod approach in defending the field from its critics, criticizing detractors for failing to recognize that claims in neuroeconomics are based on more than just functional imaging results (Camerer, 2008). But does this description coincide

with what most neuroeconomists are actually doing?

To get a sense of what methods are being used in neuroeconomics research, we can examine two sources of data. The first textbook for the field, *Neuroeconomics: Decision making and the brain* (Glimcher, Camerer, Fehr, & Poldrack, 2009), provides one source of data. The references for this volume presumably contain the most influential early research in neuroeconomics. What do these references show about what methods are being used? Of the total number of references (1,744), a minority (260) were research articles that collected neuroscience data in human subjects. Other references were reviews (256), theoretical papers (220), papers using nonhuman subjects (438), or papers concerning behavioral phenomena in human subjects (254). We can classify the human neuroscience papers according to method used, excluding a subset that had primarily clinical aims (e.g., anatomical or functional imaging to identify differences between patients and controls). By far most (70.0%) of the human neuroscience papers used fMRI. The second largest group (9.6%) studied subjects with brain damage. Overall, 81.7% of the cited human neuroscience papers provided tests of association, 12.5% tests of necessity, 2.1% tests of sufficiency, and 3.8% a combination of these (Figure 1).

A second source of data is the abstracts from the Society for Neuroeconomics conferences in the 5-year window, 2005–2009 (http://www.neuroeconomics.org/conference/annual-conference). Here, close to 60% of the total number of abstracts reported neuroscience studies in human subjects (200/344), with the remainder composed of behavioral studies in human subjects (60), studies using theoretical or computational approaches (26), and studies using nonhuman subjects (58). Again we can classify the human neuroscience abstracts according to method used, excluding a small number that had primarily clinical aims. Here the predominance of fMRI was even more pronounced: 85.3% of the abstracts used fMRI, with no other method represented in more than 3% of the abstracts. Accordingly, 93.4% of the human neuroscience abstracts provided tests of association, 2.5% tests of necessity, 1.5% tests of sufficiency, and 2.5% a combination of these (Figure 1).

These data illustrate a bias toward using test of association, and particularly fMRI. But how significant is this bias? One comparison point is the field of cognitive neuroscience as a whole. Fellows and colleagues note that publications using functional imaging increased dramatically after the development of fMRI and began to outnumber those using lesion methods between 1997 and 2001 (Fellows et al., 2005). In the editorial accompanying the Fellows paper, Chatterjee identifies a wider gap in 2005 when consulting abstracts for the Cognitive Neuroscience Society meeting (Chatterjee, 2005). Those data show a ratio of about six-to-one between studies using functional imaging (fMRI, PET, ERPs) and those using the lesion method or TMS. The bias toward tests of association in the *Neuroeconomics* references is of roughly the same size, while that in the conference abstracts is much larger.[4] In terms of gathering converging evidence from multiple methods, it appears neuroeconomics is certainly not doing better than field of cognitive neuroscience as a whole, and may be doing much worse.

It is important to recognize that there are several strong theoretical reasons to rely heavily on fMRI. There are few techniques that test necessity and sufficiency, and each has significant limitations. As a test of association, fMRI has several important strengths. It is currently unparalleled in the ability to image the entire human brain at high spatial resolution. Researchers have also developed several advanced fMRI design and analysis techniques, which allow one to ask questions that are much more sophisticated than mere localization. This includes repetition suppression designs, model-based fMRI analyses, pattern classification methods, and functional and effective connec-

[4] There are several potential explanations for the differences between the citations and conference abstracts data. One possible explanation is that the two datasets differ because they sample different time periods. This explanation can be ruled out, because restricting the citations data to 2005–2009 does not dramatically change the overall percentages (association, 81.1%; necessity, 13.5%; sufficiency, 1.8%; combined, 3.6%). Other possible explanations include that the one source of data is more representative of the field as a whole, or that, compared to studies using other methods, fMRI studies have a greater chance of not being published and/or not being cited.

