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Controlled recall of verbal material in temporal lobe epilepsy

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Abstract

This study used a guided process-dissociation procedure to examine the contribution of controlled and automatic uses of memory to a cued recall task in 24 patients with unilateral temporal lobe epilepsy (TLE: 12 left-sided; 12 right-sided), and 12 neurotypical controls. In an inclusion task, subjects attempted to complete three-letter word stems using previously studied words, in an exclusion task they aimed to avoid using studied words to complete stems. Patients with left TLE produced less target completions under inclusion conditions. Completion rates were not significantly different under exclusion conditions. Estimates derived from process dissociation calculations, confirmed that the cued recall deficit in left TLE patients arose entirely from impairment in controlled memory processes. There were no group differences in the estimates of automatic processes. Recognition judgements of stems corresponding to studied words did not differ between the groups. Overall the results support the view that controlled and automatic memory processes are mediated by separable neural systems. Hippocampal and related structures within the left medial temporal lobe are more important than corresponding right hemisphere structures for the controlled retrieval of verbal material. In contrast, the findings from this study do not suggest that the left and right temporal lobes make a differential contribution to automatic memory processing. The theoretical and clinical relevance of these findings are discussed.

Since the case of H.M (Scoville & Milner, 1957), studies of patients with medial temporal lobe lesions (MTL) have continued to make a significant contribution in helping to elucidate the neurological and cognitive bases for indirect (automatic/implicit) and direct (controlled/explicit) forms of retrieval from long term memory (see Kopelman, 2002 for a review). Direct retrieval refers to a deliberate, controlled effort to recollect a prior event. In contrast, indirect retrieval is revealed when prior exposure to an event influences subsequent behaviour automatically. One of the most intriguing findings to emerge from these studies is that MTL patients who demonstrate impaired performance on direct memory tasks (e.g. cued-recall), often perform within normal limits on indirect tasks (e.g. word stem completion), which suggests that controlled but not automatic retrieval is dependent upon the integrity of MTL structures.

Numerous imaging studies have shown that patients with temporal lobe epilepsy (TLE) commonly present with atrophy to the hippocampus and related structures within the MTL (Marsh et al., 1997), and consistent with cerebral dominance it is well documented that patients with left TLE are commonly impaired on direct verbal memory tasks (Naugle et al., 1993). Although the magnitude of this impairment is modulated by a number of seizure-related factors (Hendriks et al., 2004), left TLE patients generally exhibit poorer direct verbal memory performance compared to neurotypical controls and patients with right TLE. Because direct tests measure retrieval that is purportedly deliberate and controlled, one interpretation of the verbal memory deficit in patients with left TLE is that it reflects impairment in controlled uses of memory. One problem with this interpretation is that it is based on the task dissociation premise that performance constitutes a process pure measure. That is, direct tests exclusively involve controlled uses of memory, whereas indirect tests exclusively involve automatic uses of memory. However, this assumption has been vigorously contested within the context of indirect memory where a number of studies have shown that contamination from controlled uses of memory can inflate indirect measures (Toth et al., 1994). Contamination from automatic influences on direct tests of retrieval has received much less attention (but see Jacoby et al., 1993), although it would seem feasible that automatic facilitation is instrumental in studies where memory impaired groups perform at normal or near to normal level on direct tests designed to measure intentional uses of memory (Graf et al., 1984). Contamination confounds a clear interpretation of the direct verbal memory deficit in left TLE. Relative to right TLE, patients with left TLE may be impaired in either automatic or controlled memory processes, or both automatic and controlled memory processing. To date, these hypotheses remain untested, because conventional task dissociation approaches to memory preclude distinguishing between controlled and automatic processes since both forms of retrieval are facilitative.

