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Memory encoding and hippocampally-based novelty/familiarity discrimination networks

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Abstract

Novelty discrimination refers to the ability to decide whether information is new or has been previously encountered. Recent functional neuroimaging work has demonstrated that the hippocampus plays an important function in novelty discrimination. In the study described here, we explored the idea that novelty discrimination does not depend on the hippocampus alone but involves large-scale functional neural networks consisting of spatially remote brain regions. We measured blood flow with positron emission tomography (PET) while subjects semantically encoded visually and auditorily presented situationally novel and familiar words. Following each PET scan, subjects' memory was tested with a standard yes/no recognition test. Blood flow data were analyzed with the covariance-based seed partial least squares (PLS) method. Behaviorally, subjects' recognition performance was higher for novel than familiar words. Neurally, two large-scale functional networks involving the same region of the hippocampus were identified which showed coherent activity either during the encoding of situationally novel (but not familiar) items or situationally familiar (but not novel) items. These findings indicate that different neural networks are active in the processing of situationally novel and familiar information. The observation that the hippocampus participates in both networks supports the principle of neural context.

Keywords: Memory encoding; Novelty discrimination; Positron emission tomography; Functional connectivity; Partial least squares

1. Introduction

Among the many achievements of organisms is the ability to discriminate between novel and familiar stimuli. Novelty/familiarity discrimination (also known as novelty detection, or novelty assessment) is useful for the organism in a variety of situations, can take a number of specific forms, and can serve several functions (see reviews by [1–4]). The hippocampal system has been found to be critically involved in many tasks involving neural novelty/familiarity (henceforth just 'novelty') discrimination [1,2,5–20]. In this report, we describe a positron emission tomography (PET) study whose purpose was to explore the idea that novelty discrimination does not depend on the hippocampal system alone but is subserved by large-scale neuronal networks which include but go beyond the hippocampal system.

Earlier work suggested that novelty discrimination is a component of the process of encoding incoming information for long-term memory storage [19,20]. Regional cerebral blood flow (rCBF), measured during a yes/no recognition memory test, was higher for novel than for familiar items at a number of sites in the extended limbic system. Other research has corroborated the general thrust of these early findings [7,9,15,17,18], and has extended the novelty assessment networks to other cerebral regions beyond the limbic system, including a number of anterior and posterior neocortical sites [11,12,19]. We proposed a specific relation between novelty assessment and memory encoding in the form of a novelty encoding hypothesis. According to this hypothesis, the novelty of incoming information co-determines the extent to which such information is encoded for long-term memory storage: the greater the novelty, the greater the probability of encoding [20]. Since then, the novelty encoding hypothesis has received empirical support from two sources. First, purely behavioral studies have shown that under conditions in which all other possibly relevant variables are held constant, recognition memory is better for novel than familiar information [21,22] (see also [23]). Second, functional neuroimaging studies have identified brain regions whose activity at encoding (i) is correlated with novelty, and (ii) predicts subsequent retrieval of the encoded material [12].

The present study was designed to extend our previous experiment in two ways. First, the novelty/familiarity independent variable has typically been confounded with the task

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outcome: novel test items were (usually) correctly judged to be "new" whereas familiar test items were (usually) correctly judged to be "old". Neuronal differences between the two kinds of material, therefore, could also reflect differences in the task outcome. In the present study, we used a design in which the novelty/familiarity variable was orthogonal to other independent and dependent variables [24], thereby allowing us to examine both behavioral and neural correlates of novelty free of confoudings. Second, the existence of the postulated novelty "networks" was based on indirect evidence, namely observed differences in the activity (blood flow) levels for novel and familiar items in different cerebral regions. In the present study, we sought evidence for functional networks more directly by using the multivariate seed voxel partial least squares method (seed PLS) to identify functional networks of spatially distributed cerebral regions whose activity is correlated across subjects [25–28].

2. Methods

2.1. Subjects

Eight right-handed male and eight right-handed female subjects between the ages of 18 and 35 ($\mu = 24$) participated in the experiment. Each subject was paid $80. The study was approved by the ethics committee of Baycrest Centre for Geriatric Care, University of Toronto.

2.2. Design

The experiment consisted of a $2 \times 2 \times 2$ factorial design. Modality of presentation (auditory/visual), levels of processing (semantic/physical), and novelty of material (novel/familiar) were manipulated within subjects. The eight experimental conditions which arise from crossing these three independent variables were counterbalanced across subjects such that each condition appeared in each of the eight possible scan positions. Following each condition, a recognition test was administered. Because of our interest in identifying functional networks underlying the encoding of novel and familiar words into episodic memory, only data from the four semantic encoding conditions, which are more likely to foster long-term encoding, will be reported here [29,30].

2.3. Material

A total of 480 five- to eight-letter English words were used (frequency 1–324, $\mu = 25.7$). The words were divided into 16 lists of 30 words each. Eight lists were assigned to the auditory condition and the other eight to the visual condition. Within each modality, four lists were assigned to the semantic condition and four lists were assigned to the physical condition. From each set of four lists, one was assigned to the novel condition, another to the familiar condition, and the remaining two served as distractors for the post-scan recognition tests. For the auditory conditions, the words were digitized in a female voice on a personal computer.

2.4. Procedure

Prior to scanning, subjects were familiarized with 8 of the 16 word lists (240 stimuli). Four of these lists (120 stimuli) were presented visually and the remaining four (120 stimuli) were presented auditorily. In the first stage of the familiarization phase, subjects were instructed to read or listen to a list of words and try to remember them for a later memory test. Auditory words were presented over speakers connected to a computer. Visual words were presented on a computer monitor suspended over the scanning bed. Words were presented at a rate of 1.5 s per item. Immediately following the learning phase, subjects were given a recognition test. The recognition test was the second stage of the familiarization phase, and contained only target items from the previous study phase. Subjects, however, were not informed of this fact, and were merely instructed to decide whether they had seen or heard each word. Subjects entered their response by pressing one of two buttons on a computer mouse. The test phase was self-paced. Following familiarization in both modalities, the eight scans, as described earlier, were administered.

Prior to injection of the tracer, subjects were given instructions for the upcoming scan. Depending on the experimental condition, subjects were told that they would either see or hear a list of words, and that they were to either make living/non-living decisions (semantic condition) about each word or decide whether each word began with a vowel (physical condition). No mention of the prior history of the words (novel/familiar) was made. The task was started at the time of radio-tracer injection, which preceded actual blood flow measurement by approximately 30 s. During the task, subjects either heard words spoken over speakers connected to a computer or saw them on a computer screen suspended over the scanning bed. In each scan, one list of words (30 stimuli) was presented at a rate of 3 s per item plus a 1 s ISI. Responses were made using a two-button mouse. The task continued for approximately 30 s after the end of the 1 min scan.

Immediately after each scan, subjects were administered a recognition test. They were informed that they would either see or hear a list of words and would have to decide whether each word was present in the immediately preceding study list. The test consisted of all of the words presented during the preceding scan and an equal number of distractors. For the novel conditions, the distractors were new words, whereas for the familiar conditions, the distractors were taken from the familiarization phase. Subjects entered their response using a computer mouse. The recognition test was self-paced. This procedure was repeated following each of the eight scans.