Brain Imaging Techniques and Their Applications in Decision-Making Research

Gui XUE[1], **Chuansheng CHEN**[2], **Zhong-Lin LU**[1], and **Qi DONG**[3]

[1] Department of Psychology, University of Southern California, Los Angeles, CA 90089-1061, USA

[2] Department of Psychology and Social Behavior, University of California, Irvine, Irvine, CA 92697-7085, USA

[3] State Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University, Beijing 100875, China

Abstract

Advanced noninvasive neuroimaging techniques such as EEG and fMRI allow researchers to directly observe brain activities while subjects perform various perceptual, motor, and/or cognitive tasks. By combining functional brain imaging with sophisticated experimental designs and data analysis methods, functions of brain regions and their interactions can be examined. A nascent field called neuroeconomics has recently emerged as a result of the enormous success of applications of functional brain imaging techniques in the study of human decision-making. In this article, we first provide an overview of brain imaging techniques, focusing on the recent developments in multivariate analysis and multi-modal data integration. We then present several studies on risky decision making, intertemporal choice, and social decision making, to illustrate how neuroimaging techniques can be used to advance our knowledge on decision making. Finally, we discuss challenges and future directions in neuroeconomics.

Keywords

cognitive neuroscience; decision making; EEG; fMRI; functional imaging; neuroeconomics

The last 20 years have witnessed the emergence and rapid development of the field of cognitive neuroscience. This new field combines two traditionally distinct disciplines—cognitive psychology and neurology—to address the neural underpinnings of human cognition. The impact of cognitive neuroscience has been felt beyond psychology and extended to disciplines as diverse as anthropology, philosophy, linguistics, sociology, and economics. This article aims at providing readers with an overview of the recent advances in neuroimaging techniques and their applications in the study of human decision-making.

Brain Imaging as a Window into the Mind

Many brain imaging tools are available to cognitive neuroscientists, including positron emission tomography (PET), near infrared spectroscopy (NIRS), magnetoencephalogram (MEG), electroencephalography (EEG), and functional magnetic resonance imaging (fMRI). We focus on EEG and fMRI in this article because they are the most widely used tools.

Correspondence should be addressed to Dr. Gui Xue, Department of Psychology, University of Southern California, Los Angeles, CA 90089-1061, USA. gxue@usc.edu Fax: (1)213-821-4270.

Electroencephalography (EEG)

First discovered about a century ago, EEG measures electrical activities of the brain from electrodes placed on the scalp. Usually, EEG is collected from tens to hundreds of electrodes positioned on different locations on the scalp. Most EEG systems used in cognitive neuroscience research today employ 64 to 256 electrodes.

Scalp EEG represents the aggregates of post-synaptic currents of millions of neurons. The recorded EEG signals usually reflect two types of brain activities, *spontaneous* and *event-related activities*. Spontaneous EEG reflects neuronal responses that occur unprovoked, i.e., in the absence of any identifiable stimulus, with or without behavioral manifestations. Spontaneous EEG has long been used in clinical settings to evaluate seizure disorders, and has not been used often in cognitive neuroscience research (but see Williamson, Kaufman, Lu, Wang, & Karron, 1997). Recently, there are growing interests in examining how the background brain activities as measured by spontaneous EEG affect current cognitive activities (Ergenoglu et al., 2004; Romei et al., 2008). In addition, spontaneous EEG may hold the key to unraveling the patterns of functional connectivity and synchronicity among brain regions underlying the states of consciousness (also known as the default network) (Mantini, Perrucci, Del Gratta, Romani, & Corbetta, 2007). By combining with resting-state fMRI, generators of spontaneous EEG activities can be localized (Salek-Haddadi, Friston, Lemieux, & Fish, 2003).

Event-related potentials (ERPs) are associated with specific stimuli or thoughts. The amplitudes of ERPs tend to be low, ranging from less than a microvolt to several microvolts, compared to tens of microvolts for spontaneous EEG. To detect these low-amplitude potentials against the ongoing background EEG, EKG (cardiac artifacts), EMG (muscle activation artifacts) and other biological signals and ambient noise, repeated stimulus presentations and signal processing techniques (e.g., averaging) are required in ERP studies. The major techniques to detect event-related potentials can be divided into two categories, *time-locked averaging* techniques and *spectral analysis* techniques. Time-locked averaging techniques are usually used to detect *evoked activities,* which are time-locked to the presentation of stimuli. Because most noise occurs randomly, time-locked averaging techniques can greatly reduce the noise while preserving the event-related signals in the EEG. Time-locked averaging can be either stimulus-locked or response-locked.

In addition to time-locked responses, there may also be signals in the EEG that are related to stimulus processing without a well-defined temporal relation to the event. These responses are called *induced activity*. An example of induced activity is oscillatory activity (e.g. gamma oscillations), which might have a different phase in each single measurement and therefore would cancel one another in time-locked averaging. However, *induced activity* can be detected using spectral analysis, in which EEG recordings are decomposed into a number of frequency (sinusoidal) components, such as delta (0-3Hz), theta (4-7Hz), alpha (8-12Hz), beta (12-30 Hz), gamma (30-50 Hz), and high gamma (80-150 Hz). Among the various spectral analysis techniques, Fourier transform (FT) is traditionally the preferred method because it is time-shift invariant in both the time and frequency domains. However, in FT, any time-varying spectral content of the signal is ignored because it assumes that the signal is stationary over time. This assumption is in contradiction to the fact that EEG signals are non-stationary. To overcome this limitation, Wavelet transform (WT) is now considered to be more suitable than Fourier transform in analyzing induced activities (Akin, 2002).

Functional magnetic resonance imaging (fMRI)

fMRI is one of the most recently developed forms of neuroimaging technique. Since the early 1990s, fMRI has become the dominant method in cognitive neuroscience because of its low

invasiveness, lack of radiation exposure, and relatively wide availability. In the brain, neural activities often lead to metabolic activities such as increased blood flow and oxygen supply to the local vasculature. Several techniques can be used to detect changes of metabolic activities following neural activities, including *contrast fMRI*, *blood-oxygen-level dependent (BOLD) fMRI*, and *perfusion fMRI*. Contrast fMRI requires injection of contrast agents, such as iron oxide coated with sugar or starch. The signals associated with contrast agents are proportional to the cerebral blood volume (CBV). Although this method can provide relatively strong signals, researchers are reluctant to use this semi-invasive method with healthy volunteers. Perfusion fMRI uses "arterial spin labeling" (ASL) to magnetically label hydrogen nuclei in the arterial blood and then images their distribution in the brain. This method is sensitive to cerebral blood flow (CBF), which is considered as a good correlate of neuronal activity. This method does not require any contrast agents. Compared to the BOLD responses (to be discussed below), the signal in perfusion fMRI is more stable and the noise is much whiter. However, the relatively weak signal and the length of image acquisition time have limited the use of perfusion fMRI in cognitive neuroscience.