The process-dissociation procedure is an oppositional method developed to overcome the problem of contamination (Jacoby, 1991). The procedure contrasts performances under inclusion and exclusion conditions to derive estimates of controlled and automatic memory processes within the same task[1]. Recently Del Vecchio et al. (2004) deployed the procedure to examine the contribution of controlled and automatic memory processes to a cued-recall task in patients with left TLE. In the study phase of this experiment, subjects read aloud and were instructed to remember a list of target words. In the test phase three-letter word stems were completed under inclusion and then exclusion conditions. For inclusion conditions the aim was to use a studied word to complete the stem – under these instructions the probability of completing a stem with a target word is the additive probabilities of controlled (C) and automatic (A) influences of memory when recollection fails: C + A(1 – C). For exclusion conditions the aim was to avoid using a studied word – under these instructions the probability of producing a target completion depends on automatic processes and the failure of controlled processes: A(1 – C). The estimates derived from the process-dissociation calculations revealed that controlled memory processing [inclusion – exclusion] was significantly greater for the neurotypical than for the left TLE group, whereas automatic memory processes [exclusion/(1 – C)] were invariant between the two groups.

Although the process-dissociation procedure has been widely deployed to examine memory processing in a number of neuropsychological groups, the method has attracted some debate. A particularly pertinent issue relates to the complexity of the instructions that participants are required to follow; this is argued to be particularly problematic under exclusion conditions, to the extent that concerns have been raised over the validity of the memory processing estimates that are derived (Graf & Komatsu, 1994). The present study further examines the contribution of automatic and controlled uses of memory to the retrieval of verbal material in left TLE. It is a partial replication of Del Vecchio et al. (2004) but with two principle exceptions. First, a guided version of the process-dissociation method described by Stern et al. (2003) is used. This procedure is preferred because it clearly instructs subjects how to respond according to inclusion and exclusion conditions through a sequence of prompts, thus eliminating the constraint of participants having to understand and remember a complex set of instructions[2]. Second, in this study left TLE patients are compared to neurotypical controls and a group of TLE patients with a right seizure focus. In contrast to neurotypical controls, left and right TLE patients share clinical (e.g. mood and cognitive dysfunction) and seizure-related factors (e.g. seizure type, frequency, duration, effects of medication) that are known to adversely effect memory performance (Hendriks et al., 2004), therefore this comparison is important in order to be confident of ascribing any observed differences in memory processing to lateralization per se.

Method

Subjects: Twenty four TLE patients referred by Hull and East Yorkshire Hospital NHS Trust to the researchers for neuropsychological assessment participated in this study. Twelve patients had a left-sided focus and 12 had a right sided focus. Five patients (2 left and 3 right) had undergone an anterior temporal lobectomy, which included the temporal pole, the amygdala and hippocampal structures. The inclusion criteria for the patients consisted of unilateral temporal lobe seizure onset verified by MRI and EEG evidence of epileptiform discharges. No patients had a history of: head trauma or condition (other than relating to epilepsy) known to impair the central nervous system and/or cognitive function; psychiatric diagnosis or mental illness resulting in hospitalization; alcohol or drug abuse. There was no significant difference between the left and right groups for age, emotional status (Hospital Anxiety and Depression Scale, Zigmond & Snaith, 1987) general intellect (WAIS-R, Wechsler, 1981), sustained attention (Information Processing Tasks A and B from the AMIPB, Coughlan & Hollows, 1985), executive functions (Letter Fluency, Miller, 1984; Trail Making A and B, Armitage, 1946; Elevator Counting with Distraction from the Test of Everyday Attention, Robertson et al., 1994) short-term verbal (Digit Span) and visual memory (Corsi Block Tapping, Milner, 1971), long-term visual (Design Learning and Complex Figure from the AMIPB, Coughlan & Hollows, 1985) or verbal memory (RAVLT, Rey, 1964). Ninety-five percent of tests in the neuropsychological battery were completed. A neurotypical control group consisting of 12 people (mean age = 34, SD = 9.5; 7 female and 4 male) were recruited through opportunity sampling. All subjects participating in the study had normal or corrected to normal vision and gave informed consent prior to participating in the study.

