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Contextual modulation of hippocampal activity during picture naming

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A B S T R A C T

Picture naming is a standard task used to probe language processes in healthy and impaired speakers. It recruits a broad neural network of language related areas, among which the hippocampus is rarely included. However, the hippocampus could play a role during picture naming, subtending, for example, implicit learning of the links between pictured objects and their names. To test this hypothesis, we recorded hippocampal activity during plain picture naming, without memorization requirement; we further assessed whether this activity was modulated by contextual factors such as repetition priming and semantic interference. Local field potentials recorded from intracerebral electrodes implanted in the healthy hippocampi of epileptic patients revealed a specific and reliable pattern of activity, markedly modulated by repetition priming and semantic context. These results indicate that the hippocampus is recruited during picture naming, presumably in relation to implicit learning, with contextual factors promoting differential hippocampal processes, possibly subtended by different sub-circuitries.

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1. Introduction

Picture naming is a standard task used to probe language processes in healthy (e.g. Cattell, 1886; Glaser, 1992) and impaired speakers (e.g. DeLeon et al., 2007; Goodglass & Blumstein, 1973). This task is associated with a broad neural network, including visual areas, bilateral temporal lobes for semantic processing, the left mid- and infero-temporal areas for word retrieval, left inferior frontal areas for conflict resolution and response programming, and pre-motor and motor areas for articulation (for reviews see: Indefrey, 2011; Llorens, Trébuchon, Liégeois-Chauvel, & Alario, 2011; Munding, Dubarry, & Alario, 2015).

Picture naming can be said to engage both language and memory processes, for example during semantic processing and during word retrieval. Still, much research based on picture naming is construed in the context of language processing hypothesis (see references above), without explicit consideration of memory research (for discussion, see Introduction in Hamamé, Alario, Llorens, Liégeois-Chauvel, & Trébuchon-Da Fonseca (2014)). Recently, however, a processing model has highlighted the connections between language and memory, and has implemented them to account for picture naming performance. Oppenheim, Dell, and Schwartz (2010) propose that a memory process, namely incremental learning between semantic and lexical representations, occurs during word/lexical retrieval. It is not unreasonable to assume that incremental learning can occur incidentally during picture naming, as the task requires the implicit association between picture, concept and word. A critical aspect of Oppenheim et al. (2010) model is that learning drives a process that is central to many psycholinguistic models, namely lexical retrieval.

Oppenheim et al. (2010) speculated that the Left Inferior Frontal Gyrus (LIFG) might play a role in the modulations of learning and selection efficiency induced by semantic context; they did not intend to discuss possible neural loci beyond that point. Incremental or associative learning is well studied in memory research, and has been consistently linked to hippocampus (Gluck, Meeter, & Myers, 2003; Meeter, Myers, & Gluck, 2005; Yang et al., 2003). Hippocampal activity has been repeatedly investigated in memory tasks involving picture processing (e.g. Squire, Stark, & Clark, 2004; Stern et al., 1996), but this structure is not commonly included in the picture naming network. The considerations above suggest that the hippocampus could be active during picture naming, driving incidental learning and/or the processes of retrieval, and that its activity is sensitive to repeated naming.

The available literature does not provide a clear view of the recruitment of the hippocampus during picture naming. In fMRI studies, the hippocampus was not among the regions showing

repetition suppression due to repeated naming (Van Turennout, Bielamowicz, & Martin, 2003; Van Turennout, Ellmore, & Martin, 2000), although hippocampal repetition suppression (i.e. a decrease of bold signal driven by repetition) has been reported during the retrieval of learned face-name pairs (Kremers et al., 2014; Rand-Giovannetti et al., 2006; Vannini, Hedden, Sullivan, & Sperling, 2013; Zeineh, Engel, Thompson, & Bookheimer, 2003). Patients with hippocampal lesions showed intact priming during repeated naming of pictures (Cave & Squire, 1992). HM, the most famous hippocampal patient whose medial temporal lobe resection included both hippocampi, is typically described as having no language deficit (although see MacKay, James, Hadley, & Fogler, 2011; and footnote 1 in Hamamé et al. (2014)). These and other observations have prompted the conclusion that repetition in picture naming involves "an implicit, nonhippocampal form of memory" (Francis, 2014). In short, efficient naming or intact priming without hippocampal involvement has suggested that the task does not depend on the structure.

More recently, however, a number of reports highlighted the possible role of the hippocampus in picture naming. Hippocampal sclerosis has been associated with degraded performance in naming tasks (Bonelli et al., 2011; Hamberger, Seidel, Goodman, & McKhann, 2010; Hamberger, Seidel, McKhann, & Goodman, 2010). Some of these deficits are thought to reflect degraded word retrieval *per se*, with preservation of meaning (Miozzo & Hamberger, 2015; Trebuchon-Da Fonseca et al., 2009). Intra-cerebral recordings performed during pre-surgical investigations revealed sustained hippocampal activity that was closely tied to naming behavior (i.e. to naming latencies and, in one patient, to word finding difficulties; Hamamé et al., 2014). Finally, two fMRI studies exploring picture naming in a protocol combining repetition with a semantic context manipulation reported a modulation of left hippocampal activity that was related to lexical processing (De Zubicaray, Johnson, Howard, & McMahon, 2014; Hocking, McMahon, & de Zubicaray, 2008).

