Effects of Vascular Risk on Item and Associative Memory Performance in Cognitively Normal Older Adults

By

Demi van den Ende (7271689)

Minor Research Internship Report (33 EC)

Department of Cognitive Neuropsychology, Tilburg University

MSc Neuroscience and Cognition, Utrecht University

December, 2023

Abstract

Background: This study investigates the relationship between global vascular risk and item and associative memory performance in older adults, while also examining hypotheses regarding age-related effects on memory.

Method: A total of 328 cognitively healthy older adults, aged between 60 and 90 years (mean age = 70.88; SD = 5.96), participated in the study. The study employed the Item and Associative Memory Task, using face-name stimuli with a recognition procedure involving intentional encoding. Global vascular risk was calculated using a point-based scoring system.

Results: Repeated measures ANOVA revealed performance differences between the memory tasks, with the lowest performance on associative memory and superior memory for names compared to faces. Three separate multiple linear regression analyses examining the influence of global vascular risk on memory performance, did not reach significance. A trend was observed for predicting associative memory, however this was attributed to the individual predictor age.

Conclusion: Findings confirm an age-related associative memory deficit. Contrary to the common view, memory for names was found to be superior to faces. While no significant correlation between global vascular risk and memory was found, the study presents an overview of the literature and suggestions for future research, providing a foundation for future studies in this field.

Keywords: Associative Memory, Cognitive aging, Memory Performance, Older adults, Vascular Risk

Layman summary

Background: Episodic memory, which enables people to remember past events, is one of the first memory systems to show age-related decline. Specific memory tests show that associative memory, the ability to learn and remember relationships between items, such as a name and a face, is specifically affected by aging. Conversely, age has minimal to no impact on the ability to remember single items. Existing literature indicates that cognitive changes are not only caused by "old age", but instead are influenced by a variety of factors related to the aging process. One such potentially influential factor is vascular risk. The presence of multiple vascular risk factors (such as: advanced age, female sex, diabetes and high blood pressure) increases the global vascular risk of getting vascular health problems. This study investigates the relationship between global vascular risk and item and associative memory performance in older adults, while also examining hypotheses regarding age-related changes in memory.

Method: In total 328 older adults participated in this study, aged between 60 and 90 years (mean age = 70.88). They were all functioning on a normal cognitive level. The study used the Item and Associative Memory Task, with stimuli as faces, names and face-name pairs. The tasks started with a learning phase, were stimuli were shown and participants were told to remember these. During the testing phase, participants saw the stimuli again and had to indicate whether they recognized these from the learning phase. Global vascular risk was calculated using a point-based scoring system. Within this scoring system, points are assigned for several risk factors including: congestive heart failure, high blood pressure, age, diabetes mellitus, previous stroke or transient ischemic attack, vascular disease, and being the female sex.

Results: Findings showed differences in performance between the memory tasks with the memory for associations being lower than memory for single items. Also, participants were

better at remembering names than faces. The influence of global vascular risk on memory could not be predicted in the present study, only effects of age were found.

Conclusion: The findings confirm that older adults have lower associative memory compared to memory for single items. Contrary to the common belief, memory for names was found to be better than for faces. Although the influence of global vascular risk on memory could not be predicted by the current this, an informative overview of the literature and suggestions for future research are presented. It lays a foundation for future studies in this field.

Keywords: Associative Memory, Cognitive aging, Memory Performance, Older adults, Vascular Risk

Content

Introduction

Episodic memory, which enables people to remember past events, is one of the first memory systems to show age-related decline.[1,2] Targeted memory tests reveal that associative memory, the cognitive ability to learn and remember relationships between items, such as a name and a face, is specifically affected by aging. Conversely, age has minimal to no impact on memory for single items.[3,4,5] Associative memory is essential for connecting people, places and moments in one's personal history, making it crucial for daily cognitive functioning. Supported by structures of the medial temporal lobe (MTL) and prefrontal cortex (PFC),[5,6] associative memory is used throughout the day, shaping interactions with others, facilitating observations, and aiding in learning new information.[3] Consequently, when associative memory falters, it can profoundly affect people's quality of life and autonomy.[4] This is a global concern, as the population over 60 is expected to double to about 2.1 billion people worldwide by 2050.[7] In the Netherlands specifically, the elderly population has already increased tenfold over the past century and now makes up 20.2% of the total population.[8,9] According to the projections of the Central Statistical Office (CBS)[9], the Dutch population over 65 is expected to continue to increase to 25% by 2070.

The associative deficit hypothesis (ADH) states that age-related episodic memory decline can be explained by difficulty in linking and retrieving associations between items.[4,10] In order to investigate this, the foundational work of Naveh-Benjamin,[4] compared memory performance between younger and older adults. The study comprised four experiments, where participants had to remember single items (i.e., item memory) and associations between two initially unrelated items (i.e., associative memory). The stimuli used for these tasks included words, non-words, or fonts. Aligning with the predictions of the ADH, results from all four experiments consistently showed that older adults performed significantly worse on associative memory tasks than younger adults. Nevertheless, item-memory was relatively

well-preserved in the older adults and reflected the younger adults' performance. Furthermore, the study showed that older adults did not benefit from intentional encoding strategies in the associative memory task, while younger adults did benefit from these strategies.

By employing more ecologically relevant stimuli, such as face-name pairs, subsequent studies from 2004[10] and 2009[11] improved the external validity of earlier research. Similar to the results obtained when using word stimuli, these studies verified the existence of an associative deficit in older adults with regard to names and faces. Rather than reduced hit rates, this age-related associative deficit appeared to be the due to higher false alarm rates, suggesting that older adults frequently misremembered distractor pairs.

Even though item memory is thought to be less influenced by age, Naveh-Benjamin et al.[10] identified disparities in performance within item memory task. Specially, their findings revealed better performance on item memory for faces compared to names. This is consistent with the dominant view suggesting that memory for faces is superior to memory for names.[11–14] However, some studies, such as Burton et al.[15] have found contrasting results with better item memory for names instead of faces.

Vascular risk

The literature suggests that cognitive changes are not solely attributable to "old age"; instead, they are influenced by a variety of factors associated with the aging process. Vascular risk is such a potential influential factor affecting the trajectory of cognitive aging. Given the vascular system is responsible for the brain and body's oxygen and nutrients supply, the consequences of poor vascular health are diverse. These include increased oxidative stress, decreased cerebral blood flow, and neuroinflammation, all of which can impact cognitive functioning.[16]

Identified vascular risk factors (VRF), also referred to as cardiovascular risk factors, include high blood pressure, physical inactivity, obesity, abnormal lipid levels, smoking, poor nutrition, cardiovascular diseases, and diabetes mellitus.[16–18] For the purpose of this report, the terms "vascular risk factors" and "cardiovascular risk factors" are used interchangeably due to their overlap.