[INSERT TABLE I ABOUT HERE]

Stimuli: The critical stimulus set (see Appendix A) consisted of 64 five-letter words taken from Jacoby (1998); the three-letter word stem of each word was unique within the set and formed the beginning of several English words. The number of five-letter word completions for the stems that have actually been given by participants in Jacoby's studies (set size) ranged from four to nine (mean = 5.67). This set was divided into four blocks. For any one subject, two blocks were used for each test condition. Of these, one block was studied; the other block was unstudied and was used as an index for base rate completions. The blocks were rotated to allow each word to appear in each condition equally. Each study list started and concluded with two buffer words.

Procedure: Participants were tested individually in a quiet room. All stimuli were in black lowercase font, presented horizontally in the centre of a computer screen.

During the study phase each subject was presented with 36 words (32 critical items and 4 buffer words) and asked to read aloud and remember each word. The study phase was untimed but the experimenter encouraged prompt responses, as soon as a word was read the Enter key was used to advance the next trial. Each word was presented for approximately 2-3 seconds. The study phase was immediately followed by the test phase. In the test phase, the patients participated first under inclusion conditions; secondly, under exclusion conditions. For both inclusion and exclusion test conditions, a three-letter word stem appeared on the screen immediately beneath the question, “Do you remember seeing a word that begins like this?” subjects were directed to press 1 to indicate “Yes” and 2 to indicate “No”. Under both conditions, if a “No” response was given the instructions, “What word begins like this?” appeared on the screen and subjects were prompted to type two letters to form the first word that came to mind. If a “Yes” response was entered, in inclusion conditions they were asked, “What was the word?” in exclusion conditions they were instructed to “Form a word that you haven’t seen earlier”. The presentation order of word stems corresponding to studied and new words was random. The test phase was self-paced and the whole experiment took around 30 minutes to complete.

Results

The proportion of target word completions was calculated for each participant (see Table II) and entered into separate one-way ANOVA’s. Four subjects (2 right TLE, 1 left TLE and 1 neurotypical) who were tested obtained zero scores in the exclusion task and their data were not included in the analyses. Zero scores under exclusion instructions may be indicative that subjects have used a generate-recognise retrieval strategy and therefore target completions that have been automatically generated may be witheld. If a generate-recognise strategy is adopted the process-dissociation calculations will yield artificially low estimates of automatic memory processes, therefore zero scores under exclusion conditions are commonly discarded for purposes of analyses (Jacoby, 1998). The demographic and neuropsychological characteristics of the final TLE sample can be found in Table 1. Under inclusion conditions, the performance of healthy controls and patients with right TLE did not significantly differ, and both groups produced a greater proportion of target completions than patients with left TLE [$F (2, 29) = 5.696, p < .008$]. There were no significant differences between the groups neither for target completions produced under exclusion conditions [$F (2, 29) = .623, p > .543$] nor for the proportion of base rate completions [$F (2, 29) = .177, p > .838$]. Analyses of the completion rates across the stimulus blocks showed no significant effect of word list neither for inclusion [$F (3, 28) = .119, p > .948$] nor exclusion conditions [$F (3, 28) = 1.234, p > .316$].

Using the process-dissociation calculations, estimates of controlled and automatic processes were derived for each group. Analyses of these values indicated that relative to healthy controls and right TLE patients who did not significantly differ, patients with left TLE were impaired in deploying controlled uses of memory [$F (2, 29) = 4.427, p < .02$]. In contrast there were no group differences for automatic influences of memory [$F (2, 29) = .249, p > .780$]. Estimates of automatic memory processes were significantly above base rate [$t (31) = 2.932, p < .003$]. The guided procedure has the advantage of obtaining recognition responses to stems prior to completion. To examine whether the deficit in cued retrieval in left TLE relative to right TLE and healthy controls originated from impaired stem recognition, the proportion of hits and false alarm response were converted into d' values using Macmillan and Creelman's (1991) formula. Analysis of the d' prime data failed to reveal a significant difference between the three groups.

