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Sequential Information Processing: The "Elevated First Response Effect" Can Contribute to Exaggerated Intra-Individual Variability in Older Adults

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In this study we examined attention-related reaction time (RT†) and intra-individual variability (IIV) in younger and older adults using an iPad-based visual search test, in which, for each trial, participants were required to sequentially press a series of on-screen stimuli numbered from 1 to 8. Although overall performance RT was significantly slower, with greater IIV for the older compared to the younger adult group, there was also a disproportionately slowed RT and greater IIV for the first item in the series compared to all other responses within the trial. When the response to the first stimulus was removed from statistical analysis, the significant age-related RT slowing effect remained, but IIV was no longer significantly greater for the older compared to the younger adults. This pattern of results reveals a dichotomy between the preservation of RT and IIV in aging, and one that is strongly related to research methodology. A finding that may account, at least in part, for the outcome heterogeneity in the study of IIV in aging.

INTRODUCTION

Slowed reaction time (RT) and increased intra-individual variability of RT (IIV) associated with attention-related processing are commonly described behavioral characteristics differentiating older from younger adults with levels exceeding those expected in aging associated with dementia and MCI [1-5]. Although clinically the importance of examining information processing speed in relation to attentional function is emphasized in DSM-5 [6], the fact that research evidence reveals that study outcome can be heterogeneous lacks acknowledgement and investigation. Contributing to such outcome variability is the fact that RT and IIV can be influenced by var-

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†Abbreviations: RT, reaction time; IIV, intra-individual variability; TMT, trails making test; MILO, multi-item location; MoCA, Montreal Cognitive Assessment; PHQ-9, Patient Health Questionnaire; GAD-7, Generalized Anxiety Disorder; MFQ, Memory Functioning Questionnaire.

Keywords: Reaction time, Intra-individual variability, Attention, Aging

ious methodological, demographic, age, and other person-related factors. These include the type of attentional function measured, the inherent variation introduced by the differences in the choice of test and methodological approach used to measure that function [3,4,7]. Greater understanding of the integrity of information processing speed and its intra-individual variability in aging, particularly with respect to clinical application, therefore, requires further investigation into person- and paradigm-related, factors and their possible interaction.

In some research and clinical paradigms, the integrity of attention-related RT and IIV is measured using tests in which a series of consecutive responses make up the total task or trial. For example, in the trails making test (TMT) part A, a one-trial pen and paper test [8], participants are required to draw a continuous line joining a series of circled numbers in ascending order as fast but as accurately as possible, with outcome the time taken to complete the whole sequence [4,9], and see [10] for a computerized version of this task. A research example of such a test configuration is the multi-trial, iPad-based MILO (multi-item location) visual search task [11,12] in which for each trial, the participant is required to sequentially press a series of "billiard ball" stimuli numbered from 1 to 8 (see Figure 1) as fast and accurately as possible. There appears however to be tacit assumptions in the use of such a "sequential response" paradigm, namely that responses for each individual are relatively invariant across each stimulus within a given sequence and that all participants adopt a similar performance strategy. Evidence that this assumption cannot always be met has been provided by the work of Thornton and colleagues [11-13].

A prominent feature of the MILO RT function is a highly elevated first response compared to all other responses [11-13]. Thornton and Horowitz (2004) suggested that this elevation was due to implicit forward planning and were able to eliminate the difference by shuffling future targets, such that later response times were also slowed. Tsui *et al.*, (2013) [13] showed that responses to the first target were proportional to the length of the entire sequence and were also able to substantially reduce first response latency, although not eliminate it, by repeating the same sequence over and over or by providing a preview of the display before response onset. They concluded that the slowed first response is a combination of set-up time for registering a new visual layout, response preparation, and forward planning. Although whether such hesitancy effects reflect natural variation in one or more of the components identified above or are more strategic in nature is yet to be determined [11-13], it is clear that such effects need to be considered when examining the results of RT and IIV studies.

