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Memory function after resolution of post-traumatic amnesia

A. BAIRD[1], K. PAPADOPOULOU[1], R. GREENWOOD[2] & L. CIPOLOTTI[1]

[1]*Department of Neuropsychology and* [2]*Acute Brain Injury Unit, National Hospital for Neurology and Neurosurgery, London, UK*

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Abstract
Primary objectives: The aims of this pilot study were (1) to examine neuropsychological, particularly memory functions immediately after post-traumatic amnesia (PTA) resolution according to the Galveston Orientation and Amnesia Test (GOAT), and (2) to provide a preliminary exploration of pattern of performance on GOAT items across PTA duration.
Methods and procedures: Thirty-seven head injured patients were administered the Recognition Memory Tests on the day that PTA resolved. Formal neuropsychological assessment was conducted on average 10 days after PTA resolution.
Main outcomes and results: All the patients in the series showed memory impairment which varied in severity but was typically characterized as global and severe. Deficits in executive and speed and attention functions were common. GOAT items relating to orientation were typically passed, while items concerning anterograde and retrograde recall were most commonly failed across all stages of PTA duration.
Conclusions: These findings suggest that reliance on memory performance as a measure of PTA is not ideal and highlight the need for further research of this issue.

Keywords: *Post-traumatic amnesia, memory, traumatic brain injury*

Introduction

Traumatic brain injury (TBI) is associated with a range of cognitive sequelae. Impaired memory function is widely considered to be the most severe and persistent residual cognitive deficit in this population [1–3]. Prediction of cognitive outcome after TBI is of clinical importance and can assist in planning rehabilitation and advising patients and families. Numerous studies have found injury severity to be highly predictive of outcome after TBI. In particular, Glasgow Coma Scale (GCS) scores and duration of post-traumatic amnesia (PTA) are important predictors of cognitive [4], functional [5–8] and psychosocial outcome [7, 9].

PTA is a transient state after brain injury characterized by anterograde amnesia and behavioural disturbance [10, 11]. The Galveston Orientation and Amnesia Test (GOAT [12]) is the first and most widely used standardized scale developed for prospective assessment of PTA. It comprises 10 items that assess orientation and recall of events before and after injury. Duration of PTA as assessed by the GOAT has been found to be a strong predictor of functional outcome as measured by the Glasgow Outcome Scale [5], return to productivity [6, 7], psychosocial function [9] and distress [7].

Few studies have examined cognitive functioning during PTA. Early studies focused on memory function [13–17]. For example, Fodor [13] found that patients in PTA had difficulty with delayed recall of related but not unrelated objects. Gasquoine [14] observed a high number of intrusion errors on cued recall compared with free recall of a word list in patients in PTA. In both these studies, recognition memory was intact. Procedural memory has been shown to be relatively intact during PTA [15]. Levin et al. [16] compared rates of forgetting of

Correspondence: Dr Lisa Cipolotti, Department of Neuropsychology, National Hospital for Neurology and Neurosurgery, Queen Square, London WCIN 3BG, UK. Tel: +44 207 8298793. Fax: +44 207 8132516. E-mail: l.cipolotti@ion.ucl.ac.uk

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colour slides in patients in PTA to those out of PTA and neurologically normal controls. Patients in PTA demonstrated accelerated rates of forgetting, while patients out of PTA showed rates of forgetting comparable with controls [16]. Schwartz et al. [17] assessed patients prospectively using recall and recognition of three words and pictures and the GOAT. They found that recall of words followed the achievement of the GOAT criterion by a significant interval and that picture recognition and recall preceded that of words by ~1 day. Schwartz et al. [17] concluded that three-word recall is a more reliable measure of emergence from PTA as the orientation items of the GOAT obscure the determination of recovery of continuous memory.