[INSERT TABLE II ABOUT HERE]

Discussion

This study utilised a guided process-dissociation procedure to examine the contribution of controlled and automatic memory processes to a cued recall task in patients with TLE. Under inclusion conditions, both healthy controls and patients with right TLE completed a greater proportion of stems with target words than patients with left TLE. Moreover, as indicated by the WAIS-R VIQ scores the verbal memory impairment in left TLE did not arise from a deficit in verbal ability. The estimates derived from the process-dissociation calculations confirmed that patients with left TLE were markedly compromised in the ability to deploy controlled memory processes, whereas there was no significant difference between patients with right TLE and the control group. These findings support those of Del Vecchio et al., (2004) who reported the same pattern of results in left TLE patients relative to neurotypical individuals on a similar process-dissociation task. However, by including right TLE patients this is the first study to demonstrate that the impairment in controlled memory processing is specifically related to lateralisation and not attributable to non-specific epilepsy-related factors, such as an increased incidence of anxiety and depression, or the adverse effects of anti-epileptic medication. Importantly, our patient groups were well matched on a range of neuropsychological measures, including; IQ, verbal fluency, attention and executive functioning. Therefore the verbal memory deficit in left TLE patients observed here is not likely to be an artefact of extraneous neurocognitive factors. Moreover, no significant group differences were found for the proportion of correct recognition judgements given to stems during the test stages, which shows that the deficit in controlled uses of memory in left TLE arose from impaired retrieval per se and not from impaired stem recognition.

Stem completion under exclusion conditions is dependent upon automatic processing when recollection fails. On this task performance was invariant between the control and patient groups. Irrespective of seizure focus, TLE did not reduce the ability to deploy automatic memory processes. Thus, the results from the present study support the view that controlled and automatic memory processes are mediated by dissociable neurological structures. The integrity of hippocampal and related neural structures within the left medial temporal lobe have shown to be more critical than corresponding right hemisphere structures for subserving controlled recollection of verbal material. In contrast, the left and right temporal lobes do not appear to differentially contribute to automatic memory processing. This view is consistent with other research (Billingsley et al., 2002; Zaidel et al., 1994); but these studies have deployed task dissociation methodologies that can be vulnerable to contamination and therefore preclude associating memory processes with subserving neural structures.

It should however be noted that the process-dissociation estimates can be sensitive to exceptionally high levels of performance and ceiling effects may lead to aberrant conclusions. As controlled influences of memory increase, exclusion scores decrease and if exclusion scores are equal to zero there is a danger that the contribution of automatic memory processes will be underestimated. In order to counter this potential confound, we adopted procedures advocated by Jacoby (1998). First, we selected stimuli that had previously been shown to produce sufficiently high base rate completions to help avoid zero scores in exclusion conditions. Second, similar to other studies (e.g. Schmitter-Edgecombe, 1999) we excluded data from participants who nevertheless achieved zero scores under exclusion conditions prior to calculating the parameter estimates of controlled and automatic memory processing. With these procedures, estimates of automatic influences of memory were found to be significantly above base rate. Moreover, further support for the authenticity of our automatic memory estimates can be derived from a recent review of studies that have used the process-dissociation procedure (Yonelinas, 2002). In this analysis only experiments with estimates of controlled memory processing that exceeded .60 were associated with aberrantly low indices of automatic influences of memory. In the present study, each group demonstrated levels of controlled memory processes below that datum. Therefore based on previous process-dissociation studies, our measure of automatic possessing would appear to be valid.

