



Review

Rehabilitation of Memory Disorders

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Abstract: Memory disorders are common in clinical practice. This review focuses on the rehabilitation of anterograde amnesia, the inability to learn and retrieve new information, in non-degenerative brain disease. Diverse mnemonic strategies may be helpful in learning specific pieces of information. Their success also depends on the severity of associated cognitive failures, in particular, executive dysfunction. However, unless transfer to everyday activities is specifically trained, such strategies are of limited value in promoting independence in daily life. External memory aids are often necessary to allow for independent living. Learning to use them requires intact capacities such as procedural learning or conditioning. This review further discusses the rehabilitation of confabulation, that is, the emergence of memories of events that never happened. The rehabilitation of memory disorders needs to be tailored to patients' individual capacities and needs.

Keywords: amnesia; explicit memory; rehabilitation; orbitofrontal reality filtering; errorless learning; memory aids; confabulation; disorientation

1. Memory Systems

When people complain about having a bad memory, they typically refer to their difficulty in remembering names, remembering items on the shopping list, or learning the way around in a vacation spot. When a specialist talks about memory impairment, they have to specify what they refer to. The mentioned memory difficulties reflect an impairment of *declarative memory* (also called *explicit memory*), a system handling information that can, at least theoretically, be exchanged consciously between individuals, by telling, showing, or looking at [1]. The acquisition and maintenance of such information depends on intact medial temporal lobes (hippocampus and surrounding cortex), their connections, and associated areas [2]. The inability to normally acquire, store, and retrieve new information is called *anterograde amnesia* [3]. The loss of information acquired before the occurrence of brain injury is called *retrograde amnesia*. The declarative memory system has been supposed to have two partially overlapping components [1]: (1) *episodic memory* handles information acquired at distinct points in time, i.e., for which the spatio-temporal context is particularly relevant. It includes *autobiographical memory*, which refers to personally experienced episodes in one's life and often has an affective character. (2) *Semantic memory* represents the general stock of knowledge not tied to specific episodes. While previously acquired semantic memory is typically spared in anterograde amnesia [4], the acquisition of new semantic memory is at least partially impaired [5,6]. This review is mainly about the rehabilitation of anterograde amnesia in non-degenerative disorders, as it occurs, e.g., after stroke, traumatic brain injury, or Wernicke–Korsakoff syndrome. However, in a rehabilitation setting, anterograde amnesia seldom comes as a pure disorder; depending on the pathology, it may be associated with difficulties in planning and executing actions. The review also presents basic principles of the rehabilitation of “memory impairment” that does not fulfil the strict criteria of amnesia, where the focus is on a person's ability to function in everyday life.

Anterograde amnesia does not abolish all forms of learning. An amnesic subject may learn a new skill such as performing a sport, playing a musical instrument, or mirror



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reading, in addition to other capacities [7]. Skill learning, also called *procedural learning*, depends on intact basal ganglia and cerebellum rather than the medial temporal memory system [8,9]; however, depending on associated, primarily executing, failures, individual learning capacity varies [10]. Amnesic people may also learn as easily as healthy people to avoid a stimulus that has been perceived as harmful before, a form of *conditioning* dependent on the amygdala [11], or to blink when a warning sound was previously associated with a visual threat, a form of conditioning dependent on the cerebellum [12]. They improve their recognition of distorted or partially visible items if they have seen them in a full representation before, a form of learning called *priming* which is dependent on the association cortex [13]. Most importantly, amnesic subjects may acquire new habits and learn associations through repeated exposure, a form of learning called *habit learning*, which depends on intact basal ganglia [14]. These forms of learning, which are collectively called *nondeclarative memory*, require personal exposition to and practice of the to-be-learned capacities. They contribute to the compensation of amnesia.

Anterograde amnesia leads to a relative lack in available episodic information in memory. However, brain damage may also induce a confusion of memories: patients may remember events that never happened. This form of false memory is called *confabulation* and is often associated with disorientation in time and place [15]. This review will also briefly cover the rehabilitation of confabulation.