Currently, the most widely used fMRI method is BOLD imaging, which detects the difference in magnetic susceptibility between oxygenated hemoglobin and deoxygenated hemoglobin. Hemoglobin is diamagnetic when oxygenated but paramagnetic when deoxygenated. The magnetic property of blood therefore depends on its oxygenation level. Although neuronal activities consume some oxygen, the increase in blood flow following neuronal activities supplies more oxygen than the neuronal consumption, resulting in an increase in oxygenated hemoglobin and therefore increased BOLD response. Although BOLD fMRI is an indirect measure of neuronal activities, there is strong empirical evidence that the BOLD signals are highly correlated with neuronal activities (Logothetis et al., 2001). Because the BOLD signals are usually stronger and require less time to acquire than perfusion signals, BOLD fMRI is more popular than perfusion fMRI.

One major technical challenge for fMRI is that the hemodynamic responses are relatively slow, weak, and noisy. The typical BOLD hemodynamic response following a single stimulus event starts to rise after 1 to 2 seconds, peaks at 4-6 seconds, and returns to its baseline after 12-16 seconds. The typical BOLD signal change following a single stimulus event captured on a 3T scanner is about 1-2% and varies greatly across different event types and different brain regions. To increase the statistical power of fMRI studies, many repetitions of the same event type are necessary. In the early years of fMRI research, *block design*, in which the same types of stimuli are grouped together in each block, was used in many studies. A block design can generate strong BOLD signals that are relatively easy to process. However, block design has several limitations. First, in some experimental paradigms, the events cannot be blocked. For example, in an oddball paradigm, the target trials are presented amongst more common stimuli. Such target trials cannot be blocked. Second, in some experiments, the nature of each particular trial cannot be predetermined to allow for a block design. For example, in memory research, trials remembered vs. forgotten cannot be discovered prior to the recall/recognition test. Similarly, trials won vs. lost in a gambling task cannot be known prior to subject's response. It is therefore impossible to use a block design to examine the neural bases of winning vs. losing bets or remembering vs. forgetting. To overcome these limitations, *event-related design* was introduced. The early event-related design studies usually used long inter-trial intervals (12 to 20 s) to avoid the overlap of the BOLD responses between trials. Slow event-related designs turned out to be very boring for subjects and were highly inefficient in data collection. Currently fMRI studies usually use rapid event-related designs, in which different types of events are pseudo-randomly mixed together. Two key features of rapid event-designs are trial order randomization and random time jittering between trials (Xue, Dong, & Zhang, 2003a). The development of rapid event-related design has significantly changed cognitive neuroscience research (Xue, Dong, & Zhang, 2003b). A third type of design is the mixed design, which

combines the block design and the event-related design (Wang & Dong, 2007). In a mixed design, trials from different conditions are grouped into blocks, and also randomly jittered within blocks. An obvious advantage of the mixed design is the reduction of switches between different experimental conditions, e.g., decision making under a winning situation and under a losing situation (e.g., Xue et al., 2008). In studies of cognitive control, the mixed design can also help to dissociate sustained cognitive control and transient cognitive control (Wang, Kuhl, Chen, & Dong, In press).

In order to identify the regions that show significant signal changes in response to a task (thus presumed to be involved in that task), imaging data must be analyzed with statistical methods. Many techniques have been developed. Currently, most analysis approaches, for both block and event-related designs, have been integrated into the general linear model (GLM) framework (Friston et al., 1995). The aim of the GLM is to explain the variance in the BOLD time course (i.e., the BOLD signal acquired from the scanner) in terms of a linear combination of explanatory variables (i.e., the experimental design matrix) and an error term. By finding the magnitudes of the parameters that corresponds to each variable in the design matrix, the presence or absence of activation can be detected. In the GLM model, one can either assume the shape of the BOLD response function (e.g., a double-gamma function) and then simply estimate the amplitude of the response, or do not assume the shape of the BOLD response function and estimate the amplitude of each time-point of the BOLD response, resulting in an estimate of the shape of the BOLD response for each event type. The latter method is commonly called *deconvolution*. Obviously, with deconvolution, more parameters must be estimated and the results are always noisier. The advantage of deconvolution, however, is that the results are less affected by the theoretical shape of the BOLD response function.

Comparison of EEG and fMRI

EEG and fMRI have their respective strengths and weaknesses. Ideally experiments employing these methods must be carefully designed and conducted to maximize their strengths and minimize their weaknesses. The most salient feature of EEG is its high temporal resolution at a level of milliseconds. It is also a direct measure of neuronal response. Nevertheless, EEG has several limitations. First, EEG is only sensitive to post-synaptic potentials generated in the superficial layers of the cortex. It is not sensitive to neuronal responses from structures that are deep in the brain, such as the striatum or hippocampus. In addition, currents that are tangential to the skull make little contribution to the EEG signal. Second, the spatial resolution of EEG is very low. Third, it is almost impossible to reconstruct a unique intracranial current source distribution for a given EEG signal, although substantial recent progress has been made in this area.

In contrast, fMRI has high spatial resolution and a comprehensive coverage of the whole brain. Conventional BOLD fMRI has a typical spatial resolution of 3-6 millimeters; high resolution fMRI can reach about 1 millimeter spatial resolution at the expense of whole-brain coverage. fMRI is sensitive to the BOLD signals from both the cortical surface and deep brain structures. The only limiting factor for coverage is susceptibility artifacts in the ventromedial prefrontal cortex and temporal poles. This problem has been partly resolved by some newly developed scanning sequences, or by using contrast fMRI and perfusion MRI. The major limitation of fMRI is its temporal resolution because the BOLD response is very slow. Moreover, the BOLD signal is only an indirect measure of neuronal activity, and is therefore susceptible to influence by many physiological activities of the body that are un-related to neuronal processes.