One possible caveat of the experiment conducted here concerns the study phase procedures. To ensure stimulus encoding whilst allowing for possible inter-individual variations in cognitive slowing arising from non-specific epilepsy-related factors we elected to use a presentation format that was untimed. However to ensure that the observed differences in controlled memory processing are not confounded by variations in exposure duration, future studies may opt to control word exposure time during the study phase. Moreover, it has been posited that the critical factor that distinguishes between impaired and intact memory performance in TLE is the type of processing that the task involves, and not whether retrieval involves controlled or automatic uses of memory. For example, Blaxton (1992) found left TLE patients showed deficits in conceptual processing on direct and indirect memory tests, but were unimpaired on both types of test when performance involved perceptual processing. Whereas in contrast, Billingsley et al. (2002) found irrespective of processing requirements, TLE only produced impairments on measures of direct memory retrieval. Although the stem completion task used in this study involved perceptual processes, our study phase did afford more elaborate processing. To speak to the processing versus systems debate more directly, it may be worthwhile for future process-dissociation studies of TLE to contrast these perspectives by manipulating perceptual versus conceptual encoding at study.

With the process-dissociation procedure it is possible to examine memory processing without assuming task performance represents a process pure measure, or that populations with different neuropsychological profiles perform memory tasks using identical forms of processing. The standard procedure however, has been criticised because of the complexity of the instructions required and it is thought that these may be particularly problematic for cognitively impaired individuals (Graf & Komatsu, 1994). Although this confound is an obvious constraint on the clinical utility of the process-dissociation approach, Stern et al's (2003) guided procedure deployed in this study used a series of prompts which were designed to circumvent task complexity, and we found that all participants were able to engage with the test procedures comprehensively. Neuropsychological assessment plays a vital role in the clinical management of TLE in many areas; these include: a) aiding diagnosis (Jones-Gotman, 1992), b) the localisation and lateralisation of cognitive dysfunction (Jones-Gotman et al., 1993), c) evaluating the side effects of anti-epileptic medications (Thompson & Trimble, 1996), d) monitoring cognitive change (Strauss et al., 1995) and d) assessing the suitability of patients for epilepsy surgery and predicting post-operative outcomes (Chelune, 1995). If obtaining uncontaminated estimates of memory processing is considered important then the guided process-procedure may prove to be a valuable assessment tool.

FOOTNOTES

[1] The validity of the process-dissociation estimates depends on the assumption that controlled and automatic memory processes are independent. This assumption and other issues of contention relating to the procedure have been debated elsewhere and will not be discussed in detail here (see Reingold and Toth, 1996; Richardson-Klavehn et al., 1996).

[2] The guided procedure also encourages participants to adopt a direct retrieval strategy which is considered important for a number of key assumptions underlying the process-dissociation procedure to be met (see Stern et al., 2003).

TABLE I

Demographic and neuropsychological data for patients with left or right temporal lobe epilepsy (omitting patients with zero exclusion scores)

Participant variables	Left temporal lobe (n = 11)	Right temporal lobe (n = 10)	*P* <
Sex (male/female)	5/6	7/3	
Hand preference			
Right/left/ambidextral	8/0/3	8/0/2	
Age	38.8 (5.4)	37.6 (9.6)	0.88
General intellect			
WAIS-R VIQ	89.0 (11.5)	89.7 (13.1)	0.90
WAIS-R PIQ	93.1 (10.8)	87.5 (14.8)	0.34
WAIS-R FSIQ	89.4 (10.8)	87.7 (13.0)	0.75
Sustained attention			
AMIPB-Info. Pro-A	60.7 (23.4)	53.7 (18.0)	0.46
AMIPB-Info. Pro-B	63.7 (24.4)	61.0 (25.8)	0.82
Executive			
Fluency-FAS	35.1 (9.2)	32.4 (7.3)	0.47
Trail making-A	42.1 (14.1)	42.5 (15.3)	0.96
Trail making-B	104.1 (53.8)	103.8 (68.8)	0.98
Trail making-B-A	62.0 (47.5)	61.3 (60.8)	0.97
Elevator counting	5.9 (3.1)	6.0 (3.4)	0.94
Short-term memory			
Digits-Forwards	7.8 (1.6)	7.1 (3.5)	0.55
Digits-Backwards	5.8 (1.4)	6.5 (3.1)	0.51
Blocks-Forwards	7.6 (1.2)	7.6 (2.9)	0.97
Blocks-Backwards	7.6 (1.6)	7.6 (2.1)	0.96