A number of studies link VRFs to age-related cognitive decline.[19–21] For example, the continuing Longitudinal Aging Study Amsterdam, thoroughly evaluated cognitive performance of Dutch older adults (aged 55 and over). Using a variety of data, including blood samples, medical records, diagnoses, and outcomes of cognitive tests, this study found a negative correlation between global cognitive performance and low-density lipoprotein (LDL) cholesterol.[22] Another study, involving 396 male participants (aged 40-80), evaluated cognitive performance between those without cardiovascular disease (CVD), with sub-clinical CVD, and with prevalent CVD. The findings indicated a link between sub-clinical and prevalent CVD and lower memory performance compared to those who did not have CVD. Participants without CVD also had better global cognitive functioning, as demonstrated by higher Mini-Mental State Examination (MMSE) scores.[23] Dahle et al.[21]**,** investigated the predictive ability of specific VRFs, such as fasting blood glucose levels and arterial pulse pressure, in terms of minor age-related cognitive changes. Their study found that, on top of the expected age-related performance differences, these VRFs separately influenced cognitive performance in distinct ways.

Given that the number of VRFs tends to increase with age and they correlate with each other,[24] investigating global vascular risk - a composite score that incorporates a number of risk factors - might be more valuable than examining the impact of individual VRFs on cognitive functioning. Global vascular risk has been used in diverse studies and models, including one model that predicts the 10-year cardiovascular risk of a patient/person, derived

from the Framingham Heart Study cohort.[25] This model integrates a number of important cardiovascular risk factors, shaped by 36 years of research. These factors include age, systolic blood pressure, use of antihypertensive medications, diabetes, smoking status, history of cardiovascular disease (CVD), atrial fibrillation (AF) and left ventricular hypertrophy (LVH). Incorporating this model, Elias et al.[26] found positive correlations between a higher risk of cardiovascular disease and a variety of cognitive deficits, spanning a wide range of cognitive domains. In a recent longitudinal study conducted over 21-years with yearly follow-ups, Song et al.[24], employed a more refined version of the Framingham model to predict vascular risk. They examined a cohort of 1588 older adults who were reported to be free of dementia at the beginning of the study. Correlations were found between a rapid decline in several areas of cognitive functioning and the accumulated burden of VRFs. In particular, there was a faster deterioration in working memory, episodic memory, perceptual speed, and general cognitive performance among those with more risk factors. These findings show a link between cognitive performance and vascular health and offer insight into older adults' cognitive changes with different levels of vascular risk.

Predicting the likelihood of vascular events over time can be achieved by creating a global vascular risk score. In earlier sections of this report[24,26] and as comprehensively outlined by Sofogianni et al.[27], various predictive models have been proposed. SCORE2,[28] a popular model in Europe, enhances its predictive capabilities by incorporating variables such as ethnicity and socioeconomic status. However, the majority of these models rely on blood samples or other medical measurements, which may present logistical challenges or may not be feasible in certain contexts. A viable alternative is the $CHA_2S_2DS_2$-VASc scoring system from the 2009 Birmingham Schema[29], which requires only medical records. This acronym stands for Congestive Heart failure, hypertension, Age ≥75 [doubled], Diabetes mellitus, previous Stroke or transient ischemic attack (TIA) [doubled], Vascular disease, age 65-74 and

female. Demonstrated as effective in predicting the risk of thromboembolic events over a one-year period, the $CHA_2S_2DS_2$-VASc system has undergone validation in multiple clinical studies and it has been included in clinical practice recommendations.[30–32]

Relevance and research question

The aim of this study is to investigate the relationship between global vascular risk and cognitive performance of (cognitively normal) older adults in both item and associative memory tasks. Findings obtained from this, may hold implications for developing targeted interventions or preventive measures that protect older adults' cognitive health.

To achieve these objectives, initial hypotheses are examined regarding age-related effects on associative memory. In particular, advanced age is expected to negatively affect associative memory performance, resulting in lower associative memory compared to item memory in older adults (H1). Furthermore, older adults are expected to perform better on item memory for faces compared to names (H2). Additionally, this study investigates the effect of global vascular risk on memory performance, with the expectation that higher global vascular risk will have a negative effect, particularly on associative memory (H3).

Materials and method

Participants

The initial study sample comprised 338 cognitively healthy older adults, aged between 60 and 90 years. To be eligible for the study, participants had to meet the age criterion (≥60 years) and exhibit normal general cognitive functioning. Exclusion criteria were: (a) significant visual impairment, (b) inability to independently or with the assistance of a research team member, complete an electronic device-based questionnaire (on a PC or tablet). A brief cognitive screening tool, The Cognitive Telephone Screening Instrument (eCOGTEL), was used to confirm eligibility of the participants for the study.[33] Within a short administration time of 10-15 minutes, the eCOGTEL assessed six cognitive domains -

prospective, short-term, long-term, and working memory, verbal fluency, and inductive reasoning - in addition to general cognitive functioning. eCOGTEL can distinguish individual performance levels within the range of healthy cognitive functioning and has good test-retest reliability ($r = 0.85$, $p < 0.001$) and convergent validity ($r = 0.95$, $p < 0.001$) when compared to the MMSE.[33]

Various methods were used to recruit participants, including social media platforms, newsletters from different elderly association, such as Higher Education for Elderly (Hoger Onderwijs voor Ouderen, HOVO), and local elderly organizations across the Netherlands (e.g., Catholic Associations of Elderly/Katholieke Bond van Ouderen, KBO). Additionally, participants were sourced through the personal network of the researchers. All participants participated voluntarily without compensation and provided written consent prior to participating. This study received approval from the ethical review board of the Tilburg School of Social and Behavioral Sciences at Tilburg University (RP609) on 7 September 2021, and adhered to the principles of the Declaration of Helsinki.

Measures

a. Item and Associative Memory

The Item and Associative Memory Task (IAMT) was employed involving three separate memory tasks, assessing (1) item memory for Faces, (2) item memory for Names, and (3) associative memory for Face-name pairs. Responses were assigned a value: 1 = Hit (correctly identifying an old item as old), 2 = False alarm (incorrectly identifying a new item as old), 3 = Correct rejection (correctly identifying a new item as new), 4 = Miss (incorrectly identifying an old item as new). Reaction times were recorded in seconds. Performance was operationalized as the ratio of hits minus the proportion of false alarms to the total responses, resulting in a score between -1 and 1. Performance was additionally calculating using d-prime (d') from the Signal Detection Theory[34], these results are presented in the Appendix.

b. Vascular risk

The $CHA_2S_2DS_2$-VASc scoring system[35] was used to determine the global vascular risk for each participant. This scoring system involves assigning a numeric score to each VRF, and subsequently, summing these scores to obtain a composite vascular risk score per participant. The total score can be interpreted on its own, with higher scores indicating higher vascular risk, or it can be used to classify individuals into low-, intermediate- or high-risk groups, with scores of 0, 1 and ≥ 2 respectively.[29,35] The components of the $CHA_2S_2DS_2$-VASc scoring system and their weights are exhibited in Table 2.