Recent Advances in Neuroimaging Techniques

Functional brain imaging is a rapidly developing field. Many new techniques and improvements to existing techniques continue to emerge. Some recent examples include the

development of simultaneous high-intensity EEG and high field fMRI recording techniques, new data acquisition protocols, better data preprocessing methods, and better analysis models to improve the sensitivity in detecting the BOLD responses. Among all these advances, two most significant developments are multivariate analysis and multi-modal data integration.

Multivariate Analysis

Traditional data analysis methods treat each single voxel as an independent measure of brain activity. The BOLD responses in surrounding voxels are usually averaged (through certain types of spatial filters) in order to increase statistical power. The BOLD responses are usually thresholded to generate activation maps. Although averaging and thresholding help to reduce noise, they also remove potentially useful information. Second, the univariate approach does not explore interactions among different brain regions. In recent years, multivariate analysis methods are increasingly used in fMRI data analysis. For example, *multiple-voxel pattern analysis* (MVPA) has been used to identify the subtle differences in activation patterns across voxels, whereas *neural connectivity analysis* has been used to examine functional interactions among brain regions.

In the first fMRI study that used pattern analysis methods, Haxby et al. (2001) illustrated that activation patterns of distributed voxels in the ventral visual pathway can be used to effectively discriminate which types of visual objects participants were viewing. In this study, they asked subjects to passively view several categories of visual objects (e.g., faces, houses, chairs, shoes, bottles) that were grouped in blocks. The imaging data from each category were split in half (i.e., odd blocks vs. even blocks). They first used the GLM approach to identify the responses in the ventral temporal cortex (VTC), separately for each half of the blocks and for each category. Unlike the traditional approach, they did not smooth the data, nor did they threshold the statistical maps. Instead, they extracted the pattern of activation within VTC for each category, as well as for each half of the blocks, and then calculated the within-category correlation (e.g., the first-half patterns with the second-half patterns) and between-category correlation (e.g., "faces" vs. "houses"). The results indicate that each category was associated with a reliable and distinct pattern of activity in the VTC (i.e., the degree of within-category match was significantly higher than the degree of between-category match), challenging the view that these visual categories are processed in isolated brain regions. More significantly, this study demonstrates that the multivariate approach is able to provide a high degree of discrimination across different mental states, suggesting the superiority of pattern analysis over the traditional approaches.

Following this seminal study, many more sophisticated pattern-classification algorithms, such as support vector machines (SVM) (e.g., Mourao-Miranda, Bokde, Born, Hampel, & Stetter, 2005) and linear discriminant analysis (LDA) (e.g., Hampton & O'Doherty J, 2007), have been used in fMRI data analysis. These methods have significantly improved the sensitivity of the MVPA approach. For example, in the correlational approach, all voxels have the same discrimination weight, whereas the SVM approach can identify the voxels that maximize the *margin* between the two states (i.e., the support vectors), and thus assign the optimal discrimination weights to the voxels. These pattern-analysis algorithms usually include a training/learning stage and a test stage. In the training stage, the fMRI data and their associated mental states are both submitted into the learning algorithms to develop a classifier for each mental state. In the test stage, only the fMRI data that are not used for training are supplied to the classifiers to examine whether the classifiers can correctly label the associated mental states. Using these approaches, researchers have shown that fMRI responses can be successfully decoded as neural representations of different visual objects (Haxby et al., 2001), different word types (Mitchell et al., 2008), and different mental mathematical manipulations (e.g., addition vs. multiplication) (Haynes et al., 2007).

Both the traditional GLM approach and the MVPA approach can address the question of functional localization, with the former focusing on discrete brain regions and the latter on contiguous groups of brain voxels. However, results from these analyses suggest that even a very simple cognitive function may involve a large cooperative and/or competitive neural network. These findings point to the importance of understanding the communications and interactions among different brain regions when studying brain functions. A number of neural connectivity analysis (NCA) approaches have been developed to address this issue.

The simplest neural connectivity analysis approach is *functional connectivity analysis*, which is developed to evaluate coupling of neural activations in different brain regions. This can be done by simply extracting BOLD responses in two brain regions and calculating their correlation. As an extension of the method, the time course of the BOLD response in one brain region can be extracted and correlated with that of the rest of the brain. This approach can provide a comprehensive connectivity map of the whole brain with one particular region. Although the same method can be used to examine mutual connectivities of each voxel/region in the brain, the resulted connectivity map is usually very complicated. Additional informatics techniques are necessary to characterize the connectivities. For example, it has been shown that connectivities among brain regions during resting states exhibit "small-world" attributes, i.e., high levels of clustering and short path lengths (Hagmann et al., 2008).

Another approach is to examine how different tasks and mental states modulate functional connectivity. Friston and colleagues (1997) developed a method called psychophysiological interaction (PPI) to address this issue. They rely on task- or context-dependent inter-regional covariance to determine statistically associations among brain activities in different regions. However, all functional connectivity approaches are based on correlations, and therefore cannot be used to identify the directions and causal relations of the connections (i.e., effective connectivities).

A number of other approaches have been developed to examine effective connectivities. For example, covariance modeling (e.g., structural equation model, SEM) has been used successfully to evaluate effective connectivities among a given set of brain regions when subjects perform a particular task. It can also be used to test the differences in effective connectivities involved in different cognitive tasks, thus illustrating the time- and task-dependent nature of these patterns (McIntosh & Gonzalez-Lima, 1994). It shall be kept in mind that SEM makes causality inferences based on the covariance structure but not temporal information of neural activities in different brain regions. A causality model that emphasizes temporal information is the Granger causality model (Goebel, Roebroeck, Kim, & Formisano, 2003). This model, for example, has been applied to EEG as well as fMRI time series and has provided information about directional interactions between neural elements in cognitive tasks (Brovelli et al., 2004).

Dynamic Causal Modeling (DCM), developed by Friston et al. (2003), is based on the construction of a reasonably realistic neuronal model of interacting cortical regions with neurophysiologically meaningful parameters. The idea is to use a full Bayesian approach to estimate neuronal responses from the measured BOLD response data. Applications of DCM have examined modulatory effects of attention on connectivity in the visual system (Mechelli, Price, Friston, & Ishai, 2004). The DCM approach has also been expanded to model EEG and MEG data (David et al., 2006). It is important to note that both SEM and Granger causality model make causal inferences based on the BOLD response, but not neuronal activities.

