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Associative reinstatement: A novel approach to assessing associative memory in patients with unilateral temporal lobe excisions☆

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ABSTRACT

We investigated whether unilateral medial temporal lobe (MTL) damage disrupts associative reinstatement, which represents the gain in item memory when the studied associative information is reinstated at retrieval. We were interested to see whether associative reinstatement relies on the same relational binding operations that support other types of associative memory (associative identification and recollection) thought to be subserved by the MTL. In addition, we examined whether such damage affects the different types of associative memory to a greater extent than item memory and item familiarity, and whether a different pattern is seen in patients with language dominant relative to non-dominant temporal lobe resection when the studied material consists of verbal information. To do so, we used a word pair recognition paradigm composed of two tasks: (1) a pair recognition task that provides measures of associative reinstatement and item memory, and (2) an associative identification recognition task that provides a measure of associative identification memory. Estimates of item familiarity and recollection were derived from performance on both tasks using a variant of the process-dissociation procedure. Our results showed that associative reinstatement, like other types of associative memory measures, was impaired in patients with unilateral resection, irrespective of the side of damage. Item familiarity, however, was impaired solely following language dominant resection. The lack of a laterality effect in our relational measures was likely due to using an encoding task that promoted formation of both verbal and visual associations, whereas item-based familiarity could rely exclusively on verbal operations. We propose that associative reinstatement provides a sensitive measure of relational memory that is less dependent on strategic processing and therefore more appropriate for evaluating MTL function in patients.

Memories of newly experienced events are composed of single pieces of information (item memory) and links or associations between these elements (associative memory). Several dissociations have been documented between these types of memory using recognition memory tasks in which participants are required to discriminate between studied and novel items (item memory) or between studied and novel pairings of previously encountered items (associative identification). These dissociations pertain to the cognitive operations required at encoding and at retrieval, the underlying memory processes, and the neural substrate of these types of memory (see Eichenbaum, Yonelinas, & Ranganath, 2007; Yonelinas, 2002, for reviews). Notably, associative identification, to a greater extent than item memory, requires the creation of links between items during the encoding phase via relational binding operations, which have been shown to be dependent on the medial temporal lobes (MTL; see Davachi, 2006, for review). Furthermore, associative identification requires the instantiation of self-directed strategic operations at retrieval, which are thought to be more dependent upon frontal lobe regions (Achim & Lepage, 2005; Lepage, Brodeur, & Bourgouin, 2003). From the perspective of dual-process models of recognition memory (Mandler, 1980; see Yonelinas, 2002, for a review of these models), these strategic retrieval operations are strongly involved in supporting recollection-based memory. Recollection is typically defined as an effortful and slow process (but see Dewhurst, Holmes, Brandt, & Dean, 2006) that permits retrieval of contextual or associative information. In contrast, these operations are not as necessary to retrieve item information via familiarity, which is a fast process characterized by a decontextualized feeling of oldness.

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Importantly, we showed in previous behavioural studies that not all types of associative memory require these strategic retrieval operations or recollection (Cohn, Emrich, & Moscovitch, 2008; Cohn & Moscovitch, 2007). Specifically, associative reinstatement, which refers to gains in item memory seen when items are presented in their studied pairings relative to novel pairings (akin to cueing), clearly does not. In contrast to associative identification and in some cases item memory, associative reinstatement is not affected by conditions that prevent participants from undertaking elaborate retrieval operations (e.g., speeded retrieval, short response deadline, overlapping pairing condition in which a target word has several studied associates). It is also unaffected, along with item familiarity, in older adults who show deficits in associative identification and recollection, which can be attributed to suboptimal frontal lobe functioning. However, unlike item familiarity, associative reinstatement appears to require some kind of relational binding operations. Notably, it is reduced, as is associative identification, following dividing attention at encoding (Castel & Craik, 2003) and following shallow encoding of the relational information between items (Cohn & Moscovitch, 2007). In sum, associative reinstatement is like associative identification and recollection as it requires relational binding operations at encoding, but differs from these at retrieval as it does not necessitate elaborate retrieval operations. Therefore, we propose that associative reinstatement may provide a 'purer' index of relational binding ability and of MTL function than other associative memory tasks.

The main goal of the current study was to verify whether associative reinstatement and the relational binding operations that support it rely on the MTL, as do associative identification and recollection. While several studies have documented associative identification deficits following bilateral MTL lesions, either of greater (Giovanello, Verfaellie, & Keane, 2003; Giovanello, Keane, & Verfaellie, 2006; Holdstock, Mayes, Gong, Roberts, & Kapur, 2005; Mayes, Holdstock, Isaac, Hunkin, & Roberts, 2002; Mayes et al., 2004; Turriziani, Fadda, Caltagirone, & Carlesimo, 2004; Vargha-Khadem et al., 1997) or of equal magnitude than deficits in item memory (Cipolotti et al., 2006; Stark, Bayley, & Squire, 2002; Stark & Squire, 2003), only two studies have investigated associative reinstatement in these patients. In one study, associative reinstatement was impaired in amnesic patients despite intact associative priming, suggesting that the relational binding operations underlying reinstatement depend on MTL regions and were dissociable from those underlying associative priming subserved by the posterior neocortex (Goshen-Gottstein, Moscovitch, & Melo, 2000). In another study, amnesic patients also showed impaired reinstatement, even when item memory was equated with that of control participants (Kan, Giovanello, Schnyder, Makris, & Verfaeillie, 2007). The latter suggested that reinstatement is dissociable from item familiarity, though item memory is not a pure measure of this process as recollection also contributes to it.

