The Face-Name Associative Memory Exam (FNAME) as an early indicator of cognitive decline.

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Abstract

Associative memory (AM) is one of the first cognitive domains to be impaired in Alzheimer's disease, thus, there is an increasing need to develop sensitive tools that can detect those early, subtle impairments. Further, AM is not only an issue in AD, but also declines significantly in healthy aging. The Face-Name-Associative-Memory-Exam (FNAME) is a test of associative memory that has shown promising results in detecting impairments in AM in both, healthy older adults and older adults with aMCI or subjective cognitive decline (SCD). The aim of the current research was to assess which subscales of the FNAME were most sensitive to aMCI, and how age and cognitive reserve (CR) affect FNAME scores in such clinical populations, to get a more comprehensive and realistic picture of FNAME performance in a clinical environment. *Methods:* 206 participants were recruited from the ongoing Cogmax study and divided into an SCD and an aMCI group. A Dutch, extended version of the FNAME was administered to all participants. CR was assessed by the level of education, corresponding to the Dutch education system. *Results:* In a linear regression model, spontaneous name recall was most sensitive to group membership (β=-.185, t (203) =-6.045, p<.001), whereas face-name matching was most sensitive to aging (β=-2.592, t (203) =-6.965, p<.001). Age was a significant predictor for each subscale, even when accounting for group membership. The least sensitive subscales to both, group membership and age, were face and name recognition. CR was only significant at .05 level for some subscales, but not all, with very low effect sizes. *Discussion:* Age and group membership differentially affect the FNAME subscales. The small effect sizes for name and especially face recognition implicate that item recognition is not much affected by age or aMCI, however a subsequent suggestion is the use of face recognition as a performance validity test (PVT) and to develop a sensitive cut-off score. The small and often non-significant effects of CR indicate that the FNAME is a promising screening tool for early cognitive impairments, which is less prone to the effects of higher education than other tests of memory functioning (e.g., CVLT). It is recommended to use the FNAME only in combination with age-norms and to observe the overall pattern of performance, instead of a single score, and to pay special attention to impaired recognition abilities.

Keywords: FNAME, associative memory, Alzheimer's disease, mild cognitive impairment, ageing, cognitive reserve

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Associative memory impairments in Alzheimer's disease

Alzheimer's disease (AD) has been typically associated with deficits in episodic memory and learning, and other cognitive domains, however, these impairments are not becoming obvious until advanced progression of the disease (Markova et al. 2022). The cognitive and behavioral changes associated with AD are already clinically significant when a diagnosis is provided, however an earlier identification is becoming more important considering its significant psychosocial and economic impact (Markova et al. 2022, Rubiño & Andrés, 2018). A more specific type of memory, associative memory, has been shown to be more sensitive to the early development of AD, and could be an important target for early diagnosis (Rubiño & Andrés, 2018). Associative memory is a type of episodic memory that involves binding processes that create associative links between unrelated items and contexts, and the ability to recall them as a single unit (Bastin et al. 2014).

The measurement of associative memory appears to be a promising target, as it has been shown to be impaired in the early stages of AD (e.g., subjective cognitive decline [SCD], or mild cognitive impairment [MCI] due to AD), even preceding other episodic memory deficits and in the absence of any other clinical signs (Rubiño & Andrés, 2018) (for more detailed information on AD diagnosis and progression, refer to Appendix A). One widely accepted explanation for this finding is the associative deficit hypothesis (ADH; Naveh-Benjamin, 2000). The ADH holds that deficits in episodic memory occur as an inability to form and retrieve links among single bits of information, as memories, or "episodes" consist of several components such as semantic and contextual information, that is bound together to form a coherent unit (Naveh-Benjamin & Mayr, 2018). The neuropathological changes observed in the AD progression, especially structural and functional changes in the medial

temporal lobe (including the hippocampus, parahippocampal, perirhinal, and entorhinal regions) (Corriveau et al. 2021, Hugeri et al. 2022, Markova et al. 2022, Oedekoven et al. 2014, Troyer et al. 2012), and the presence of certain biomarkers in the preclinical stages (Rentz et al. 2011, Trelle et al. 2021), are thus hypothesized to interfere with these processes, thus leading to a more generalized episodic memory impairment, even though memory for single items may be still intact.

Associative memory and healthy aging

Associative memory deficits have not only been related to Alzheimer's disease, but also to healthy aging. A body of research found consistent associative memory deficits in older adults compared to younger adults, that were significantly higher in magnitude than deficits in other memory domains, such as single item memory (Clark et al. 2018, Pitarque et al. 2015, Ratcliff & McKoon, 2015, Silver et al. 2012). In line with the associative deficit hypothesis, these deficits lead to a more generalized deficit in episodic memory in healthy older adults. In contrast to individuals with AD, these deficits in healthy older adults are not due to neuropathological changes, but rather due to a natural decline and alterations in connectivity in the hippocampus and hippocampal-cortical systems that occur with increasing age (Clark et al. 2018, Oedekoven et al. 2014).

The Face-Name Associative Memory Exam (FNAME)

The outlined evidence suggests that it is crucial to develop tests that are able to sensitively measure the subtle changes observed in older individuals and in individuals at risk for developing AD. To date, a number of experimental paradigms to measure associative memory exist, including item-item associations such as a product and a price (Fine et al. 2018), or a word (e.g., banana) and a picture (e.g., a face of a famous person) (Trelle et al.

2021); or item-context associations such as a face and a scene/landscape (Jonin et al. 2021). Some tests are used in clinical practice as well, such as the Visual Association Test (VAT; Lindeboom & Schmand, 2003), which presents two items that interact with each other and have to be remembered in combination (e.g., a dog riding a bike). Another promising tool that has recently received considerable attention in its potential to aid the early diagnosis of AD, is the Face-Name Associative Memory Exam (FNAME, Rentz et al. 2011). The FNAME is a cross-modal measure of associative memory and is able to detect the subtle cognitive changes observed in early AD while more traditional neuropsychological tests (e.g., the California Verbal Learning Test) are not (Kormas et al. 2020, Rubiño & Andrés, 2018).

