Neurology, Psychiatry and Brain Research 25 (2017) 1–8

Contents lists available at ScienceDirect

Neurology, Psychiatry and Brain Research

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

Recall of semantically related word-lists in two patients with herpes simplex encephalitis

Z.K. Kouvatsou[a,*], E. Masoura[a], E.Z. Papadaki[b], V.K. Kimiskidis[c]

[a] School of Psychology, Department of Experimental Cognitive Psychology, Aristotle University of Thessaloniki, Greece
[b] Department of Radiology, MRI Unit, University of Crete, Heraklion, Crete, Greece
[c] Laboratory of Clinical Neurophysiology, AHEPA Hospital, Aristotle University of Thessaloniki, Greece

ARTICLE INFO

Keywords:
Medial temporal lobe
Herpes simplex encephalitis
Working memory
Word-lists task

ABSTRACT

Objective: The aim of the present study is to provide further insight into semantic processing in Working Memory (WM) in two amnesic patients with extensive medial temporal lobe (MTL) by adopting a short length word-lists recall task.

Background: It is still unclear whether the medial temporal lobe structures and especially the hippocampus is recruited in semantic processing in the context of WM.

Materials & methods: Two severely amnesic patients with extensive MTL damage due to herpes simplex encephalitis (HSE) and a control group (n = 36) underwent an experimental task involving the immediate free recall of 9 word-lists in three different conditions: 1. semantically related words clustered according to semantic category (SRC), 2. semantically related words non-clustered (SRnC), 3. semantically unrelated words (SU). Additionally, standard cognitive measures were administered [Digit Span Forward & Backward, Greek Verbal Learning Test (GVRT), Verbal Fluency Test (VFT), Logical Memory I & II (LM-I & LM-II) of Wechsler Memory Scale (WMS)].

Results: Both patients obtained normal performance in WM tests (Digit Span Forward & Backward), but were impaired in GVRT, VFT, LM-I and LM-II. With regard to the word-list task, the number of words recalled by both patients' did not differ from controls. However, semantic facilitation effects were not recorded in patients' performance for the SRC and SRnC conditions (SRC = SRnR = SU), unlike controls (SRC > SRnC > SU).

Conclusions: Our results suggest that the effects of semantic facilitation in short length word-lists recall are diminished to a certain degree in HSE patients that suffer from MTL damage.

1. Introduction

A number of studies have demonstrated that Medial Temporal Lobe (MTL) may contribute in certain aspects of Working Memory (WM), especially in supporting the encoding of relations between items (Allen, Vargha-Khadem, & Baddeley, 2014; Berlingeri et al., 2008; Eichenbaum & Cohen, 2014; Hannula et al., 2006; Moses & Ryan, 2006; Monti et al. (2015); Hassabis, Kumaran, Vann, & Maguire, 2007; Eichenbaum, Otto, & Cohen, 1992; see Eichenbaum, 2004; Konkel and Cohen, 2004; Graham, Barense, & Lee, 2010 for reviews). Studies in amnesic patients suffering from MTL pathology have reported contradicting evidence with regard to the ability to effectively process semantically related information during WM tasks (Bäuml, Kissler, & Rak, 2002; Bueno, Bertolucci, Oliveira, & Abrisqueta-Gomez, 2008; Channon & Daum, 2000; Goodrich-Hunsaker & Hopkins, 2009; Isaac & Mayes, 1999; O'Kane, Kensinger, & Corkin, 2004). More precisely, Channon and Daum (2000) administered 16 word-lists, containing either semantically related (both clustered and non-clustered) or unrelated words, and found that amnesic patients were unable to take the advantage from the semantic information to enhance recall; this deficit resulted in a general lower performance when compared with healthy control group. The authors suggested that the complex comparative operations, necessary to encode semantically related material may be impaired in amnesic patients (Channon & Daum, 2000).

