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# Unfamiliar facial identity discrimination and recognition impairment in prodromal Alzheimer's disease: A behavioral pattern separation and completion study

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#### ARTICLE INFO

# Keywords: Pattern separation Pattern completion Face identity discrimination Face recognition Prodromal Alzheimer's disease Mild cognitive impairment

#### ABSTRACT

Background: Impairment of face identity recognition (FIR) in prodromal Alzheimer's disease (AD) is not clearly established, and the cognitive processes underpinning a potential FIR impairment remain elusive. The influential pattern separation (PS) and completion (PC) framework may offer a fascinating insight in this respect. Indeed, efficient FIR implies PS to encode facial identities in distinct memory representations, while PC is involved in matching the perceived facial patterns to these memory representations at retrieval. Based on this functional dissociation, the present study investigated FIR using a PS and PC paradigm in prodromal AD patients.

 $\it Method:$  Thirty-one cognitively unimpaired (CU) older individuals and 16 amyloid-positive patients with amnestic Mild Cognitive Impairment (A $\beta$ + aMCI) were familiarized with 40 facial identities, using a viewpoint-matching task. They then performed a forced-choice recognition task assessing the extent to which these unfamiliar faces were implicitly learned. Subsequently, they underwent separate Yes/No recognition tasks involving parametrically controlled blurred or morphed faces, designed to solicit PC and PS processes respectively. Finally, in two separate discrimination tasks, participants had to determine whether two simultaneously displayed faces, a proportion of them being blurred or morphed, corresponded to the same identity or not.

Results:  $A\beta$ + aMCI patients obtained lower performance than CU older individuals in each task, including the tasks that did not involve FIR demands in episodic memory. There was no disproportionate performance decrease with increasing levels of PC and PS requirements.

Conclusions: No isolated PS/PC deficit was evidenced in FIR in prodromal AD patients. Importantly, besides a general FIR deficit, discrimination of simultaneously presented unfamiliar facial identities was impaired.

Humans are constantly exposed to faces in their environment. Accurately and quickly creating new facial representations in memory is socially necessary to dissociate familiar faces from unfamiliar ones and identify individuals. This function is dramatically impaired at the

dementia stage of Alzheimer's disease (AD; Moss et al., 1986; Seelye et al., 2009; Werheid and Clare, 2007 for review) but its impairment in the prodromal stages of the disease is less well established. Some studies revealed poorer recognition of newly learned faces in patients with Mild

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Cognitive Impairment (MCI; Petersen, 2004), which may represent a transitional stage between normal aging and dementia, compared to cognitively unimpaired older individuals (Nguyen et al., 2014; Rahmani et al., 2019; Zhang et al., 2024), while other studies did not (Seelye et al., 2009). These discrepancies may be linked to several factors, including sample sizes, the various experimental tasks that were used to assess newly learned facial identities recognition (FIR), and the heterogeneous nature of the MCI diagnosis. Regarding the latter aspect, previous studies did not systematically use biomarkers to identify MCI patients presenting a high risk of evolving to AD dementia. By referring to recently proposed thresholds, such as for the quantification of the cerebral amyloid- $\beta$  (A $\beta$ ) pathology, it is now possible to reliably discriminate MCI patients with the highest risk of progressing to AD dementia from those who will most likely remain clinically stable in the following years (B. J. Hanseeuw et al., 2021).

