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Article

The recency ratio as an index of cognitive performance and decline in elderly individuals

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Abstract

Individuals with Alzheimer's disease have been found to present a typical serial position curve in immediate recall tests, showing poor primacy performance and exaggerated recency recall. However, the recency advantage is usually lost after a delay. On this basis, we examined whether the recency ratio (Rr), calculated by dividing recency performance in an immediate memory task by recency performance in a delayed task, was a useful risk marker of cognitive decline. We tested whether change in MMSE performance between baseline and follow up was predicted by baseline Rr, and found this to be the case ($N = 245$). From these analyses, we conclude that participants with high Rr scores, who show disproportionate recency recall in the immediate test compared to the delayed test, present signs of being at risk for cognitive decline or dysfunction.

1 Introduction

An important feature of memory is the relationship between the *input* temporal sequence of the to-be-learned information, that is the order/sequence in which something is learned, and the likelihood of its recall. In particular, stimuli presented at the beginning and end of a list are typically remembered better than stimuli presented in the middle (Murdock, 1962). These are known as primacy and recency effects, respectively. Although there is not a complete consensus on which account best explains these effects (see e.g., Bjork & Whitten, 1974; Brown, Neath & Chater, 2007; Neath, 2010; Tan & Ward, 2000), a popular interpretation is based on postulating two separate processes (Glanzer, 1972). Primacy relies on increased rehearsal opportunities due to the fact that fewer items are competing for attention at the start of the list (Brown, Della Sala, Foster & Vousden, 2007; Rundus, 1971; but see also Sederberg, Gauthier, Terushkin, Miller, Barnathan & Kahana, 2006, for an account that incorporates enhanced attentional processes). In contrast, recency relies on short term memory processing: recent information is fresh in memory and therefore more accessible, at least in immediate memory tasks.

Regardless of the specific theoretical interpretation of primacy and recency effects (i.e., serial position effects), recent evidence, using standardized neuropsychological memory tests (e.g., Rey Auditory Verbal Learning Test, AVLT), has shown that they can play a role in differentiating between individuals with mild cognitive impairment (MCI) and Alzheimer's disease (AD; Martin et al., 2013; but see also Howieson et al., 2011), and between individuals with late-life depression and AD (Foldi, Brickman, Schaefer & Knutelska, 2003). Moreover, primacy performance has been shown to predict conversion from MCI to AD (Egli et al., 2014), and cognitive decline from a healthy baseline (Bruno, Reiss, Petkova, Sidtis & Pomara, 2013).

In a seminal study, Carlesimo, Sabbadini, Fadda and Caltagirone (1995; see also 1997 for a comparison of young and older cognitively intact participants) analysed the serial position performance of participants with AD and controls, comparing immediate and delayed performance, and concluded that participants with AD (and, incidentally, amnesics) suffered the "(…) most forgetting (…)" over time due "(…) to a loss of information from the recency part of the serial position curve" (p. 743). This conclusion suggests that individuals with AD may be overly reliant on

recency and short term memory processing in immediate memory tasks due to a comparatively greater loss of longer term memory ability (although, notably, individuals with AD have also been found to report working memory deficits, and especially issues with the central executive; Baddeley, Bressi, Della Sala, Logie & Spinnler, 1991; Rutherford & Bruno, 2015). If presented information is not successfully maintained and/or consolidated, it will be rapidly lost as new information is presented; it stands to reason then that only the most recently learned information will be preserved. Therefore, the typical immediate memory pattern emerges in people with AD where a reduction in primacy and an exaggerated recency recall are observed (e.g., Foldi et al. 2003). However, in delayed tasks, when information related to items from the recency position does not benefit anymore from *actual* temporal recency, most of the information will be lost, and individuals with AD will show a most dramatic drop in memory for recency items since that was best preserved in the immediate task. In contrast, primacy recall will be relatively comparable, since we know that retention of primacy information is poor at both stages in AD.[1] Of note, therefore, this pattern of results is not analogous to the recency to primacy shift (e.g., Brown & Lewandosky, 2010) in that primacy recall does not improve over time.