The FNAME requires an individual to learn and recall face-name and face-occupation pairs, whereas the faces are presented as visual stimuli on a screen, and the names/occupations as words below the face (Rentz et al., 2011). More recent versions of the FNAME (Flores-Vázquez et al. 2021) only use face-name pairs, because previous studies have found that only face-name pairs were sensitive to cognitive changes, whereas no significant differences were found in the performance on face-occupation pairs between different groups (Rentz et al., 2011, Sanabria et al., 2018). The FNAME measures immediate and delayed cued recall ability, where an individual is provided with a cue (a face) and needs to recall the corresponding name, and recognition, where multiple choices (faces or names) are presented and the participant has to pick the correct target that has been previously learned. Recently, two new scales were introduced by Flores-Vázquez and colleagues (2021), namely free name recall and face-name matching.

FNAME performance in healthy aging

Consistent with the extensive body of research finding significant declines in associative memory abilities with aging, studies that have been conducted on FNAME and aging have supported this notion. Two studies found a significant age effect, where younger adults generally perform better on the FNAME than older adults (Enriquez-Geppert et al. 2021, Flores-Vázquez et al. 2021). Since age is the highest risk factor for developing AD (Alzheimer's Association, 2023), it is crucial for future research to develop norms for different age groups to determine which scores can be considered normal for a certain age group and which ones indicate pathological cognitive changes. To date, such norms do not exist for the FNAME.

FNAME in asymptomatic stage and SCD

Impairments in FNAME performance were also found for individuals at risk for developing AD, before the onset of clinically significant symptoms. Even though mixed, there is evidence for a relationship between FNAME performance and SCD. Typically, traditional neuropsychological measures do not correlate with subjective cognitive complaints (De Simone et al. 2022), however the FNAME has shown some more promising results in that regard. De Simone and colleagues (2022) assessed FNAME performance in a group of older individuals with SCD and age-matched healthy controls without any cognitive complaints. SCD group was found to score significantly worse on certain subscales of the FNAME (i.e., delayed recall and recognition) than healthy, age-matched controls without any cognitive complaints. Similar results were found in other studies (Chapman et al. 2021, Kormas et al. 2020), however, there is also contradicting evidence: Flores-Vázquez and colleagues (2022) compared performance on the FNAME between older individuals with aMCI, SCD, and healthy controls, and failed to find any significant differences between the SCD and control group. Alegret and colleagues (2015) also did not find a significant relationship between SCD

and FNAME performance. Differences in methodology and participant recruitment might account for some of the inconsistent results.

FNAME results in (a)MCI

The FNAME has been administered to individuals with MCI or aMCI in several studies, and it was found that their performance was highly affected in comparison to healthy individuals or individuals with SCD (Alegret et al. 2015, Flores-Vázquez et al. 2022, Kormas et al. 2020, Papp et al. 2014). It was also found that worse FNAME performance correlated with higher biomarker levels (e.g., Aβ1-42/Aβ1-40 ratio) and lower cortical volume in certain brain areas, such as associative visual, prefrontal and temporo-parietal areas, in aMCI individuals (Alegret et al. 2022).

Recognition versus recall tasks on the FNAME

It is well known by now that recognition abilities generally are more resilient to cognitive impairments or aging than recall abilities (Meyer et al. 2022, Pitarque et al. 2015), and this pattern of memory decline is also found on the FNAME: Research has pointed out that not every subscale differentiated equally well between healthy individuals and individuals with cognitive impairments. In fact, only small effect sizes were found for face and name recognition in discriminating aMCI group from healthy or SCD group, whereas moderate to large effect sizes were found for immediate and delayed recall (Kormas et al. 2020), as well as free name recall and face-name matching (Flores-Vázquez et al. 2022). These results indicate the presence of ceiling effects for individuals with aMCI on the recognition scales, which are not present for the recall conditions, implicating that immediate or delayed recall of face-name pairs is a more demanding task and thus, discriminates better between groups (Flores-Vázquez et al. 2021). Similar results were found for healthy individuals, whereas

recognition scales differed not significantly between healthy younger and older individuals or showed a clear ceiling effect in both groups (Enriquez-Geppert et al. 2021, Flores-Vázquez et al. 2021). Thus, not only in clinical but also in healthy populations it appears that some subscales of the FNAME are more sensitive to declines in associative memory abilities than others. It is thus important to consider the clinical utility of each subscale, and how much they add to diagnostic procedures.

Associative memory and cognitive reserve and its possible influence on FNAME

Definition and maintenance of cognitive reserve

Cognitive reserve (CR) is a concept that might potentially influence the presentation of associative memory deficits among individuals with SCD and aMCI who additionally are of higher age and thus, have a higher risk of progressing to AD. CR is defined as the adaptability of cognitive processes that explain differential susceptibility of cognitive abilities to brain aging or pathology (Stern et al. 2020). These cognitive processes are supported by underlying adaptable functional brain processes, i.e., increased connectivity (Stern et al. 2020). CR thus actively operates on brain networks efficiency, rather than on the structure of individual brain areas (Serra et al. 2017). Further, the level of CR is not fixed, but rather a result of modifiable factors that can build higher reserve, such as higher educational attainment, bilingualism, social engagement, physical activity, leisure activities (such as playing musical instruments), and certain dietary habits (Amanollahi et al. 2021).

Protective mechanisms of cognitive reserve in neurodegenerative disorders

Research has consistently shown that CR protects from the impact of neurodegenerative diseases such as AD. Higher cognitive reserve significantly decreased the risk of progressing to MCI or AD by delaying its onset, even in the presence of biomarkers

and neuropathology related to AD (Nelson et al. 2021). Further, individuals with MCI that accumulated a higher CR performed better on neuropsychological tests (such as verbal fluency tests) than individuals with a lower CR, additionally exhibiting altered functional brain connectivity, i.e., increased connectivity in fronto-parietal network (Bozzali et al. 2015, Serra et al. 2017). Two mechanisms have been suggested to explain this neural implementation of CR: Neural compensation, where individuals with high CR are able to better recruit alternative brain areas or networks to preserve their premorbid level of functioning in the case of brain damage, and neural reserve, referring to neural networks with increased efficiency and less susceptibility to damage (Amanollahi et al. 2021). It should be noted that even though CR operates on neural networks, it is a qualitatively different concept from brain reserve (BR) (refer to Appendix B for more detailed information on BR).