Multi-modality data integration

Another significant development in functional imaging is multi-modality data integration. In a sense, like reaction times and many other physiological responses, functional imaging is just

another measure of human brain activities. Each of these measures provides different insights into the human mind. In addition, as mentioned before, different functional imaging techniques measure different aspects of brain responses and have their own strengths and limitations. Thus, integrating different measures is not only useful but very necessary. There are four types of integrations. First, different imaging techniques can be integrated to take advantage of their respective strengths. Second, behavioral and functional imaging data must be integrated when interpreting imaging results. Third, data on brain structures and functions must be integrated. Finally, there are also methodological reasons to integrate multi-modality data. For example, recordings of subjects' head movement, eye blinking, breathing, and heart rates can be used to reduce the noise in functional imaging data. Using multi-modal data to reduce noise in fMRI has become a standard affair in modern functional imaging analysis. We focus on the first three types of integrations in the following sections.

Multi-modality data integration has not only furthered our understanding of old problems, but also addressed many new questions. For example, researchers have long been puzzled by the sources of resting-state BOLD fMRI. Mantini et al. (2007) recorded simultaneous EEG and fMRI when subjects were instructed to lie down quietly in the scanner without thinking about anything. Using independent component analysis on the fMRI data, they identified six widely distributed resting state networks. The BOLD signal fluctuations associated with each network were correlated with EEG power variations in the delta, theta, alpha, beta, and gamma bands. Each functional network was characterized by a specific electrophysiological signature that involved combination of different brain rhythms (Mantini et al., 2007). Another classical example is to identify the relationship between the BOLD response and neuronal activities. Logothetis et al. (2001) simultaneously recorded neuronal activities (single neuron spikes and local field potentials) and the BOLD responses on monkey subjects, and found that the BOLD responses were highly correlated with local field potentials, providing support that the BOLD responses at least partially reflect neuronal activities. Similar studies have been conducted on human patients (due to the invasive nature of this procedure) and have generally confirmed this observation (Nir et al., 2007)

The multi-modality data integration approach has also been used to identify the relationship between anatomical connectivities and functional/effective connectivities. In a recently study, Hagmann et al. (2008) found a very high degree of overlap between structural and functional connectivities by combining diffusion spectrum imaging (a non-invasive method to examine the white-matter anatomical connectivities) and resting-state fMRI imaging.

One of the ultimate goals of cognitive neuroscience is to use functional imaging to reveal the neural basis of human behavior. At a minimum, behavioral data must be correlated with fMRI data. As illuminating as such correlations may be, it is even more important to have such analyses guided by computational models. Recent successful applications of the state-space model (Law et al., 2005; Smith et al., 2004) and reinforcement-learning model (Sutton & Barto, 1998) in imaging illustrates the importance of theory-driven integration of behavioral and imaging data (O'Doherty et al., 2004). As it will become clear in the next section, an important feature of neuroeconomics research is the integration of functional imaging with decision-making models from economic research. Computational models and theories provide important hypotheses to guide imaging data analysis.

In sum, cognitive neuroscience has experienced a rapid development, in large part due to recent advances in functional imaging techniques and their obvious advantages over traditional neurological and animal physiological methods. Cognitive neuroscience has become highly influential not only in the field of neuroscience and psychology, but also in disciplines such as sociology, economics, and philosophy. Researchers of different disciplines have begun to use brain imaging to connect human behaviors with brain activities. Among the most rapidly

developing areas is neuroeconomics, which combines cognitive neuroscience with experimental and behavioral economics. In the next section, we provide some illustrative examples of research in neuroeconomics.

Neuroeconomics: Applications of Brain Imaging in Decision Making Research

Neuroeconomics is a multidisciplinary area of research that incorporates neuroscience, economics, and psychology, with the goal of building a biological model of decision-making in economic environments. By combining techniques from cognitive neuroscience and experimental economics, neuroeconomic studies examine how real-time neural activities are associated with various decision making processes, such as evaluating options, assessing risks and rewards, making decisions, and interacting with others who may be affected by the decisions (Camerer, Loewenstein, & Prelec, 2005).

Before the emergence of neuroeconomics, researchers in behavioral economics had developed various models to describe, predict and guide human economical decision-making. These models can be roughly divided into two categories. One category, the so-called normative or prescriptive models, is about optimal decisions. By assuming people are absolutely rational and fully informed, and possess unlimited computational power, these models describe how people *should* make optimal decisions. The other category, the so-called predictive or descriptive models, is about how people *actually* make decisions in real life. One focus of neuroecnomics is to understand why people often do not make optimal decisions, i.e., neural mechanisms of irrationality.

Research in neuroeconomics covers a wide range of topics. In the first comprehensive handbook in this field, *Neuroeconomics: Decision Making and the Brain*, there are 33 chapters and the topics range from axiomatic neuroeconomics to social preference in primates. Due to space limitation, the current article focuses on three specific areas, decision under uncertainty, intertemporal choice, and game theory. For each area, we first introduce the general research questions and then review some representative studies to exemplify the diverse set of research topics in neuroeconomics.

Decision under uncertainty

Many decisions, such as whether to invest in the stock market or to accept a new job, involve the possibility of gaining or losing relative to the status quo. The economics literature makes distinctions between two types of decision-making under uncertainty, decision under risk and decision under ambiguity. When the probabilities of the possible outcomes are known to the decision maker, such as in the dice game, gambling on a roulette wheel, and certain lottery, it is called risky decision making or decision making under risk. In most daily decision-making situations, such as whether or not to take a job offer, to marry someone, and to invest in the stock market, the probabilities of possible outcomes are not available. Decision under these situations is called decision under ambiguity.

The difference between risky and ambiguous decision-making is illustrated by the Ellsberg paradox (Segal, 1987). Imagine one deck of 20 cards composed of 10 red and 10 blue cards (the risky deck), and another deck has 20 red or blue cards, but the composition of the red and blue cards is completely unknown (the ambiguous deck). A successful bet on a color wins a certain amount of money if a card with the chosen color is drawn. Otherwise the participant loses a certain amount of money. This gambling task reveals two important characteristics of human decision making under uncertainty. First, when faced with such decisions, most people are markedly risk aversive. For instance, if you offer people $10 gain (when betting correctly)

and otherwise $10 loss, people will reject this gamble. On average, people will not accept the gamble unless the amount that may be gained is at least twice the amount that may be lost (e.g., gain $20 or lose $10). Second, people also have ambiguity aversion. They are more likely to reject the gamble in the ambiguous situation (e.g., when the distribution of the red and blue cards is unknown). That is, when asked to choose between a risk decision and an ambiguous decision, subjects prefer the risk decision task over the ambiguous decision making task.