Table 2. Global vascular risk computation[35]

Risk factor		Score
Age	<65 years	0
	65 to 74 years	1
	≥ 75 years	2
Sex	Male	0
	Female	1
Congestive heart failure history		1
Hypertension history		1
Stroke/TIA/thromboembolism history		2
Vascular disease history (prior MI, peripheral artery disease or aortic plaque)		1
Diabetes mellitus history		1

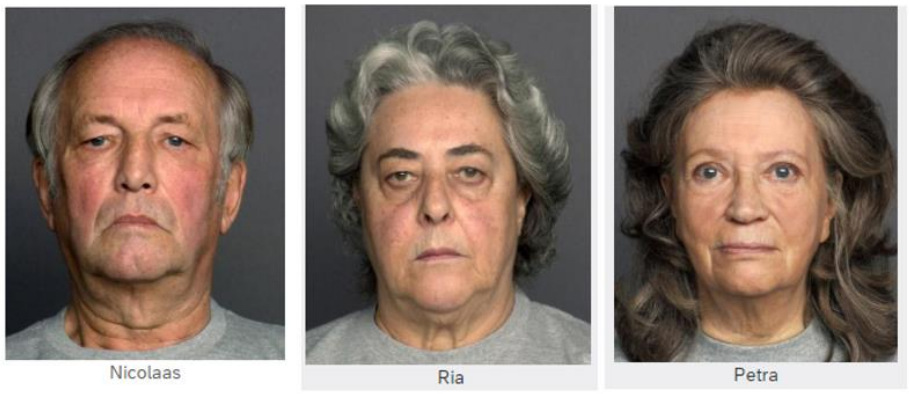
Abbreviations: TIA, Transient Ischaemic Attack; MI, Myocardial infarction. Calculation is based on the $CHA_2S_2DS_2$-VASc Scoring system. This table was adapted from Lip et al.[35]

Procedure

Participants received a Qualtrics survey (the current study was a small part of a much larger study[36]) via a link on a PC or tablet directed them to the IAMT. The IAMT employed a recognition procedure with intentional encoding, along with a structured order of the tasks.

In the encoding phase, stimuli were presented for 3 seconds, requiring participants to learn 24 Face-name pairs. A 60-second distraction task followed, involving solving mathematical problems. Subsequently, participants continued with three memory tasks: item-memory for (1) Faces, (2) Names and (3) associative memory for Face-name pairs. Each task involved presenting a series of stimuli on the screen, some of which participants had seen before (presented in the encoding phase) and some were new (not presented in the encoding phase). In the two item-memory tasks participants identified whether the item was new or old, and in the associative memory task, participants indicated whether the face and name belonged together or not. Each task featured 16 items (8 old, 8 new), and the administration time was approximately 10 minutes. Prior the main assessment, participants underwent a training phase with stimuli that were not used in the main assessment.

Figure 1. Example of face-name pairs presented in the Encoding phase



Statistical Analysis

To prepare for statistical analysis, the dataset underwent cleaning. In case of missing data, removal of cases was chosen rather than imputing missing values, to minimize potential

bias in the results. A total of 10 participants did not fully complete the IAMT, resulting in missing data and thus removal from the dataset. Subsequently, outliers were identified using the boxplot method. Using boxplots, the interquartile range (IQR) was automatically calculated and values above 1.5 IQR were identified as outliers, and values above 3 IQR as extreme values. In total, five outliers were identified in IAMT performance (four in item-memory for Faces and one in associative memory) and eight in the covariates (seven in education level, one in age). Each of these values were thoroughly examined (e.g. by inspecting data entry errors, response patterns and response time) and revealed that none of the outliers were the result of data entry or measurement errors or problems with the sampling process. Rather, they were due to natural variations within our sample and should be considered valid. As such, these outliers were not be removed.[37] The initial dataset comprised n = 338 cases, after data cleaning n = 328 cases remained.

For the first analysis, a one-way repeated measures Analysis of Variance (ANOVA) was performed, including performance on the three tasks within the IAMT as within-subject factors: item-memory for Faces and Names, and associative memory for Face-name pairs. This analysis involved verifying three assumptions: independence, normality and sphericity.[38] The assumption of independence of observations was met as all cases represented individual participants. Q-Q plots and histograms were visually inspected to assess normality of the dependent variables. Normality was assumed as the data points generally followed the diagonal line in the Q-Q plots and a bell shape in the histograms. The p-value of Mauchly's Test of Sphericity was <.05, meaning that the assumption of sphericity was violated. This indicated that the variances of differences between repeated measurements were not equal. In order to correct for the degrees of freedom, it is typically recommended to interpret Greenhouse-Geisser for epsilon (ε) values below .75, and Huyn-Feldt for values over .75.[39]

Post-hoc Tukey's Honestly Significant Difference (HSD) tests were used to identify task-to-task differences.

The second analysis involved three separate multiple linear regression analyses, one for item-memory for Faces, one for item-memory for Names and one for associative memory. Performance on the tasks was the dependent variable and global vascular risk the predictor. Covariates were age, sex and education level. Before conducting the analysis, the following key assumptions of multiple linear regression analysis were assessed: linearity, normality of residuals, no multicollinearity and homoscedasticity.[40] Scatterplots showed a linear relationship between the dependent and independent variables. Q-Q-plots displaying the distribution of the errors between the observed and predicted values, showed datapoints along the reference line, reflecting a normal distribution of the residuals. Residual plots revealed homoscedasticity of the data. The correlation matrix of all independent variables demonstrated no correlations exceeding .80, indicating the absence of multicollinearity. Collinearity statistics, the variance inflation factor (VIF), confirmed this finding by indicating no multicollinearity (VIF > 5).[41] To ensure for reliable regression analysis, a minimum of two independent observations per independent variable is required.[42] In this study, given the inclusion of four independent variables, the required minimum sample size of 8 cases was substantially exceeded.

All statistical analyses were performed using IBM SPSS Statistics software (version 28.0.1.0). The significance level α was set to < 0.05. The interpretation of the results uses a two-tailed approach, including the anticipated directional hypothesis (H3). This deliberate choice comes from the expected direction in only two specific predictors within that model.