Cognitive reserve and its effect on associative memory

Evidence on the effect of CR specifically on associative memory is mixed. There is some research that was not able to find better associative memory performance in older individuals with high CR compared to low CR, but rather a general age-related associative memory decline regardless of the level of CR (Peterson et al. 2017). Another study found a significant improvement in an associative memory task in healthy older adults with high CR compared to those with low CR, however this effect was not found for individuals with aMCI (Algarabel et al. 2016). The mixed results might be attributed to the use of different paradigms in measuring associative memory and CR. In fact, for the FNAME, no effect was found for CR on FNAME performance in cognitively normal older adults (Rentz et al. 2011). However, in this study, CR was measured by the American National Adult Reading Test IQ (AMNART-IQ), whereas in the aforementioned studies, CR was measured by education level. In addition, the effect of CR in Rentz and colleagues' (2011) study was only assessed in

cognitively normal individuals, whereas more recent research found that CR exerts its effect only in individuals with progressed cognitive impairment (Bozzali et al. 2015, Serra et al. 2017). Further, to date no studies have investigated the effect of CR on the newly introduced subscales of the FNAME (spontaneous name recall and face-name matching). The inconsistent results and use of different methodologies and measurement approaches to associative memory underline the importance of further assessing the effect of CR on FNAME performance, especially taking the new subscales and clinically relevant populations (e.g., individuals with MCI) into account. This is crucial because of the lack of knowledge on which factors contribute to FNAME performance, especially when FNAME is to be used in clinical practice and relevant decisions have to be made on the basis of an individual's score.

Research question

The aim of the current thesis is to further assess the differences in FNAME performance between individuals with SCD and aMCI, in order to investigate which of the subscales are most discriminating between the two risk states of AD. The findings that certain subscales may be of limited use for certain populations and show a ceiling effect might indicate that not all subscales are clinically useful. Further, the effect of age on FNAME performance has been examined in healthy, but not in cognitively impaired individuals so far. Thus, in the current thesis the aim is to investigate how age contributes to the presentation of associative memory impairments as measured by the FNAME in cognitively impaired individuals. Lastly, the influence of cognitive reserve on the FNAME performance has not been investigated in individuals with SCD and aMCI while accounting for the influence of age, thus the goal is to establish how cognitive reserve, as measured by level of education, contributed to FNAME performance.

H1.

SCD will score significantly higher than aMCI group on all subscales. More specifically, the greatest differences will be found in recall ability as measured by the immediate and delayed recall tasks, as well as free name recall of the FNAME, whereas the recognition scales will result in small effect sizes only, while accounting for age.

H0. Every subscale will differentiate to the same extend between SCD and aMCI group.

H2.

Age will significantly predict performance on the FNAME, even when accounting for group membership. More specifically, increasing age is associated with decreasing FNAME scores. The aim is to create a regression model that can predict FNAME scores based on age and group membership (SCD versus aMCI).

H0. Age will not be a significant predictor of FNAME scores when accounting for group membership.

H3.

FNAME performance will significantly differ between the education levels, with higher education level being associated with significantly higher FNAME scores, while accounting for group membership and covarying for age.

H0. No significant differences will be found between the different education levels on FNAME scores, when accounting for group membership and age.

Methods

Participants

The participants recruited for this study were informed beforehand and gave written consent. The study was approved by the University Medical Center of Groningen/ University of Groningen and conducted by the Declaration of Helsinki.

SCD and aMCI participant data were used from the ongoing Cogmax study (https://www.cogmax.nl/). The Cogmax study investigates the effects of transcranial alternating current stimulation (tACS) on cognitive functions in older individuals with aMCI. Individuals were recruited via advertisement and were invited to the study if they experienced subjective cognitive complaints. The data collection took place in the Universitair Medisch Centrum Groningen (UMCG). Only baseline data, i.e., before any intervention took place, was used for this study. For HC participants, archival data from an earlier study (Enriquez-Geppert et al. 2021) was used. In total, 231 participants were sampled. Additionally, 6 participants were further excluded for from the analyses for not completing the FNAME, 14 were excluded because of technical issues while administering the FNAME, and 5 were excluded for having incorrectly scored tests or misunderstanding tasks that might influence the validity of the data. Demographic information of the remaining 206 participants (SCD=116; aMCI=90) is depicted in table 1.

Materials

Baseline assessment

The baseline neuropsychological assessment conducted at Cogmax included a battery of cognitive as well as behavioral measures, including the FNAME.

FNAME extended

Individuals in the SCD and aMCI group completed the Dutch version of the extended FNAME (Flores-Vázquez et al. 2022). The following steps are part of the procedure: *Familiarization*. 12 faces are shown for 2 seconds each. *Learning phase I*. Each face is shown with the corresponding name for 6 seconds, one after another. *Immediate recall I (IR1)*. Each face is shown for 8 seconds, participant has to recall the name. *Learning face II*. Face-name

pairs that were not remembered in the previous step are shown again for 6 seconds each. *Immediate recall II (IR2).* Participants are shown each face again for 8 seconds and have to recall their name. *Learning phase III*. Participants are shown each face-name pair they couldn't remember for 6 seconds. *Spontaneous Name recall (SNR).* After a 30-minute delay, the participant has 30 seconds to freely recall every name they can remember. *Face recognition (FR)*. The participant is shown 4 different faces for 5 seconds, and has to choose the face they encountered previously among 3 distractor faces. *Delayed recall (DR)*. The participant is shown each face for 8 seconds and has to recall their name. *Name recognition (NR).* The participant is presented with the names they could not recall in the previous phase together with three distractor names for 6 seconds each, and has to choose the correct name. *Face-Name matching (FNM)*. All faces and all names are presented on one slide, for 2 minutes. The participant has to match the names with the corresponding faces by pointing at them. For all phases, the total number of correctly recalled names/faces is scored. An exception is name recognition, where the number of errors is scored.

Table 1. Demographic information of the sample.

Group	N	Age Mean(SD)	Gender Male/Female	Education level (1/2/3/4/5/6/7)
SCD	116	70.39 (.78)	60/56	1/1/3/13/34/46/18
aMCI	90	72.36 (.77)	62/28	0/1/3/12/20/42/12

Procedure

Every individual underwent a baseline assessment including the extended FNAME, MMSE, 15 Word test (Dutch version), and other neuropsychological tasks. The assessment was conducted in a single session of about 2.5-3 hours. A score below the 9th percentile on the 15 Word test indicated aMCI and was an inclusion criteria for receiving the intervention of the study. Those individuals form the aMCI group of the current study. Individuals who did

not fulfill the criteria for aMCI were excluded from the further study and will form the SCD group.