The cognitive processes underlying a potential FIR impairment in prodromal AD remain elusive. When it was evidenced, the impaired newly learned FIR in MCI and AD was interpreted as being potentially linked to impaired perceptual discrimination abilities between targets and foils (Nguyen et al., 2014), impaired general memory encoding deficit (Rahmani et al., 2019) or to a deleterious interference due to an overload of facial inputs disrupting memory for unified facial representations (Nguyen et al., 2014; Rahmani et al., 2019). These hypotheses are not necessarily mutually exclusive and could depend on the spatio-temporal dynamics of the AD pathology spreading across the visual ventral stream. In our view, these hypotheses could even be reconciled through the unifying concepts of "Pattern Separation" (PS) and "Pattern Completion" (PC), which may account, at least partly, for FIR performance in MCI and AD patients, depending on the demands that the experimental task places on these processes. PS refers to the ability to operate discrimination between similar input patterns by reducing the overlap between their respective representations (see Hunsaker and Kesner, 2013 for review). This neural process is considered to form new representations that prevent catastrophic interference across similar input patterns (Kent et al., 2016; Yaros et al., 2019). Besides PS that operates at encoding, PC is a neural process enabling the retrieval of a previously stored representation based on partial cues (Hanson and Madison, 2010; Hunsaker and Kesner, 2013; Yassa and Stark, 2011; Yassa et al., 2010). Compelling evidence from behavioral and neuroimaging studies suggests that the hippocampus, which undergoes significant morpho-functional changes early in AD (Dickerson and Sperling, 2008; B. J. Hanseeuw et al., 2011), critically supports these processes (Yassa and Stark, 2011).

Traditionally, PS and PC are assessed using recognition tasks implying new, repeated and lure object pictures (Ally et al., 2013; Stark et al., 2013; Yassa et al., 2010). Lures are similar but not identical to previously presented stimuli (e.g., two similar exemplars of a piano). In such tasks, participants indicate whether the displayed object is new, old or similar but not identical to a previously viewed object. Responses to lures are the measure of interest. While "similar" responses to lures are viewed as revealing a successful PS process, "old" responses to lures are interpreted as impaired PS abilities associated with a bias towards PC.

This behavioral propensity towards PC at the expense of PS has been evidenced in normal aging, concordantly with the "representational rigidity" highlighted in some hippocampus subfields (i.e., CA3 – dentate gyrus) that need a higher degree of dissimilarity for the network to encode the stimulus as new instead of treating it as a repetition (Toner et al., 2009; Yassa, Michael A, Lacy, Joyce M, Stark, Shauna, Albert, Marilyn, Gallagher Michela, Stark et al., 2011). However, healthy older adults performed at the level of younger participants when correctly identifying the repeated stimuli as "old" and the new stimuli as "new" (Toner et al., 2009).

In the AD spectrum, patients with amnestic MCI (aMCI), an MCI subtype considered as prodromal AD given the high likelihood of progression to AD (B. Hanseeuw and Ivanoiu, 2011), similarly demonstrated a higher tendency to consider lure object pictures as old items

compared to healthy older adults (Ally et al., 2013; Stark et al., 2013). This evidence argues in favor of a PS deficit in aMCI patients, consistent with the structural and functional changes occurring in the hippocampus since the early stages of AD (Dickerson and Sperling, 2008; B. J. Hanseeuw et al., 2011, 2016). Moreover, performance on mnemonic PS recognition tasks involving objects and/or scene pictures was evidenced to correlate with the level of amyloid-beta 42 (A $\beta$ 42) in the cerebrospinal fluid and the Apoliprotein-E (APOE) genetic risk factor in mild to moderate AD patients (Wesnes et al., 2014).

While most prior research on PS/PC has concentrated on the memory domain and its prominent cerebral substrate, i.e. the hippocampus (Yassa and Stark, 2011), PS is increasingly recognized as a fundamental process reducing interference and representational similarity of inputs, regardless of whether the task involves memory demands (Kent et al., 2016). Moreover, converging evidence from both animal and human studies supports that PS represents a multistage process implemented by interacting brain regions that are differentially recruited depending on the task demands (e.g., fronto-parietal cognitive control regions, occipito-temporal sensory regions; Amer and Davachi, 2023). In humans, FIR is known to rely on specific regions in the ventral occipito-temporal cortex (VOTC; Duchaine and Yovel, 2015; Jacques et al., 2020), with a right dominance (Rossion, 2014). The Occipital Face Area (OFA; Gauthier et al., 2000) and the Fusiform Face Area (FFA; Kanwisher et al., 1997) are traditionally viewed as supporting the building of invariant facial representations, while anterior and medial temporal regions support semantic, episodic and affective memory functions (see Rossion et al., 2024 for a review and alternative view). One may assume that processes analogous to PS/PC most probably intervene in this interacting network to optimize FIR. Indeed, an efficient FIR system should ideally be able to disentangle faces that are similar but belong to different individuals and create non-(or only partially) overlapping representations to avoid any misrecognition between people who are alike, which corresponds to the PS process (Yaros et al., 2019). Furthermore, humans learn to recognize their acquaintances' faces in various contexts from infancy (Hill et al., 1997). Therefore, an efficient FIR system should also tolerate variability in the inputs originating from the same identity and be able to fill in the currently perceived facial pattern based on a mnemonic representation despite this variability, which corresponds to the PC process (Yaros et al., 2019). However, to our knowledge, little investigation of FIR has been conducted in the light of the PS/PC framework.