In our (Tales and colleagues) own pilot work using the MILO test and the TMT, we have also observed this elevated first response and that it can be highly variable between participants despite the provision of set numbers of practice trials designed to promote familiarity with the task requirements and responses. At the end of the testing session some participants reported that they had considered the various strategies described by Thornton and colleagues [11-13]. Some also reported anxiety at the beginning of each trial, a factor that may further influence or contribute to the elevated first response effect [14,15].

Using the MILO test, the first aim of this study was to investigate whether an elevated first response effect occurred for IIV as well as for RT. The second aim was to compare any RT and IIV elevated first response effects in younger and older adults and whether they varied with respect to general cognitive and subjective memory function and non-clinical levels of anxiety and depression [1,7,16-18]. Although educational level was matched as closely as possible within our study, group mean level was significantly greater for the older adults. We therefore also investigated the potential association between educational level and RT and IIV.

METHODS

Community dwelling older adults (n = 84, 50 to 80 years, 32 male and 52 female) were recruited via the Swansea Psychology Department research volunteer database, social network, and public advertisements throughout Swansea, Wales, UK. Younger adults (n = 58, 18 to 25 years, 13 male and 45 female) were recruited from the Swansea University Psychology Department student research credit system. Demographic details are displayed in Table 1. Four younger and five older adults were left-handed. All participants reported good medical, mental, and cognitive health, no history of such conditions and with no visits to the general practitioner about such conditions. Exclusion criteria included clinical levels of anxiety and or depression, poor general medical, mental and psychological and cognitive health, past history of head injury or neurological, medical or psychological problems, self-reported medication likely to influence cognitive function and physical barriers to task performance. All participants had normal or corrected to normal vision and hearing. Payment was not provided for participation. Travelling expenses were however reimbursed. Ethical approval was gained from the Psychology Department ethics committee at Swansea University and all participants gave written informed consent.

General cognition was measured using the Montreal Cognitive Assessment (MoCA) tool [19,20]. Depression and Anxiety were measured by the Patient Health Questionnaire (PHQ-9) [21] and the Generalized Anxiety Disorder (GAD-7) [22] respectively. For the older adults, subjective memory function was measured using

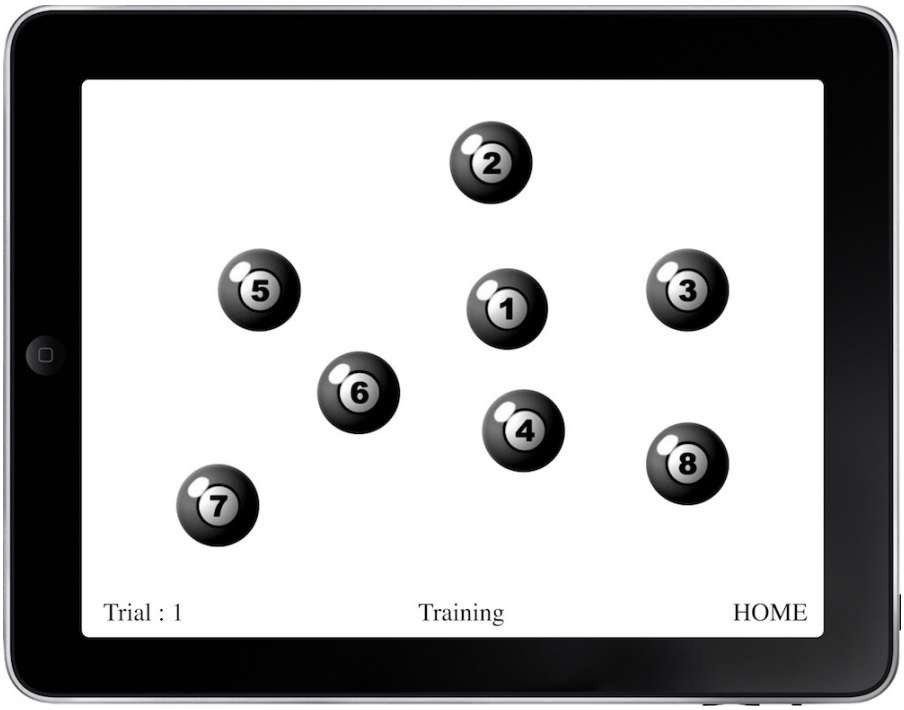

Figure 1. Representation of MILO stimuli with all eight numbered billiard balls.