Prospect Theory, the most successful behavioral model on decision-making under risk (Kahneman & Tversky, 1979; Tversky & Kahneman, 1992), explains risk aversion for "mixed" (gain/loss) gambles using the concept of loss aversion: People are more sensitive to the possibility of losing objects or money than they are to the possibility of gaining the same objects or amount of money. To examine the neural substrates of loss aversion, Poldrack and colleges (2007) collected fMRI data while participants decided whether to accept or reject mixed gambles that offered a 50/50 chance of either gaining one amount of money or losing another amount. They systematically manipulated the amount of gain and loss so that some gambles were appealing to the participants whereas the others were not. The amounts of wins and losses were essentially orthogonal to each other across the entire pool of trials. By comparing trials with potential gains and those with potential losses, the researchers could separate the neural responses associated with possible gains and possible losses. In the first analysis, they correlated the brain responses with potential gains and potential losses. They found that largely overlapping areas (including the midbrain dopaminergic regions and their target regions, such as the ventral striatum and ventromedial prefrontal cortex) exhibited increased activities as potential gains increased and decreasing activities as potential losses increased. More importantly, the slope of decrease associated with losses was steeper than that of increase associated with gains, consistent with the notion that losses loom larger than gains in Prospect Theory. Using the slopes for gains and losses, they calculated the neural loss aversion factor (λneural) for each brain region: $\lambda_{neural} = [-\beta_{loss}-\beta_{gain}]$. They also calculated, based on the participants' choices, the behavioral loss aversion factor (λ). They found that individual differences in behavioral loss aversion were well predicted by the measure of neural loss aversion in several brain regions, including the ventral striatum and prefrontal cortex. The study provides a neural account of behavioral loss aversion.

According to Prospect Theory, human decision-making involves maximization of a single measure of expected utility (EU), which is a combination of subjective weighting/probability and subjective value. Despite its parsimony and significant explanatory power, expected utility models have not led to a satisfactory understanding of the decision impairments observed in some of the patients with VMPFC lesions who displayed intact processing of reward levels (Bechara & Damasio, 2005). This points to the possibility that other factors, such as risk sensitivity, i.e., the fear of unknown, might also be important in understanding individuals' risky decision making. To test this hypothesis, Xue et al. (2008) used the Cups Task to study the neural mechanisms of risky decision-making, especially the inter-play of risk and reward (Xue et al., 2008). The Cups Task includes a Gain domain and a Loss domain (Weller, Levin, Shiv, & Bechara, 2007). In the Gain domain, each trial consists of a certain option of winning $1 for sure, and a risky option with a probability, as determined by the number of cups, of winning more than the sure bet, or not winning at all. Similarly, each trial in the Loss domain consists of a certain option of losing $1 for sure and a risky option of losing more than the sure loss, or not losing at all. Participants were asked to choose between the risky option and the safe option, and received the outcome after their choice. Simple as it is, this task has been shown to be sensitive to decision deficits in a group of medial prefrontal lesion patients (Weller et al., 2007).

In analyzing the fMRI data, Xue et al. (2008) first quantified the amount of experienced risk and experienced reward for each trial by considering participants' choice (risk vs. no risk) and

outcome (gain vs. loss). Following existing literature (Holt & Laury, 2002), risk was defined as the variance of the outcome. The experienced risk was defined as the variance of the possible outcome of the risky option, multiplied by the choice (1 for risk and 0 for no risk), i.e., they experienced no risk if they did not gamble. By correlating the experienced risk and experienced reward with brain activations, Xue et al. (2008) found that two adjacent brain regions in the medial prefrontal cortex (MPC) conveyed distinct decision signals: the dorsal MPFC was more activated when individuals experienced higher level of risk; in contrast, the ventral MPFC was parametrically modulated by the received gain/loss. In a further analysis, the authors calculated participants' risk preference based on their behavioral choices and correlated it with activations in the ventral and dorsal MPFC. This analysis revealed that the degree of dorsal MPFC activation to risk across subjects was negatively correlated with their behavioral risk preference, whereas the degree of ventral MPFC activation to reward was positively correlated with their behavioral risk preference. These results suggest risk decision making is a combat between two competing neural forces: the "lure" of gain in the ventral MPFC and the "fear" of risk in the dorsal MPFC.

Other studies have directly compared decision making under ambiguity and under risk. For example, Hsu, Bhatt, Adolphs, Tranel, & Camerer (2005) found that the level of ambiguity in choices was correlated positively with activations in the amygdala and orbitofrontal cortex, and negatively with that in the striatal system. Essentially, the same system treats ambiguity and risk as limiting cases of uncertainty. In contrast, another study (Huettel, Stowe, Gordon, Warner, & Platt, 2006) has also compared ambiguous vs. risky decision-making and found that decision under ambiguity might involve neural mechanisms that are different from those involved in decision under risk. The authors found that activation of the lateral prefrontal cortex (Ambiguity > Risk) was correlated with individuals' ambiguity preference, whereas activation of the posterior parietal cortex (Risk > Ambiguity) was correlated with individuals' risk preference.

Although the majority of studies on risky decision-making have used fMRI as their primary research tool, there is an increasing number of studies using EEG. For example, one ERP study has shown that the ERP response recorded from the medial frontal electrodes can quickly separate two decision components: Feedback negativity that occured 200-300ms after the feedback significantly differentiated gain and loss trials, whereas the P300 component was associated with outcome amplitude (regardless whether they were gain or loss trials) (Yeung & Sanfey, 2004). As mentioned earlier, EEG studies can provide important insights into the time-course of neural responses associated with different decision parameters.