Therefore, the primary aim of this study was to investigate newly learned FIR abilities in prodromal AD patients compared to healthy older adults in PS and PC conditions. Participants were familiarized with 40 faces using a viewpoint-matching task, followed by FIR tasks involving parametrically controlled blurred or morphed faces to incrementally solicit PC or PS abilities, respectively. Given the pathophysiological changes occurring on the ventral occipito-temporal pathway, mostly in medial-temporal and temporal regions, since the early stages of AD (Braak and Braak, 1991), we expected impaired newly learned FIR in prodromal AD patients compared to controls, with dramatically impaired performance in PC and PS trials. Previous studies on PS (and PC) mostly used objects as stimuli and the ones that manipulated the similarity degree of items are scarce. Stark et al. (2013) highlighted a shift in the PS performance curve of MCI patients compared to healthy older individuals, depending on the similarity degree of objects, supporting the idea that patients need greater level of dissimilarity between items to correctly reject lures. Therefore, we here expected an interaction between group and the degree of PS or PC demands in the FIR tasks.

Moreover, to test whether upstream high-level face perceptual processes would be preserved in prodromal AD patients and whether deficits would be limited to memory-based recognition, we assessed facial discrimination abilities in no-delay tasks that did not involve any FIR demand from episodic memory. In these tasks, participants had to determine whether two simultaneously presented faces, a proportion of them being blurred or morphed, were identical or not. Little is known

about the integrity of the face identity discrimination abilities at the prodromal stage of AD. Indeed, most of the previous studies included AD patients who were at a dementia stage and their results are inconsistent (Becker et al., 1995; Chang et al., 2016; Cronin-Golomb et al., 2000; Della Sala et al., 1995; Lee et al., 2006, 2007). Therefore, in the current study, we aimed at exploring the integrity of these abilities in prodromal AD patients to test whether impairment would be limited to FIR tasks placing demands on episodic memory and especially on mnemonic PC and PS processes.

A terminology precision is needed about the PS/PC terms, which originally refer to computational processes that are implemented at the cell population level (Santoro, 2013). In line with previous behavioral studies on PS/PC (e.g., Ally et al., 2013; Stark et al., 2013), the current work used these concepts to specifically refer to the behavioral perceptual or mnemonic discrimination performance, although no cell ensemble PS/PC could formally be inferred.

#### 1. Method

#### 1.1. Participants

Participants included 31 cognitively unimpaired (CU) older individuals, recruited through advertisement, and 16 amyloid-positive patients with amnestic Mild Cognitive Impairment (A $\beta$ + aMCI, considered as prodromal AD), recruited from a local Memory Clinic research cohort (UCL-2010-412; Ivanoiu et al., 2014, Table 1).

The cognitive status was determined through a cognitive assessment that evaluated: (1) global cognitive function using the Mini-Mental State Evaluation (MMSE; Folstein et al., 1975) (2) episodic memory using the Free and Cued Selective Reminding Test (FCSRT; Van der Linden et al., 2004), and (3) language using the Category Fluency Test for animals and the Letter Fluency Test for the letter P (de Partz et al., 2001).

Each CU older individual: (1) denied memory complaints, (2) had preserved daily living functioning, (3) obtained a MMSE score  $\geq$ 28/30, and (4) obtained age-typical performance on the FCSRT (i.e., both the sum of the three free recalls and the sum of the three total recalls >-1.3 SD compared to an independent group of 26 amyloid negative CU older individuals; data collected in Ivanoiu et al., 2015). They did not undergo any amyloid status examination.