Education level was assessed in seven levels corresponding to the Dutch education system: Level one depicts less than basic education ("minder dan basisonderwijs"), level 2 depicts basic education ("basisonderwijs"), level 3 depicts less than LBO ("minder dan LBO"), level 4 depicts LBO, level 5 is compromised of mavo/MBO, level 6 is compromised of havo/VWO/HBO, and level 7 depicts university education.

Statistical design

H1.

Multiple linear regressions will be conducted for each FNAME subscale and the total score. The FNAME scores will be used as the dependent variable, and age and group membership will be entered as the independent variables. Differences between the three groups and correlations between group membership and FNAME subscores will be examined to determine which subscale of the FNAME discriminates best between the diagnostic groups. The regression coefficients will indicate for which subscale group membership leads to the greatest change, while age is held constant and thus controlled for.

H2.

Linear regressions are used to determine the effect of age, i.e., whether it remains a significant predictor in the model if group membership is held constant. Further, the magnitude of its contribution will be examined by comparing the effect sizes of age for each FNAME subscale.

H3.

Two way-ANCOVAs will be conducted for each FNAME subscale. FNAME score will be the independent variable, whereas group membership and education level will be

entered as the fixed factors, and age as a covariate. F-statistic, p-value and effect size for education level will be examined, and additionally, pairwise comparisons between each individual education will be conducted. Because of the small sample sizes for the first three education levels, those will be merged together with the 4th level, representing a lower education level altogether.

Statistical assumption checks

For all FNAME scales, as well as the variable "age", the assumptions of normality and homogeneity of variances between the aMCI and SCD groups were tested. Additionally, multicollinearity between the independent variables of and the presence of a linear relationship between the dependent variable and independent variables were tested. Homogeneity was tested with Levene's test and revealed significant differences for *spontaneous name recall* (F=5.838, p=.017*), face recognition* (F= 17.714, p<.001), *name recognition* (F=56.686, p>.001), and *total FNAME* score (F=6.190, p=.014). Normal distribution was tested by examining the normal probability plots (Q-Q plots). *Only face and name recognition* deviated from the expected values and show a negative, left skewed distribution, which was however expected due to the ceiling effects for these scales.

Multicollinearity was tested by examining the correlation between the variable age and group membership, and a non-significant correlation was found (r=.123, p=.079). Lastly, the variables age and group membership were both linear related to each FNAME scale, as presented in Table 3.

Interpretation of statistical results

The strengths of the correlations are interpreted in light of Cohen's classification of effect sizes, were small >.10<.30, medium >.30<.50, and large >.50 (Cohen, 1992).

Results

Hypothesis 1.

Mean scores and standard deviations of each FNAME subscore in the SCD and aMCI group can be found in Table 2. Multiple linear regression results revealed that each of the subscores differ significantly between aMCI and SCD group (Table 4). The greatest change is observable for *spontaneous name recall*, β=-2.592, t (203) =-6.965, p<.001. The slope indicates a - 2.592 points change (decrease) in *spontaneous name recall* score for an individual being in the aMCI group compared to the SCD group, with a medium correlation between the scale and group membership, r=.453, which was the highest among all other scales. The second largest change was found for *delayed recall*, β=-2.567, t (203) =-6.467, p<.001, with a medium correlation between the scale and group membership, r= .400. The smallest, but still significant change was found for *face recognition*, β=-.604, t (203) =-3.173, p=.002, indicating a change in its score of -.604 only for individuals being in the aMCI group compared to SCD group, with a small effect size, r=.233. The second lowest change was found for *name recognition*, β=-1.320, t (203) =-5.632, p<.001. For *face-name matching* there was a significant, medium sized effect found, r= .403, β=-2.543, t (203) =-7.034, p<.001, which is similar in magnitude to the recall scales. The hypothesis that the recall scales are superior in discriminating between the groups than the recognition scales is thus only partially supported, as the scale *face-name matching* makes an exception in this relationship.

Table 2. FNAME mean scores and SD per group.

	F-total	F-IR1	F-IR2	F-DR	F-SNR	F-FR	F-NR	F-FNM
SCD	56.91(1.22)	4.97(.24)	7.21(.26)	7.02(.29)	7.1(.23)	11.55(.08)	11.53(.08)	8.02(.29)
aMCI	41.78(1.78)	3.02(.28)	4.42(.33)	4.11(.38)	4.32(.32)	10.87(.20)	10.13(.24)	5.11(.37)

Note. Standard deviations (SD) are displayed in brackets.

Table 3. Correlations FNAME and age, group membership

	F-total	F-IR1	F-IR2	F-DR	F-SNR	F-FR	F-NR	F-FNM	Age
Age[a]	-.440	-.383	-.423	-.426	-.304	-.239	-.216	-.452	-
	< .001	<.001	<.001	<.001	<.001	<.001	.002	<.001	
Group[b]	-.449	-.347	-.426	-.400	-.453	-.233	-.380	-.403	.123
	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	.079
Education	.190	.161	.182	.171	.187	.143	.072	.166	-
level[c]	<.001	.004	<.001	.002	<.001	.019	.226	.003	

a. Pearson correlation, p-value below.
b. Biserial rank correlation, p-value below.
c. Kendall's tau, p-value below.
d. F-total: FNAME total score. F-IR1: immediate recall 1. F-IR2: immediate recall 2. F-DR: delayed recall. F-SNR: spontaneous recall. F-FR: face recognition. F-NR: name recognition. F-FNM: face-name matching

Table 4. Multiple regression results.