Bueno et al. (2008) further addressed this issue and used semantically related (both clustered and non-clustered) and unrelated −lists

Abbreviations: GVLT, Greek Verbal Learning Test; HSE, herpes smplex encephalitis; LM-I & LM-II, logical memory I & II of the Wechsler Memory Scale-III; LTM, Long Term Memory; MTL, Medial Temporal Lobe; SRC, semantically related-clustered words; SRnC, semantically related-non-clustered words; SU, semantically unrelated words; VFT, verbal fluency task; WM, Working Memory

* Corresponding author at: Papaflessa 10a, Syros, Greece.
E-mail addresses: zoikouvatsou@yahoo.gr (Z.K. Kouvatsou), emasoura@psy.auth.gr (E. Masoura), fpapada@otenet.gr (E.Z. Papadaki), kimiskid@auth.gr (V.K. Kimiskidis).

http://dx.doi.org/10.1016/j.npbr.2017.05.001
Received 7 April 2017; Accepted 26 May 2017
Available online 09 June 2017
0941-9500/

that varied in length in two groups of Alzheimer's Disease patients (mild and moderate stage of Alzheimer's Disease). The results showed that the semantic facilitation did not emerge in the 15 word-list condition (in line with the results reported in Channon & Daum, 2000), but it was detectable in the 9 word-list condition. In the light of this evidence, the authors suggested that with smaller sets of material, the appropriate semantic information might still be available to support the semantic binding processes in AD patients (Bueno et al., 2008).

A similar pattern of results emerged also with patients MTL damage due to herpes simplex encephalitis (HSE). The ability to take the advantage of a limited amount of semantic information for a brief interval was maintained, but as soon as the amount of to be recalled information increased, their performance was heavily disrupted (Cermak, 1976; Baldivia, Saa, Rocha, & Brucki, 2008). Baldivia et al. (2008) described the cognitive profile of a patient with extensive bilateral damage due to HSE. They found that his performance was intact in WM tasks (digit span forward and backward), while his performance in Rey Auditory Verbal Learning Test was found to be severely impaired. It was suggested that the immediate recall of lists with 15 semantically related words depends on Long Term Memory (LTM) processes, as a larger number of information has to be maintained in comparison with the digit span tasks.

The aforementioned experimental findings have suggested that beneficial effects from semantic encoding are observed in amnesic patients under specific circumstances, when WM is sufficient in order to support performance. In accordance with this aspect, Jeneson and Squire (2012) in their review regarding the role of MTL in memory, argued that MTL activity is of critical significance when WM capacity becomes overloaded and the contribution of LTM is necessary, while at lower memory loads and short retention times, this particular brain area is not critically involved. Even more recently, Zanto, Clapp, Rubens, Karlsson, and Gazzaley (2015) investigated the effect of various manipulations of task demands (manipulating delay duration, distraction method, and memory probes) on MTL involvement in healthy participants. Results from fMRI imaging suggested that when the task is expected to be more challenging, then MTL involvement is more activated during both encoding and maintenance periods. On the other hand, MTL involvement was not found to be recruited during low-demand memory tasks (Zanto et al., 2015).

To further address this issue, we studied two patients with MTL damage due to herpes simplex encephalitis (HSE). Patients were assessed with a brief neuropsychological battery including a classical measure of immediate recall (immediate prose recall) and an experimental task involving the immediate free recall of three 9 word-lists. The length of the word-lists was set up to 9 words in order to explore whether semantic processing was preserved in short length word-lists. The content of the three lists was manipulated so as to include semantically related-clustered words (SRC), semantically related-non-clustered words (SRnC) and semantically unrelated words (SU). We assumed that if MTL is necessary in order to encode complex semantic associations even in a short word-lists task, then our patients would exhibit impaired recall in the three word-lists task and no significant advantage in recalling the semantically related items versus the unrelated items should be evident. On the contrary, if normal immediate recall and facilitation effects are manifested for semantically related items, then it would be suggested that MTL involvement is not initial during the encoding phase of semantic information in a short word-lists task.