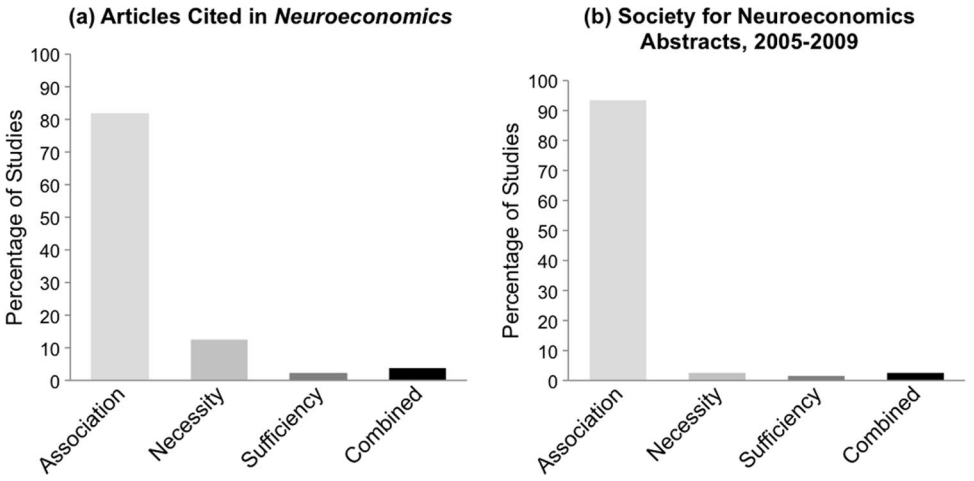

Figure 1. Percentage of studies in the field of neuroeconomics that use tests of association, necessity, and sufficiency. (a) Data from articles cited in the textbook *Neuroeconomics: Decision making and the brain* (Glimcher et al., 2009).[5] (b) Data from abstracts presented at the Society for Neuroeconomics conference.[6]

tivity techniques. All of these go beyond asking whether there is an association between *increased neural activity in brain area X* and *psychological process Y,* to investigate the relationship between the pattern of neural activity within and across regions and the pattern of instantiations of the psychological process.

There are also practical concerns contributing to the heavy reliance on fMRI. Most research institutions now have an MRI scanner, and user-friendly software is readily available for the analysis of fMRI data. There are very few barriers to beginning fMRI research, even though fMRI is more expensive and technically challenging than many of the other methodologies in human neuroscience. As one important contrast, access to subjects with brain damage has historically been limited to clinicians and their collaborators, even though in principle creating the support structure for patient-based research would require (at most) comparable resources to establishing an imaging center.

An important question for neuroeconomists is whether we should reduce some of the practical barriers to using methods other than fMRI, or otherwise encourage a greater degree of multimethod research. There are several reasons for doing so. A stated standard of the field is that claims should be defended with evidence gathered using multiple methodologies (Camerer, 2008). Furthermore, as discussed above, the strongest arguments in neuroscience rely on converging data that speak not just to association, but also to necessity and sufficiency. To the extent that researchers in the field want findings in neuroeconomics to have similar impact, they should follow the same approach.

[5] From the articles cited in *Neuroeconomics*, the tests of association included fMRI (168), PET measuring blood flow (17), EEG (2), anatomical studies (3), invasive recordings (1), PET measuring neurotransmitter receptors (4), and genetics (1). The tests of necessity included lesion or patient studies (23), TMS (4), cathodal tDCS (1), and antagonist pharmacology (2). The tests of sufficiency included anodal tDCS (2) and agonist pharmacology (3). Combinations included neuroimaging studies in subjects with brain damage (5) and neuroimaging combined with pharmacology (4).

[6] From the Society for Neuroeconomics abstracts, the tests of association included fMRI (168), PET (1), EEG (5), NIRS (1), anatomical studies (1), invasive recordings (2), hormone measurements (1), and genetics (5). The tests of necessity included lesion or patient studies (3) and TMS (2). The tests of sufficiency included agonist pharmacology (3). Combinations included neuroimaging studies in subjects with brain damage (2), neuroimaging combined with pharmacology (2), and patient studies combined with pharmacology (1).

How Can Neuroscience Methods Be Used to Inform Theories in Economics and Psychology?

Many economists are skeptical that research incorporating neuroscience methods can better inform theories in economics (Camerer, 2007; Camerer et al., 2004; Camerer et al., 2005). They argue that a better understanding of the neural mechanisms of decision making will not necessarily lead to better predictions about economic behavior. This critique is similar to earlier critiques of cognitive neuroscience (Coltheart, 2004). As cognitive psychologists have said, "Why should we study the brain in order to understand the mind?" This is an important debate, and many neuroeconomists have outlined how research in the field can inform economics and psychology as well as neuroscience (Camerer, 2007; Glimcher, 2010; McCabe, 2008). Many neuroeconomists believe that a multilevel investigation of brain-behavior relationships, aimed at building mechanistic theories of decision making, will ultimately lead to a coherent integration at the border of neuroscience and economics/psychology (Glimcher, 2010; Kable & Glimcher, 2009). While some scholars of decision making may doubt this possibility, a similar integration has already occurred in perception, and arguably in other domains of cognitive psychology (language, memory) as well.