Impulsivity and inter-temporal choice

"Should I apply for graduate school or go to the job market now?" "Should I save for the future or should I consume now?" Life is full of inter-temporal choices like this. Most such choices require decision-makers to trade off costs and benefits at different points in time. According to Irving Fisher (1930), rational decision makers will make the decision (e.g., borrow or lend) based on the market interest, so that present and future money can be equated. However, even with interest rates and other factors taken into account, human behavior deviates greatly from predictions of prescriptive decision theories. Most economic agents prefer current rewards to delayed rewards of similar magnitude. In economics, the theory of discounted utility is the most widely used framework for analyzing inter-temporal choices. Normative models either assume a zero discount or a constant discount, i.e., an *exponential* discounting function $D(t) = \delta^t$, where δ represents the discounting rate, t represents time and D represents the discount. In contrast, the *hyperbolic* discount function has been widely adopted as a more-realistic way of describing how people (and animals) value future outcomes. Two major *hyperbolic* discount functions have been proposed. The first is the quasi-hyperbolic time-discounting function,

sometimes referred to as beta-delta preference. It posits that the discounted value of a reward of value u received at delay t is equal to u at $t = 0$ and $\beta\delta^t{}_u$ at $t > 0$, where $0 < \beta \leq 1$ and $\delta \leq 1$. The ß parameter represents the special value placed on immediate rewards relative to rewards received at any other point in time. When $\beta < 1$, all future rewards are uniformly downweighted relative to the immediate reward. The δ parameter is simply the discount rate in the standard exponential formula, which treats a given delay equivalently regardless of when it occurs. Another hyperbolic function is $SV = 1/(1+kD)$, where SV is subjective value (expressed here as a fraction of the immediate value), D is delay (in days) and k is a subject-specific constant. Both versions of the hyperbolic discount function have obtained support from fMRI studies.

McClure and colleagues hypothesized that the two parameters in the first hyperbolic discount function are mediated by two distinct neural systems: The ß system is mediated by the limbic structures and the δ system by the lateral prefrontal cortex and associated structures supporting higher cognitive functions (McClure, Laibson, Loewenstein, & Cohen, 2004). To test these hypotheses, they asked participants to make a series of inter-temporal choices between early monetary rewards and later monetary rewards while their brains were scanned in fMRI. In some choice pairs, the early option was available "immediately" (e.g., $20 now vs. $23 in 1 month). In other choice pairs, the early option was available only after a delay (e.g., $20 in two weeks vs. $23 in 1 month and two weeks). According to their dual-system hypothesis, the cognitive system is involved in both choices, whereas the limbic region is only involved in the first choice. To identify the ß system, they compared neural activations between the two types of choices. This comparison revealed regions in the ventral striatum (VStr), medial orbitofrontal cortex (MOFC), medial prefrontal cortex (MPFC), posterior cingulate cortex (PCC), all having been implicated in reward processing. To identify the δ system, they compared all trials with the baseline. Since this comparison included regions that are involved in visual and motor processing, they did a further analysis comparing the easy and difficult trials (based on the reaction time data). The idea here is that the cognitive system is engaged to a greater degree in difficult trials than the easy trials. This comparison revealed significant activations in the dorsolateral prefrontal cortex, ventrolateral prefrontal cortex, left orbitofrontal cortex, and inferoparietal cortex. If the two systems, i.e., the ß limbic system and the δ cognitive system, are differentially involved in immediate and future rewards, a further prediction is that the ß system is more activated when an immediate reward is selected and the δ system is more activated when a future reward is selected. This prediction was also confirmed by the interaction of the two systems and the two types of choices, with δ areas showing greater activity when future reward was chosen.

Kable and Glimcher (2007) investigated neural mechanisms of the second hyperbolic discount function. The authors employed a psychometric-neurometric technique in the study to identify the subjective values of delayed rewards (as compared to the immediate reward) based on economic models, and brain regions whose responses are correlated with the subjective values. To achieve this goal, they asked participants to make a series of choices between a future reward (with the reward amplitude and time delay parametrically varied) and a fixed amount of immediate reward (i.e., $20). By examining participants' choices, they estimated the behavioral discounting parameter k (i.e., behavioral k) for each individual participant, which varied from .005 (the most patient subject) to .1189 (the most impatient subject). Within each participant, they used the estimated parameter k to calculate the subjective value of each individual trial, and then correlated the subjective values with brain activations. This analysis identified that, across all subjects, activities of the medial prefrontal cortex, posterior cingulate cortex, and the ventral striatum, were significantly correlated with subjective values. To further confirm this result, they extracted the brain responses in the three regions in different temporal delay conditions, and estimated the neural discount parameter k (i.e., neural k). They found that across all subjects, the neural k was highly correlated with the behavioral k. Taken together, the study

provides compelling evidence that the limbic reward regions quantitatively track subjective values, for both immediate and future rewards.

Game theory

Game theory has been developed to understand a wide class of social interactions, including competition, cooperation, and coordination. A game is usually played by two or more people, thus provides the ground to connect individual decision making with group-level outcomes. Traditional studies of game theory focus on developing and describing *strategies* in social interactions. A normative game theory usually develops a set of equilibria in these games, i.e., a set of strategies that individuals may follow so that they are unlikely to change their behavior. One important equilibrium state is the so-called Nash Equilibrium, which is reached if each player has chosen a strategy and no player can benefit by changing his or her strategy while the other players keep their strategies unchanged. For example, in the Ultimatum Game (UG), two players are randomly and anonymously matched, one acts as proposer and the other as responder. The proposer is endowed with a given amount of money (say, $10). He is then asked to suggest a way of sharing the money with the responder. The responder can either accept the offer or reject the offer. If he accepts the offer, the money is split according to the proposal. If he rejects the offer, neither of them gets the money.

The Nash Equilibrium in this game is reached if the proposer gives the responder a smallest division of the money (like one cent). This is because, once the proposer sticks to this strategy, no matter what the responder chooses to do, either accept or reject the offer, the outcome for the responder will not be better. A rational responder would accept whatever proposal (except that the proposer keeps all the money), otherwise he gets nothing. Surprisingly, many studies have shown that the responders actually reject quite often low offers; they reject about half of the offers that are below 20% of the endowment. The interesting question here for neuroeconomics is to understand the neural mechanisms underlying the decision making process of the responder.

Sanfey and colleagues were the first to use fMRI to study social exchanges in Ultimatum Games (Sanfey, Rilling, Aronson, Nystrom, & Cohen, 2003). It should be noted that in the UG paradigm, it is important to keep the responder and proposer anonymous to each other. In addition, the mechanisms involved in single-shot games (i.e., a pair of proposer and responder play only one round of the game) and its results are different from those of multi-shot games in which multiple rounds of game are played between them. In the latter case, one reason the responder would reject an unfair offer is to pressure the proposer to increase the subsequent offers, but such a tactic is not possible in the single-shot games. In this study, the authors first introduced 10 anonymous people to the participants and told them that they would be the partners with them in the game. In another condition, the participants were told to play with a computer who makes random proposals. Essentially, participants received exactly the same offers from the computer as from the 10 anonymous people, with half of the offers being fair ($5:$5 split) and the other half being unfair (two offers of $9:$1, two offers of $8:$2 and one offer of $7:$3). There were two important behavioral results. The first result is that the participants accepted all fair offers and the rejection rate increased as the offers became more unfair. The second result is that the participants rejected significantly more unfair offers proposed by humans than those by the computer.