These studies involved patients with bilateral MTL lesions or degeneration with severe functional memory deficits. In Kan et al. (2007), to equate performance between patients and controls and to avoid floor effects in patients or ceiling effects in controls, patients received six presentations of the study material, while controls received only one. A fundamental problem with this approach is that it assumes that this manipulation enhances all types of recognition memory and processes to the same extent. However, repetition at study in healthy participants enhances item memory but has little or no effect on associative identification (Cleary, Curran, & Greene, 2001). Thus, the difference between the tasks completed by patients and by controls creates confounds and makes interpretation difficult, especially if one argues for dissociations between memory types. It is thus preferable to use the same study procedure, but test patients with milder memory deficits. Such patients include individuals with unilateral MTL dysfunction (e.g., temporal lobe epilepsy) or lesion [e.g., unilateral temporal lobe excision (TLE) for the treatment of epilepsy]. These patients are not functionally amnesic, but typically show memory impairments on standardized neuropsychological tests that are specific to the material preferentially processed by the damaged hemisphere (e.g., left hemisphere for verbal material; Jones-Gotman, 1997; Milner, 1974; Morris, Abrahams, & Polkey, 1995).

To our knowledge, there are no studies investigating associative reinstatement or associative identification in these patients. There are only a few published studies that investigated recollection and familiarity for single items using other paradigms (e.g., remember-know procedure and source memory), but their findings are mixed. All studies showed recollective deficits in this population, which were interpreted as impaired relational binding operations, but some showed deficits only for material processed by the damaged hemisphere (Bird, Shallice, & Cipolotti, 2007; Moscovitch & McAndrews, 2002), only in dominant TLE patients irrespective of the type of material used (Blaxton & Theodore, 1997) or in all TLE patients regardless of side of lesion and material (Moran, Seidenberg, Sabsevitz, Swanson, & Hermann, 2005; Thaiss & Petrides, 2003). All studies also suggest that familiarity is intact for material processed by the undamaged hemisphere, but some suggest that it is impaired solely for material processed by the damaged hemisphere (Bird et al., 2007; Blaxton & Theodore, 1997; Thaiss & Petrides, 2003) whereas others report that it is intact regardless of the type of material or side of lesion (Moscovitch & McAndrews, 2002).

In the current study, our first goal was to verify whether associative reinstatement is impaired in memory-impaired but non-amnesic patients with unilateral TLE, and thus, verify whether this type of associative memory relies on relational binding operations subserved by MTL regions, as suggested by previous studies with amnesic patients (Goshen-Gottstein et al., 2000; Kan et al., 2007). Our second goal was to investigate potential differences in associative and non-associative memory between patients with language dominant and non-dominant hemisphere resections to help resolve some of the mixed results noted in the literature. To do so, we employed a word pair recognition paradigm previously used with young adults under various experimental conditions (Cohn & Moscovitch, 2007) and with older adults (Cohn et al., 2008). This paradigm includes two old–new recognition tasks: (1) a pair recognition task in which participants must discriminate between pairs containing at least one unstudied word (new and half-old pairs) from pairs composed of two studied words (intact pairs and rearranged pairs), and (2) an associative identification recognition task in which participants are required to endorse pairs that reinstate the studied pairings (intact pairs) and reject all other pairs (new, half-old and rearranged pairs). The associative reinstatement and item memory measures are derived from performance on the pair recognition task, the associative identification measure is derived from the associative identification recognition task, and estimates of familiarity and recollection are derived from performance on both tasks using a variant of the process-dissociation procedure (Jacoby, 1991; Yonelinas, Regehr, & Jacoby, 1995).

1. Method

1.1. Participants

1.1.1. Patients

Twenty-four patients with unilateral TLE were recruited from the Epilepsy Clinic at Toronto Western Hospital and participated in this study. The temporal excision typically included resection of the hippocampus (3 cm), parahippocampal gyri (including portions of perirhinal, entorhinal and parahippocampal cortices), amygdala and anterior portion of the inferior and middle temporal lobe gyri. Twelve patients underwent dominant TLE (all left hemisphere resections) and twelve underwent non-dominant TLE (three left hemisphere and nine right hemisphere resections). Hemispheric dominance was determined based on findings from clin-