Each patient met the criteria for amnestic Mild Cognitive Impairment (aMCI), as they: (1) attended the Memory Clinic for memory complaints, (2) presented an objective memory impairment as defined by a score inferior to -1.3 *SD* compared to an independent group of 26 amyloid

negative CU older individuals (data collected in Ivanoiu et al., 2015) for the sum of the three free or total recalls on the FCSRT, (3) had essentially spared general cognitive function as defined by a MMSE score ≥24/30, (4) demonstrated globally preserved daily living skills, and (5) did not meet the DSM-V criteria for Major Neurocognitive Disorder (Association American Psychiatric, 2013).

In the UCL-2010-412 parent cohort, the amyloid status was determined through a [ $^{18}$ F]Flutemetamol (marketed as  $^{TM}$ Vizamyl, GE Healthcare) positron emission tomography (PET) scan. Quantitative standard uptake value ratios (SUVr) were computed using PVIEW and PFUS v3.2.2 software modules (Pmod Technologies Ltd Z, Statistical Parametric Mapping, n.d.) and then transformed into Centiloid values using the following equation: Centiloid =  $(120.2 \times \text{SUVr}) - 144.5 \text{ (B. J. Hanseeuw et al., 2021}$ ). The amyloid status was considered positive when the Centiloid value exceeded a threshold of 26. This threshold optimally predicted progression to dementia 6 years after PET (B. J. Hanseeuw et al., 2021).

Cognitive impairment stemming from another known neurological condition, psychiatric disease, and substance abuse were exclusion criteria for the parent research cohort. Each participant had normal or corrected-to-normal vision.

This study received approval from the Ethical Committee of Saint-Luc University Hospital in Brussels (2012/28FEV/085) and was conducted in accordance with the Helsinki Declaration. Each participant provided informed consent before participating. CU older individuals were paid to participate in the experiment.

#### 1.2. Materials

Two hundred fifty-eight (258) colored pictures of Caucasian faces of young people (i.e., undergraduate university students; 80 % women) displaying a neutral expression were used. Among these pictures, there were 178 different identities presented in a full-front view. Forty of these 178 different identities were presented in two different profile views (30° to the right and 30° to the left) in the familiarization part of the experimental task (see *Procedure*). All pictures were taken under standardized conditions in terms of lighting, background and distance from the camera. External features (i.e., hair and ears) were cropped out using Adobe Photoshop CS 5.1. and a neutral grey background was used with the resulting isolated faces. The height of the final pictures was 300 pixels (width = 223.4  $\pm$  10.7 pixels), corresponding to 7.26° (width = 5.37°).

We used blurred faces to investigate PC processes since they can be

**Table 1**Demographic characteristics, cognitive scores, viewpoint-matching and forced-choice recognition performance.

	CU older individuals $N=31$ Mdn (Q25-75)	Aeta+ aMCI N=16 Mdn~(Q25-75)	p	Effect size r
Demographic characteristics				
Age (years)	71.0 (66.0–75.0)	75.5 (60.0–78.3)	0.529	-0.092
Education (years)	17.0 (16.0–18.0)	13.5 (12.0–17.0)	0.007	-0.396
Sex (% W/M)	58/42	44/56	0.533	1.78 <sup>a</sup>
Standard cognitive assessment				
Global cognitive function				
MMSE (/30)	29.0 (28.5-30.0)	26.5 (25.0-28.0)	< 0.001	-0.578
Memory				
FCSRT-FR sum of trials (/48)	34.0 (31.0-38.5)	16.0 (7.75–20.8)	< 0.001	-0.810
FCSRT-TR sum of trials (/48)	48.0 (47.0-48.0)	31.5 (25.3-40.3)	< 0.001	-0.767
Language				
Category Fluency	37.0 (31.0-46.5)	29.0 (23.0-33.3)	< 0.001	-0.501
Letter Fluency	26.0 (20.5–29.0)	22.5 (18.0-23.3)	0.024	-0.330
Experimental tasks				
Viewpoint-matching task	0.97 (0.93-0.98)	0.86 (0.82-0.94)	< 0.001	-0.535
Forced-choice recognition	0.78 (0.74–0.85)	0.73 (0.63-0.76)	0.005	-0.407

Note. CU = cognitively unimpaired; aMCI = amnestic Mild Cognitive Impairment; W = Women; M = Men; MMSE = Mini-Mental State Examination; FCSRT = Free and Cued Selective Reminding Test; FR = Free Recall; TR = Total Recall. <sup>a</sup> Odds ratio.