the Memory Functioning Questionnaire (MFQ) in which higher scores represent lower levels of concern regarding memory function [23].

The MILO test [11,12] is composed of a representation of eight billiard ball-type stimuli each containing a number from 1 to 8 randomly distributed around the iPad screen (Figure 1). The participant was required to tap each billiard ball in sequence (from number 1 to 8) with the index finger of their dominant hand. Once tapped the ball disappeared from the screen. Once all 8 balls were tapped, they appeared again, randomly distributed on screen, after a 2-second interval, for 30 trials. In advance of the testing phase, the participants were instructed (using identical written and verbal instructions), that the aim of the task was to tap each ball in consecutive order (from number 1 to number 8) using their dominant index finger, as quickly but as accurately as possible. The iPad was placed flat on the desk ensuring there was no reflective light shining on the screen that would obscure or reduce the clarity of the stimuli. The participant was asked to keep their dominant hand at the edge of the iPad and given strict instructions to start performing the task as soon as the stimuli appeared on screen and to tap each billiard ball as quickly and accurately as possible. The researcher completed one trial as a demonstration, after which the participant performed three practice trials. The practice trials also ensured that participants were able to physically and correctly tap the screen and that responses were not hindered by factors such as long nails [24]. The three practice trials were not included in the statistical analysis. Immediately upon completion of the practice phase, the program reverted to the testing mode and participants completed all 30 trials. If a mistake was made a further trial was administered until 30 successful trials had been completed. As in the Trails Making Test-Part A, the outcome is the time taken (reaction time, RT) to complete the full and correct sequence of 8 taps (RT8), *i.e.*, from the onset of the test screen to when the last, 8^{th}, billiard ball is tapped. In addition, the time taken from stimulus onset to tapping the first billiard ball (RT1) was also recorded. Subtracting the RT to the first billiard ball (RT1) from the total task completion time (RT8) provided a measure of the influence of the first billiard ball in the sequence, upon test outcome. Individual median RT and its interquartile range (IQR) (the measure of intra-individual variability of RT) were obtained (see Table 1) and from this, group mean performance was obtained (see Boxplot Figures 2, 3, 4, and 5) entered into statistical analysis. In response to the non-normal distribution of the data (according to the Shapiro Wilkes test) for most conditions, SPSS (Statistical Package for the Social Sciences) non-parametric analysis was employed.

Table 1. Mean baseline demographics for the older adult and younger adult groups. Standard deviation in parenthesis.

	Age (Years)	Education (Years)	MoCA	MFQ	PHQ-9 (depression)	GAD-7 (anxiety)
Young adults	20	14	27	_	6	5
	(1.7)	(3.1)	(2.1)		(4.0)	(4.1)
Older adults	66	15	27	293	3	2
	(5.6)	(4.8)	(2.3)	(50.6)	(3.2)	(2.5)

MoCA, Montreal Cognitive Assessment; MFQ, Memory Functioning Questionnaire; PHQ-9, Patient Health Questionnaire; GAD-7, Generalized Anxiety Disorder 7-item scale.

Table 2. Group mean RT (Standard deviation in parenthesis) and IIV (interquartile range).