Setting aside the prospects for a broad integration, we can consider specific ways that the neuroscience methodologies reviewed above can be used to inform research questions in economics and psychology. As most of the research in the field has used fMRI, the examples discussed here reference that technique, but could apply similarly to other tests of association. One place to start, though, is to note one way that fMRI data are (commonly) used that provides poor inference regarding psychological processes. This involves making an assumption about the function of a brain region based on past studies, and inferring based on activation in that region that the task the subject performed involved a particular psychological process. For example, one might find that decisions under risk are associated with activity in the amygdala, note that the amygdala has previously been implicated in the emotion of fear, and then conclude that decisions under risk involved fear. This kind of reasoning is called "reverse inference," and reverse inference is generally problematic (Aguirre & D'Esposito, 1999; Poldrack, 2006). The central problem is that it assumes there is only one psychological process associated with activity in a given brain region (e.g., the amygdala is *only* active when you experience fear). Such a one-to-one mapping is unlikely. Poldrack works through an example in probabilistic terms to show that reverse inferences are unlikely to provide very strong information, at least at the spatial scale of brain activity and coarseness of the cognitive ontology that are typically used (Poldrack, 2006; though see Ariely & Berns, 2010, for a more promising example).

There are several more promising ways, though, that fMRI (and other tests of association) might be used to inform economic and psychological theories. First, model-based fMRI can provide information about what variables and quantities are encoded in the brain when an individual makes decisions. One example of this is the demonstration of prediction error signals in the human brain, consistent with those posited in reinforcement learning models (McClure, Berns, & Montague, 2003; O'Doherty, Dayan, Friston, Critchley, & Dolan, 2003). Current work is using these signals to test competing learning models (Hampton, Bossaerts, & O'Doherty, 2006). Another example is the demonstration of utility-like value signals during human choice (Kable & Glimcher, 2007; Plassmann, O'Doherty, & Rangel, 2007; Tom, Fox, Trepel, & Poldrack, 2007), consistent with those posited in decision theory. Current work is illuminating the inputs to those signals and the domains in which they operate (Hare, Camerer, & Rangel, 2009; Smith et al., 2010; Wunderlich, Rangel, & O'Doherty, 2009). Second, fMRI can demonstrate whether two different kinds of decisions use similar or different neural processes, and thus whether they are likely to use similar or different cognitive processes. Examples include prominent debates in the field over whether decisions under risk and ambiguity involve similar or different mechanisms (Hsu et al., 2005; Levy, Snell, Nelson, Rustichini, & Glimcher, 2010), and whether decisions about immediate and delayed rewards involve similar or different mechanisms (Kable & Glimcher, 2007; McClure,

Laibson, Loewenstein, & Cohen, 2004). Third, in addition to identifying similarities and differences across tasks, fMRI can also be used to test whether different individuals perform the same decision in different ways. Venkrataman and colleagues provide one example of this with regards to decision strategy (Venkatraman, Payne, Bettman, Luce, & Huettel, 2009), and Houser and colleagues discuss how the discovery and validation of different types of decision makers could improve econometric predictions (Houser, Schunk, & Xiao, 2007). Fourth and finally, directly incorporating neural measures into models could improve predictions of economic behavior. Early neuroeconomic studies demonstrated that neural activity could be used to predict simultaneously measured choices (Knutson, Rick, Wimmer, Prelec, & Loewenstein, 2007). More recent studies have shown how neural activity can predict individual behavior outside of the scanner (Levy, Lazzaro, Rutledge, & Glimcher, 2011), and how neural measures can predict what products will be successful (Berns, Capra, Moore, & Noussair, 2009).

Because it is the most widely used technique in the field, this discussion has so far focused on fMRI. However, considering how neuroscience methods can best inform theories in economics and psychology provides yet another rationale for a multimethod approach. In tests of necessity and sufficiency, behavior is the dependent variable. Because this is also the variable economists and psychologists are usually most interested in, these techniques could provide more compelling evidence to them. Consider the question of whether two kinds of decisions involve similar or different cognitive processes. The search for double dissociations in neuropsychology is entirely motivated by these kinds of concerns. Though this may not be how they are commonly used, TMS, tDCS, and pharmacology can uncover similar dissociations. Indeed the question "Why should we study the brain in order to understand the mind?" might have seemed strange to earlier human neuroscientists. For more than a hundred years before the advent of modern imaging techniques, human neuropsychologists studied the effects of brain damage in order to elucidate mental structure. In addition to providing evidence about the causal role of brain structures in behavior, tests of necessity and sufficiency, since they treat behavior as the dependent variable, can also provide evidence that further strengthens the neuroeconomist's answer to why studying the brain enlightens us about how people make decisions.

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