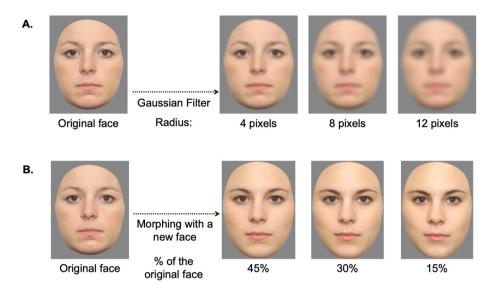


Fig. 1. Blurring and morphing manipulations. A. The blurring manipulation was implemented by adding Gaussian blur to face pictures (radius = 4, 8 or 12 pixels). Blurred faces constituted partial/degraded versions of familiarized faces, whose correct recognition is assumed to solicit PC abilities. B. The morphing manipulation was implemented by merging each familiarized face with a new face to one of three possible similarity degrees: morphed faces contained 15 %, 30 %, or 45 % of familiarized faces. This parametrically controlled manipulation created facial stimuli that were similar but not identical to familiarized faces, which is supposed to place demands on PS abilities.

considered as partial or degraded versions of previously presented faces. The blurring manipulation was implemented by adding Gaussian blur to face pictures in Adobe Photoshop CS 5.1. Three blurring levels created three increasing blurring degrees (Gaussian filter with a radius of 4, 8, and 12 pixels; Fig. 1A).

We used morphed faces to tax PS abilities since they are similar but not identical to the face identities from which they originate. The morphing manipulation was implemented by merging pairs of faces in *PsychoMorph* (Tiddeman et al., 2001). Three increasing morphing degrees were used: (1) morphed faces containing 15 % of the previously seen faces and 85 % of new faces (i.e., faces "poorly" similar to the previously seen faces), (2) morphed faces containing 30 % of the previously seen faces and 70 % of new faces (i.e., faces "moderately" similar to the previously seen faces), and (3) morphed faces containing 45 % of the previously seen faces and 55 % of new faces (i.e., faces "strongly" similar to the previously seen faces; Fig. 1B).

#### 1.3. Procedure

During the experiment, participants sat at 60 cm from the computer screen. The stimuli were presented on a computer screen with a 1366  $\times$  768 pixels resolution.

The experimental task, programmed in Psychtoolbox running under MATLAB (MathWorks, Inc. R2010a, 2010), was divided into six parts. In each part, trials were self-paced but a maximum period of 15 s was allowed for responding. Stimuli were displayed on the screen until the participant responded by pressing either the left or the right "control" key on an AZERTY keyboard. A green sticker covered the left "control" key, while a red sticker covered the right "control" key (see below). In each task, trials were randomly presented and separated by a 500 ms interval.

#### $1.3.1.\ \ Viewpoint-matching\ task-familiarization$

The first task consisted of a viewpoint-matching task to familiarize participants with 40 face identities. In this task, three faces were displayed on the screen during each trial. One full-front view face was centered in the upper half of the screen (i.e., the reference face). Each of the 40 faces was displayed four times as the reference face, leading to 160 trials. Two profile faces were presented simultaneously in the lower half of the screen (Fig. 2. A.). One of these faces represented the same

identity as the reference face but was shown under another viewing perspective ( $30^{\circ}$  to the right or  $30^{\circ}$  to the left). The other profile face was randomly selected among the profile viewing perspectives of the 39 remaining faces. Participants were instructed to indicate which profile face corresponded to the same identity as the reference face. They had to press the left or right button when they thought that the left or right profile face corresponded to the reference face, respectively. Participants were not informed that they would have to recognize faces later.