Functional imaging results showed that several brain regions, including the anterior insula, anterior cingulate cortex, and dorsal prefrontal cortex, exhibited stronger activations to unfair offers than to fair offers. The bilateral insula activation was also significantly greater when the unfair offers were from humans than when they were from the computer, suggesting that it is not simply the amount of money but rather the perceived unfair treatment from people that drove the insula activation. Across all the participants, it has been shown that individuals who

showed more insula activation to unfair offers were more likely to reject the offer. In light of the fact that the anterior insula has been implicated in processing negative emotions, these results suggest that the rejection of unfair offers is driven by negative emotion experienced by the responders during the ultimatum game. Consistent with this view, it has been shown that allowing participants to express their negative emotion toward the proposer actually increased the rate of acceptance of unfair offers (Xiao & Houser, 2005).

Knoch and his colleagues used repetitive transcranial magnetic stimulation (rTMS) to examine effects of left and right dorsolateral PFC disruption on rejection decision (Knoch, Pascual-Leone, Meyer, Treyer, & Fehr, 2006). They found that rTMS stimulation of the right DLPFC significantly reduced the rejection rate of unfair offers, i.e., 10% rejection of offers below 20% of the endowment, as compared to 50% rejection rate when the left DLPFC was disrupted by rTMS. One interpretation of this result is that the right DLPFC, but not the left DLPFC, can override participants' self-interest and guide their decision towards benefits to the society, i.e., to foster the social order and fairness. According to this interpretation, the motivation of rejecting unfair offers is prosocial rather than selfish, which is guided by the high-level executive control system but not by the emotional system. This study has led to many interesting debates. Further studies are necessary to resolve these debates.

The Ultimatum Game is an elegant paradigm to study social exchanges as well as their neural mechanisms. Researchers have also used other games, such as the prison's dilemma game, the trust game, and the public goods game, to study social trust, competition, and collaboration. Due to space limitation, brain imaging research using these other games is not reviewed in this article. Interested readers are referred to Camerer's chapter (Camerer, 2008).

Summary

Although we have covered a very small sample of current neuroeconomics studies on decision-making, several features are already evident from these studies. From a theoretical point of view, these studies have generated important insights into human decision-making. For example, theses studies have shown that decision making usually involves complex psychological and neural processes, including competitions between automatic and controlled processes, between cognitive and emotional processes, as well as between different emotional processes, such as the "lure" of reward and "fear" of risk. These findings suggest that, contrary to normative models' claim that human beings are perfectly rational and possess unlimited power for cognitive processing, human decision-making is usually affected by emotions and by habitual and automatic mental processes. These processes have clear neurobiological bases. These studies also reveal that many important social motivations, such as altruism and prosocial morals, social order and hierarchy, and social comparison, could profoundly affect human decision making. Some of them, such as social fairness (Tabibnia, Satpute, & Lieberman, 2008), charity giving (Harbaugh, Mayr, & Burghart, 2007), and social comparison (Fliessbach et al., 2007) might function through the common reward circuits that are responsive to primary rewards, such as water, food, and sex. Finally, these studies have started to reveal the neural mechanisms underlying individual differences in decision-making. As is evident in these studies, individual differences in decision-making might be associated with variations in the functionality of brain regions implicated in the decision process.

From a methodological point of view, all these studies have set good examples of combining models from decision theories (e.g., the Prospect Theory) with brain imaging techniques. The high degree of correlation between decision parameters (such as expected utility, risk, probability) and brain activations are crucial in identifying the neural substrates of decision-making. Generally, both within-subject correlation and between-subject correlation have been shown to be extremely useful. For example, Xue et al. (2008) used a model from the finance literature to quantify the experienced risk in each trial, and examined, within each individual

subject, the trial-by-trial variations in the BOLD signals as a result of different levels of experienced risk. This within-subject analysis revealed highly consistent results across all subjects in the dorsal MPFC. To further examine the association between dorsal MPFC and risk preference, Xue et al. (2008) examined whether individual differences in dorsal MPFC activations were associated with individual differences in risk preference. In this between-subject correlational analysis, they found that individuals showing strong activations in dorsal MPFC also exhibited low levels of risk behaviors. A similar approach has been used in a number of studies reviewed in this article (e.g., Hsu et al., 2005; Kable & Glimcher, 2007; Tom et al., 2007). Identifying consistent correlations at both the within- and between-subject levels has provided a highly useful method to integrate functional imaging measures with decision models.

Challenges and Future Directions

Despite the impressive applications of functional imaging in decision-making studies, neuroeconomics is still in its infancy. This discipline has great promises, but also faces many challenges.

First, functional imaging studies can only discover the brain regions that are involved in performing a task, but cannot establish whether the regions are necessary for the task. For example, although the anterior cingulate cortex (ACC) has been consistently found to be involved in cognitive control, patients with ACC lesions perform normally in the Stroop and go/no-go tasks (Fellows & Farah, 2005). In order to establish the necessary and sufficient conditions of a brain region in a task, it is important to combine neuroimaging and lesion techniques. For example, Hsu et al. (2005) used fMRI to discover that the orbitofrontal cortex is involved in risky decision-making. In another experiment, they applied the same task to a group of patients with orbitofrontal lesions and confirmed that damage to this region impaired decision-making. The study by Xue et al. (2008) has taken a different approach: They adapted a task that has been shown to be sensitive to medial PFC lesions and used the information to guide their analyses of the fMRI data collected from healthy participants. Both approaches have proved to be effective. One major limitation for the combined imaging and lesion studies on human subjects is that (irreversible) lesions can only be studied with patients. The nature of the lesions (size, severity, location, etc.) is beyond researchers' control. Reversible "lesion" techniques such as transcranial magnetic stimulation (TMS) and pharmacological research methods also have their own limitations. For example, TMS can only target cortical regions but not subcortical nuclei, and drug effects are often too widespread for researchers to target a particular brain area. Major breakthroughs are necessary to overcome these limitations.