Research examining cognitive functions other than memory during PTA is even scarcer. Mandelberg [18] found that Wechsler Adult Intelligence Scale (WAIS) results were significantly lower in patients in PTA compared with those out of PTA. He reported both a qualitative and quantitative difference in performance. Wilson et al. [19] compared patients in PTA with pure amnesics, patients with chronic memory impairment and normal controls on a range of cognitive measures. They found that patients in PTA differed from all other groups on measures of semantic processing, verbal fluency and simple reaction time. The authors suggested that patients in PTA exhibit a wider range of cognitive deficits than the other two patient groups. They concluded that PTA is not solely a disorder of memory and orientation, as implied by the GOAT. A subsequent study by Wilson et al. [20] confirmed and extended this finding by exploring the nature of PTA recovery. They found that the most useful measures for determining the end of PTA were reaction time, digit span backwards, speed of information processing and verbal recognition in addition to orientation. Simple reaction time was the best measure for distinguishing between patients in PTA and patients at a later stage post-brain injury. Patients in PTA showed a gradual improvement in performance on all measures over time except verbal recognition. Wilson et al. [20] commented that the term PTA is misleading given that patients in PTA show cognitive deficits which are intact in pure amnesics. Further, patients with amnesic syndrome or severe memory impairment post brain injury may fail the orientation items of the GOAT despite being 'out' of PTA. Thus, it appears that the GOAT confounds confusion and amnesia, and therefore may not be an accurate measure of PTA. Indeed, a recent study by Nakase-Thompson et al. [21] concluded that the use of a single measure such as the GOAT which is limited to assessment of orientation and memory results in a poor characterization of the multi-faceted symptoms during the early stage of recovery after brain injury which they term 'post-traumatic confusion'.

This issue has been further addressed by Stuss et al. [22], who compared pattern of performance on attention and memory tests with results of the GOAT. Memory function was assessed using free recall and recognition of three words and three pictures after a 24 hour period. They found that word recognition recovered earlier than word recall and that ability to perform on the GOAT was recovered before word retrieval, but overlapped with word recognition. Performance on simple attentional tasks recovered before word recognition and ability to perform more demanding attentional tasks recovered before free recall. Stuss et al. [22] concluded that PTA is primarily a confusional state with prominent attentional problems and proposed the new term 'post-traumatic confusional state'. In addition, the authors argued that the GOAT score indicates a stage of recovery that is concurrent with recovery of recognition. They suggest that this is consistent with the use of orientation questions in the GOAT which are less demanding than free recall, and propose that after severe TBI, actual amnesia contributes to the GOAT score, whereas in mildly injured patients the primary contributors are attentional problems and confusion.

The current literature suggests that the GOAT is limited in its ability to characterize the initial post-traumatic recovery period and assesses orientation rather than memory *per se*. While there is evidence supporting the GOAT as a predictor of outcome, to the best of the authors' knowledge, there has been no previous study that has specifically examined the relationship between patient performance on neuropsychological tests, in particular memory tests, immediately after PTA resolution (results greater than 75 on the GOAT). The aim of this pilot study was to examine the relationship between recognition memory function immediately after PTA resolution according to the GOAT and performance in a variety of cognitive domains. Furthermore, this study aimed to provide a preliminary exploration of the pattern of performance on specific items of the GOAT over PTA duration.

Methods

Participants

Patients who had sustained a brain injury and were consecutively admitted to the Acquired Brain Injury Unit of the National Hospital for Neurology and Neurosurgery between October 2000 and December 2003 were eligible for participation in the study. Exclusion criteria were previous history of

epilepsy, brain injury, psychiatric illness or alcohol dependence.

Forty-eight patients were eligible for participation in the study. Six of these patients were discharged prior to PTA resolution and were therefore not included. Of the remaining 42 patients in whom PTA resolved, four patients refused to participate in the study, leaving a sample of 37 patients.

Measures

Glasgow coma scale (GCS) scores on admission to the Accident and Emergency Department were obtained from patient medical files as a measure of injury severity. PTA duration was assessed using the GOAT [12]. Memory function was assessed using the Recognition Memory Tests (RMT) for words and faces [23]. Neuropsychological assessment utilised measures of intellectual ability (Wechsler Adult Intelligence Scale × Revised (WAIS-R) [24]), nominal skills (Graded Naming Test [25]; Oldfield Naming Test [26]), visuoperceptual and visuospatial skills (sub-tests of the Visual Object and Space Perception Battery (VOSP) [27]), frontal executive abilities (including Weigl Sorting Test [28]; Controlled Oral Word Association Test [29] and Stroop Test [30]) and speed of information processing (Letter or Number Cancellation, Trail Making A and B Test [31]).