Results

Participant characteristics

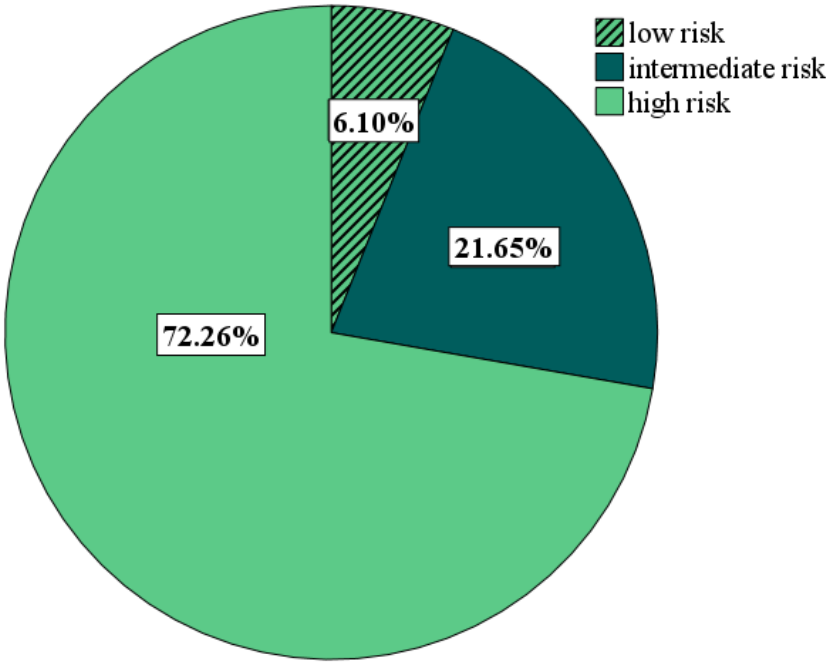
In total 328 participants completed the full IAMT, and their characteristics are displayed in Table 1. The mean age of the participants in this study was 70.88 years, with a large range. Notably, the majority of participants fell into the category of 'young-olds,' as defined by Lee et al.[43]. Moreover, a large proportion of participants (n = 237) exhibited a high global vascular risk, as illustrated in Figure 2. The sample demonstrated an average education level of 5.80, indicative of a middle-to-high level of education. Furthermore, there was a higher participation rate among females compared to males.

Table 1. Participant characteristics (n= 328)

Characteristic	Mean ± SD (range)
Age (years)	70.88 ± 5.96 (60.02-90.81)
Global vascular risk	2.18 ± 1.18 (0-6)
Education level	5.80 ± 1.04 (2-7)
Female %	60.7

The level of education was categorized according to Verhage[44], ranging from 1 (<6 years of primary education) to 7 (university degree). For a more detailed description read [44]. Global vascular risk was calculated using $CHA_2S_2DS_2$-VASc.[35]

Figure 2. Vascular risk distribution across sample (n = 328)

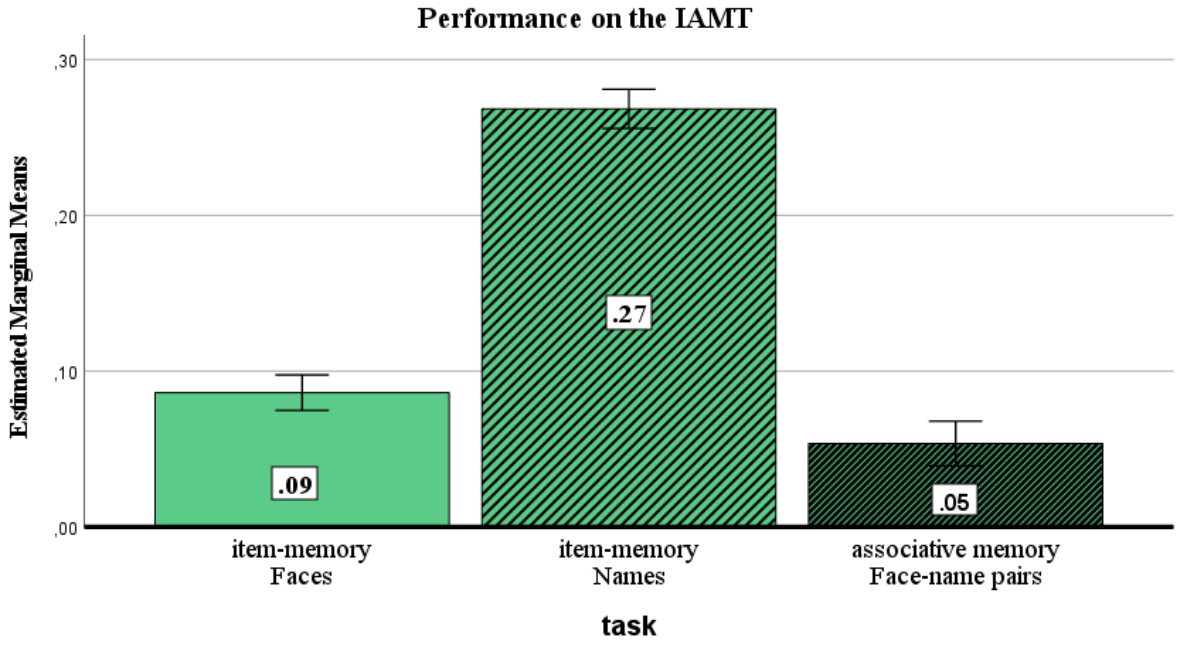


High risk indicates a score of ≥ 2 on the $CHA_2S_2DS_2$-VASc scoring system, while intermediate risk equals a score of 1 and low risk equals 0.[29]

Performance IAMT

A repeated-measures ANOVA was performed to see if memory performance differed across tasks. Mauchly's Test of Sphericity indicated that the assumption of sphericity had been violated, $\chi^2(2) = 11.39$, $p = .003$, and therefore, degrees of freedom were corrected using Huyn-Feldt estimates of sphericity ($\varepsilon = .967$). Memory performance differed significantly across all three tasks ($F(1.95, 636.98) = 4.52$, $p < .001$), with a large effect size of $\eta_p^2 = .502$. IAMT performance is displayed in Figure 1. Tukey's HSD showed performance differences among all three tasks. Associative memory performance (Face-name pairs) was lower than item memory for Faces (mean difference = -.33, SE = .01, p = .003) and Names (-.215, SE = .01, p <.001). Furthermore, item-memory performance for Names was higher than for Faces (mean difference = .18, SE = .01, p <.001). The level of significance was adjusted for multiple comparisons using Bonferroni correction. Similar results were obtained when using d' to calculate performance, as described in the Appendix.

Figure 1. Mean performance on the IAMT



Mean performance is visualized for each IAMT task, with standard deviations of .10, .12 and .13, respectively. Error bars represent the 95% confidence interval (CI). ANOVA showed significant ($p < .05$) performance differences across all task.

Regression analysis

Three separate multiple regression analyses were run to predict performance on the IAMT, outcomes are represented in Table 2-4. However, none of the regression models in this study significantly predicted memory performance. Specifically, the model that was expected to predict associative memory performance did not reach significance ($F(4, 323) = 2.140$, $p = .076$, $R^2 = .026$), suggesting that the included predictors did not collectively explain a significant proportion of the variance in the outcome variable. Despite not reaching statistical significance, this regression model with a p-value of .076, demonstrated a noticeable trend caused by the predictor Age. The other models predicting item memory for Faces ($F(4, 323) = 1.161$, $p = .328$, $R^2 = .014$), and Names $F(4, 323) = 1.964$, $p = .100$, $R^2 = .024$, were also non-significant. As no model reached significance, the individual predictors could not be interpreted.