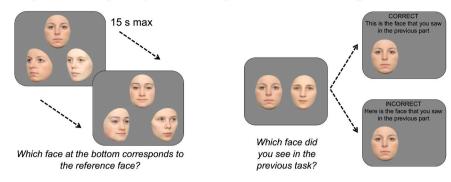
#### 1.3.2. Forced-choice recognition task

After the viewpoint-matching task, participants immediately completed a forced-choice recognition task to assess how well they had encoded the 40 faces. Each of the front view faces presented in the familiarization task (i.e., then referred to as "old" faces) was displayed with a new front view identity, leading to a total of 40 trials (Fig. 2. B.). Participants were asked to identify the old faces by pressing the left or right button if they thought they had seen the left or right face in the familiarization task. Participants received feedback for each response. If the response was correct, the sentence "Correct. This is the face that you saw in the previous part." was displayed on the screen, above the correct face. If the response was incorrect or the participant gave no answer, the sentence "Incorrect. Here is the face that you saw in the previous part." was displayed above the correct face. This feedback was aimed at strengthening the learning of the 40 faces.

#### 1.3.3. Yes/no recognition task with blurred faces - PC condition

Participants then performed a Yes/No recognition task to solicit PC processes. This task was composed of 60 trials, in which faces were displayed one at a time in a front view (Fig. 2. C.). Among the displayed faces, there were ten intact non-blurred old faces, ten slightly blurred old faces (i.e., radius of the added Gaussian blur = 4), ten moderately blurred old faces (i.e., radius of the added Gaussian blur = 8), ten strongly blurred old faces (i.e., radius of the added Gaussian blur = 12), and 20 new faces (five non-blurred new faces, five slightly blurred new faces, five moderately blurred new faces, five strongly blurred new faces). The new faces differed from those presented in the forced-choice recognition task. Even though some faces were blurred, participants were instructed to press the left key (green key) if they thought they had seen the displayed face in the previous parts of the paradigm and the right key (red key) otherwise. No more feedback was provided. In the

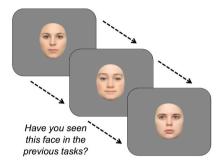
#### A. Viewpoint-Matching Task (Familiarization) B. Forced-choice recognition task



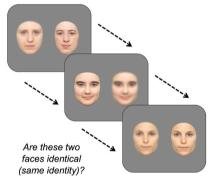
#### C. PC Yes/No recognition task

# Have you seen this face in the previous tasks?

#### D. PS Yes/No recognition task



#### E. PC Discrimination task



#### F. PS Discrimination task

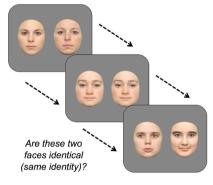


Fig. 2. Examples of facial stimuli used in the: A. Viewpoint-matching task, B. Forced-choice recognition task, C. PC Yes/No recognition task, D. PS Yes/No recognition task, F. PS discrimination task.

current Yes/No recognition task, a high rate of yes responses to blurred old faces would suggest that the participant could complete the facial pattern based on a previously stored representation of the face.

#### 1.3.4. Yes/no recognition with morphed faces - PS condition

PS processes were then assessed using a Yes/No recognition task comprising 50 trials, in which faces were displayed one at a time in a front-view (Fig. 2. D.). Among the displayed faces, there were ten intact non-morphed old faces, ten morphed faces slightly similar to the old faces (i.e., morphed faces containing 15% of old faces), ten morphed faces moderately similar to the old faces (i.e., morphed faces containing 30% of old faces), ten morphed faces strongly similar to the old faces (i. e., morphed faces containing 45% of old faces), and ten new faces. Of note, the new faces differed from those presented in the forced-choice recognition task and the PC Yes/No recognition task. Participants were drawn to the fact that, in some trials, faces might be similar but not identical to faces they had seen in the previous parts. They were, therefore, instructed to respond yes by pressing the left key (green key) only when they thought that they had seen the exact face in the previous

parts and respond no by pressing the right key (red key) otherwise. In the current recognition task, a high rate of yes responses given to morphed faces suggests that the participant could not separate similar facial patterns.