Procedure

Patients were administered the GOAT every day from the date of admission until they scored 75 and were considered to be out of PTA [12]. Participants were administered the verbal (words) and visual (faces) versions of the RMT on the same day that the GOAT score reached 75. Formal neuropsychological assessment was conducted on average 10 days (SD = 37 days) after PTA resolution.

Analysis

Patients were classified according to RMT scores; (1) severe global memory impairment (scores on both RMT faces and words ≤ 5th percentile), (2) mild global memory impairment (scores on both RMT faces and words > 5th × 25% percentile, (3) severe selective memory impairment (≤5th percentile on one RMT and >25 percentile on the other RMT), (4) mild selective memory impairment (5th × 25% percentile on one RMT and >25% percentile on the other RMT).

Analyses of variance (ANOVA) were conducted to explore differences between the memory groups on clinical variables including PTA duration, GCS score and age. The independent variable was memory group and the dependent variable PTA duration, GCS score or age. Chi-square analyses were used to explore sex differences between memory groups.

Neuropsychological assessment results for each cognitive domain were classified into two groups; (1) failed (≤5%ile for GNT/Oldfield, 5% cut-off for VOSP tests; failure of two frontal tests; ≥2 SD from the mean for speed of information processing tasks) and (2) passed. Given the small number of patients in each memory group, qualitative descriptions are used to examine differences in cognitive functioning between the memory groups.

An item analysis of the GOAT was conducted across certain time intervals of PTA duration. In particular, the percentage of patients who failed each GOAT item at the acute stage (day 1), middle stage (day 5) and final stage of PTA duration (day 10) according to the mean PTA duration for the sample (11 days) was calculated.

Results

Clinical features

Overall, the sample comprised 27 males and 10 females with a mean age of 39 years (SD = 15 years). The mean GCS score for the sample was 9 (SD = 5) and the mean PTA duration as measured by the GOAT was 11 days (SD = 10 days).

Table I shows the clinical features of the four memory groups. The majority of patients showed a global memory impairment (73%). Within this group, the greatest number of patients had a severe global memory impairment (74%). A selective memory impairment was rarer. In this group, all patients except one presented with a visual memory impairment.

There was no significant difference between memory groups in clinical variables such as age ($p = 0.08$) or sex distribution ($p = 0.93$). Interestingly, there was no significant difference between memory groups in injury severity as measured by GCS score ($p = 0.26$). However, it is noteworthy that the least impaired memory group (mild selective memory impairment) had the highest GCS score. There was also no significant difference between memory groups in injury severity as measured by PTA duration determined by GOAT score ($p = 0.51$). Nevertheless, the pattern of results reveals that a longer duration of PTA is associated with more severe memory impairment. Specifically, patients with a severe global memory impairment had the longest duration of PTA, while those with a mild selective memory impairment had the shortest duration of PTA (see Table I).

Table I. Clinical features of the memory groups.

Clinical variable	Memory group post-PTA resolution ($n = 37$)			
	Severe global memory impairment	Mild global memory impairment	Severe selective memory impairment	Mild selective memory impairment
Number of patients	20	7	6	4
Age, *M* (SD)	38 (14)	41 (19)	35 (16)	47 (13)
Sex, male (*n*)	14	5	5	3
Female (*n*)	6	2	1	1
GCS score(n)[a]	19	6	6	4
M (SD)	9 (4)	8 (6)	9 (5)	11 (5)
Range	3–15	3–15	3–14	3–15
Duration of PTA (days)				
M (SD)	12 (12)	9 (7)	10 (5)	5 (4)
Range	1–42	2–21	6–15	1–8
Selective⋆ (*n*)				
RMT words	N/A	N/A	0	1
RMT faces			6	3
RMT (words)[b], *M* (SD)	33 (5)	41 (2)	47 (2)	45 (5)
RMT (faces)[b], *M* (SD)	31 (4)	36 (4)	33 (3)	41 (3)

PTA = Post-traumatic amnesia, GCS = Glasgow Coma Score, RMT = Recognition Memory Test.
⋆ Number of patients with a selective verbal (words) or visual (faces) memory impairment.
[a]GCS scores were unavailable for two patients.
[b]Maximum score 50.