Participant variables	Left temporal lobe	Right temporal lobe	*P* <
Verbal memory			
List Learning			
Total A1-A5	44.7 (8.6)	49.3 (12.8)	0.36
Delay (1)	6.6 (3.7)	9.0 (3.6)	0.17
Delay (2)	6.7 (3.4)	9.7 (4.0)	0.09
Recognition	13.1 (3.6)	13.4 (2.6)	0.82
Story Recall %			
Immediate	25.0 (23.0)	17.0 (14.3)	0.36
Delayed	17.5 (17.6)	10.5 (5.5)	0.24
Retained	18.0 (21.3)	22.0 (28.0)	0.72
Visual memory			
Complex Figure %			
Recall	23.5 (27.6)	23.5 (22.9)	1.00
Delay	19.5 (23.5)	21.0 (21.0)	0.88
Retained	35.5 (27.9)	34.5 (34.1)	0.94
Design Learning %			
Total A1-A5	49.0 (28.4)	48.3 (31.0)	0.96
Delayed	32.0 (28.0)	37.7 (22.7)	0.63
Intrusions	42.0 (24.6)	49.4 (30.3)	0.56
Emotional status			
Anxiety	7.3 (3.6)	6.0 (4.1)	0.43
Depression	5.4 (2.5)	4.7 (4.3)	0.63

Note. Standard deviations are in parentheses ().

TABLE II

Proportion of target completions and estimates of controlled and automatic processes for patients with left or right temporal lobe epilepsy and healthy control participants

	Left temporal lobe		Right temporal lobe		Healthy controls	
	Mean	SD	Mean	SD	Mean	SD
Condition						
Inclusion	.57	.15	.70	.13	.74	.06
Exclusion	.25	.11	.20	.19	.18	.07
New words	.26	.11	.29	.11	.27	.12
Estimate						
Controlled	.33	.22	.50	.22	.55	.09
Automatic	.36	.11	.37	.22	.40	.14

APPENDIX A

Word frequency and set size of target stimuli used in the study

Block 1			Block 2			Block 3			Block 4		
Target	F	Set size	Target	F	Set size	Target	F	Set size	Target	F	Set size
alien	13	5	angle	30	5	batch	3	4	berry	29	5
spoke	AA	7	squaw	3	5	stand	AA	9	stick	A	6
thick	A	7	torch	17	6	tramp	24	9	treat	A	5
broke	A	8	choke	27	5	chunk	3	6	clamp	4	8
limit	A	4	merry	38	4	mouse	34	6	panic	19	5
clerk	A	5	click	10	5	clump	9	4	cloth	A	8
troop	A	5	truth	AA	7	twist	42	5	value	AA	5
radio	41	4	rebel	25	4	route	A	5	sauce	27	4
study	AA	8	swamp	29	9	swing	A	9	tally	2	4
black	AA	8	blind	A	5	block	A	6	bride	41	8
patch	34	5	plate	A	7	porch	A	4	quack	7	5
frost	41	7	glaze	9	5	glory	A	6	grind	18	6
shift	A	6	slump	6	4	small	AA	4	snack	1	5
dream	AA	4	flick	4	4	forge	17	6	freak	5	4
couch	28	7	crack	48	9	crime	A	5	diver	4	5
guide	AA	5	heavy	AA	5	human	AA	4	knock	A	4

Note. Set size is the number of five-letter completions that have been produced by participants based on Jacoby's (1998) data. Word frequency (F) is based on Thorndike & Lorge (1944), A and AA have a high frequency of occurrence.

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