Moreover, additional analyses using d' as performance (see Appendix) showed no significant effect of global vascular risk on memory performance. However, a similar trend was found for associative memory and the model predicting item memory for Names was significant, due to the individual predictor Age.

Table 2. Regression Coefficients for Predicting Item-memory for Faces

Model 1	B	95% CI	β	t	p
Vascular risk	-.010	[-0.02,0.00]	-.115	-1.44	.152
Age	.000	[-0.02,0.00]	.007	.10	.925
Sex	.011	[-0.02,0.38]	.054	.84	.402
Education	-.008	[-0.19,0.03]	-.079	-1.40	.161

R^2_{adj} = .002 (N = 328, p = .328), CI = confidence interval for B.

* less than .05

** less than .01

Table 3. Regression Coefficients for Predicting Item-memory for Names

Model 2	B	95% CI	β	t	p
Vascular risk	.007	[-0.08,0.02]	.075	.942	.347
Age	-.003	[-0.06,0,00]	-.144	-2.00	.047*****
Sex	.018	[-0.01,0.05]	.078	1.23	.221
Education	.001	[-0.01,0.01]	.012	.22	.824

R^2_{adj} = .012 (N = 328, p = .100), CI = confidence interval for B.

* less than .05

** less than .01

Table 4. Regression Coefficients for Predicting associative memory for Face-name pairs

Model 3	B	95% CI	β	t	p
Vascular risk	.008	[-0.01,0.03]	.067	.85	.399
Age	-.004	[-0.01,-0.00]	-.186	-2.59	.010*
Sex	-.004	[-0.38,0.03]	-.014	-.23	.822
Education	.004	[-0.01,0.02]	.035	.63	.532

R^2_{adj} = .014 (N = 328, p = .076), CI = confidence interval for B.

* less than .05

** less than .01

Discussion

The goal of this study was to enhance our understand of the relationship between global vascular risk and cognitive performance of older adults in both item and associative memory tasks. This was done in several steps, first performance differences on memory tasks were examined, and subsequently memory performance was assessed in relation to global vascular risk.

Associative memory

In line with the ADH, cognitively normal older adults were expected to perform worse on associative memory than item memory. Our sample's results confirm this finding as participants demonstrated lower performance on associative memory, compared to both item memory tasks. This aligns with the foundational work of Naveh-Benjamin.[4,10,11]

Many studies sought to uncover the underlying factors contributing to the age-related associative deficit. Inspired by Naveh-Benjamin's study in 2000,[4] the current study incorporated intentional encoding instructions, mirroring their approach of instructing participants to actively remember stimuli. The observed lowest performance in associative memory aligns with ADH that suggests a binding difficulty. A subsequent replication of Naveh-Benjamin's study[11], explored whether encoding instructions played a role in the associative deficit. Their findings showed an associative deficit exclusively under intentional learning conditions, and no such deficit under incidental learning instructions. If the associative deficit is indeed exclusive to intentional encoding, a possible explanation based on literature, could be older adults' difficulty in using effective cognitive strategies during intentional encoding.

Two other studies[45,46], investigated whether limited availability of attentional resources could contribute to the associative deficit. It is postulated that as the reservoir of attentional resources decreases with age, initiating in-depth encoding processes becomes

more challenging, leading older adults to remember the gist of a memory rather than specific details. Greene and Naveh-Benjamin[47] also researched the specificity of memory, and found that older adults depend on a gist-based strategy and therefore, compared to young adults, retrieve associations at a less detailed level.

Bartsch et al.[48] tried to explain the associative deficit by the limited working memory capacity of older adults. Participants in this study had to remember word-pairs, with varying amounts of words in a learning set. Interestingly, associative memory performance remained unaffected by the number of words in the set, leading to the conclusion that limited working memory capacity was not the root cause of the associative deficit. Nevertheless, the study did reveal that a prolonged encoding time served as a compensatory mechanism for the associative deficit.

Performance differences in item memory

In the current study, performance differences were examined between the two item memory tasks, anticipating better performance for faces over names, in line with the prevailing perspective in the literature.[10,11] Contrary to our expectations, participants exhibited better performance for names than faces. This finding is, however, consistent with the results of Burton et al.[15], who also used a recognition task for unfamiliar faces. They similarly observed better memory for names compared to faces. In an attempt to investigate this discrepancy, Burton et al.[15] conducted several experiments involving recognition memory tasks. They posited that the apparent ease of remembering names could be attributed to the dual engagement of visual and phonological memory representations, whereas faces predominantly rely on visual representations.

Moreover, the observed superior memory for names compared to faces was only exhibited when involving faces participants had not encountered before (unfamiliar faces; as in the present study). However, when it came to familiar faces, this performance difference

was not observed.[15] This could indicate that the mechanisms involved in memory for names and faces may vary based on familiarity.

Global vascular risk and memory performance

Contrary to our expectations, the current study did not find a negative correlation between global vascular risk and associative memory. This contradicts previous research findings that higher vascular risk can affect a range of cognitive domains, including episodic memory.[24,26] These studies used a longitudinal design, which allowed for a more nuanced assessment of changes over time compared with the current cross-sectional design. Furthermore, their method of calculating vascular risk differed from ours in terms of samples they collected. Both studies[24,26] used the Framingham General Cardiovascular Risk Score[25] and included measurements of systolic blood pressure and cholesterol, factors that were not integrated in the $CHA_2S_2DS_2$-VASc. The $CHA_2S_2DS_2$-VASc only incorporates hypertension history, represented with a binary yes/no classification. However, as both are widely used and validated models, the difference between their predictive abilities should be minimal.

A plausible explanation for the absence of a correlation between global vascular risk and associative memory in the present study might be the unequal distribution of vascular risk within our sample, failing to represent distinct risk groups. With a mean global vascular risk of 2.18 out of 9, the majority of the participants are categorized into the high risk group ($\leq$ 2 VRFs) despite having only a few risk factors. Grouping participants according to Hindricks et al.[29] criteria, might therefore not be very insightful as it lacks specificity for the high-risk category, spanning a broad range of scores from 2 to 9. Additionally, individuals in this population effortlessly accumulate 2 points (high risk group), as individuals aged between 65 to 74 accumulate 1 point, and those aged 75 and above garner 2 points. Considering this, it can concluded that the current sample, on average, lacks other VRFs beyond advantaged age, possibly contributing to the absence of significant results.

Strengths and limitations

This study has several strengths. One strength lies in the method that was used for calculating vascular risk, which is validated and widely employed in clinical and research settings. This ensures the reliability of our measurements and also facilitates comparisons with other studies. The substantial sample size is another strength. Furthermore, the transparent documentation of methods allows other researchers to replicate the findings. Finally, incorporating ecologically valid stimuli in the memory tasks improved the external validity of the study, enhancing the practical relevance and allowing for a better understanding of memory in real-life situations.

