Serial position effects scoring in the assessment of memory in Alzheimer's disease and major depression

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Improvement scoring of the Rey Auditory Verbal Learning Test

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Submitted

Abstract

The objective was to test the validity of serial position effects (SPE'S) scoring of the Rey Auditory Verbal Learning Test. The RAVLT, a multi-trial free recall test, is a much used clinical method for assessing memory performance. The method of scoring, however, obfuscates that two memory functions underlie free recall. This is suggested by serial position effects (SPE'S) of single-trial free recall, although the extent of the effects is not defined.

Research is reviewed in which the internal and external validity of SPE'S of the RAVLT is studied.

The internal validity of SPE'S was tested by means of confirmatory factor analysis. It is shown that the recency effect comprises the last two to three items, while the primacy and middle (prerecency) effect comprise the remaining items in a list, implying that they arise from two memory functions. Studies testing their external validity show that they play a variant role in memory impairment of AD and MD patients and are found to be differentially related to stress hormones activity in these patients, and in healthy human subjects.

Scoring of accurately determined SPE'S in the RAVLT is a valid improvement of clinical memory assessment. Their neuropsychological significance is discussed.

Introduction

A much used clinical method for assessing memory performance is the Rey Auditory Verbal Learning Test (RAVLT) [62]. The method of scoring, however, obfuscates the fact that two memory functions underlie this multi-trial free recall test. This is suggested by extensive research into cognitive [1,3] and medical influences [35,44] on serial position effects (SPE'S) of single-trial free recall [4,70]. These effects come evident the frequency of recall of a word list is plotted against the position of an item in a list. Typically, the first and last few items – called the primacy and recency effects – are more readily recalled than items in the middle, resulting in the U shaped serial position curve (SPC). It has been hypothesized that the recency effect is representative of short-term store (STS) performance and the primacy and middle effect of long-term store (LTS) performance [26].

However, deploying SPE'S scoring in the RAVLT is complicated by their limited internal and external validity. The extents of the effects are not defined. When done in single-trial free recall they have been based on the shape of the SPC. This is an arbitrary method as the extents of SPE'S have been found to vary considerably [16,23,25,28,30,33,43,49,70]. Further, it is unclear what influence rehearsal has on the extent of these effects. According to the dual store explanation of SPE'S [26] rehearsal will modulate the extent of the primacy and middle effect and the recency effect.

The internal validity of serial position effects in the Rey Auditory Verbal Learning Test

The internal validity of SPE'S of multi-trial free recall was studied in two very large (n=± 500) heterogeneous groups of psychiatric patients, ranging in age from 17 to 91, by means of confirmatory factor analysis [8] using a modified version of the RAVLT [6,62]. Before offering the standard five trials of a 15-word list, five trials of the first six and remaining nine words were offered and immediate free recall was tested after every trial. The reason for this modification was to ensure a gradual increase of task load and to avoid a too great emotional involvement in the task. The groups were chosen in order

to ensure the greatest amount of variability in the data. In addition, we studied the internal validity of SPE'S of single-trial verbal free recall analysing free recall performance of the first trial of the test. Confirmatory factor analysis showed that SPE'S in the RAVLT arise from two functions. One function arises from the recency effect, comprised of two items for the six-word list and three items for the nine- and fifteen word list; the other function arises from the remaining items on the lists (hereafter denoted as the prerecency effect). The same division was found for SPE'S of single-trial free recall. This argues against the dual store explanation of SPE'S [26] as it implies that rehearsal has no influence on the extent of the SPE'S, even though it modifies the frequency of recall of items on these effects.

The external validity of serial position effects in the Rey Auditory Verbal Learning Test

The external validity of SPE'S in the RAVLT was tested when defined on the basis of the shape of the SPC [7] and when defined accurately [9,10]

In mild to moderate AD group we [6] explored the role of AD in SPE'S. We were particularly interested in what role AD plays in the emergence of the primacy effect of short lists, as no evidence for this has yet been found [20,43,55,58]. We found a primacy effect on the 6-word list, to a lesser extent on the 9-word list, but not of the 15-word list. However, as a similar performance was found in the age-matched, normal, control group, it was argued that these impairments are probably general for aging and not specific to AD.

In the group of MD patients we [7] explored the relations between SPE'S and hypothalamic-pituitary-adrenal (HPA)-axis activity in a group of 15 elderly MD patients. Plasma cortisol (CORT) was used as a parameter of HPA-axis activity. To ensure that a possible influence of diurnal rhythm of CORT would not go unnoticed, plasma CORT was assessed in the morning, at midday and in the afternoon. The extents of the primacy and recency effects were defined as comprising the first and last four items. The lumped recall on these four items was used as the measure of performance.