Based on the above, we propose that the ratio between immediate and delayed performance at the recency position should be an effective test of cognitive impairment and, possibly, a good predictor of future cognitive decline. A ratio of 1 would indicate that recency performance is the same at both stages; alternatively, a ratio below 1 would suggest that the person has increased their recall of recency items over time, thus presumably acquiring more information after the initial test, and maintaining such information until the delayed test (note that tests like the AVLT comprise multiple learning trials between the immediate and delayed phases); finally, a ratio higher than 1 would reflect the opposite: disproportionate recall of recent information as compared to information preserved in memory over the delay. As noted above, overreliance on recent information might underscore an

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[1] Although beyond the scope of this paper, it is interesting to speculate how the same pattern of results might be explained by models of memory that do not postulate a distinction between short- and long-term memory stores (e.g., Brown, Neath & Chater, 2007; Tan & Ward, 2000). Most single storage models emphasize the importance of item distinctiveness in retrieval, such that more distinctive items are more likely to be retrieved. Therefore, one could perhaps argue that in AD subjects, temporal distinctiveness is important in immediate memory tasks, as recency is preserved, but then abandoned or underused in delayed tasks, perhaps due to impaired processing of, or limited ability to use, temporal information (e.g., see also Howard, Fotedar, Datey, & Hasselmo, 2005).

underlying cognitive impairment. We tested this hypothesis by carrying out a longitudinal study to examine whether the recency ratio was related to changes in mini-mental state exam (MMSE) scores, a clinical measure of mentation, over two subsequent visits, starting from a cognitively intact baseline.

2 Methods

2.1 Participants. Volunteers for this study were recruited from the Memory Education Research Initiative (MERI; Reichert, Sidtis & Pomara, 2015) and were tested at the Nathan Kline Institute, Orangeburg, NY. The complete participant pool comprised 987 individuals at the start of the study. From this pool, participants were selected based on the following criteria: they were at least 60 years of age at baseline, had an MMSE score of at least 25, had no reported prior diagnosis of dementia, and returned for further assessment at least one year after baseline. Once these criteria were applied, we obtained 287 valid cases. Out of these, 42 participants were dropped because they had no corresponding e4 data, thus leaving us with a total of 245 subjects. Table 1 reports the demographic information.

2.2 Procedure. This procedure has been described previously in Bruno et al. (2013). All participants provided informed consent prior to the start of the data collection. After this, blood was drawn for APOE genotyping, vitals were examined, and the MMSE was administered. Subsequently, a neuropsychological test battery, lasting about 2 hours in total, was also administered; this included memory evaluation with the Rey Auditory Verbal Learning Test (AVLT). In the AVLT, participants are read the same list of 15 unrelated words five times; they are asked to recall the words immediately after each presentation. A new list of words (interference list) is then tested, followed by a recall test for the originally presented word list. Finally, 20-25 minutes later, participants are asked again to free recall the items (delayed recall task), and to complete a recognition task. One of three (or six, for participants enrolled after June 2014) alternative versions of this test, using different word lists was assigned randomly to each participant. These alternative versions were rotated over time, so that each participant received a new list in each of two consecutive visits. All participants were seen at baseline and at a follow up visit. Follow up times ranged from one year to nine years after baseline for the longitudinal sample, with a mean of 2.11 years and a *SD* of 1.57 years.