This study also has some limitations. Firstly, because of the cross-sectional study design, causality cannot be assumed and longitudinal studies are necessary to capture changes over time. Despite our effort to represent the Dutch population of older adults, the study inadvertently attracted a slightly younger cohort of older adults, with a somewhat higher levels of education, which affected generalizability. The unequal distribution of vascular risk within our sample, poses a challenge in assessing various levels of vascular risk. Furthermore, completing tasks online, although practical, brings limitations as external factors cannot be controlled to the same extent as in a laboratory environment.

Future research

Future research could replicate this study using a longitudinal study design, to capture changes over time. During the recruitment process, researchers should pay extra attention to representing the desired population while also ensuring a diverse distribution of vascular risk levels. Additionally, researchers could explore innovative ways to balance the practicality of using an online task with the need for controlled environments, perhaps by incorporating additional measures to control for external factors. Furthermore, investigating effective strategies to address binding difficulties in older adult, offering a partial compensation for

associative memory decline, could be interesting as understanding and implementing such strategies could improve cognitive performance and daily functioning.

Conclusion

In conclusion, this study confirms findings of an associative deficit in older adults. The unexpected higher memory performance for names, emphasizes the need for nuanced exploration and a potential shift from the common view. While no significant correlation between vascular risk and associative memory was found, the study has offered an overview of the literature and suggestions for future research, providing a foundation for future studies in this field.

Acknowledgements

First, I would like to express my gratitude to all the participants who took part in this study, and to all staff members who played a role in the collection and management of the data. Special gratitude is owed to Ruth E. Mark, Assistant Professor, for her invaluable guidance as my supervisor during writing this report. Her expertise and support significantly contributed to the completion of this work. I am also thankful to M.J.E. van Zandvoort, Professor, for serving as my examiner for this research paper.

References

1. Tulving E. What is episodic memory? *Current Directions in Psychological Science*. 1993;2(3):67-70. doi:10.1111/1467-8721.ep10770899

2. Tulving E, Szpunar KK. Episodic memory. *Scholarpedia*. 2009;4(8):3332. doi:10.4249/scholarpedia.3332

3. Naveh-Benjamin M, Mayr U. Age-related differences in associative memory: Empirical evidence and theoretical perspectives. *Psychology and Aging*. 2018;33(1):1. doi:https://doi.org/10.1037/pag0000235

4. Naveh-Benjamin M. Adult age differences in memory performance: Tests of an associative deficit hypothesis. *Journal of Experimental Psychology: Learning, Memory, and Cognition*. 2000;26(5):1170-1187. doi:10.1037/0278-7393.26.5.1170

5. Suzuki WA. Associative learning signals in the brain. *Prog Brain Res*. 2008;169:305-320. doi:10.1016/S0079-6123(07)00019-2

6. Becker N, Laukka EJ, Kalpouzos G, Naveh-Benjamin M, Bäckman L, Brehmer Y. Structural brain correlates of associative memory in older adults. *NeuroImage*. 2015;118:146-153. doi:10.1016/j.neuroimage.2015.06.002

7. World Health Organization. Ageing and health. Accessed August 28, 2023. https://www.who.int/news-room/fact-sheets/detail/ageing-and-health

8. Cijfers en feiten ouderen in Nederland | Loketgezondleven.nl. Accessed November 13, 2023. https://www.loketgezondleven.nl/gezondheidsthema/gezond-en-vitaal-ouder-worden/feiten-en-cijfers-ouderen

9. Ouderen. Accessed November 20, 2023. https://www.cbs.nl/nl-nl/visualisaties/dashboard-bevolking/leeftijd/ouderen

10. Naveh-Benjamin M, Guez J, Kilb A, Reedy S. The associative memory deficit of older adults: further support using face-name associations. *Psychology and aging*. 2004;19(3):541.

11. Naveh-Benjamin M, Shing YL, Kilb A, Werkle-Bergner M, Lindenberger U, Li SC. Adult age differences in memory for name–face associations: The effects of intentional and incidental learning. *Memory*. 2009;17(2):220-232. doi:10.1080/09658210802222183

12. Enriquez-Geppert S, Flores-Vázquez JF, Lietz M, Garcia-Pimenta M, Andrés P. I know your face but can't remember your name: Age-related differences in the FNAME-12NL. *Archives of Clinical Neuropsychology*. 2021;36(5):844-849. doi:10.1093/arclin/acaa107

13. Cohen G. Why is it difficult to put names to faces? *British J of Psychology*. 1990;81(3):287-297. doi:10.1111/j.2044-8295.1990.tb02362.x

14. Harris DM, Kay J. I recognize your face but I can't remember your name: Is it because names are unique? *British J of Psychology*. 1995;86(3):345-358. doi:10.1111/j.2044-8295.1995.tb02757.x

15.Burton AM, Jenkins R, Robertson DJ. I recognise your name but I can't remember your face : an advantage for names in recognition memory. *Quarterly Journal of Experimental Psychology*. Published online October 28, 2018. doi:10.1177/1747021818813081

16.Kucia AM, Hartley A. Risk Factors for Cardiovascular Disease. In: Kucia AM, Jones ID, eds. *Cardiac Care*. 1st ed. Wiley; 2022:35-51. doi:10.1002/9781119117810.ch5

17.Scutelnic A, Heldner MR. Vascular Events, Vascular Disease and Vascular Risk Factors—Strongly Intertwined with COVID-19. *Curr Treat Options Neurol*. 2020;22(11):40. doi:10.1007/s11940-020-00648-y

18.Knopman DS, Roberts R. Vascular Risk Factors: Imaging and Neuropathologic Correlates. *J Alzheimers Dis*. 2010;20(3):699-709. doi:10.3233/JAD-2010-091555

19.Singh-Manoux A, Marmot M. High blood pressure was associated with cognitive function in middle-age in the Whitehall II study. *Journal of Clinical Epidemiology*. 2005;58(12):1308-1315. doi:10.1016/j.jclinepi.2005.03.016

20.Waldstein SR, Giggey PP, Thayer JF, Zonderman AB. Nonlinear Relations of Blood Pressure to Cognitive Function. *Hypertension*. 2005;45(3):374-379. doi:10.1161/01.HYP.0000156744.44218.74

21.Dahle CL, Jacobs BS, Raz N. Aging, vascular risk, and cognition: Blood glucose, pulse pressure, and cognitive performance in healthy adults. *Psychology and Aging*. 2009;24(1):154-162. doi:10.1037/a0014283

22.van den Kommer TN, Dik MG, Comijs HC, Jonker C, Deeg DJH. The role of lipoproteins and inflammation in cognitive decline: Do they interact? *Neurobiology of Aging*. 2012;33(1):196.e1-196.e12. doi:10.1016/j.neurobiolaging.2010.05.024