Dependent variable	Independent variables	*B*	*SE*	*Standardized B*	*t*	*p*	95% CI for B
F-total	Constant	114.467	8.488		13.485	<.001	[97.73;131.2]
	aMCI group[a]	-13.440	1.91	-.402	-7.046	<.001	[-17.2;-9.68]
	Age	-.818	-.119	-.391	-6.856	<.001	[-1.05;-.58]
F-IR1	Constant	13.420	1.528		8.768	<.001	[10.41;16.43]
	aMCI group[a]	-1.716	.343	-.309	-5.591	<.001	[-2.39;-1.04]
	Age	-.120	.0210	-.345	-4.999	<.001	[-.16;-.08]
F-IR2	Constant	18.020	1.699		10.604	<.001	[14.67;21.37]
	aMCI group[a]	-2.485	.382	-.380	-6.507	<.001	[-3.24;-1.73]
	Age	-.154	.024	-.376	-6.433	<.001	[-.20;-.11]
F-DR	Constant	19.168	1.903		10.084	<.001	[15.44;22.94]
	aMCI group[a]	-2.567	.428	-.355	-6.467	<.001	[-3.41;-1.72]
	Age	-.173	.027	-.382	-6.003	<.001	[-.12;-.43]
F-SNR	Constant	13.910	1.656		8.399	<.001	[10.64; 17.18]
	aMCI group[a]	-2.592	.372	-.422	-6.965	<.001	[-3.33;-1.86]
	Age	-.097	.023	-.252	-4.155	<.001	[-.14;-.05]
F-FR	Constant	14.311	.880		16.254	<.001	[12.58;16.05]
	aMCI group[a]	-.604	.198	-.205	-3.173	.002	[-.99;-.21]
	Age	-.039	.012	-.214	-3.053	.003	[-.06;-.02]
F-NR	Constant	14.276	1.043		13.689	<.001	[12.22;16.33]
	aMCI group[a]	-1.320	.234	-.363	-5.635	<.001	[-1.78;-.86]
	Age	-.039	.015	-.171	-2.662	.008	[-.07;-.10]
F-FNM	Constant	21.038	1.872		11.239	<.001	[17.35;24.73]
	aMCI group[a]	-2.543	.421	-.352	-7.034	<.001	[-3.37;-1.71]

Age	-.185	.026	-.409	-6.045	<.001	[-.24;-.13]

a. Reference category: Subjective cognitive decline (SCD) group.

b. F-total: FNAME total score. F-IR1: immediate recall 1. F-IR2: immediate recall 2. F-DR: delayed recall. F-SNR: spontaneous recall. F-FR: face recognition. F-NR: name recognition. F-FNM: face-name matching

Hypothesis 2

Multiple linear regressions revealed that age was a significant predictor of each FNAME score, even when accounting for group membership, thus supporting the third hypothesis (Table 4). The strongest age effect was observable for *face-name matching*, β=-.185, t (203) =-6.045, p<.001, meaning that a one unit increase in age (i.e., one year increase) leads to a .185 decrease in *face-name matching* score. In addition, the correlation between *face-name matching* and age was the highest among all FNAME scores, r= -.452.

Surprisingly, although *spontaneous name recall* was strongest affected by group membership among all scales, the effect of age on *spontaneous name recall* is the lowest among the recall scales, β=-.097, t (203) =-4.155, p<.001.The lowest effect was found for age on *face recognition*, β=-.039, t (203) =-3.053, p=.003, and NR, β=-.039, t (203) =-2.662, p=.008. Correspondingly, *face and name recognition* had the lowest correlations with age among all subscales (Table 3), indicating that age has a small effect on recognition abilities, compared to recall abilities.

In addition, by comparing the standardized beta slopes for each predictor, it was found that for certain subscales age was an evenly important predictor than group membership (Table 4). Especially for *face-name matching, immediate recall 1 and delayed recall*, the contribution of age in the prediction model was higher than for group membership, whereas for *name recognition and spontaneous name recall* the contribution of age was lower compared to group membership.

Hypothesis 3

For the last hypothesis, education levels 1-4 (i.e., less than basic education; basic education; less than LBO; LBO) were merged into one level representing lower educational achievement. Correlations between education level and FNAME subscales were small (Table 3). For none of the FNAME subscales, education level was a significant predictor at .001 significance level. However, it was a significant predictor for some scales at .05 level, although with very low effect sizes (Table 5). The largest effect was found for *spontaneous name recall*, F (3) = 4.430, p= .005, ηp^2=.063, and the total FNAME score, F (3) = 4.037, p=.008, ηp^2=.058. When comparing the individual education levels and their mean differences on each FNAME subscale, there is a general tendency to have increased scores FNAME scores with higher education level. Generally, significant differences were especially found between the highest and lowest education level, except for *face recognition*, t=-.285, p=.424, *name recognition*, t= -.116, p=.788, and *face-name matching*, t= -.995, p=.189. No significant differences were observed between the first two education levels and the last two, except for *spontaneous name recall*, where the highest education level scored significantly higher than education level 3, t= -1.363, p=.014. The hypothesis was thus only partially supported by the data, as generally many effects were non-significant, with only few exceptions for certain subscales and education levels.

Table 5. Effect of education level on each FNAME scale, displaying *F, p, and* ηp^2 for the whole model, as well as pairwise comparisons for each individual education level (1-4).

	F	*p-value*	*Partial eta squared,* ηp^2	*Pairwise comparisons – mean difference*[a]		*Std. error of mean difference*	*p-value of mean difference*
F-total	4.037*	.008	.058	1-2	.091	2,985	,976
				1-3	-5.415	2,765	,052
				1-4	-8.781*	3,412	,011
				2-3	-5.506*	2,353	,020
				2-4	-8.872*	3,097	,005
				3-4	-3.365	2,850	,239
IR1	2.888*	.037	.042	1-2	-.177	,541	,743

				1-3	-1.086*	,501	,031
				1-4	-1.246*	,618	,045
				2-3	-.909*	,426	,034
				2-4	-1.069	,561	,058
				3-4	-.160	,516	,757
IR2	2.857*	.038	.042	1-2	-.105	,602	,861
				1-3	-.863	,558	,123
				1-4	-1.665*	,688	,016
				2-3	.758	,475	,112
				2-4	-1.560*	,625	,013
				3-4	-.802	,575	,165
DR	2.637	.051	.039	1-2	-.093	,676	,891
				1-3	-.775	,626	,217
				1-4	-1.849*	,772	,018
				2-3	-.682	,533	,202
				2-4	-1.757*	,701	,013
				3-4	-1.075	,645	,097
SNR	4.430*	.005	.063	1-2	-.176	,579	,761
				1-3	-.764	,536	,156
				1-4	-2.127*	,662	,002
				2-3	-.587	,456	,200
				2-4	-1.950*	,601	,001
				3-4	-1.363*	,553	,014
FR	2.723*	.046	.040	1-2	.441	,311	,158
				1-3	-.204	,288	,481
				1-4	-.285	,356	,424
				2-3	-.645*	,245	,009
				2-4	-.725*	,323	,026
				3-4	-.081	,297	,786
NR	.686	.562	.010	1-2	.012	,376	,975
				1-3	-.361	,348	,301
				1-4	-.116	,430	,788
				2-3	-.373	,296	,210
				2-4	-1.560*	,625	,013
				3-4	-.802	,575	,165
FNM	3.267*	.022	.048	1-2	.637	,660	,336
				1-3	-.833	,612	,175
				1-4	-.995	,755	,189
				2-3	-1.470*	,521	,005
				2-4	-1.632*	,685	,018