2.3 Design and Analysis. Primacy and recency were defined as the first and last four items on the study list, respectively. Middle words were all remaining words (7). In order to calculate the ratios, we divided the primacy, middle, and recency scores in the first AVLT learning trial (i.e., Trial 1) by the corresponding scores in the subsequent delayed memory trial, and applied a slight correction (*numerator* + 0.05 / *denominator* + 0.1) to avoid data loss from cases in which the denominator is 0. This way we obtained a primacy ratio (Pr), a middle ratio (Mr) and a recency ratio (Rr). We then performed a multiple linear regression analysis to establish whether Rr was predictive of cognitive ability over time. The regression analysis used a two-model structure with all control variables entered in the first model, and the ratios added in the second model. Model 1 predictors were: age, sex, years of education, e4-status, total memory performance in the AVLT, and time from baseline (years); Model 2 included three additional predictors: Pr, Mr, and Rr. The outcome was the change in MMSE score between baseline and the subsequent visit. The mean change score was 0.20 (*SD* = 1.41), ranging from -3 to +7, with positive values indicating cognitive decline. The MMSE change score did not fit a normal distribution (Shapiro-Wilk; $p < .001$), but in consideration of the fact that normality is not a critical assumption for linear models (Gelman & Hill, 2007), we maintained a linear regression approach.

Table 1 here

3 Results

Table 2 reports details on the ratio scores.

3.2 Prediction of cognitive ability. No issues with multicollinearity were noted (VIF $\leq$ 1.385). Both models fit the data satisfactorily (Model 1: $F_{(6,244)}=3.702$, p=.002; Model 2: $F_{(9,244)}=3.390$, p=.001), and Model 2 marginally significantly increased shared variance ($F_{(3,235)}=2.614$, p=.052) by .030 R^2. As anticipated, Rr was a significant predictor of MMSE change ($t=2.541$, $p=.012$, $\beta=.169$), whereas Pr ($t=.435$, $p=.664$, $\beta=.027$) and Mr were not ($t=.928$, $p=.355$, $\beta=.058$). This finding suggests that a higher Rr score is associated with more cognitive decline over time. The only other significant predictor was the total AVLT score ($t=-2.373$, $p=.018$, $\beta=-.171$). No other variable (age, $p=.640$; years of education, $p=.187$; sex, $p=.688$; e4-status, $p=.411$; and time, $p=.672$) yielded a significant effect on the change score. For illustrative purposes, the Figure presents the serial position curves of

participants who declined over time (i.e., they lost at least one point of MMSE at follow up; dashed-lines; n=76) and of participants who did not decline (i.e., they did not lose any point of MMSE at follow up; full lines; n=169). Notably, the distinctive serial position pattern is only present at the immediate trial. More critically, the Figure corroborates our findings by showing decliners perform more poorly than non-decliners in all portions of the serial position, except at the recency position in the immediate test. Therefore, whereas primacy and middle ratios are relatively comparable across the two groups, the recency ratio is much higher in decliners than in non-decliners.

3.3 Reliability. To assess whether the ratios scores remained consistent over time, we carried out bivariate correlations between baseline and follow-up ratios on all available scores that met our inclusion criteria. We carried out non-parametric correlations due to the non-normal distribution of the ratios. The results show that Pr (ρ=.271, *p*<.001, *N*=241) and Rr (ρ=.208, *p*=.001, *N*=241) correlated significantly, whereas Mr did not (ρ=.117, *p*=.070, *N*=241).

Table 2 and Figure here

4 Discussion

AD presents neuropathological degeneration in the hippocampal area and surrounding medial-temporal lobe (MTL) first, before affecting other regions (Raj et al., 2015). As a consequence, poor episodic memory and, particularly, a deficit in the ability to form and consolidate new memories, are early behavioural markers of the disease. Memory deficits are also identifiable when examining the serial position curve in recall, where individuals with AD tend to maintain intact retrieval of recently learned items (recency items in immediate tasks), but lose most of the preceding information. Following this pattern, we have argued that the ratio between immediate and delayed performance scores at the recency position (Rr), should be a sensitive marker of age-related cognitive dysfunction, with higher ratios suggesting greater risk for cognitive decline or dysfunction. We supported this claim by showing that Rr was a predictor of cognitive decline, as measured by change in the MMSE score, after an average follow up time of ~ 2 years; notably, this finding was obtained while also controlling for total memory performance, thus indicating that Rr provides added predictive value beyond that of more commonly used measures of memory performance.