Second, neuroimaging studies have focused on understanding brain functions (i.e., what is the function of a certain brain region?). Studies of this kind have significantly advanced our knowledge of brain functions. Nevertheless, if neuroimaging studies are ever going to advance our understanding of human decision-making, we must be able to make inferences on the ongoing cognitive processes. Although such inferences have been made (implicitly or explicitly) for a long time, by cognitive neuroscientists, their validity has only been carefully examined recently by Poldrack (2006). Poldrack pointed out this issue as a "reversal inference" problem. Typical inference in cognitive neuroscience goes like this: "When task A is presented, brain area Z is active; then we conclude that brain area Z is responsible for task A". The reversal reference, on the other hand, goes like this: "Brain area Z is active in task X and previous studies show that area Z has been involved in task A. Thus we conclude that task X engages cognitive process A." The reversal inference is guaranteed to be valid only if "Area Z is only involved in cognitive process A". However, the reality discovered from neuroimaging studies in the last 20 years is that we seldom find a brain region that is just doing one thing. Even the primary visual cortex is involved in both visual processing and visual imagery. The Broca's

area, which had been assumed to be solely associated with articulation, has been found to be active in numerous tasks. In the decision-making literature, the nucleus accombens (NAcc) is often found to be active in processing reward. However, this does not necessarily mean that whenever the NAcc is activated, the participant is experiencing reward and happiness. Indeed, other studies have found that the NAcc is also involved in processing risk (Xue et al., 2008) as well as stimulus and feedback salience (Cooper & Knutson, 2008). The logical pitfall hidden in "reversal inference" is potentially very serious and deserves careful treatment. Poldrack (2006) proposed two ways to improve confidence in reversal inference: increase the response selectivity in the brain region of interest, or increase the prior probability of the cognitive process in question. It should be noted that pattern analysis approaches, which have been developed to improve "reversal inference" (Poldrack, 2008), are using both strategies. By looking at the pattern of many voxels rather than the activation or deactivation of a single averaged region, pattern analysis approaches significantly increase the selectivity of brain responses to certain stimuli. Using the same experimental task for both the training and test dataset, it also significantly increases the prior probability of the cognitive process. However, because the same experimental task is used in both training and test stages, this design does not allow us to learn anything about the underlying cognitive process. One potential solution, for example, is to use the pattern analysis approach to train the classifier to differentiate two well-studied tasks (e.g., pictures eliciting positive vs. negative emotions) and then use this classifier to test whether the brain pattern of watching an in-group and an out-group member would match the two patterns respectively. If they match, we can then conclude with some confidence that observing an out-group member would engage negative emotions (see Miller, 2008 for similar discussion).

Third, the laboratory settings for functional imaging studies are very different from daily life. To simplify interpretations of experimental results, researchers have usually used oversimplified decision tasks and added strict experimental controls. These practices might have impaired the ecological validity of these tasks and limited their explanatory power in accounting for real-life decision-making phenomena. For example, in typical fMRI studies, participants have to stay very still in a semi-closed space for a relatively long time, and engage in very limited social interactions. Due to the weak signal levels in brain imaging, most studies require repetitions of the same decision. As a result, the decision- making tasks in this setting have to be relatively simple and can be made quickly. These requirements have placed major limitations on the research questions that can be addressed with functional imaging techniques. In addition, to dissociate the neural responses involved in different cognitive processes, special task designs are required in many functional imaging studies. For example, since the BOLD response is very slow, in order to separate the neural responses associated with decision and feedback processes, researchers have to either discard the feedback or introduce long and jittered delays between decision and feedback. Although these manipulations have been very successful, their effects on the psychological and neural processes of decision-making are not well understood and it is not clear how results from these studies can be connected to daily life decision-making, such as gambling in Las Vegas. One possible way to increase the ecological validity of functional imaging studies is to associate laboratory task performance with performance in daily-life decision-making. For example, the Iowa Gambling Task (IGT), developed by Bechara and colleagues (1994) to examine risky decision-making in laboratory settings, has been shown to be able to predict decision-making behavior in daily life situations. Our hope is that, with technical advances, a lot of these issues can be resolved in the near future.

Finally, the fundamental question is whether we can make better predictions of human decision behavior from neuroeconomical studies. Since the birth of neuroeconomics, researchers have been debating whether neuroimaging can provide theories for economists or whether economic theories can provide frameworks for neuroscience (Glimcher, Camerer, Poldrack, & Fehr, 2008). Ultimately, critics are skeptical whether neuroimaging can provide better descriptions

and predictions of human decision-making behaviors than behavioral theories. In a 2005 article by two economists at Princeton University, Faruk Gul and Wolfgang Pesendorfer, "The Case for Mindless Economics", the authors argued that neuroscience cannot transform economics because what goes on inside the brain is irrelevant to the discipline. What matters are the decisions people make--in their jargon, the "revealed preferences"--not the process by which they reach them (Gul & Pesendorfer, 2005). The argument is similar to that of "mindless" psychology used by behaviorists and that of "brainless" psychology used by cognitive psychologists. Although it would be easier to argue for "mindless" decision making than "brainless" decision making, since the latter is based on traceable physical responses, many enthusiasts of neuroeconomics like Daniel Kahneman have acknowledged that the findings in neuroeconomics have so far generally just confirmed the expectations of behavioral theorists and behavioral economists (Kahneman, 2008). This is a methodological issue as well as a theoretical issue, and it is not limited to functional imaging techniques but also applies to other methods in neuroeconomics. So far we are nowhere close to a solution to this issue, but we have reasons to be optimistic since neuroeconomics is in its infancy and its potential in describing the neural bases of decision-making and predicting future decision making has just begun to be revealed.

Conclusion

This paper provides an overview of brain imaging techniques, with an emphasis on functional MRI and EEG, and their applications in studying human decision-making. With its rapid development and wide applications, brain imaging has profoundly changed the landscape of cognitive neuroscience research. One prominent application of brain imaging in the last few years is neuroeconomics, an emerging field that has roots in economics, neuroscience, and psychology. By combining theoretical models from experimental and behavioral economics and real-time measurements of brain activities, neuroeconomics has significantly advanced our understanding of the neural mechanisms underlying a wide range of decision behaviors, such as decision under uncertainty, intertemporal choice, and game theory. We believe neuroeconomics will fully realize its potentials by addressing several theoretical and methodological challenges.

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