	3-4	-.162	,631	,798

* significant at .05 level.

a. Education level 1: less than basic education; basic education; less than LBO; LBO. Education level 2: mavo/MBO. Education level 3: havo/VWO/HBO. Education level 4: university.

b. F-total: FNAME total score. F-IR1: immediate recall 1. F-IR2: immediate recall 2. F-DR: delayed recall. F-SNR: spontaneous recall. F-FR: face recognition. F-NR: name recognition. F-FNM: face-name matching

Discussion

The aim of the current study was to investigate which subscales of the FNAME were able to discriminate best between individuals with subjective cognitive complaints and amnestic mild cognitive impairments, while also assessing the influence of age and CR on FNAME performance. Multiple linear regressions were conducted to investigate which subscale would be most and least sensitive to group membership, as well as the predictive value of age on FNAME score while controlling for group membership. A significant age effect was found for each subscale; further, it was found that some subscales were more sensitive to group membership (e.g., spontaneous name recall), and others were more sensitive to age (e.g., face-name matching). Face and name recognition were robust to both predictors, age and group membership. Below the implications of these findings will be discussed. Further, to examine the effect of CR on FNAME score, two-way ANCOVAs were conducted to assess the differences in FNAME scores between different education levels. Interestingly, only small and inconsistent effects were found. The implications of these results on the cognitive reserve hypothesis will be discussed below.

Performance of the individual subscales in discriminating SCD from aMCI

Good discrimination ability of recall scales

As hypothesized, the greatest differences between the groups were found in recall abilities, with the largest effect size found for spontaneous name recall. This finding has

several implications: It appears that spontaneous name recall is a more challenging task for cognitively impaired individuals than immediate or delayed recall. This may be due to the lack of a cue, as the names have to be freely recalled without the cue of a face given. In fact, previous research found that free recall is often impaired before cued recall in individuals developing MCI due to AD (Grober et al. 2018), which is supported by the current data as well. The free recall task at hand is additionally challenging by the nature of the items that have to be recalled: Names are very abstract, and their recollection cannot be facilitated by the use of semantic cues (Kormas et al. 2020). Research has examined the effect of schematic support (i.e., schemas or prior knowledge that can enhance memory by facilitating encoding and retrieval) on associative memory by manipulating the items so that schematic information could be used to improve performance. For instance, Delhaye and colleagues (2019) created word-word pairs from either related categories (e.g., animals, or vehicles) or unrelated categories and measured their participant's ability to remember those pairs. Performance improved in individuals with mild AD when being presented with the semantically related words. This makes the FNAME inherently less prone to the use of semantic knowledge, as no such categories can be formed for names. As an implication, the FNAME could be superior in detecting subtle memory impairments than other tests of associative memory that are using items that have a semantic meaning. Of another consideration should be the position of the spontaneous recall scale in the FNAME procedure, i.e., free recall takes place immediately after the 30-minute break, followed by the cued delayed recall task. Participants could benefit from recalling the names in the spontaneous name recall trial, thus slightly enhancing performance on cued delayed recall.

Limited ability of the recognition scales in discriminating groups

Partial support was found for the notion that for the recognition scales the smallest effect sizes would be found. As expected, face and name recognition yielded the smallest effect sizes among all scales, however, face-name matching yielded a moderate effect size and discriminated nearly as well between the two groups as the recall scales, even though face-name matching also is a recognition task. Face-name matching and simple face or name recognition appear to be substantially different tasks from each other; in fact, face-name matching measures associative recognition, whereas face or name recognition measure item recognition. Previous research has shown that individuals with aMCI exhibited worse associative recognition memory than item memory (Troyer et al. 2012). There is evidence suggesting that item recognition is often reliant on familiarity judgments only, which is relatively spared even in more progressed cognitive impairments, whereas associative recognition, as in the face-name matching task, is more reliant on recollection, i.e., it is not sufficient to be familiar with the two items, but it is necessary to actively recall the association to determine which items belong together (Fine et al. 2018, Old & Naveh, 2008, Troyer et al. 2012).

Face recognition had the smallest effect size in discriminating between the SCD and aMCI group. The difference between SCD and aMCI on this scale is mainly attributable to outliers in the aMCI group scoring in the very low range of the scale. Name recognition had a higher discrimination value, and it is of interest why name recognition appears to be a slightly more challenging task than face recognition. As a suggestion, the items on the name recognition scale are verbal, whereas face recognition is a visual recognition task, and some literature has shown that visual material is easier to remember than verbal material, even in individuals with aMCI or AD (Ally et al. 2009).

Possible use of the recognition scales as a PVT or to identify high-risk individuals

The utility of a face recognition task in the FNAME procedure may thus seem questionable as its effect in discriminating between SCD and aMCI participants is too small to be clinically significant. However, the information obtained from the face recognition score can still be valuable. First, it is known that generally item recognition abilities are relatively unaffected by early cognitive disorders such as aMCI (Troyer et al. 2012). A low score on face recognition should thus not be treated as an outlier but has to be evaluated very carefully. It is possible that the face recognition scale can detect individuals who are at an especially high risk of progressing to AD, as impaired familiarity might implicate advanced neurodegeneration of the hippocampal areas (Troyer et al. 2012). Another possibility that should be considered is the utility of the face recognition scale as a performance validity test (PVT) (see Appendix C for more information of PVTs). Embedding PVTs into a neuropsychological examination can decrease the risk of misdiagnosis and save valuable resources (Meyer et al. 2017). The implementation of the face recognition scale as a PVT within the FNAME should thus be considered as an effective tool to differentiate genuine memory impairments from noncredible performance. In fact, a previous study has implemented a multiple-choice recognition task as a PVT into a test of visual associative memory (Visual association task, VAT; Lindeboom & Schmand, 2003) and found that it was highly discriminative between MCI and AD patients, and individuals who were instructed to feign (Meyer et al. 2017). The rationale behind using a multiple-choice recognition task as a PVT is that recognition by familiarity is usually preserved in MCI and early AD, however individuals who intentionally respond non-credibly are most often unaware of this pattern of memory functioning (Meyer et al. 2017). The face recognition scale of the FNAME thus appears to be an ideal target to test this assumption. Future research could focus on developing a sensitive cutoff to determine noncredible versus credible performance on the FNAME. However, it must be noted that interpretation of noncredible performance must be