2. How to Improve Memory in Amnesia

Many strategies that healthy subjects use to improve their memory are also applied in the rehabilitation of amnesic subjects [16]. As the automatic storage of information characteristic of a healthy memory is not amenable to neurorehabilitation techniques, most strategies focus on enhancing information encoding, with the aim to secondarily improve memory retention [17,18]. Promoting *deep encoding* is such a strategy. It refers to the principle that new information that is mentally associated with previous knowledge and linked to a meaningful context is stored better than when encoding relies on ‘shallow’ (e.g., perceptual) characteristics [19]. Applied to everyday memory, a shopping list is easier to remember if it is thought about as the components of a whole menu rather than single and dissociated items. Likewise, the learning of names can be facilitated if a mental image is attached to the name [20]. Some patients use this strategy spontaneously [21]. The mere writing down of names may improve their storage, in particular in patients with relatively light memory impairment.

Some studies compared different learning methods. In a pioneering study, Glisky et al. [22] taught amnesic subjects two lists containing 15 words of a programming language under two conditions. In the *vanishing cues* condition, subjects first learned the full words, which were subsequently presented with more and more missing letters at the end. In the second condition, called *anticipation*, subjects recalled the words on the basis of their definition. As it turned out, the vanishing cues condition led to slightly but significantly better recall of the words, an effect which was maintained after a 6-week delay. Another study failed to confirm an advantage of this method [23]. A review of studies using the method of vanishing cues concluded on a discrete, but nonsignificant effect [24]. A more recent study with patients having suffered traumatic brain injury concluded that the efficacy of the technique depended on two parameters: first, it was generally more efficient when subjects were explicitly instructed to memorise the presented words (intentional learning) than when they were asked to produce the first word coming to mind (automatic learning); second, this advantage was not present in patients with more severe memory and executive failures [25].

Weakly stored information is prone to confusion upon recall. This principle is relevant for the occurrence of false memory in healthy and amnesic subjects [15]. *Errorless learning* has, therefore, been promoted as a means to improve memory in amnesia. In a seminal study, Baddeley and Wilson [26] compared the effect of errorless and errorfull learning. In the errorless condition, instructions were precise: “I am thinking of a word beginning

with QU, and the word is QUOTE. Please write that down". In the errorfull condition, subjects had to guess the word: "I am thinking of a word beginning with QU. Can you guess what it might be?". After the subject had guessed, the correct word was provided. The result was remarkable: both young and healthy elderly people recalled words learned in the errorless condition slightly but significantly better. Amnesic subjects overall learned fewer words, but the effect of condition was much more pronounced: words learned in the errorless condition were recalled about twice as well as the other words. Subsequent studies confirmed the beneficial effect of errorless learning of word lists or names [27–29] but found no advantage for route learning or acquisition of the ability to handle a personal organiser [27]. Middleton and Schwartz [30] confirmed the beneficial effect of errorless learning in a review but warned that the advantage of errorless learning may be offset by the therapeutic potential of difficult and potentially errorfull retrieval practice, which may be necessary for robust learning and prolonged performance gains. Whether errorless learning also supports independence in everyday activities is unclear: Rensen et al. [31] found that institutionalised patients with chronic Korsakoff syndrome improved their daily activities under errorless learning, while Ownsworth et al. [32] found errorfull learning to be more efficient for an everyday activity (cooking) in patients with traumatic brain injury. Errorless learning may be particularly suited for patients with severe amnesia, while patients with slight or moderate memory problems benefit more from errorfull conditions.

Most of the mentioned studies concerned the learning of specific pieces of information—word lists, names, and the like. However, amnesic patients may suffer from an inability to remember personal events. Some patients profit from taking and reviewing notes [33], but a proficient use of this technique requires repetitive practice and gradual adaptation [34]. As an alternative, technical equipment such as small portable cameras (e.g., SenseCam, Narrative clip) have been tested as a means to improve patients' memory of their own experiences. Pictures are recorded during chosen events at a determined frequency and later reviewed on a computer [35,36]. This intervention allowed patients to remember more details of events, even after weeks and months, and was clearly appreciated. To date, it has only been used in the context of studies, under the control of an investigator. As interesting as it may be for select patients, it requires considerable investment by the patient to review their daily experiences and poses the (legal) problem of people not accepting to be photographed [36].

