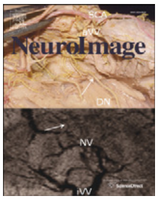
NeuroImage 71 (2013) 147–157

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg



Temporal prediction errors modulate cingulate–insular coupling

Roberto Limongi [a,b,*], Steven C. Sutherland [a], Jian Zhu [a], Michael E. Young [c], Reza Habib [a]

[a] Southern Illinois University Carbondale, USA
[b] Venezuelan Institute for Scientific Research, Venezuela
[c] Kansas State University, USA

ARTICLE INFO

Article history:
Accepted 29 December 2012
Available online 17 January 2013

Keywords:
Dynamic causal models
Prediction error
Cingulate cortex
Insular cortex
Predictive behavior

ABSTRACT

Prediction error (i.e., the difference between the expected and the actual event's outcome) mediates adaptive behavior. Activity in the anterior mid-cingulate cortex (aMCC) and in the anterior insula (aINS) is associated with the commission of prediction errors under uncertainty. We propose a dynamic causal model of effective connectivity (i.e., neuronal coupling) between the aMCC, the aINS, and the striatum in which the task context drives activity in the aINS and the temporal prediction errors modulate extrinsic cingulate–insular connections. With functional magnetic resonance imaging, we scanned 15 participants when they performed a temporal prediction task. They observed visual animations and predicted when a stationary ball began moving after being contacted by another moving ball. To induced uncertainty-driven prediction errors, we introduced spatial gaps and temporal delays between the balls. Classical and Bayesian fMRI analyses provided evidence to support that the aMCC–aINS system along with the striatum not only responds when humans predict whether a dynamic event occurs but also *when* it occurs. Our results reveal that the insula is the entry port of a three-region pathway involved in the processing of temporal predictions. Moreover, prediction errors rather than attentional demands, task difficulty, or task duration exert an influence in the aMCC–aINS system. Prediction errors debilitate the effect of the aMCC on the aINS. Finally, our computational model provides a way forward to characterize the physiological parallel of temporal prediction errors elicited in dynamic tasks.

Introduction

The neural coding of predictive behavior has gained substantial attention in the last decade (Bar, 2009). Research on predictive behavior includes areas as diverse as neuroeconomics (Platt and Huettel, 2008), learning (Behrens et al., 2007; den Ouden et al., 2009; O'Doherty et al., 2001; O'Doherty et al., 2004), and brain function (Friston and Kiebel, 2009). In all these domains, researchers test their theories using both animal and human models.

Human predictive behavior comprises the prediction of the outcome of an event: the winner of a football match, whether it will rain, or which product will sell better. Critically, humans also predict the temporal dynamics of events. For example, while walking down the street, a person might witness a rear-end collision. As an anticipatory physiological response, the witness' body may shrink away a few milliseconds before the collision. The witness not only predicts the occurrence of the collision but also *when* the collision occurs.

Prediction error likelihood is associated with a linear increase in the activity of the anterior mid-cingulate cortex (aMCC, Brown and Braver, 2005).[1] Furthermore, in tasks demanding either time processing (Kosillo and Smith, 2010), the prediction of an event's onset (Forster and Brown, 2011), or predictions under uncertainty (Singer et al., 2009) activity in the anterior insula (aINS) increases. For the current study, we consider crucial, however, that uncertainty in the outcomes of future events conjointly increases the activity of the aMCC and the aINS (Critchley et al., 2001).

The aMCC and the aINS constitute an input–output system (Medford and Critchley, 2010; Taylor et al., 2009) with anatomical (Mesulam and Mufson, 1982; Mufson and Mesulam, 1982) and functional (Taylor et al., 2009) reciprocal connectivity. These facts suggest that effective connectivity (i.e., neuronal coupling) might mediate the functional aMCC–aINS connectivity in uncertainty-related temporal prediction tasks. Based upon the observed BOLD responses elicited during a temporal prediction task that generated different levels of uncertainty in the participants, we used a dynamic causal modeling (DCM) approach (Friston et al., 2003) to test two hypotheses. First, task context (i.e., the main effect of temporal prediction) would directly increase within-region coupling in the aINS. Second, signals

---

* Corresponding author at: 8424 NW 56th St., Suite CCS 00202, Doral, FL 33166, USA. Fax: +58 212 5041764.
E-mail address: Roberto.Limongi@fulbrightmail.org (R. Limongi).

[1] According to the four-region neurobiological model of the cingulate organization (Vogt, 2009; Vogt et al., 2003), the aMCC comprises the caudal parts of areas 32, 24, and 33 encompassed between the vertical plane of the anterior commissure and the diagonal from the vertical plane of the genu of the corpus callosum.

1053-8119/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.neuroimage.2012.12.078

associated with prediction errors would modulate the connection strength of the aMCC–aINS system.

From a DCM perspective, regional activity in the aMCC–aINS system can be produced via either direct or modulatory inputs. The main effect of an uncertainty-related prediction task is an increment of the insula's hemodynamic response (Critchley et al., 2001). Thus, we predicted that a model generating the fMRI data would include direct inputs to the aINS. In addition, neural activity associated with prediction errors modulates cortical–cortical (den Ouden et al., 2009) and cortical–subcortical (den Ouden et al., 2010) connections. Therefore, we predicted that temporal prediction errors would modulate aMCC–aINS connections. No previous studies, however, allowed us to anticipate whether prediction errors would modulate forward or backward connections. Thus, we evaluated this issue via model comparison.