Neuropsychological functioning

Neuropsychological assessment results of each memory group are shown in Table II. Patients with a global memory impairment underwent neuropsychological assessment a greater number of days after PTA resolution compared with those in the other memory groups. Patients with a global memory impairment had a slightly lower pre-morbid IQ than those patients with a selective memory impairment. In general, all patients showed cognitive impairments. The cognitive domains most frequently impaired were executive abilities and speed and attention functions (see Table II).

Overall, patients with a global memory impairment (Groups 1 and 2) were more cognitively impaired than those with selective memory impairment. Patients with global memory impairment showed deficits in intellectual, nominal, executive, speed and attention functions. In contrast, patients with a selective memory impairment (Groups 3 and 4) showed no impairment in intellectual ability. Deficits in nominal skills were somewhat less common. Nevertheless, deficits in executive abilities and speed and attention functions were also present in these patients. Visuoperceptual functions were intact across all memory groups (see Table II).

GOAT performance across duration of PTA

The number of patients failing each GOAT item across duration of PTA (specifically on days 1, 5 and 10) is shown in Table III. In general, items 3, 4 and 5 (relating to the date of admission and first and last event recalled) appear to be the most difficult and were most commonly failed, while items 1 and 2 (relating to orientation) were the easiest and were less commonly failed. Specifically, item 5b (Can you describe in detail the last event you recall before the injury) is most commonly failed by patients on days 1 (87%) and 5 (100%), while item 3a (On what date were you admitted to hospital) is most commonly failed on day 10 (100%).

Discussion

This pilot study has provided a preliminary investigation of the relationship between PTA resolution as determined by GOAT score and neuropsychological outcome, specifically memory performance in patients with TBI. The findings regarding the relationship between memory outcome and clinical features, neuropsychological outcome and GOAT performance will be discussed in turn.

Clinical features

All the patients were assessed immediately after PTA resolution and all showed memory impairment which varied slightly in terms of severity. It was found that the majority of patients in this sample showed a global memory impairment that could be characterized as severe. This is in keeping with previous research that has documented a high incidence of memory impairment after TBI [1, 2, 32]. Previous neuroimaging research has demonstrated that the frontal and temporal regions are the most common lesion sites in patients with TBI [33], suggesting that memory impairment after TBI

Table II. Neuropsychological assessment results of the memory groups.

Variable	Memory group post-PTA resolution ($n=37$)			
	Severe global memory impairment ($n=20$)[a]	Mild global memory impairment ($n=7$)[b]	Severe selective memory impairment ($n=6$)	Mild selective memory impairment ($n=4$)[c]
Days post-PTA NP, assess. *M* (SD)	17 (51)	3 (2)	3 (3)	1 (2)
Pre-morbid IQ				
NART, *M* (SD)	92 (29), $n=13$	93 (3), $n=3$	102 (20), $n=4$	117 (1), $n=2$
Ed/Occ (level)	$n=3$ (Av)	$n=1$ (Av)		$n=1$ (HAv)
Schonell (level)			$n=1$ (Av)	$n=1$ (Av)
Verbal IQ	$n=15$	$n=5$	$n=5$	$n=3$
M (SD)	84 (13)	77 (6)	91 (5)	99 (7)
Performance IQ	$n=16$	$n=5$	$n=3$	$n=3$
M (SD)	76 (18)	88 (19)	89 (15)	91 (18)
Full scale IQ	$n=16$	$n=5$	$n=3$	$n=3$
M (SD)	83 (9)	93 (30)	89 (7)	94 (7)
Nominal[d]	$n=15$	$n=5$	$n=5$	$n=3$
Failed, *n* (%)	9 (60)	2 (40)	2 (40)	0
Passed, *n* (%)	6 (40)	3 (60)	3 (60)	3 (100)
Visuoperceptual	$n=15$	$n=5$	$n=5$	$n=3$
Failed, *n* (%)	0	0	0	0
Passed, *n* (%)	15 (100)	5 (100)	5 (100)	3 (100)
Executive abilities	$n=16$	$n=5$	$n=5$	$n=3$
Failed, *n* (%)	10 (63)	4 (80)	3 (60)	1 (33)
Passed, *n* (%)	6 (37)	1 (20)	2 (40)	2 (67)
Speed/attention	$n=16$	$n=5$	$n=4$	$N=3$
Failed, *n* (%)	11 (69)	4 (80)	3 (75)	1 (33)
Passed, *n* (%)	5 (31)	1 (20)	1 (25)	2 (67)