We found impaired primacy effect performance in the group of elderly MD patients. This complies with the results of previous research where impaired performance on the primacy effect [12], respectively prerecency effect [25] was found in MD, using single-trial free recall. As performance on the primacy effect has been associated with effortful processing [38], this complies with the hypothesis that memory impairments in MD are characterized by problems with effortful processing [32].

We also found that plasma CORT, within reference values, is positively related to the reduced performance on the primacy effect and negatively related to normal performance on the recency effect. This suggests that plasma CORT is differentially related to the memory functions arising from these effects. However, as plasma CORT does not appear to contribute to the impaired performance on the primacy effects in MD, a possible alternative may be dysfunction of the central noradrenergic system [15,65], which has been conjectured central to memory impairment in depression [61].

In a group of healthy human subjects we studied [9] the role of central noradrenergic activity and glucocorticoid activity in the SPE'S. Central noradrenergic activity has been found to play a role in memory performance [27], and plasma norepinephrine (NE) is a parameter of central noradrenergic activity [79]. We hypothesized that plasma CORT is positively and plasma NE is negatively related to memory performance on the prerecency effect. In order to increase the sensitivity and specificity of collapsed recall on SPE'S scores individual item scores were multiplied by the factor score coefficients [8]. In order to avoid confounding effects of free recall on stress hormone activity [42,53], memory performance was assessed after the last venipuncture.

We found that plasma CORT and plasma NE are respectively positively and negatively related to collapsed recall on the prerecency effect, while plasma CORT is negatively related to collapsed recall on the recency effect. With regard to the recall performances based on the SPE'S and plasma CORT, our findings support previous results in MD patients [8], and suggests, moreover, that plasma CORT and plasma NE are oppositely involved in the memory function arising from the prerecency effect.

In a group of elderly moderate to advanced AD patients we also studied [10] the role of

central noradrenergic activity and glucocorticoid activity in the SPE'S. AD is accompanied by hypercortisolism in about half of the cases [50,54], and an altered function of the central and peripheral noradrenergic system [35,61]. On the basis of this it was hypothesized that plasma CORT and plasma NE are negatively related to memory performance on the prerecency effect. The same design was used as in the previous study [9]. The sensitivity of the prerecency and recency effects was further increased by multiplying the individual item scores by factor score coefficients derived from data of a previous study [8]. Suppressed performance on the prerecency and the recency effects was found. Yet impairment on the prerecency effects was found to be qualitatively specific to AD, as revealed by repeated measures of analysis. To the best of our knowledge this has not been reported before.

Hypercortisolism was found in AD, but no enhanced peripheral noradrenergic activity was found. A possible reason why no significant difference was found between the AD group and the normal controls, may be due the lack of statistical power to discriminate the two groups because of the small number of control subjects in which noradrenergic activity was determined. In accordance with our hypothesis it was found that plasma CORT is negatively related to the recall performance on the prerecency effect, suggesting that hypercortisolism promotes problems with effortful retrieval of information from the LTS. According to the glucocorticoid cascade hypothesis the hippocampal cell loss in AD will result in hypercortisolism that in turn will act as a co-factor in further hippocampal degeneration [64]. Yet no evidence for this has been found in ageing or AD [54]. Hypercortisolism has been found to result in dendritic remodelling and a suppression of neurogenesis in the dentate gyrus that normalize when CORT concentrations normalize [68].

Contrary to our hypothesis plasma NE was found positively related to memory performance on the prerecency effect suggesting that central noradrenergic activity promotes effortful retrieval from the LTS. It may inferred that the negative influence hypercortisolism has on dendritic remodelling and suppression of neurogenesis in the dentate gyrus is counteracted by central noradrenergic activity.

The neuropsychological significance of memory functions arising from serial position effects of free recall of a word list

Up till now, three neuropsychological interpretations of SPE'S of free recall of a word list have been discerned: two two-memory modality interpretations [1,19,26] and one processing interpretation [38]. The more prominent of the two-memory modality interpretations has been that the prerecency effect is a reflection of long-term store (LTS) performance, while the recency effect is a reflection of short-term store (STS) performance [1,26], an interpretation based on the 'modal' model [1]. According to this model two serially coupled memory modalities exist i.e. STS and LTS. The STS, which is believed to be a partial activation of the LTS, contains all control processes and regulates information transference to and from the LTS. The STS is a limited capacity buffer. Initially, this buffer is empty. When items enter the buffer, the time they stay in the buffer determines how often they are rehearsed and how much information about the items is transferred to the LTS.