done very carefully. As noted earlier, an exceptionally low score on the face recognition scale might as well indicate the presence of high impairment and is not necessarily related to intentional feigning. Research on the use of PVTs within the context of early-onset AD has shown that a substantial number of patients completing neuropsychological evaluation, including the test of memory malingering (TOMM), was misdiagnosed due to failing the TOMM, even though they had biomarker evidence confirming the presence of the disease (Corriveau-Lecavalier et al. 2022). Thus, failing a PVT, in this case the face recognition task, should not automatically lead to the believe of uncredible performance, but rather indicates the need for a more thorough examination to determine the reason for an exceptionally low performance on that task.

Age as a significant predictor of FNAME scores

Age was a significant predictor in FNAME scores, even when accounting for group membership. However, the relationship between age, group membership and FNAME scores differs somewhat between the different scales, which has important implications for clinical practice and future research.

Differential sensitivity of the recognition scales to aging

Among all FNAME subscales, face-name matching was affected by age the strongest. This is an interesting result, given that recall is a more challenging task for individuals with aMCI, however when it comes to age only, associative recognition as measured by the face-name matching task appears to be more difficult than the recall tasks. One possible explanation could be that face-name matching is measuring both, recollection and familiarity, as the individual items need to be recognized, and their association has to be recalled. One could argue that in the delayed recall task the face also needs to be recognized first in order to

correctly retrieve the associated name, however in this task every face is presented one-by-one, whereas in face-name matching all the stimuli (every face and name) are presented at once, possibly making the task more difficult. Future research could further examine the effects of multiple stimuli presentation versus single stimuli presentation on recognition and recall ability.

In contrast to face-name matching, face recognition and name recognition were affected by age only weakly. This further supports the notion that face-name matching and face/name recognition are two distinct types of recognition memory that are differently affected by aging. There is a body of research confirming that item recognition that works by using familiarity is generally preserved in older adults, compared to associative recognition that needs a degree of recollection (Old & Naveh-Benjamin, 2008, Pitarque et al. 2015, Ratcliff et al. 2015, Silver et al. 2012). Thus, the current results add to the literature stating that item recognition is relatively unaffected by age. The results also further support the idea of implementing face recognition as a PVT, as it is not only robust to diagnostic group membership but also to aging effects.

Free recall is less sensitive to aging than to diagnostic group membership

Interestingly, among the recall scales, spontaneous name recall was the least sensitive to aging, even though it was highly affected by group membership. In fact, spontaneous name recall may not be directly measuring associative memory, as the task only requires the free recall the learned names, without the necessity of binding it with a face. Previous research has suggested that free recall of items is less affected by aging than recall of associations, as is required by the other recall tasks of the FNAME (Old & Naveh-Benjamin, 2008). The current results support this notion and are in line with the associative deficit hypothesis (Naveh-

Benjamin, 2000), suggesting that associative memory is more sensitive to aging than other types of memory. Further, the current results indicate that patterns of memory decline related to aMCI are not just an exacerbation of age-related memory decline but are distinct in nature.

Practical implications of differential performance patterns of pathological versus age-related memory decline

As an implication, knowing about the patterns of memory decline on the FNAME for older individuals compared to younger individuals and for individuals with cognitive impairments such as aMCI, can help to differentiate between healthy aging individuals and cognitively impaired ones. The FNAME could be implemented as a screening tool in clinical settings to estimate an individual's risk of developing AD, based on the pattern of performance. For instance, based on the current results, a highly impaired performance on spontaneous name recall compared to immediate or delayed recall might implicate the presence of (a)MCI, whereas a higher performance on spontaneous name recall in combination with more impaired performance on face-name matching and delayed recall indicates an age-related decline in memory. Performance on the face and name recognition scales then further indicate either the severity of impairment, or the possible presence of noncredible performance. Another important implication that arises from the current results is that both variables, group membership and age, stay significant in predicting FNAME score, i.e., even in the presence of aMCI, age still significantly contributes to FNAME performance. This underlines the importance of developing age norms to be able to compare an individual's performance to that of similarly aged individuals, as higher age may exacerbate the observed impairments in individuals who are cognitively impaired and thus, could lead to an overestimation of the contribution of the underlying disease to the observed memory complaints.

Inconsistent and small effect of cognitive reserve on FNAME

No strong support was found for the notion that CR as measured by education level could improve performance on the FNAME, when accounting for group membership and age. The effect was only significant at .05 level for some subscales. Within the individual subscales, only the lowest and highest education level continuously differed significantly, indicating a general tendency to improve FNAME performance with the highest education level (i.e., university level), however for the lower levels no clear pattern of performance could be observed. Even though some results were significant, the magnitude of their effect questions their clinical utility. It appears that FNAME performance is relatively unaffected by the level of CR in the present study, which also adds to Rentz and colleagues' (2011) results.

One possibility to explain these unexpected results is the nature of the measurement of CR in the current study. Some of the education levels used in this study consist of educational degrees that are qualitatively quite different from each other, e.g., level 6 consists of VWO, which is the highest level of Dutch high school, and HBO, which is the Dutch college/university of applied sciences. This could account for some of the variability found in the FNAME performance of each education level.