	Information Processing Speed (seconds)	Intra-Individual Variability (seconds) (IQR)				
	RT1	RT8	RT1-RT8	IIV1	IIV8	IIV1-IIV8
Young adults	1.24 (0.29)	4.52 (0.69)	3.28 (0.61)	0.37	0.8	0.43
Older adults	1.6 (0.44)	6.06 (1.04)	4.47 (0.86)	0.57	1.08	0.51

RESULTS

Mann-Whitney analysis revealed that non-clinical levels of depression and anxiety were significantly greater for the young compared to older adults (U = 1468, $p < .001$, effect size (r) = .38) and (U = 1278.5, $p < .001$, effect size (r) = .32) respectively. Mean MOCA score and mean years of education did not vary with respect to group (all p values > .05).

RT1 and IIV1 represent the time taken to respond to the first stimulus (billiard ball) in the sequence and the intra-individual variability of this response respectively. RT8 and IIV8 represents the time taken from the start of the trial to the completion of each trial, *i.e.*, pressing all eight billiard balls in the sequence (*i.e.*, including the first ball) and the associated intra-individual variability.

RT8 and IIV8 Overall Performance

Mann-Whitney analysis revealed that the time interval between when the stimuli appeared to when all eight billiard balls had been tapped (RT8), was significantly slower (U = 399, $p < .001$, effect size r = .71) and more variable (Greater IIV; U = 1121, $p < .001$, effect size r = .44), for the older compared to the younger adults. Note that for both the older and younger adult groups, the outliers in Figures 4 and 5 are not the same participants as for the outliers in Figures 2 and 3.

For the older adults, RT8 and IIV8 were not significantly correlated with anxiety or depression, subjective memory function or educational level (all p-values > .05). RT8 and IIV were however significantly negatively correlated with MoCA score, (r = -.254, $p = .023$) and (r = -.269, $p = .016$) respectively with faster and less variable performance related to better general cognition. For the younger adults, both RT8 and IIV8 were not significantly correlated with anxiety or depression, MoCA score, or educational level (all p-values > .05).

RT1 and IIV1

Mann-Whitney analysis revealed that the group mean time interval between when the stimuli appeared to tapping billiard ball one (RT1), was significantly slower (U = 737, $p < .001$, effect size r = .58) and more variable (greater IIV; U = 958, $p < .001$, effect size r = .50), for the older compared to the younger adults.

For the older adults, RT1 was not significantly correlated with non-clinical levels of anxiety and depression, MoCA score or education, but it was significantly correlated with subjective memory function, with less perceived detrimental change associated with faster RT speed. IIV1 was not significantly correlated with non-clinical levels of depression, subjective memory function, MoCA score or education, but it was significantly correlated with non-clinical levels of anxiety (r = .26, $p = .021$) with greater anxiety associated with higher variability. For the younger adults, both RT1 and IIV1 were not significantly correlated with non-clinical levels of anxiety or depression, MoCA score, or education.

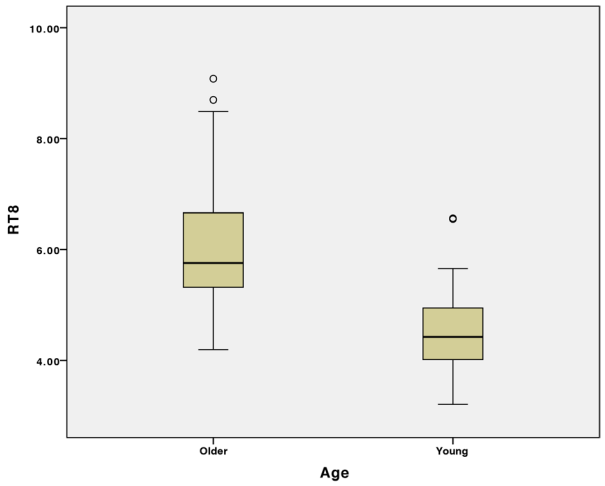

Figure 2. Box plot of RT median and interquartile range in seconds for responding to all 8 balls (RT8) for the young and older adults.