23.Muller M, Grobbee DE, Aleman A, Bots M, van der Schouw YT. Cardiovascular disease and cognitive performance in middle-aged and elderly men. *Atherosclerosis*. 2007;190(1):143-149. doi:10.1016/j.atherosclerosis.2006.01.005

24.Song R, Xu H, Dintica CS, et al. Associations Between Cardiovascular Risk, Structural Brain Changes, and Cognitive Decline. *Journal of the American College of Cardiology*. 2020;75(20):2525-2534. doi:10.1016/j.jacc.2020.03.053

25.D'Agostino RB, Vasan RS, Pencina MJ, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. *Circulation*. 2008;117(6):743-753. doi:10.1161/CIRCULATIONAHA.107.699579

26.Elias MF, Sullivan LM, D'Agostino RB, et al. Framingham stroke risk profile and lowered cognitive performance. *Stroke*. 2004;35(2):404-409. doi:10.1161/01.STR.0000103141.82869.77

27.Sofogianni A, Stalikas N, Antza C, Tziomalos K. Cardiovascular Risk Prediction Models and Scores in the Era of Personalized Medicine. *J Pers Med*. 2022;12(7):1180. doi:10.3390/jpm12071180

28.Kist JM, Vos RC, Mairuhu ATA, et al. SCORE2 cardiovascular risk prediction models in an ethnic and socioeconomic diverse population in the Netherlands: an external validation study. *EClinicalMedicine*. 2023;57:101862. doi:10.1016/j.eclinm.2023.101862

29.Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). *European Heart Journal*. 2021;42(5):373-498. doi:10.1093/eurheartj/ehaa612

30.Ntaios G, Lip GYH, Makaritsis K, et al. CHADS2, CHA2DS2-VASc, and long-term stroke outcome in patients without atrial fibrillation. *Neurology*. 2013;80(11):1009-1017. doi:10.1212/WNL.0b013e318287281b

31.Friberg L, Rosenqvist M, Lip GYH. Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study. *European Heart Journal*. 2012;33(12):1500-1510. doi:10.1093/eurheartj/ehr488

32.Okumura K, Inoue H, Atarashi H, et al. Validation of CHA_2DS_2-VASc and HAS-BLED scores in Japanese patients with nonvalvular atrial fibrillation: an analysis of the J-RHYTHM Registry. *Circ J*. 2014;78(7):1593-1599. doi:10.1253/circj.cj-14-0144

33.Ihle A, Gouveia ÉR, Gouveia BR, Kliegel M. The Cognitive Telephone Screening Instrument (COGTEL): A Brief, Reliable, and Valid Tool for Capturing Interindividual Differences in Cognitive Functioning in Epidemiological and Aging Studies. *Dement Geriatr Cogn Dis Extra*. 2017;7(3):339-345. doi:10.1159/000479680

34.Stanislaw H, Todorov N. Calculation of signal detection theory measures. *Behavior Research Methods, Instruments, & Computers*. 1999;31(1):137-149. doi:10.3758/BF03207704

35.Lip GYH, Nieuwlaat R, Pisters R, Lane DA, Crijns HJGM. Refining Clinical Risk Stratification for Predicting Stroke and Thromboembolism in Atrial Fibrillation Using a Novel Risk Factor-Based Approach. *Chest*. 2010;137(2):263-272. doi:10.1378/chest.09-1584

36.van den Elzen EHT, Brehmer Y, Van Deun K, Mark RE. Stimulus material selection for the Dutch famous faces test for older adults. *Front Med (Lausanne)*. 2023;10:1124986. doi:10.3389/fmed.2023.1124986

37.Osborne JW, Overbay A. The power of outliers (and why researchers should ALWAYS check for them). doi:10.7275/QF69-7K43

38.Zach. The Three Assumptions of the Repeated Measures ANOVA. Statology. Published November 23, 2021. Accessed November 2, 2023. https://www.statology.org/repeated-measures-anova-assumptions/

39.Correction for Violation of Sphericity in Repeated Measures Designs | Laerd Statistics. Accessed November 3, 2023. https://statistics.laerd.com/statistical-guides/sphericity-statistical-guide-2.php

40.Assumptions of Multiple Linear Regression. Statistics Solutions. Accessed November 9, 2023. https://www.statisticssolutions.com/free-resources/directory-of-statistical-analyses/assumptions-of-multiple-linear-regression/

41.Frost J. Multicollinearity in Regression Analysis: Problems, Detection, and Solutions. Statistics By Jim. Published April 2, 2017. Accessed November 9, 2023. http://statisticsbyjim.com/regression/multicollinearity-in-regression-analysis/

42.Austin PC, Steyerberg EW. The number of subjects per variable required in linear regression analyses. *Journal of Clinical Epidemiology*. 2015;68(6):627-636. doi:10.1016/j.jclinepi.2014.12.014

43.Lee SB, Oh JH, Park JH, Choi SP, Wee JH. Differences in youngest-old, middle-old, and oldest-old patients who visit the emergency department. *Clin Exp Emerg Med*. 2018;5(4):249-255. doi:10.15441/ceem.17.261

44.Verhage F. *Intelligentie En Leeftijd Bij Volwassenen En Bejaarden*. Koninklijke Van Gorcum; 1964.

45.Wong BI, Lecompte M, Yang L. The age-related associative deficit simulated by relational divided attention: encoding strategy and recollection. *Memory*. 2021;29(3):406-415. doi:10.1080/09658211.2021.1898645

46.Kim SY, Giovanello KS. The effects of attention on age-related relational memory deficits: Evidence from a novel attentional manipulation. *Psychology and Aging*. 2011;26(3):678-688. doi:10.1037/a0022326

47.Greene NR, Naveh-Benjamin M. A Specificity Principle of Memory: Evidence From Aging and Associative Memory. *Psychol Sci*. 2020;31(3):316-331. doi:10.1177/0956797620901760

48.Bartsch LM, Loaiza VM, Oberauer K. Does limited working memory capacity underlie age differences in associative long-term memory? *Psychology and Aging*. 2019;34(2):268-281. doi:10.1037/pag0000317

49.dprime analysis. Accessed October 29, 2023. http://phonetics.linguistics.ucla.edu/facilities/statistics/dprime.htm

Appendix: Analysis using d-prime as performance

Additional analyses were performed using a different calculation method for performance within tasks of the IAMT, that is, d-prime (d') from the Signal Detection Theory.[18] The d' is a standardized measure of sensitivity, that allows performance assessment while minimizing the influence of response bias.