A key hypothesis in this paper is that Rr indexes possible age-related cognitive dysfunction or decline, and that higher ratio scores should suggest greater risk. The rationale behind this hypothesis is two-fold. First, individuals with signs of cognitive impairment are postulated to suffer comparatively more loss of long-term than short term memory ability; consequently, they are expected to rely more on short-term memory processing than long-term consolidation. Therefore, in immediate memory tasks, individuals with cognitive impairment may compensate for the relative loss of long term memory by relying on, for example, a relatively intact phonological loop. As a consequence, in immediate performance tasks, where interference is reduced to a minimum, impaired participants will present relatively high levels of recency recall. This is noticeable in the Figure, where the decliners maintain the same level of performance as non-decliners at the recency position. Second, due to impaired ability to consolidate and preserve memories long term, individuals with cognitive impairment are also expected to show more generalized memory loss in the delayed task than controls. Consistent with this expectation, the Figure shows a stable memory advantage for non-decliners in the delayed trial across all serial positions. Of note, the repetition of the study list benefits primacy recall more than recency recall, as performance in the delayed task slopes downwards. This pattern of findings is generally consistent with the two-process account of serial position effects, and the common observation that the primacy advantage is preserved in delayed tasks, whereas the recency advantage often disappears, perhaps due to interference. As noted previously, however, the aim of this paper is not to debate accounts of the serial position effects, but rather to highlight the possible usefulness of examining Rr for the purposes of predicting cognitive impairment.

In this report, we have argued that Rr should provide a marker of cognitive decline based on its potential in identifying participants whose consolidation ability is declining or hampered. As noted, individuals with AD tend to present a reduction in primacy paired with comparatively better recency (e.g., Foldi et al. 2003), a pattern we have replicated with cognitively intact participants (see decliners vs. non-decliners in Figure). This emphasis on recency in decliners and individuals with AD, who we can class for convenience here as high-recency performers (HRPs), is interesting, and can be explained in at least two ways, or perhaps a combination. First, it is possible that the deficit to form new memories would leave little competition to recency items (i.e., the last items learned), which in

turn would be more easily retrieved in immediate memory tasks. If this is true, we should predict also reduced effects of proactive interference in HRPs as compared to controls. However, a correlation between Rr and a measure of proactive interference derived from dividing the list 6 (interference list) performance score by the trial 1 score (Vakil, Greenstein & Blachstein, 2010; cf. Loewenstein, Acevedo, Agron & Duara, 2007) did not yield a significant result ($r = -.018$, $p = .785$, $N = 245$). Alternatively, it may be possible that HRPs are aware of an existing memory deficit and, strategically, focus on recency items to maximise performance. In this case, it would be expected that HRPs might also show better response monitoring for recency items than for items presented previously (e.g., Higham, Perfect & Bruno, 2009). However, as these questions fall outside of the current focus of this report, they are best left for consideration by further research.

An alternative approach to calculating ratio measures is to divide performance at the last learning trial (i.e., trial 5 in the AVLT) by performance in the delayed trial. Performance at trial 5 should reflect how much a participant is able to learn; thus, contrasting trial 5 score (learning) with the delayed recall score could provide an estimation of the person's long-term retention of information. A higher learning ratio be it with primacy (LPr), middle words (LMr) or recency (LRr) would then reflect more memory loss over the delay, and potentially poorer consolidation. We tested this hypothesis by running a separate regression analysis with the learning ratios in place of the original measures – note that due to multicollinearity, the learning ratios cannot be simply added to the original analysis. The new ratio measure did not significantly add to Model 1 predictive value ($p=.134$), but we did observe LRr to be a significant predictor ($t=-2.033$, $p=.043$, $\beta=.136$), unlike the other two ratios. Of note, Rr produced a higher coefficient value than LRr (0.169 vs. 0.136), but both ratios were positively correlated with change in MMSE so that more drop in performance is predicted by a higher ratio. Future studies should investigate potential differences between Rr and LRr.