[a]Four patients, no neuropsychology assessment; [b]two patients no neuropsychology assessment; [c]one patient no neuropsychology assessment; [d]Graded Naming Test (GNT) or Oldfield Naming test (ONT): Group 1 GNT ($n=13$), ONT ($n=10$), Group 2 GNT ($n=5$), ONT ($n=2$), Group 3 GNT ($n=3$), ONT ($n=4$), Group 4 GNT ($n=2$), Oldfield ($n=1$); [e]Incomplete Letters (IL) or Object Decision (OD) tests from the VOSP: Group 1 IL ($n=12$), OD ($n=7$), Group 2 IL ($n=4$), OD = 1, Group 3 IL ($n=3$), OD ($n=3$), Group 4 IL ($n=2$), OD ($n=2$).
PTA = Post Traumatic Amnesia; NP = Neuropsychological, Assess = Assessment, NART = National Adult Reading Test, Ed/Occ = Pre-morbid IQ based on educational/occupational history, Av = Average, HAv = High Average, WAIS R = Wechsler Adult Intelligence Scale-Revised, GNT = Graded Naming Test, ONT = Oldfield Naming Test.

Table III. Pattern of failure of GOAT items on days 1, 5 and 10 of PTA.

GOAT question	Day of PTA		
	Day 1 ($n=37$), *n* (%)	Day 5 ($n=12$), *n* (%)	Day 10 ($n=7$), *n* (%)
Q1a	4 (11)	0	0
Q1b	9 (24)	2 (17)	0
Q1c	9 (24)	2 (17)	2 (29)
Q2a	7 (19)	2 (17)	1 (14)
Q2b	12 (32)	3 (25)	3 (43)
Q3a	30 (81)	11 (92)	7 (100)
Q3b	26 (70)	7 (58)	5 (71)
Q4a	27 (73)	7 (58)	3 (43)
Q4b	31 (84)	10 (83)	5 (71)
Q5a	30 (81)	10 (83)	5 (71)
Q5b	32 (87)	12 (100)	6 (86)
Q6	20 (54)	4 (33)	3 (43)
Q7	18 (49)	5 (42)	1 (14)
Q8	21 (57)	5 (42)	3 (43)
Q9	13 (35)	3 (25)	3 (43)
Q10	12 (32)	2 (17)	1 (14)

reflects damage to the medial temporal lobe memory system [1].

In the current series, visual memory function was more commonly impaired than verbal memory function in those patients with selective memory impairment. However, rather than suggesting a laterality effect implicating that right temporal functions are more commonly affected after TBI, this finding is likely to be an artefact reflecting task difficulty. Previous research has found that young people typically perform poorly on the RMT for faces and that performance on verbal recognition memory tests are less discriminant [34].