#### 1.3.5. Discrimination task with blurred faces – PC condition

We included a discrimination task, including the blurred faces shown in the PC Yes/No recognition task, to assess PC processes without any long-term memory requirement. This task was composed of 60 trials, in which two front-view faces were simultaneously displayed on the screen (Fig. 2. E.). For 40 of the 60 trials, each old face was displayed with the corresponding face presented in the PC Yes/No recognition task. For example, if a non/slightly/moderately/strongly blurred version of face A was presented during the PC Yes/No recognition, this non/slightly/moderately/strongly blurred face A was displayed with its original non-blurred face A in the current phase. In the 20 remaining trials, each new blurred or non-blurred face displayed during the PC Yes/No recognition task was presented with another new non-blurred face. Participants were asked to determine whether the two front-view faces displayed on

the screen were identical or not (i.e., whether they represented the same identity, although one might be blurred). They were instructed to press the left button (green key) if they thought the two faces were identical and the right button (red key) otherwise. Here, a high rate of *yes* responses to the trials implying old blurred faces suggests that the participant could match the simultaneously displayed facial patterns despite one being blurred.

#### 1.3.6. Discrimination task with morphed face - PS condition

The last task aimed to assess PS processes without any long-term memory requirement by using a discrimination task. The task comprised 50 trials, in which two front-view faces were displayed on the screen (Fig. 2. F.). For 10 of the 50 trials, the ten intact non-morphed faces displayed in the PS Yes/No recognition task were shown twice next to each other (i.e., identical trials). For 30 of the 50 trials, morphed faces presented in the PS Yes/No recognition were displayed with the faces from which they originate (i.e., old faces). That is, if a morphed face slightly/moderately/strongly similar to face A seen during the familiarization phase was displayed in the PS Yes/No recognition task, this morphed face slightly/moderately/strongly similar to face A was shown with face A. Each of the ten new faces displayed in the PS Yes/No recognition task was presented with another entirely new face for the remaining trials. Participants had to determine whether the two frontview faces displayed on the screen were identical (i.e., whether the two represented the same identity) by noticing that faces might be similar but not identical in some trials. They were instructed to press the left button when they thought two faces were exactly identical and the right button otherwise. Here, a high rate of yes responses to the trials implying morphed faces suggests that the participant could not discriminate the two similar facial patterns that are simultaneously displayed.

#### 1.4. Statistical analyses

Statistical analyses were performed using R version 4.2.2 (R Core Team, 2022). The alpha statistical significance threshold was set at 0.05.

#### 1.4.1. Participants' characteristics

Group differences in demographic characteristics (i.e., age and education) and standard cognitive measures were examined using Mann-Whitney tests, given that these variables were non-normally distributed, and the homoscedasticity assumption was not systematically met. A chi-squared test was implemented for sex.

#### 1.4.2. Experimental tasks

Performance on the viewpoint-matching and forced-choice recognition tasks was assessed by calculating the correct response rates (number of correct responses divided by the total number of trials).

We used behavioral detection theory in the PC and PS Yes/No recognition tasks and the PC and PS Discrimination tasks (Davison and Tustin, 1978). We calculated the discriminability measure  $\log d$  for each degree of item manipulation (i.e., blurring or morphing) according to the following equation:

$$\log d = \frac{1}{2} \log 10 \left( \frac{Hits}{Misses} \cdot \frac{Correct \ Rejections}{False \ Alarms} \right)$$

Like the more widespread d' discriminability measure derived from the signal detection theory (Green and Swets, 1966), the  $\log d$  measure is theoretically not supposed to be contaminated by response bias (Davison and Tustin, 1978) and does not suffer from ceiling effects since its scale is not bounded. The latter measure was preferred to the d' measure as it is considered more reliable when the trial number is under 100 (Kadlec, 1999). To avoid an infinite value of  $\log d$  measures due to highly accurate and errorless performance, we added the constant 0.5 to all cells of the behavioral detection matrix, regardless of their content (i.e.,

percentages of hits, misses, false alarms, correct rejections) and regardless of their values (Goodman, 1970). This correction was demonstrated to limit the discriminability overestimation to an acceptable level (Brown and White, 2005). Regarding interpretation, high log d values (e.g., >1) indicate strong discriminability and few errors, while values close to 0 suggest that performance is at chance level