Because the BOLD response is unspecific for excitatory and inhibitory connections that instantiate cortical activity (Logothetis, 2012). Our study relied on two assumptions regarding the dynamics of the synaptic plasticity within and between our regions of interest. First, synaptic plasticity of cortical within-region intrinsic connections comprises changes in both excitatory and inhibitory neuronal subpopulations. Second, between-region extrinsic inter-regional connections comprise changes mainly in excitatory couplings (Douglas and Martin, 2004). Thus, we assumed that direct influence of task context would produce changes in both excitatory and inhibitory connections whereas temporal prediction errors would cause changes only in aMCC–aINS extrinsic connections.

We tested our predictions in two stages. First, we identified a set of inter-regional connections in an optimal DCM. Several candidate models with different interregional configurations could accommodate our hypotheses and assumptions. By means of model comparison, we selected the model with the highest probability of having produced the fMRI data. To represent a more realistic decision making circuit in the model, we also added connections from the ventral striatum. Second, we tested our optimal model against models with alternative direct and modulatory inputs.

Temporal prediction task

We used a variant of a task that has been traditionally used in research on causation: the Michotte's launching effect task (Thines et al., 1990). Participants predicted the movement's onset of a stationary ball contingent to the contact of a second ball. In this basic condition, the movement's onset of the stationary ball was highly predictable because the spatiotemporal contiguity between both balls cued the launching time (see Supplemental Video 1). We introduced different levels of uncertainty by modifying this basic stimulus in the temporal and spatial dimensions. In the temporal dimension, we introduced two delays between the termination of the first ball's movement and the onset of the stationary ball's movement. Empirical data and mathematical models support the thesis that subjective time is not linearly related to objective time (Beckmann and Young, 2009; Catania, 1970; Gibbon, 1977, 1981; Gibbon and Church, 1981; Young et al., 2005). Failing to predict an objective sensory magnitude produces uncertainty in future predictions (Schultz et al., 2008; Singer et al., 2009), which increases the probability of committing prediction errors. Although in our task the trial instructions informed the participants on the duration of the programmed delay, higher uncertainty for longer delays was expected. In some timing tasks, individual differences in prediction accuracy arise due to variations in the strategy that participants might adopt for time estimation. For example, when participants are instructed to predict long durations spontaneous language-based counting increases the accuracy. The use of this chronometric strategy could confound the interpretation of the fMRI data (Hinton et al., 2004). In our task, however, chronometric timing unlikely caused any individual differences because the delays lasted less than 1500 ms. In the spatial dimension, we introduced two different spatial discontiguities (gaps). The effect of delay depends on the spatial gap between the objects (Young et al., 2005). Thus, for example, for a given delay we expected greater uncertainty-driven prediction errors in the presence of large gaps than in the presence of small gaps.

In this task, the computational value of each prediction error could produce adjustments in subsequent predictions. More accurate adjustments, however, would occur after explicitly delivering objective feedback (e.g., “your prediction was 230 ms late”) as an instance of supervised learning. Nevertheless, because we wished to ensure a high level of error commission across trials for the same condition (to avoid ceiling effects) we did not deliver feedback after the familiarization trials.

Modeling prediction errors

In previous fMRI studies using prediction errors as either a covariate (e.g., in linear models of the hemodynamic responses) or as exogenous inputs (e.g., in dynamic causal models), the experimenters have not used a direct measure of such errors. They have created continuous distributions of either the prediction errors or the probabilities of committing such errors. To construct the distributions, they have estimated the most-likely parameter values of theoretical behavioral models. Examples of these types of models are the Rescorla–Wagner model (Rescorla and Wagner, 1972), the temporal difference model (Sutton and Barto, 1998), and the Bayesian learning models (Behrens et al., 2007; den Ouden et al., 2010; Mathys et al., 2011). In the Rescorla–Wagner and the temporal difference models, the investigators estimate the free parameters (e.g., the learning rate) and then use such estimators to compute the prediction errors (O'Doherty et al., 2007). Conversely, by means of Bayesian learning the investigators construct distributions of prediction-error probabilities.

Although these strategies account for the behavioral data and serve the purpose of constructing continuous distributions that enter fMRI/DCM models, they implicitly rely on the assumption that the models mirror how the brain executes the tasks. Consequently, the problem of selecting the best possible behavioral model accompanies these strategies (see, for example, den Ouden et al., 2010). Because there always exists a more probable behavioral model that could produce a prediction-error/probabilities distribution, the investigator remains uncertain of the exact relationship between the neurophysiological and the behavioral data. To avoid this problem, we used a model-free direct measure of temporal prediction errors as a continuous variable.

Materials and methods

Participants

Fifteen right handed students (10 female), between 19 and 26 years of age (M = 21.76, SD = 2.26) and with no neurological history participated in the study. Participants signed informed consent forms and received a $25 gift card for participating. The study was approved by the Human Subjects Committee of Southern Illinois University at Carbondale.

Stimuli

The stimulus set consisted of nine types of visual animations with three gap sizes (0, 1, and 2 cm; 0.0, 0.9, and 1.9° of visual angle respectively) and three delay durations (0, 300, and 1200 ms). Each animation lasted 2700 ms and began with two balls appearing on the computer screen, one ball to the left of the screen and the other ball in the middle of the screen. Each ball was 1.34 cm (1.28° of visual angle) in diameter. At the beginning of each animation sequence, the left-most ball began to move to the right and continued at a constant