Virtual reality is another tool increasingly used in cognitive rehabilitation [37]. Its role for the rehabilitation of memory disorders is not yet clear. It allows exploration of the effects of impaired memory in natural environments, e.g., the effects on spatial navigation [38], that is not otherwise possible. It has also been used to train daily activities in patients suffering from stroke, with greater effects on global cognitive functioning, attention, and executive functions than conventional therapy [39]. Virtual reality offers the possibility to adapt the difficulty of exploration and training to the patient's capacities. In addition, it is stimulating [40]. Its potential for the rehabilitation of memory disorders has yet to be exploited.

Whereas the available evidence suggests a beneficial effect of strategies such as errorless learning, possibly also vanishing cues, on the learning of specific information, their weakness is also obvious. These methods demand the preparation of the to-be-learned material and an effort, at least partially conscious, on the part of the learner. They may, therefore, help with the acquisition of names or word lists, but cannot make up for deficient automatic processing and learning of new information, as it is mediated by the medial temporal memory system.

Thus, is there no hope for amnesic subjects to ever improve their automatic memory acquisition? Recent developments in brain stimulation methods—repetitive transcranial magnetic stimulation (rTMS) or transcranial direct current stimulation (tDCS)—hold some promise [41]. The stimulation of cortical areas implicated in memory networks (prefrontal, parietal) improved learning and retention of name–face associations or word lists in healthy subjects [42,43]. However, these positive effects were typically short-lived. While it ap-

pears unlikely that cortical stimulation might compensate for a severely damaged medial temporal lobe, it appears plausible that enhancing plasticity in association areas during encoding may improve memory in moderately amnesic patients. At the current stage, however, optimal stimulation parameters and receptive patient populations remain to be determined.

3. Compensation of Impaired Memory

One of the main goals of rehabilitation is to render a person as independent as possible. As useful as the above-mentioned methods may be to learn specific pieces of information (e.g., word lists, names, or number codes), they are not sufficient to promote independent daily functioning (such as prospective memory, the ability to execute a planned action at the right time [44]). Indeed, memory-impaired subjects have a strong tendency to spontaneously rely on external aids. In an early study, Wilson [21] asked patients with chronic amnesia about their memory strategies. A long list of strategies emerged, among them asking others to remind one of things to do, putting objects in specific places, using notebooks or wall charts, or the dressing of lists. One of these methods, the regular use of a notebook, trained over several weeks, has been shown to decrease the number of memory failures in everyday activities [45].

Despite the arrival of new technologies, the spontaneous strategies have not markedly changed over time. A recent study found that up to 90% of patients would leave objects in noticeable places, mentally retrace steps, or practice activities repeatedly [46]. A similar percentage used external aids such as asking someone to remind them of things to do, using a paper diary for future events, making lists on paper, or using a notebook. A smaller percentage of patients applied modern technologies. Less than 40% used a mobile phone or an external timer as a reminder or asked somebody else to send a text message at the time a specific activity had to be completed. In most cases, these strategies and aids were considered helpful. Apparently, patients rapidly find out which strategy fits them best.

Many of these strategies depend on intact nondeclarative memory. Learning how to use the electronic agenda invokes procedural memory. Learning that, in case of doubt, helpful information can be found in a specific location (for example, placed there by the spouse), reflects a combination of conditioning and habit learning. Indeed, external memory aids such as an electronic agenda may allow for the acquisition of certain habits, such as taking medication at the specific time [47]. This was also suggested by an early study testing the usefulness of a pager system. Wilson et al. [48] asked memory-impaired subjects to indicate activities they wanted to be reminded of. The list contained activities such as a “good morning” message indicating the day and date and reminders to take medication or to prepare the sandwich for lunch. Over a 2 to 6 week baseline observation period, patients executed an average of less than 40% of the desired activities. This percentage rose to almost 90% during 12 weeks, in which they received a reminder for all activities through the pager system. After this, the pager was removed. Notably, over the following 3 weeks, the patients still executed about 75% of the intended actions. Apparently, they had taken the habit of performing them. A replication study indicated that this long-term benefit is attenuated or lost in patients having more severe executive dysfunction [49].