More recently it has been conjectured that the recency effect is associated with a short-term memory buffer, while the prerecency effect is associated with episodic memory performance [19]. The buffer is distinct from episodic memory. During storage as well as recall, the lexical-semantic system is activated by the short-term memory buffer. Subsequently, the activated information is placed in the correct context and stored in the episodic memory. The strength of association with which information is stored in the episodic memory depends on how well lexical-semantic activities are coupled to the context, and determines the amount of recall.

Neither interpretation of SPE'S of free recall of a word list is, however, tenable, .the most important reasoning being that we [8] found that the extents of the recency and prerecency effects, in single- and multi-trial free recall of a word list, are the same. If rehearsal facilitates the transfer of information from the STS to the LTS or from the short-term buffer via activation of the lexical-semantic system and coupled to a context to episodic memory the recency effect should have dissipated or its extent should at least have diminished. Another reason why these interpretations of SPE'S are not

tenable is because we [6-10] and others [1,75] found SPE'S in a word list which length is well within the STS capacity of 7±2 [48].

A third interpretation based on the encoding model [33] is that the recency effect is indicative of automatic processing and the primacy part of effortful processing [38]. According to this model two forms of encoding exist: effortful and automatic encoding. The first form is believed to seize a large part of the limited attentional capacity, to occur intentionally, and to improve with practice. Examples of effortful processing are rehearsal, organization and mnemonic techniques. The second form, on the other hand, is believed to function without attention, to occur with intention, and not to improve with practice. Examples of mental functions in which automatic processing is believed to play a role are a sense of time, space and reading and writing [33].

When the three explanations are integrated, it may be hypothesized that SPE'S of free recall of word list are representative two control processes i.e. effortful and automatic that regulate information transference to and from the LTS. This hypothesis explains why we [8] found that the extent of the recency and prerecency effect is not sensitive to rehearsal. It also explains why recall is fleeting, when automatic retrieveal of information not yet permanently stored is delayed, and why it is not fleeting when it is permanently stored. Examples of the latter condition are the U shape SPC'S found when recalling the names of previous presidents of the USA [63], recalling which rugby matches one has attended in the last season [2], recalling which pictures one has seen during the previous year [36], and recalling which operas one has gone to in the last 25 seasons [66], a phenomenon which has become known as the long-term recency effect.

With regard to the sequence of these control processes the impression is gained that automatic processing precedes effortful processing. When small amounts of information are processed, it has been found that only recency effect occurs in immediate recall, primacy and recency effect after a certain time delay, and primacy effect after a long delay [40,52,75].

Neuropsychologically, SPE'S of free recall of a word list appear to be representative of distinct brain systems. Impaired performance on the prerecency effect has been found

associated with hippocampal c.q. medio temporal lobe damage [34,67,69,74], impaired performance on the recency effects has been found associated with posterior parietal damage [44,72], and impaired performance on both SPE'S has been found associated with frontal lobe damage [21]. Electrophysiological evidence supports this. The prerecency effect of free recall of a word list has been found associated with frontal and parietal activity, while the recency effect has been found associated with parietal activity [74]. Neurochemical evidence also supports this. We found that stress hormones are differentially related to performance on the SPE'S [7,9,10]. Diazepam [46], desglycinamide-arginine-vasopression, a synthetic vasopressin analogue [56], glucose [47] have been found to have a differential influence on SPE'S.

On the nature of serial position effects

Although SPE'S behaviour has predominantly been studied in free recall of a word list [4], evidence is converging that SPE'S are not modality-dependent nor sense-specific effects, and general to all type of memory performance in man and in animals. SPE'S have been found in declarative i.e. episodic memory [5,10,23], semantic memory performance [45], non-declarative memory performance, such as priming [13], and classical conditioning [57]. They have also been found in judging contests when end-of-sequence procedures or step-by-step procedure were used evaluating candidates [14], in forward and backward recall, where it was found that responding was faster to initial and final positions than to center positions [29], and in visitors to a website who demonstrated an increased probability to click to the first link and the last link in a list [51]. They further appear to be sense-independent as they have been found for ical conditioning [57], and for different senses such as hearing, sight [40, 52, 76]. Evidence is further increasing that SPE'S of different memory forms are supported by other brain areas than SPE'S of free recall of a word list (see fig 1).

