SHORT REPORT

Association learning in the acute confusional state

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Abstract

The usefulness of cognitive rehabilitative treatment in the acute stages after brain injury seems questionable because patients in severe acute confusional state early after coma clinically seem unable to learn and store new information. Therefore, the capability of patients in acute confusional state to learn and retain associative information was assessed. On two occasions pairs of simple nouns were presented to six patients in severe acute confusional state. Stimuli were presented repeatedly either in written form only or with additional pictorial representations. Immediate and 20 minutes delayed recall was measured. Patients in acute confusional state were able to learn progressively more word pairs across several presentations. They retained some information over an interval of 20 minutes. In addition, they learned and remembered pictorially supported associations better than pure verbal associations. Patients in severe acute confusional state may retain some explicit information and may profit from an imagery mnemonic aid. These results were not expected on the basis of clinical findings alone and they have potential implications for the care of patients in acute confusional state.

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The acute confusional state is a common consequence of head trauma, stroke, infections, or other diseases of the brain, and reflects severe and global disturbance of attention in these conditions.[1] Patients in acute confusional state fail to focus on relevant stimuli, react slowly, and fail to sustain their attention in conversation.[2] Alertness and the sleep-wake cycle are usually disturbed, resulting in lethargy or agitation.[3] Some features of the acute confusional state—for example, disorientation, hallucinations, language, and thought disorders—may sometimes be secondary to attentional difficulties.[4]

Clinical evidence suggests that patients in acute confusional state fail to store ongoing events and that after resolution of the acute confusional state only "islands of memory" remain.[5] However, a systematic investigation of explicit memory capabilities of patients with head injury in severe acute confusional state has never been done.

Despite this lack of knowledge and the very severe memory disturbance of acutely confused patients, there has been growing demand to start rehabilitative treatment early in the course of illness.[6] However, the ability to acquire declarative knowledge is important for rehabilitative efforts and may even enhance or facilitate procedural learning.

The present study investigated declarative memory in severe acute confusional state. The goals of this study were to test whether patients in acute confusional state are able to retain simple associations after several presentations of the material and whether they benefit from a visual mnemonic.

Subjects and methods

Patients in severe acute confusional state, several of them just gaining consciousness after coma, were selected. Waxing and waning of

Table 1 Demographic and clinical characteristics of the patients with acute confusional state

Age	*Sex*	*Education (y)*	*Time after injury (days)*	*Aetiology*	*Initial CT findings*	*Orientation score**
27	f	12	40	TBI	Bilateral frontotemporal, right medial temporal, and thalamic contusion	11
27	m	13	14	TBI	Right medial temporal contusion	10
19	m	13	5	TBI	Right anterior medial temporal lobe, basal ganglia, and basal forebrain contusion	13
35	f	17	44	TBI	Left frontotemporal contusion	8
32	f	11	21	TBI	Left parietotemporal contusion	14
55	m	16	25	Aneurysm rupture (right A cerebri media)	Subarachnoidal haemorrhage in right sylvian fissure	13

TBI=traumatic brain injury.
*A score <15 indicates disorientation.[14]

attention was mandatory for the diagnosis. Patients showed marked disturbances in consciousness and attention, diurnal fluctuations, and disorientation. Reduced vigilance, drowsiness, and lethargy were common features of all patients even during the short phases of relative wakefulness. Consensus of three independent clinicians on the diagnosis of acute confusional state was required to include patients. Informed consent was obtained from the caregivers of all subjects. From 11 patients, five were unable to complete experimental sessions due to their impaired arousal. The table presents demographic characteristics of the six patients included in the study.

For the severe attentional failure of our patients, two simple associate learning paradigms were used. Sixteen concrete and imageable words were used to prepare two lists of four semantically unrelated word pairs. This limited number of items was considered to be relevant because patients may lose motivation and score at bottom if the amount of information surpasses their capacities. In one condition (WORD), word pairs were printed on white sheet (for example, BUTTER-LANDSCAPE). The other condition (PICT) consisted of both words and line drawings representing the concepts (for example, the picture of an APPLE on the head of a NUN).

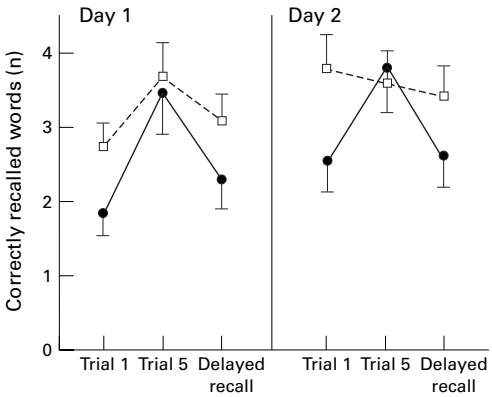
On two consecutive days, patients participated in a total of four experimental sessions. Each session consisted of five learning trials of either the WORD or PICT condition followed by a 20 minute delayed recall. In each of the five learning trials, patients first saw every item for 5 seconds and attempted to read it aloud. If a patient did not succeed at reading, words were read aloud by the investigator. Immediately after presentation of the entire list, in both conditions the first word of the word pair was presented in written form only and subjects were asked to recall the second word. Presentation of items was random in every trial. Twenty minutes later without further learning a delayed recall followed. Beginning with the WORD condition, WORD and PICT were learned in two separate sessions on day 1. This procedure was repeated on day 2, using the same word lists.