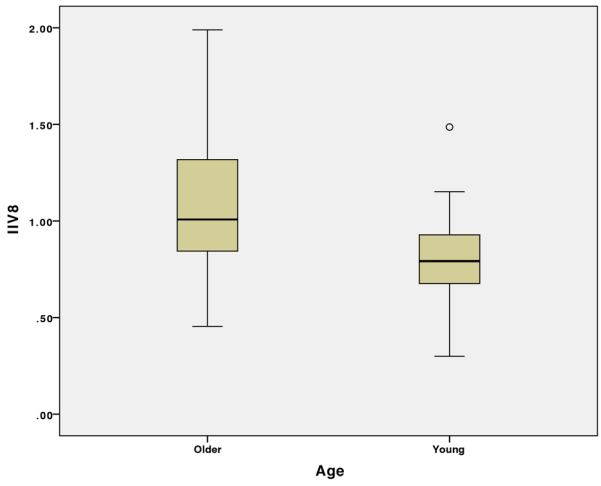

Figure 3. Box plot of median IIV (IQR) in response to all 8 balls (IIV8) in seconds, for the young and older adults.

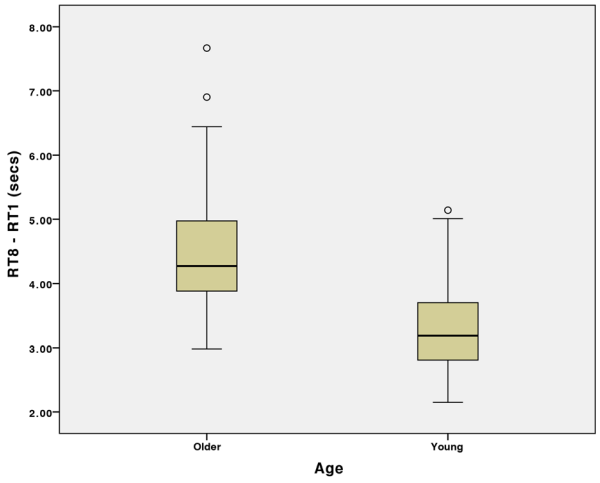

Figure 4. Box plot of RT median and interquartile range in seconds for the young and older adults when RT1 is subtracted from RT8.

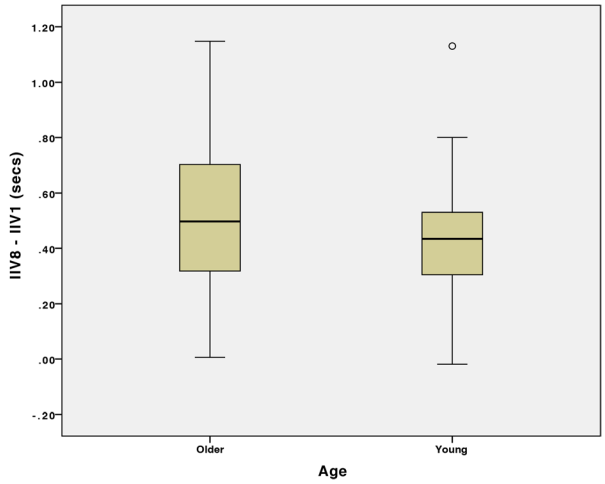

Figure 5. (IIV8 - IIV1) Box plot of IIV median and interquartile range in seconds for the young and older adults when IIV1 is subtracted from IIV 8.

RT8 - RT1

When RT1 is removed, this of course reduces the RT of each trial completion. For the young group, subtracting RT1 from RT8 reduced the RT for task completion by 1.24 seconds and for the older adult group by 1.59 seconds. For the young group, RT1 alone accounted for 27.4% and for the old, 26.4% of the total RT response.

When the first response is removed the IIV for the whole task is reduced for the young group by .37 seconds and for the older group by .57 seconds. For the young group IIV in response to the first billiard ball accounted for 46.2% of the total IIV for the whole task; accounting for 53% for the older adult group.