2. Method

2.1. Participants

2.1.1. Healthy controls

Taking into account previous investigations suggesting that the word span capacity does not differ significantly between men and women (Robert & Savoie, 2004), a group of thirty-six healthy controls (23 women, 13 men) aged between 18 and 51 years old (*mean* age = 39.5, *SD* = 5.81) and with an education level between 6 and 17 years (mean education = 13.3, *SD* = 3.18) was selected for this study. All the participants gave informed consent for the procedures before entering the study.

2.1.2. Case 1

ThV, a 43-year-old right-handed male patient (formal education = 6 years) was hospitalized and treated in 2006 for herpes simplex encephalitis (HSE). Brain MRI scans revealed extensive damage of the temporal lobes bilaterally, particularly affecting their medial parts, the insula and the orbito-frontal cortices; the rest of the brain was minimally affected (Fig. 1). In order to obtain quantitative data, a brain volumetric analysis with the dedicated software Analyze 12.0 (AnalyzeDirect, Inc, KS, USA) was performed in both patients and a group of age and sex-matched healthy subjects (n = 20) and the resulting data were compared using the SINGLIMS test (Crawford, Garthwaite, & Porter, 2010; see Statistical analyses). In the control group, the mean total brain volume was 915880.157 mm^3 (*SD* = 29613.59) and the mean volumes of left and right hippocampi were 2286.998 mm^3 (*SD* = 179,227) & 2281.608 mm^3 (*SD* = 155,311), respectively. In the case of ThV, the total brain volume was normal (984.871,84 mm^3) whereas both left and right hippocampus had significantly reduced volumes (1.586,45 mm^3 and 1.925,73 mm^3) compared to the control group ($p < 0.001$ and $p < 0.05$, respectively, Zcc = −3.909 with a 95% CI of −5.210 to −2.594 for the left and Zcc = −2.292 with a 95% CI of −3.128 to −1.438 for the right).

At the time of the scheduled evaluation in 2011, five years after the HSE infection, his gross neurological examination was normal. Severe anterograde and retrograde amnesia were presented, including both semantic and episodic memory deficits. With regard to retrograde amnesia, impaired recall of important historical or contemporary facts along with inability to retrieve basic personal information and important autobiographical events, were noticed through clinical interview. The accuracy of all responses regarding autobiographical facts and events was established in an interview with a close relative. Taking into account the observations of the extended clinical interview, as well as patients' accurate performance in Greek word and non-word repetition task, receptive and expressive language skills were classified as adequately preserved. His speech was well-articulated and non-paraphasic. Semantic memory was assessed with the Pyramids and Palm Trees test-Picture Version (Howard & Patterson, 1992). ThV's performance was mildly impaired [ThV score: 44/52, healthy controls score: 49.42 (*SD* = 1.83)], according to the Quebec-French[1] population norms (Callahan et al., 2010). His Mini Mental State Examination (Feinstein, Folstein, & McHugh, 1975) score revealed a moderate cognitive impairment (18/30). ThV's low performance was mainly due to a deficit in time- spatial orientation and in the delayed recall of the 3 words; on the contrary he showed an intact performance in the naming, immediate recall, comprehension, reading, writing and visual-constructional subtasks of the Mini Mental State Examination.

2.1.3. Case 2

NTh, a 44-year-old right-handed male patient (formal education = 11 years) that was hospitalized and treated for HSE in 2000. His brain MRI scans revealed extensive damage of the left temporal lobe including the medial-temporal structures as well as the lower and middle temporal gyri (Fig. 2). The volumetric MRI analysis revealed that the total brain volume (911.065,71 mm^3) as well as the volume of the right hippocampus (2.142,34 mm^3) were normal whereas the volume of the left hippocampus (1.053,85 mm^3) was significantly reduced compared to the control group ($p < 0.001$, Zcc = −6.880 with a 95%

[1] Quebec-French population norms were used as norms for the Greek population are not yet available.