In this context, we hypothesized that hippocampal activity should be detected during plain picture naming, and that it could be modulated by contextual factors thought to promote learning, such as repetition and semantic context. Such a learning mechanism has been proposed as a unitary cause for two robust contextual effects observed in picture naming behavior (Oppenheim et al., 2010): generic priming from repeated use (Bartram, 1973; Bartram, 1974), and specific interference from semantically related material (Howard, Nickels, Coltheart, & Cole-Virtue, 2006). We report a test of the hypothesis based on intra-cerebral electrophysiological data (Bancaud et al., 1969; Talairach et al., 1974) recorded directly from structurally healthy hippocampi that had been anatomically and functionally identified. Native French speakers overtly named pictures they had never seen before, and then named them again in a block-design protocol previously used to elicit the contextual effects of repetition priming and semantic interference (Damian, Vigliocco, & Levelt, 2001). There was no memorization or encoding requirement. The analysis sought to detect hippocampal activity during the task and its possible modulation by the two contextual factors.

2. Materials and methods

2.1. Subjects

We analyzed data from nine patients with epilepsy undergoing pre-surgical stereotactical electro-encephalographic investigations (SEEG) in La Timone Hospital, Marseille. These patients had been stereotactically implanted with intra-cerebral electrodes to define

the epileptogenic zone by recording local field potentials (LFP) with millimetric spatial resolution (Talairach et al., 1974). The implantation consists of 5–11 multi-lead linear-array depth-electrodes comprising 10–15 contact sites (3 mm spaced, 0.8 mm diameter; Alcis, Besançon, France). The electrode implantation was based strictly on clinical requirements and was decided independently of the present study.

The nine patients were right-handed (Oldfield Questionnaire) native French speakers with a left dominant hemisphere for language. All patients had left hemispheric dominance as revealed by different criteria including: (1) the recording of auditory evoked potential in auditory cortex in response to French voiced and voiceless stop consonants (/ba/, /pa/; detailed methods in Trébuchon-Da Fonseca, Giraud, Badier, Chauvel, and Liégeois-Chauvel (2005); (2) functional mapping of language using direct electrical stimulation, whereby left hemisphere stimulation induced language deficit in all patients; (3) fMRI or WADA test; (4) pattern of ictal aphasia when seizures involved left hemisphere. Anticonvulsant therapy was reduced or withdrawn during the clinical exploration in order to facilitate seizure occurrence. However, no subject had presented any seizure in the 12 h before testing. Participants or their parents (required for the two minor patients) provided written informed consents. As described below, the data analysis procedure led to exclude data from three patients, leaving a total of six.

2.2. Recording sites

The imaging analyses of the nine patients showed no hippocampal sclerosis or other structural abnormality. The functional integrity of the recorded hippocampi was tested using a visual odd-ball task. The patients had to count the number of times a rare stimulus (previously shown to the subjects) appeared on the screen while ignoring the frequent stimulus. It is well established that, within a healthy hippocampus, rare stimuli elicit a large negativity peaking around 300–600 ms (Halgren, Marinkovic, & Chauvel, 1998; Halgren et al., 1995; Knight, 1996; Ludowig, Bien, Elger, & Rosburg, 2010; Soltani & Knight, 2000). The recordings from one of these patients during this task did not reveal the expected negativity. This was interpreted as a dysfunctional hippocampus, and the patient was removed from the study. Moreover, two other patients were also excluded because the physiological activity recorded from the electrodes corresponded to far-field potentials (i.e. field potentials remotely generated, recognizable by a similar pattern of electrophysiological activity all along the electrode) and not to hippocampal local field potentials.

Among the six remaining patients, two had electrodes in the right hippocampus, three in the left and one patient bilaterally. These patients also had electrodes in perirhinal cortex (PRC), involved in object recognition processing (Buckley & Gaffan, 2006). The location and the number of contacts are listed in Table 1.

2.3. Experimental procedure

All procedures were performed in accordance with the INSERM Institutional Review Board (N 0000388).

The experiment started with a "familiarization phase" during which the patients sequentially named 108 black and white object images (Alario & Ferrand, 1999) that were novel to them. The pictures were presented in a pseudo-random order (Van Casteren & Davis, 2006) with the constraints that consecutive trials did not involve items from the same semantic category nor items beginning with the same phoneme (see Fig. S1a). This familiarization phase was followed by a "repetition phase" in which 36 items among those 108 were used in a design directly inspired by that of