Mann-Whitney analysis revealed that when the response to the first billiard ball (RT1) was removed from the data, older adults were still significantly slower compared to young adults in their overall RT performance ($U = 512.5$, $p < .001$, effect size $r = .66$), but there was no longer and significant age-related difference in IIV ($U = 1929$, $p = .092$).

For the older adult group, RT8-1 and IIV8-1 were not significantly correlated with non-clinical levels of anxiety or depression, subjective memory function or education, but they were significantly negatively correlated with MoCA score ($r = -.309$, $p = .005$) and ($r = -.28$, $p = .012$) respectively. For the younger adult group, RT8-1 and

IIV8-1 were not significantly correlated with non-clinical levels of anxiety or depression, MoCA, or education.

Although this task elicited very few errors, (only four errors in total across both groups in response to the first billiard ball), Mann-Whitney analysis revealed that in overall performance young adults' mean number of errors (2.57, sd = 1.74) was significantly greater compared to that of older adults (1.25, sd = 1.59) (U = 1150, $p < .001$, effect size (r) = .44). There was however no significant association between the number of errors and performance on any measure for both groups (all p values > .05). Finally, there were no significant gender or handedness effects (all p values > .05).

Summary of Key Findings

To summarize: overall task RT was significantly slower and of greater IIV for the older compared to the younger adults with an elevated first stimulus response effect evident for IIV as well as for RT in both groups. When the response to the first stimulus was removed from statistical analysis, the significant age-related RT slowing effect remained, but IIV was no longer significantly greater for the older compared to the younger adults. For the older adults, RT and IIV (with or without the contribution of RT1 and IIV1) was significantly correlated with general cognition (MoCA score), with faster and less variable performance related to higher levels of cognitive function. Furthermore, response to the first stimulus (RT1) was significantly correlated with subjective memory function, whereas IIV was significantly correlated with non-clinical levels of anxiety, with greater anxiety associated with higher IIV. There were no significant correlations with respect RT and IIV and these factors for the younger adults.

DISCUSSION

A diverse range of tests have been used to investigate attention-related RT and IIV in aging. One might argue that such an approach has revealed the functional integrity of information processing speed and its variability with respect to a wide range of information processing components and specific aspects of attention-related function, relevant to real life. It is however difficult to compare outcomes and how robust any given finding is because of the inherent methodological variation in this area of research. It is also clear that different tests measuring RT and IIV ostensibly in relation to the same attention-related function can also vary in outcome. Increasing evidence indicates that methodological factors related to the choice of test and paradigm, can introduce previously unrecognized factors that may directly or indirectly influence RT and IIV and that this may vary significantly with respect to age [4].

In this study we investigated a further potential methodological influence upon RT and IIV research outcome in aging studies, namely the elevated first response effect, using the iPad-based MILO test [11-13]. To reiterate, when a paradigm such as MILO is used in which each trial requires the participant to sequentially respond to a series of stimuli, a disproportionately slow response to the first in this series, compared to all other responses can be observed. This elevated first response effect appears related to the time taken to register the new stimulus conformation at the beginning of each trial, response preparation and strategy planning. Here we examined this effect and its influence upon RT and IIV in both younger and older adults *per se* and upon the group comparison of such function. The potential association between this effect and person-related factors which typically vary with aging, namely non-clinical levels of anxiety and depression, objective (MoCA score) and subjective cognitive function (MFQ score) and educational level, were also examined.