Another possibility is that the FNAME is especially robust to the effects of CR due to its abstract nature, consistent with Rentz and colleagues' (2011) and Kormas and colleagues' (2020) suggestion that CR is related to enhanced memory strategies and semantic knowledge, which is not applicable in the FNAME. In fact, previous research found that high CR is especially related to increased connectivity in the frontal areas, enhancing such strategic processes to enhance memory, but not in the medial temporal lobe, including the

hippocampus, which is crucial in associative memory functioning (Peterson et al. 2016). Possibly, as suggested by the current data, the effect of CR on FNAME might be of such small magnitude that only especially high cognitive reserve (i.e., the highest education level) exerts a significant effect. High education has been associated with other lifestyle factors that promote the maintenance of the brain's health and enhanced neural connectivity, i.e., by engaging in mentally stimulating activities throughout life, encouraging divergent thinking, or protecting from adverse habits in adulthood (Serra et al. 2016). The effects of high education starting early in life already could be thus not only restricted to improved connectivity in the frontal areas but are associated with a more general preservation and enhancement of neural efficiency, that might eventually improve memory functions as well.

Strengths and limitations

A strength of the current study was the consideration of several factors, i.e., age, CR, and cognitive impairment in the prediction of FNAME scores, which yields a more realistic picture of the composition of FNAME performance in a clinical environment. To date, the age effect on FNAME performance has been only investigated in healthy older adults (Enriquez-Geppert et al. 2021, Flores-Vázquez et al. 2021). The effect of CR on FNAME has been only investigated in cognitively normal adults, whereas the current study assessed CR in individuals with cognitive impairment. Further, the current study used participants from an older age group (50-90 years) and did not compare younger to older adults. Still an age effect was found, indicating that the consideration of age is also important for samples with a smaller age range. Lastly, compared to other studies on the FNAME, the sample size was relatively large in each group.

The conclusions drawn by the current research are limited by the unavailability of a healthy control group, without any subjective and objective complaints. Since the research on differences between HOA and SCD individuals on FNAME performance is mixed, it is not clear whether the effect of age on FNAME scores might change when taking HOA into account. Further, the current research made use of archival data only. Thus, there was no control over the recruitment process, or over the administration procedure of the FNAME. Next, the choice of statistical analysis has some limitations. Linear regression analysis is sensitive to outliers, which were especially present for the face recognition scale; however, removing those outliers would have been theoretically incorrect, as individuals scoring especially low could reflect highly vulnerable group, requiring special attention when interpreting the data. Further, the assumptions of homogeneity and normality was violated for some scales. Even though a large sample size (>50) usually is not prone to violations of normality (Hair et al. 2010), the violations of homogeneity might have negative consequences for the validity or accuracy of some of the results.

Conclusion

The current research found age to be an important predictor in FNAME performance, even when for group membership is accounted, which is in line with previous literature stating that associative memory is highly affected by age. Future research should focus on developing norms for different age groups in order to accurately interpret an individual's score in light of their age and degree of cognitive impairment. Furthermore, age and group membership affected FNAME subscales differently, i.e., age was more strongly associated with performance on face-name matching and delayed recall, whereas group membership mostly affected spontaneous name recall. Face and name recognition were only weakly affected by both variables, however their use could still be useful in clinical practice, i.e., by

implementing the face recognition scale as a PVT or a tool to identify individuals who are at an especially high risk of developing AD. The next step that is crucial to test this notion is the development of a cutoff score that indicates normal from noncredible performance on face recognition. Further, the results suggest that when implementing the FNAME as a screening tool in clinical practice, the pattern of performance rather than scores on individual scales should be considered. The effect of CR was small and often non-significant, thus underlining the potential of the FNAME as a screening tool that is robust to different education levels and thus, potentially superior to other measures of associative memory.

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Appendix

Appendix A – Symptoms and stages of AD

In general, AD is a neurodegenerative disease, characterized by neuropathological changes such as extracellular amyloid beta plaque formation and intracellular neurofibrillary tangles, as well as clinical symptoms, predominantly episodic memory problems, as well as verbal (e.g., word-finding) and executive (e.g., judgment, reasoning, problem-solving) difficulties (Alzheimers Association, 2023, Pais et al. 2020). To date, a diagnosis of probable AD is made predominantly based on aforementioned clinical symptoms, the presence of a gradual onset over many months/years, and the exclusion of other causes such as cerebrovascular diseases or Lewy bodies (McKhann et al. 2011). AD progresses in a stage-like manner, starting with a preclinical, asymptomatic stage, in which AD-related neuropathology is already present, but without otherwise objectively measurable cognitive deficits (Rostamzadeh et al. 2022); followed by a prodromal stage, which is characterized by mild cognitive impairments (MCI) (Rostamzadeh et al. 2022); and eventually developing into Alzheimer's dementia, which is further subdivided into mild, moderate, and severe (Alzheimer's Association, 2023). Further, recently a transitional phase between the preclinical and prodromal stage has been suggested, characterized by self-reported cognitive complaints (subjective cognitive decline [SCD]) which are not yet objectively measurable as in MCI (Rostamzadeh et al. 2022). Usually, a diagnosis is made when an individual has already progressed to MCI due to AD, thus, the issue with these current diagnostic procedures is that cognitive and behavioral changes are already clinically significant when a diagnosis is provided, however an earlier identification is becoming more important considering its significant psychosocial and economic impact (Markova et al. 2022, Rubiño & Andrés, 2018).

Appendix B – Brain reserve and cognitive reserve

Brain reserve refers to the intrinsic properties of the brain, such as volume or the number of synapses, which can also passively affect the threshold for the clinical expression of a disease (Alvares Pereira et al. 2022). However, even though CR and BR describe different processes, the two constructs are not mutually exclusive, as BR is also influenceable by factors that affect brain anatomy, such as health-related habits (i.e., drinking alcohol, or diet) (Alvares Pereira et al. 2022). This process is also referred to as brain maintenance (BM; Stern et al. 2020). Thus, better BM can sustain higher BR, and external factors that enhance CR can also modify the level of BR.

Appendix C – Performance validity tests

Performance validity refers to the validity of an individual's actual task performance, assessed by either stand-alone PVTs that have been developed for specifically that purpose, or embedded PVTs that are included in an actual neuropsychological test (such as the recognition scale within the FNAME) (Larrabee, 2012). The importance of implementing PVTs in neuropsychological examinations has increased over the past decades, as it has been recognized that the prevalence of noncredible performance on cognitive measures is higher than expected, not only in forensic but even in clinical contexts (Martin et al. 2020). The reasons for noncredible responding are broad and vary from external incentives (e.g., monetary gains) to internal incentives (e.g., exaggerating symptoms as a "cry for help") (Martin et al. 2020).