Interestingly, no significant difference was found between memory groups in injury severity as measured by both GCS score and PTA duration. The lack of significant difference between memory groups on these injury severity measures may be due to the small sample size and the large standard deviation, particularly in PTA duration for Group 1. However, it is noteworthy that the pattern of results is in keeping with previous research, which has identified these measures as predictors of cognitive

outcome [2, 4, 32]. Specifically, in this series the patients in the least impaired memory group (Group 4: mild selective memory impairment) were less severely injured according to these measures. In other words, patients in Group 4 had the highest GCS score and shortest PTA duration. Furthermore, patients with severe global memory impairment (Group 1) had the longest PTA duration. A number of studies have found that with increased severity of injury as measured by GCS score and/or PTA duration there is greater impairment across cognitive domains [4]. The findings support this notion as the patients with a severe global memory impairment showed greater cognitive impairment across cognitive domains, as discussed below.

Neuropsychological findings

Overall, all the patients showed cognitive impairment. In particular, deficits were most common in executive abilities and speed and attention functions. This finding supports previous research that has identified these two cognitive domains as the most commonly affected after TBI [35–37]. This is in keeping with evidence from neuroimaging and neuropathological studies which have shown that the frontal and temporal lobes are the most common sites of lesions after TBI [33, 36–37]. Interestingly, visuoperceptual functions were intact across all memory groups. This finding suggests that this cognitive domain is rarely affected after TBI.

Overall, patients with a global memory impairment (Groups 1 and 2) were more cognitively impaired than those patients with a selective memory impairment. These patients showed deficits in intellectual, nominal, executive, speed and attention functions. In contrast, patients with a selective memory impairment (Groups 3 and 4) only showed deficits in executive and speed and attention functions. Intellectual ability was relatively well preserved and deficits in nominal skills were less common. This finding suggests that global memory impairment after PTA resolution in patients with TBI may occur in the context of more generalized cognitive impairment. Two previous studies have investigated this notion and found that memory impairment after TBI was disproportionate relative to intellectual function as measured by the Wechsler Adult Intelligence Scale [1, 16]. It is noteworthy that both of these studies examined long-term outcome (years post-injury) and failed to examine potential deficits in cognitive domains other than intellectual function such as executive and speed of information processing skills. Further research is required to examine the relationship between memory impairment and deficits in cognitive domains other than intellectual function after TBI.

GOAT performance across duration of PTA

In general, across all patients GOAT items 1 and 2 relating to personal orientation were the easiest (least likely to be failed). In contrast, items 3, 4 and 5 relating to temporal orientation and first and last event recalled were the most difficult (most commonly failed). These findings are in keeping with previous research. In their development of the GOAT measure, Levin et al. [12] found that item 1 was passed by all patients, whereas only ~60% of patients correctly answered items 3, 4 and 5. Similarly, in their study examining the measurement properties of the GOAT, Bode et al. [38] found that items 3, 4 and 5 were the most difficult and item 1 the easiest. Furthermore, in their study of resolution of disorientation and amnesia during PTA, Tate et al. [39] reported that half the sample attained full orientation but never scored to criterion on GOAT item 4 (first recalled event post-injury) before the cessation of PTA testing, whereas the remaining patients passed this item before the return of full orientation. This contradictory finding highlights the significant problem with items used to assess memory in current PTA measures such as the GOAT. Previous authors have discussed these limitations and attempted to introduce alternative terms for PTA to highlight that this period of recovery encompasses a range of cognitive deficits other than memory impairment [20–22]. The findings of poor performance on the 'memory' items of the GOAT and impaired recognition memory function immediately after PTA resolution suggest that using memory performance as a measure of PTA is not ideal. Given that small sample size is a significant limitation of this study, particularly after stratification of the patients into memory groups, further research is required to clarify this issue in a larger population.

Conclusion

This study has provided a preliminary exploration of neuropsychological, in particular recognition memory performance immediately after PTA resolution according to the GOAT, and pattern of performance on the GOAT across PTA duration. It was found that all the patients in the series showed memory impairment which varied in severity but was typically characterized as global and severe. Deficits in executive abilities and speed and attention functions were common. Items of the GOAT relating to orientation were commonly passed across all stages of PTA duration, while items relating to anterograde and retrograde recall were most commonly failed. These findings suggest that reliance on memory performance as an assessment of PTA is not ideal. Further research is required to address this issue and to explore the relationship

between memory impairment after PTA resolution and other cognitive deficits.

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