The application of mnemonic strategies to learn specific pieces of information and training the use of external memory aids (e.g., taking notes or using an electronic agenda) together with punctual supervision by an external person may allow patients with severely impaired memory to lead a largely independent life in a familiar environment.

4. Confabulation

At times, brain-damaged subjects do not appear to have too little, but false memory. Confabulation denotes the emergence of memories of events that never happened [15]. Numerous theories have been advanced to explain them, such as the combination of amnesia with executive failures, deficient monitoring mechanisms [50], or a desire to fill gaps in memory. We could not confirm these mechanisms as a general explanation. Rather,

we found that there are different forms of confabulation having different mechanisms [51]. The mere evocation of words that were not present in a learned word list correlated with the retrieval of correct words. Thus, these *intrusions* provoked by the memory test reflect a subject's endeavour to retrieve maximal amounts of information from an imprecise memory. More serious are the *momentary confabulations* that subjects produce in discussions or upon questioning. Patients may invent responses to questions about their recent activities or relating to external events. Such confabulations appear to be more prevalent with anterior brain lesions but have no specified mechanism. We found them to be weakly associated with impaired mental flexibility or a tendency to fill gaps in memory [51].

Much more serious are confabulations that patients act upon or that they advance to justify activities that are inappropriate in the present context. This form of confabulation, which we have called *behaviourally spontaneous confabulation*, is associated with amnesia and disorientation [15]. It actually corresponds to the original definition of the *Korsakoff syndrome*. As an example, a psychiatrist hospitalised with severe amnesia following rupture of an aneurysm of the anterior communicating artery was convinced for months that she was a psychiatrist on the ward. She regularly searched for patients she thought she had to take care of. Another idea was that she had to organise a reception in the evening. She would regularly try to leave the unit to response to this felt obligation. This disorder, when it occurs in nondemented subjects, always indicates damage to the posterior medial orbitofrontal cortex or an area directly connected with it [52]. The mechanism appears to be specific: the patients fail to sense when an upcoming thought or memory does not pertain to present reality and thus represents a daydream or fantasy. The ability to make this distinction depends on an extinction signal from the orbitofrontal cortex, which indicates that a currently held anticipation finds no correlate in reality, and thus is not valid [53]. This signal is produced 200 to 300 ms after evocation of a thought or memory and precedes the recognition of the thought's content, which happens at 400 to 600 ms. The perception of current reality, including time, place, and one's current role, thus depends on a pre-conscious mechanism not amendable to conscious correction. We call this mechanism *orbitofrontal reality filtering* [54].

The rehabilitation of reality-confusing patients is demanding and stressful for a rehabilitation team. A patient may promise to stay on the ward but disappear shortly thereafter in the attempt to assume their felt obligations. Sheltered freedom appears to be the most promising approach [15]. In our division, patients wear a bracelet emitting a signal when a patient approaches the door or enters the elevator, which are then blocked. Orientation training is performed with an errorless approach, in order to avoid entering into conflict with a patient who may insist on the veracity of their false orientation [16]. The positive message for families is that the state of reality confusion is virtually always limited in time; patients eventually find their way back to reality, although amnesia often persists. This process may take a few days but may also last up to several months. Occasionally, neuroleptics such as risperidone may accelerate the recovery of the sense of reality [55].

5. Perspectives and Conclusions

Rehabilitation of memory disorders is complex and has multiple variables: the type and severity of the disorder, associated cognitive failures, insight and motivation of the patient, and goals of rehabilitation. For some patients, it may be useful to learn strategies to better memorise names and specific terms, a capacity explored in multiple studies. Future methods of brain stimulation (rTMS, tDCS, etc.) may possibly help to improve automatic recording of information [41,43]. Some patients rapidly turn to external aids, with an increasing choice of technical gadgets [46]. For many patients with severe memory impairment, independence in daily activities is the most important goal. Training of habits and procedures, supported by the use of external aids, may allow achieving this goal. Virtual reality may offer new, motivating ways to verify and train capacities essential for daily functioning [37,40]. In any case, the rehabilitation of memory disorders needs to be adapted to every patient's individual capacities and needs.

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