Formula

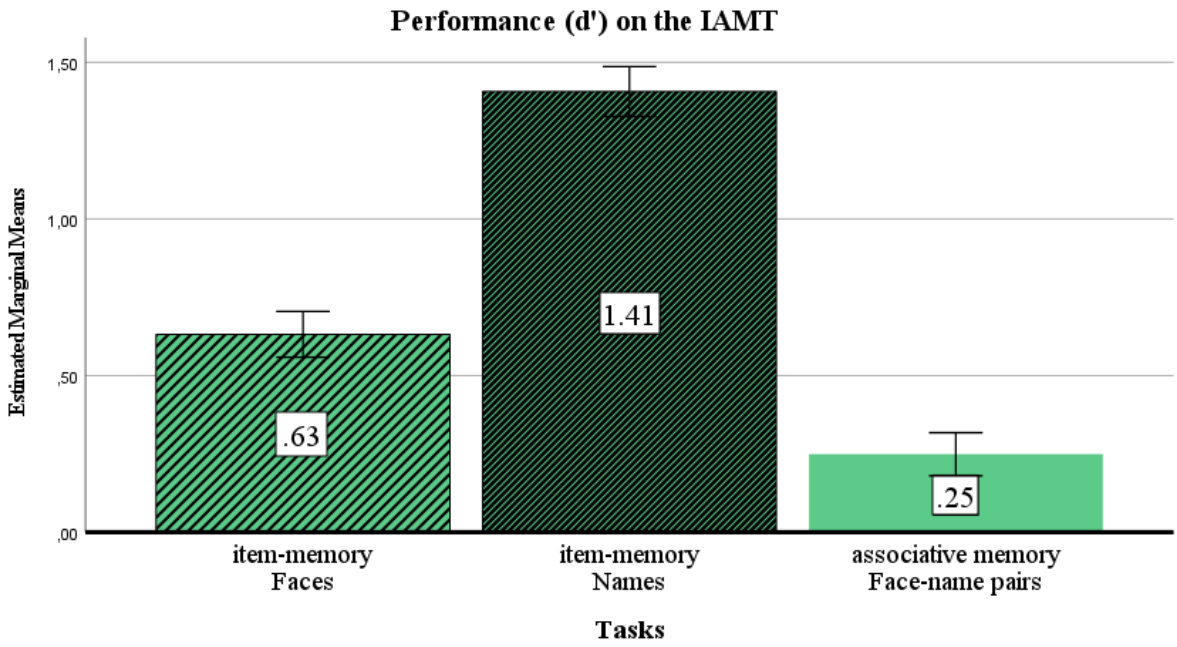
For each participant per task, the hit rate (H) and false alarm rate (F) was calculated. D' was calculated with this formula: d' = z(H) - z(F). Since H and F could not equal 0 or 1, these cases were transformed to .01 and .99. The d' allowed performance assessment while minimizing the influence of response bias. It provides insights into individuals' discrimination ability between stimuli. A higher d'-value indicates a better discrimination ability and more accurate performance. Conversely, a lower d'-value indicates a lower ability to differentiate between old and new stimuli, reflecting less accurate performance. The maximum obtainable d' - representing the highest sensitivity - is 6.93, yet the practical threshold is 4.65, with values typically ranging up to 2.0.[19]

Repeated measures ANOVA

A repeated-measures ANOVA was performed to see if memory performance differed across tasks. Mauchly's Test of Sphericity indicated that the assumption of sphericity had been violated, $\chi^2(2) = 8.97$, $p = .011$, and therefore, degrees of freedom were corrected using Huyn-Feldt estimates of sphericity ($\varepsilon = .979$). Memory performance differed significantly across all three tasks ($F(1.96, 640.48) = 265.78$, $p < .001$), with a large effect size of $\eta_p^2 = .448$. IAMT performance is displayed in Figure 1. Tukey's HSD showed performance differences among all three tasks. Associative memory performance (Face-name pairs) was lower than item memory for Faces (mean difference = -.38, SE = .05, $p < .001$) and Names (-1.16, SE = .05, $p < .001$). Furthermore, item-memory performance for Names was higher than

for Faces (mean difference = .78, SE = .05, p <.001). The level of significance was adjusted for multiple comparisons using Bonferroni correction.

Figure 1. Mean performance (d') on the IAMT



Mean performance (d') is visualized for each IAMT task, with standard deviations of .67, .73 and .63, respectively. Error bars represent the 95% confidence interval (CI). ANOVA showed significant (p <.05) performance differences across all task.

These findings closely match the findings obtained by using the calculation method described in the report and indicate a consistent pattern: lowest performance in associative memory and highest performance in item memory for Names.

Regression analysis

Three multiple regression analyses were run to predict performance on the IAMT, outcomes are represented in Table 1-3. The model that was expected to predict associative memory performance did not reach significance ($F(4, 323) = 2.377$, $p = .052$, $R^2 = .029$), suggesting that the included predictors did not collectively explain a significant proportion of the variance in the outcome variable. Nevertheless, this regression model, with a p-value of .052, demonstrated a noticeable trend. This was similar to the outcome demonstrated in the report. The model to predict item-memory for Faces was not significant ($F(4, 323) = 1.868$, p

= .116, R^2 = .011). However, in the current analysis, the model to predict item memory for Names did reach statistical significance F(4, 323) = 3.299, p = .011, R^2 = .039. Inspecting the individual predictors showed that solely age (t = -2.756, p = .006) was a significant predictor, but, global vascular risk (t = 1.554, p = .121), sex (t = .937, p = .350) and education level (t = 1.378, p = .169) were not.

Table 1. Regression Coefficients for Predicting Item-memory for Faces

Model 1	B	95% CI	β	t	p
Vascular risk	-.05	[-0.14,0.04]	-.09	-1.12	.270
Age	-.01	[-0.08,2.35]	-.06	-.80	.425
Sex	.16	[-0.01,0.33]	.12	1.81	.072
Education	-.03	[-0.10,0.04]	-.05	-.87	.383

R^2_{adj} = .011 (N = 328, p = .116), CI = confidence interval for B.
* less than .05
** less than .01

Table 2. Regression Coefficients for Predicting Item-memory for Names

Model 2	B	95% CI	β	t	p
Vascular risk	.08	[-0.02,0.17]	.12	1.55	.121
Age	-.02	[-0.04,-0.01]	-.20	-2.76	.006**
Sex	.09	[-0.10,0.28]	.06	.94	.350
Education	.05	[-0.02,0.13]	.08	1.38	.169

R^2_{adj} = .027 (N = 328, p = .011), CI = confidence interval for B.
* less than .05
** less than .01

Table 3. Regression Coefficients for Predicting associative memory for Face-name pairs

Model 3	B	95% CI	β	t	p
Vascular risk	.05	[-0.03,0.14]	.10	1.22	.223
Age	-.02	[-0.04,-0.01]	-.20	-2.81	.010**
Sex	-.02	[-0.18,0.14]	-.01	-.21	.831
Education	.03	[-0.04,0.09]	.04	.79	.428

R^2_{adj} = .017 (N = 328, p = .052), CI = confidence interval for B.
* less than .05
** less than .01