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Research article

# Relatedness-dependent rapid development of brain activity in anterior temporal cortex during pair-association retrieval

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## HIGHLIGHTS

• It is known that long-term memory can be consolidated rapidly in one or two days.

• Activity in temporal neocortex during pair-association retrieval changed in one day.

• The activity change was more rapid when paired items were semantically related.

## ARTICLE INFO

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Functional MRI studies have revealed that the brain activity in the anterior temporal cortex during memory retrieval increases over months after memory encoding. Behavioral evidence has demonstrated that long-term memory can sometimes be consolidated more rapidly in one or two days. In the present functional MRI study, we manipulated the relatedness between paired faces to be retrieved in a pairassociation task. The brain activity in the anterior temporal cortex during retrieval of paired associates increased rapidly in one day, as shown in previous studies. We found that the speed of the brain activity development was dependent on the level of semantic relatedness of paired faces. The results suggest that the semantic relatedness enhances the speed of formation of memory representation in the anterior temporal cortex.

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# 1. Introduction

It has been held that a memory trace is stabilized after its initial acquisition, a process called consolidation, by forming a memory representation, or a memory engram, in the neocortex after information is encoded into the hippocampus [1-3]. It usually takes months to years for the representation to be consolidated in the neocortex [4,5]. Recent studies have revealed that memory consolidation can occur more rapidly, in one or two days [6-8]. It has

http://dx.doi.org/10.1016/j.neulet.2016.05.044 0304-3940/© 2016 Elsevier Ireland Ltd. All rights reserved. been proposed that the rapid memory consolidation is guided by "the schema," that is, prior knowledge about learned items that is thought to be represented in the medial prefrontal cortex, if newly acquired information is compatible with the schema [6,9–13].

Previous studies using nonhuman primates have revealed the neural correlates of long-term memory representations. A population of neurons in the inferior temporal (IT) cortex has been found to be activated during performance of a pair-association (PA) task, where one of the paired stimuli is retrieved from the other of the paired stimuli [14]. The response of IT neurons was dependent on the medial temporal lobe (MTL), suggesting an interaction between the MTL and IT neurons during formation of memory representations [15]. Functional MRI studies have also demonstrated increased brain activity in the anterior temporal cortex (ATC) dur-





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**Fig. 1.** A) Participants performed a PA task. After presentation of a cue face, two faces (one a distractor and the other a paired associate of the cue) were presented, and the participants determined which face was the target. B) Three conditions of paired faces. The pairs of familiar faces were either the related (R) pairs that consisted of familiar faces of persons whose occupations were the same, or the unrelated (U) pairs that consisted of familiar faces of persons whose occupations were different. The novel (N) pairs consisted of unfamiliar faces. C) Time schedule of the experiment. On the first day, participants learned a set of pairs (R, U, N) as remote pairs. On the next day, participants learned another set of pairs (R, U, N) as recent pairs. Then, fMRI scan was administered while participants performed the PA task for all pairs. Postscan retest sessions were conducted for the same pair sets, and participants rated the confidence level of their judgments, and subjective congruency of the pairs.

ing retrieval of pair associations learned about 8 weeks before than during retrieval of recently learned pair associations [16,17]. It has also been suggested that the ATC plays a critical role as a network hub that gathers specific memory information distributed in different brain regions including the posterior temporal cortex [12,18]. Of particular relevance is the functional MRI study of Takashima et al. [8] showing that the brain activity in the anterior temporal cortex increased in one day after learning. However, it remains less understood under which condition the anterior temporal activation is formed rapidly.

In the present study using a PA paradigm (Fig. 1A), the relatedness between paired familiar faces was manipulated to differentiate the compatibility of the pairs with prior knowledge, namely related (R) and unrelated (U) pairs (Fig. 1B), with R pairs belonging to the same category (occupation) and U pairs belonging to different categories. As a reference, pairs of novel (N) faces, which are similar to those used in our previous studies [17,18], were also included (Fig. 1B). These three conditions of pairs were learned at two time points, about one day before the scan and about one hour before the scan, and these pairs were remembered during fMRI scanning (remote vs. recent conditions, respectively) (Fig. 1C). In this study, we primarily tested the hypothesis that the anterior tem-

poral activation is formed rapidly when the pair of familiar faces to be learned is compatible with prior knowledge on the faces, which allowed us to employ a small volume correction in the ATC. The brain activity during memory retrieval was examined on the basis of the condition (R vs. U) by time (remote vs. recent) interaction effects in ANOVA to detect the differential temporal characteristics of ATC activity that are dependent on the relatedness of pairs. The time effects (remote vs. recent) in N pairs were also examined to test the one-day effects for the unfamiliar face pairs.

## 2. Materials and methods

#### 2.1. Participants

Written informed consent was obtained from 32 healthy righthanded participants (14 males, 18 females; age range, 20–31 years). They were then subject to MRI under the experimental procedures approved by the institutional review board of the University of Tokyo School of Medicine. Five of the participants were excluded from imaging analyses due to the insufficient number (three or less) of remember trials under any of the six conditions (see behavioral procedures). Therefore, data from 27 participants (14 males, 13 females; age range: 20–31 years) were analyzed.

#### 2.2. Imaging procedures

Functional MRI scanning was conducted using a 3T MRI system (Philips Achieva X 3T Rel. 2.6, Best, The Netherlands). Localizer images were first collected to align the field of view centered on each participant's brain. T1-weighted structural images were then obtained for anatomical reference (120 1.20-mm-thick slices; in-plane resolution,  $0.813 \times 0.813 \text{ mm}^2$ ). For functional imaging, a gradient echo echo-planar sequence was used (32 4-mm-thick slices; TR = 2000 ms; TE = 35 ms; flip angle = 85°; field of view = 256 × 256 mm<sup>2</sup>; matrix size = 64 × 64). Each functional run consisted of 56 whole brain acquisitions. The first four functional images in each run were excluded from analysis to allow for the equilibration of longitudinal magnetization.

#### 2.3. Stimuli

Three hundred and eighty gray-scaled human face pictures were collected. The faces consisted of 100 famous athletes, 160 famous actresses or actors, and 120 non-famous persons. The faces of actresses and actors included TV entertainers, celebrities, and comedians.

Prior to each daily session, participants scored their familiarity with the faces on a scale of 1-4 (4, very familiar; 3, familiar; 2, barely familiar; 1, unfamiliar). For the faces scored as familiar (4, 3, or 2), the participants also chose the persons' occupation from three choices (actor/actress, athlete, or others). For the faces scored as unfamiliar (1), the participants rated if they knew any third person resembling the presented face on a scale of 1-3 (3, not resembling persons; 2, relatively resembling persons; 1, well resembling persons). Then, for each participant, familiar faces were defined as the faces with a familiarity score higher than 2 (i.e., 4 or 3) and correct occupation matching (actor/actress or athlete), and novel faces were defined as the faces with a familiarity score of 1 (unfamiliar), and a resemblance score of 3 (not resembling persons).

These familiar and novel faces were used to form face pairs (Fig. 1B). The face pairs were classified into three conditions based on the participants' semantic knowledge of the faces. The familiar pairs were either the related (R) pairs, which consisted of the familiar faces of the persons who have the same occupation [(actor/actress–actor/actress) or (athlete–athlete); total of 20 pairs], or the unrelated (U) pairs, which consisted of

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