Overall task RT (RT8) performance, *i.e.*, the time taken from the start of the trial to the completion of responses to all eight billiard balls in the sequence, was significantly slower and of significantly greater IIV for the older compared to the younger adults. For the young and older adults, the response to the first billiard ball (RT1) alone accounts for a disproportionate amount of the time taken to complete the task (RT8) (27.4% and 26.4% respectively). Further evidence therefore of the MILO-related "elevated first response latency effect." These comparable percentages however indicate a similar magnitude of effect in younger and older adults upon total test performance and indeed when RT1 was subtracted from RT8, the significantly slowed RT for the older compared to the younger group remained. This pattern of results indicates that when the contribution, specific to RT1, of the additional time taken in choosing, applying, adapting response strategy, together with the time taken to register different stimuli configurations and in response preparation and forward planning [11-13] is taken into account, information processing speed across the rest of the sequence remains significantly slower for the older compared to the younger group.

Intra-individual variability to the first billiard ball (IIV1) alone accounted for 46.2% for the younger, and 53%, for the older adults, of the whole task IIV (IIV8); evidence here therefore that an elevated first IIV effect can accompany the elevated first response RT effect in such a test paradigm.

The first response in both groups appears to influence the IIV of the response to a greater degree than RT. To speculate, although this first response effect contributes to some degree of overall slowing, some of this slowing may be compensated by, after several trials, the "discov-

ery" of strategy that speeds RT throughout the rest of the trial. Although such trial and error might speed overall RT, it may also result in highly variable RTs with respect to the time taken to determine and initiate these new strategies, a factor which may be less efficient and thus more variable for the older compared to the younger adults.

Whatever the origin, there is clearly a dichotomy in outcome between the RT and IIV results. Here then is further evidence that IIV and RT are not invariably related [4], but rather they may represent different aspects of information processing and their functional integrity [4] and which may be differentially affected by methodology, aging, and interaction between these and other factors.

Furthermore, for both the younger and older adults, overall RT and IIV (irrespective of whether or not the response to the first stimulus was removed from the analysis) were not significantly correlated with anxiety, depression, or educational level (or subjective memory function for the older adult group). For the older but not the younger group, they were however significantly negatively correlated with MoCA score, with faster and less variable performance associated with better general cognition. The outcome of such studies can therefore be expected to vary, at least in part, with respect to older participants' level of general cognition.

The response to the first billiard ball *per se* was also significantly slower and more variable for the older compared to the younger adult group. In contrast to the RT and IIV1 over the entire task, RT1 and IIV were not significantly correlated with MoCA score. RT1 was instead significantly correlated with subjective memory function, with less perceived detrimental change in memory associated with faster RT, whereas IIV1 was significantly correlated with anxiety, with greater levels of anxiety associated with higher variability.

The results also indicate therefore that even different components of a given task (*i.e.*, within the MILO test, the response to the first compared to the remaining stimuli) can be differentially influenced by aging, non-clinical anxiety, subjective memory function and general cognition, and that such associations can vary with respect to age. The outcome of this research may be relevant also to the decision in such studies regarding the number of practice trials provided in such paradigms. If such trials enable the prior determination of a successful strategy before actual test measurement begins, then variation in practice trials, and indeed individual differences in the number a given person requires to form a successful strategy, may affect study outcome.

Overall, these findings reveal that IIV outcome can vary as a result of both age-specific methodological- and person-related influences, and their potential interaction with different stimuli, within a given sequence. Arguably such effects can occur for any paradigm which requires sequential processing for each trial and thus need to be taken account of when using them. These findings also indicate that it may not be appropriate to generalize the outcome from such tests or to directly compare them with the results using other paradigms to measure RT and IIV in aging. These findings may also be relevant to the use of the TMT to measure attention-related (executive processing) function to measure information speed, which although only including one trial, and generally pen-and paper-based, may have similar disparity of responses between the first and subsequence stimuli. We recognize of course that we report only such results with respect to one test, MILO, and thus that further studies are required to test the robustness of our inferences from this study. Further potential study limitations include the lack of use of eye tracking to investigate strategy development and change, the fact that our participants were not necessarily medication free (although one can argue that this is in fact representative of both older and younger adults), and the fact that we did not measure the motivation, fatigue, trial number, task difficulty, and sequence length, or a greater range of age effects.

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