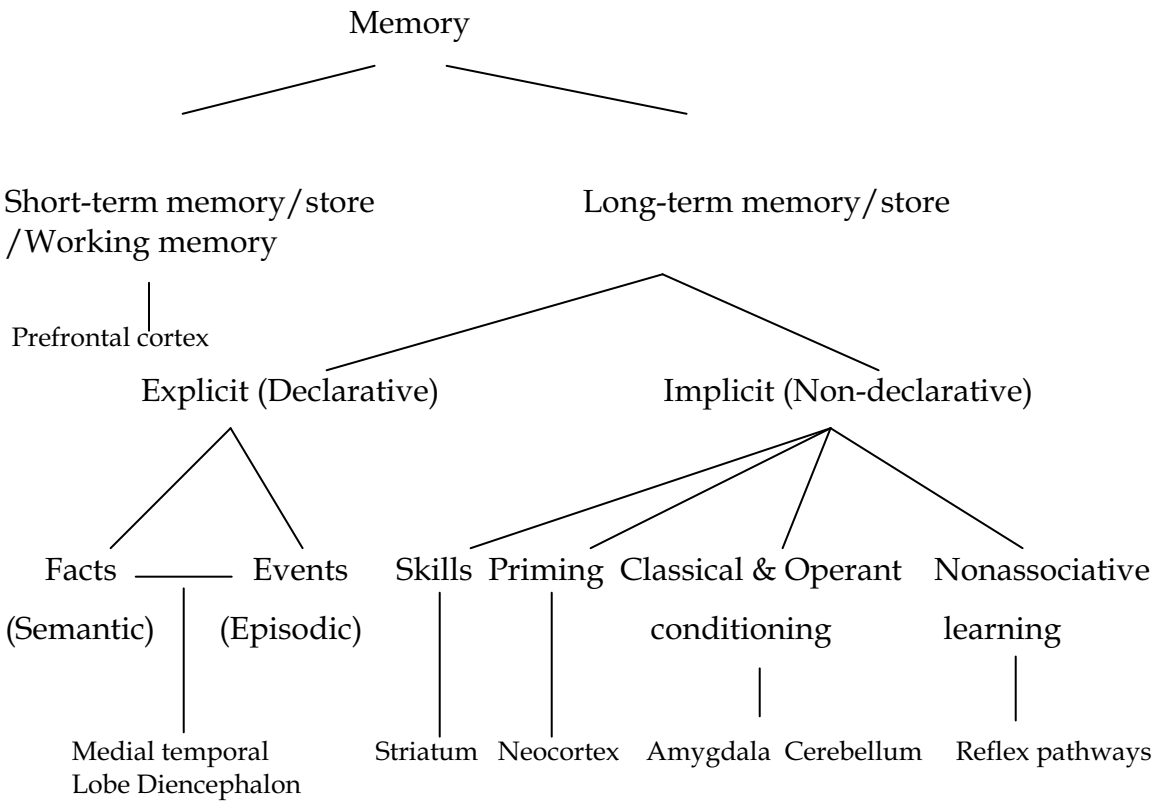

Fig 1. Classification of memory [24,71].

Paramount to this SPE'S have been found in memory behavior of animals [11,22,39,75-78], suggesting an evolutionary continuity between animals and man. As in man, they have been found not to be sense-specific and supported by similar neuroanatomical and neurochemical associations. Further, differential influence of cognitive tasks on SPE'S has been reported. For instance, delay has the same detrimental influence on the recall of the recency effect as in man [31]. SPE'S have been found on olfactory, auditory and visual memory tasks [60,77,78]. Impaired performance on the primacy effect has been found associated with left medial temporal lobe functioning [39,67]. CORT and NE have been found oppositely related to activity of the CA1 area [37], a brain area associated with working memory [73]. Benzodiazepines and atropine sulfate have been found to have differential effects on SPE'S [17,18].

In short, the nature of SPE'S appears to be general to all types of memory performance in man and in the animals suggesting that animals may be used as a model to study the

neurobiological backgrounds of SPE'S. When done a possible approach may be to focus on the functional influence of parts of the hippocampus on SPE'S. In the rodent, it was recently demonstrated that axon-sparing neurotoxic lesions of the CA3 are suppress prerecency effect performance, while damage to the CA1 area suppresses performance on all serial positions [41].

Conclusion

The internal validity of SPE'S in the RAVLT was tested by means of confirmatory factor analysis. The external validity of SPE'S was supported by (1) the role of a qualitative difference between reduced prerecency effect performance in AD compared with agecontrolled subjects, as well as by (2) the recall performance on the prerecency and recency effects in AD and MD being related in specific ways with stress-hormone concentrations. The most likely explanation of the SPE'S of free recall of a word list is that they are representative of effortful and automatic ways in which to regulate information transference to and from the LTS. In short, scoring of accurately determined SPE'S in the RAVLT is a valid improvement in clinical memory assessment.

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