In Bruno et al. (2013), we showed that delayed primacy was a better predictor than delayed recency, as well as performance in other sections of the serial position, over two to five visits. In that study, we did not examine the ratio between immediate and delayed performance, but focused on performance over the five learning trials and the delayed task. Our current results are consistent with the findings of Bruno et al. (2013; see also Bruno et al. 2015; 2016). Our main claim in Bruno et al.

(2013) was that delayed primacy was a predictor of subsequent decline because it indexed a failure to consolidate information and establish long term memories. Consistently, we argue here that individuals with cognitive impairment may rely on short term memory processing more than healthy controls because these functions remain relatively more intact following impairment than does the ability to consolidate information in the long term. Therefore, the use of Rr, which taps into the combination of relatively preserved short term memory and impaired consolidation, serves as the other side of the coin with respect to the work presented in Bruno et al. (2013).

A limitation of this study is that the longitudinal analysis only assessed participants for a relatively short period of time, and detected small, although significant, changes in performance in the MMSE score. Therefore, the clinical relevance of this finding is limited. First of all, future research may contemplate examining whether Rr is a robust predictor of future cognitive performance from a healthy baseline, when compared to other likely candidates, by extending the follow up period. A related question also is whether Rr is a useful predictor of conversion to a neurodegenerative disorder, e.g., from MCI to AD.

The Rr score at baseline was found to correlate with the Rr score at follow up only weakly, albeit significantly. This finding does suggest that Rr may suffer from low reliability. However, the relationship between Rr at baseline and Rr at follow up was stronger within the non-decliner group, $r = .211$, $p = .017$, than within the decliner group, $r = -.025$, $p = .888$, thus suggesting that reliability may also be affected by category membership. Nevertheless, further research is needed to confirm our results. Future research should consider examining brain neuroimaging indices in relation to Rr performance to determine whether a link is found between, for example, MTL grey matter volume and Rr (cf., Bruno et al., 2015). Moreover, with larger samples, it may be possible to examine also whether there are gene-dose effects on Rr.

5 Conclusion

With a longitudinal study looking at change in generalized cognitive ability, we have provided evidence that Rr, the ratio between immediate and delayed performance scores at the recency position in the AVLT, is a useful measure to identify potential age-related cognitive impairment. Higher Rr

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scores, showing disproportionate recency recall in the immediate test, appear to associate with greater

risk for cognitive decline or dysfunction.

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Table 1. *Study demographics: Number of subjects (i.e., N); Age in years (mean and standard deviation, and range); MMSE score (with standard deviation); Sex (proportion of females); Years of Education (with standard deviation);and total AVLT score (with standard deviation).*

N	245
Age	71.42 (6.33) 60-91
MMSE	29.05 (1.02)
Sex (females)	134 (55%)
e4-carriers	85 (35%)
Education (years)	15.56 (2.94)
Total AVLT	43.31 (10.97)

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Table 2. *Minimum, maximum, mean and* SD scores *of primacy ratio (Pr), middle ratio (Mr), recency ratio (Rr), immediate primacy proportion (Immediate P), immediate middle proportion (Immediate M), immediate recency proportion (Immediate R), delayed primacy proportion (Delayed P), delayed middle proportion (Delayed M), and delayed recency proportion (Delayed R).*

	Minimum	Maximum	Mean	SD
Pr	0.05	8.00	0.96	1.39
Mr	0.05	6.21	0.50	0.56
Rr	0.05	10.50	1.82	1.88
Immediate P	0.00	1.00	0.38	0.28
Immediate M	0.00	0.86	0.22	0.19
Immediate R	0.00	1.00	0.58	0.24
Delayed P	0.00	1.00	0.57	0.33
Delayed M	0.00	1.00	0.54	0.28
Delayed R	0.00	1.00	0.46	0.31

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Figure. Serial position plots. Serial positions are on the x-axis (primacy, middle and recency). On the y-axis is reported the recall score in proportion to the number of items presented in that serial position (i.e., 4 for primacy and recency, and 7 for middle). Lines depict non-decliners (full line) and decliners (dashed line) separately by delayed and immediate trials.

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