STATISTICAL ANALYSIS

Because considerable variation of the data was expected, the raw scores were square root transformed. A three way repeated measures analysis of variance (ANOVA) with main factors of experimental condition (WORD×PICT), learning trial (trial 1×trial 5×delayed recall), and day (day 1×day 2) was performed. Significant interactions were analysed using post hoc *t* tests with Bonferroni corrected significance levels.

Results

The figure shows that patients were able to learn progressively more word pairs across five learning trials and that they recalled some information even after 20 minutes (trials $F(2,10)=12.0$, $p<0.01$). This effect differed in the two experimental conditions, as reflected by the significant interaction of condition×trial ($F(2,10)=5.4$, $p<0.05$). This interaction was due to the fact that only in the WORD condition performance of trial 5 was better than trial 1 and dropped significantly after 20 minutes.



Mean performance of patients in acute confusional state learning associations between simple nouns, which were presented either in written form only (solid line) or with additional pictorial representation (dashed line). Error bars show SEM.

Recall of pictorial material was generally better than recall of words alone ($F(1,5)=8.9$, $p<0.05$). Finally, patients' performance was better on day 2 compared with day 1 ($F(1,5)=6.3$, $p<0.05$).

These results are representative of the whole study group. Five patients performed better in the PICT condition than the WORD condition, whereas one patient scored equally on both conditions. All six patients were better on trial 5 than trial 1. Finally, five patients were better on day 2 than day 1, and one patient scored equally on both days. This pattern implies that the effects found were stable and not biased by extreme distribution of scores across patients.

Discussion

Patients in this study showed a residual ability to learn simple associations and to retain some information for 20 minutes. Performance in the immediate recall during five learning trials increased significantly only in the WORD condition. This was due to the relatively good recall in the PICT condition already in the first learning trial. A ceiling effect precluded further increase in performance. A second finding was that overall performance was better on the second day. Finally, there was an effect of experimental condition with pictorial material leading to better retention than verbal material.

Cognitive functions in the acute stages after coma are rarely the subject of experimental investigation. This lack of research is due to the fact that confused or disoriented patients are often unable to cooperate. For the same reason, five of our 11 patients had to be excluded from the study. Several studies investigated memory impairment in post-traumatic amnesia. Post-traumatic amnesia is defined as the period after traumatic brain injury during which patients are unable to store ongoing events.[7] It is a related but not identical concept to acute confusional state, and some patients with post-

traumatic amnesia are clinically comparable with our patients. However, whereas memory disturbance and disorientation are the only necessary features of post-traumatic amnesia, patients in acute confusional state additionally have severe disturbance of the sleep-wake cycle, wakefulness, and attention.[8] Post-traumatic amnesia might constitute a less severe memory impairment than the amnesic syndrome.[9] In one study,[10] patients with post-traumatic amnesia were severely impaired in recognition while showing an intact capacity to learn mirror reading. The authors concluded that "rehabilitation during post-traumatic amnesia should stress direct acquisition of skills ... that the patient is likely to retain rather than repetitive, computer based exercises to improve episodic recall". However, in their study patients were not explicitly advised to learn and retain declarative information, while mirror reading was repeatedly practiced. Our patients had very serious attentional dysfunction, but nevertheless showed some declarative learning. This finding implies that repeated practice has a specific effect on declarative memory even in severely confused patients.

Another important finding is that patients in acute confusional state profited from pictorial presentation of the material. Pictorial presentation is a powerful technique to enhance recall, and the positive effect of imagery mnemonics has been demonstrated in amnesic patients.[11] According to Paivio,[12] images result in both pictorial and verbal representations in memory and thus lead to stronger memory traces than words. By contrast, verbal material is represented only in verbal form and does not automatically generate strong pictorial traces. Neurophysiologically, during acquisition imagery could activate more widespread cells in the cortex, resulting in a more complex cortical network than verbal material, which in turn would lead to better recall of the information represented in this network.[13]

The consequence of our results is that use of pictures in the rehabilitation of confused patients may be a treatment aid. Wilson[11] suggested that patients could profit from visual mnemonics to establish declarative knowledge of to-be-learned procedures.

In summary, our results show that patients in acute confusional state show a residual ability to learn and store new associations. Declarative memory is thus not completely abolished in acute confusional state. The fact that severely confused patients profited from a mnemonic aid is of potential relevance for rehabilitative approaches.

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