These log d measures were then entered in linear mixed-effects models (LME) including random intercepts to examine the effects of the group and the item manipulation degree on behavioral performance as well as their potential interaction ("nlme" R package; Log d  $\sim$  Blurring/Morphing\*Group, random =  $\sim$ 1|participant). We excluded random slopes from LMEs because models including random slopes and intercepts resulted in higher AIC and BIC values, indicating a poorer balance between model fit and complexity. Post-hoc two-by-two comparisons between the blurring or morphing degrees were implemented using the package "emmeans" (Lenth, 2024).

#### 1.4.3. Correlational analyses between scores in the experimental tasks

To obtain one unique metric for the trials involving blurred or morphed faces in the PC and PS Yes/No recognition and discrimination tasks, we computed the mean  $\log d$  obtained for the three degrees of blurring or morphing in each of these tasks for each participant.

To assess associations between scores obtained in experimental tasks, we then computed a matrix of Spearman correlation coefficients over the entire sample and within each group, including the viewpoint-matching task and forced-choice recognition correct response rates and the mean  $\log d$  obtained for the trials involving blurred or morphed faces in the PC and PS Yes/No recognition and discrimination tasks.

P-values were adjusted using the Benjamini-Hochberg correction.

# 1.4.4. Correlational analyses between scores in the experimental tasks and standard cognitive measures

Spearman correlation coefficients were computed over the entire sample and within each group between the scores in the experimental tasks (i.e., viewpoint-matching task and forced-choice recognition correct response rates, the mean  $\log d$  obtained for the trials involving blurred or morphed faces in the PC and PS Yes/No recognition and discrimination tasks) and standard cognitive measures (i.e., MMSE, FCSRT sum of free recalls, FCSRT sum of total recalls, Category fluency, Letter Fluency).

#### 2. Results

# 2.1. Demographic characteristics and performance on standard cognitive measures

There was no significant difference between A $\beta$ + aMCI patients and CU older individuals for age (W=219.5, p=.529, r=-0.092) nor sex ( $\chi^2(1)=0.389, p=.533, OR=1.78;$  Table 1). However, the educational level was significantly different between the two groups (U=368.5, p=.007, r=-0.396), being lower in patients than in controls.

Moreover, as expected, patients' performance in each neuropsychological test was significantly inferior to the control group performance (Table 1; MMSE, W=420.0, p<.001, r=-0.578; FCSRT – FR sum of trials, W=495.5, p<.001, r=-0.810; FCSRT – TR sum of trials, W=472.5, P<.001, P=-0.767; Category Fluency, P=401.0, P<.001, P=-0.501; Letter Fluency, P=349.0, P=.024, P=-0.330).

## 2.2. Performance on the viewpoint-matching and forced-choice recognition tasks

The correct response rate in the viewpoint-matching task was lower in A $\beta$ + aMCI patients than in CU older individuals (W=411.5, p<.001, r=-0.535; Table 1), even when controlling for education ( $b_{group}=-8.48, 95$  % CI [-12.49, -4.47], p<.001;  $b_{education}=-0.11, 95$  % CI

[-0.72, 0.50], p = .715).

Moreover, A $\beta$ + aMCI patients recognized fewer old faces in the forced-choice recognition task than older controls (W = 372.0, p = .005, r = -0.407), even when including education in the analysis ( $b_{group}$  = -10.83, 95 % CI [-17.46, -4.20], p = .003;  $b_{education}$  = -0.32, 95 % CI [-1.32, 0.68], p = .538).

#### 2.3. Discriminability performance on the PC yes/no recognition task

The LME with the discriminability  $\log d$  measure as the dependent variable, the group as the between-subject factor and the blurring degree as the within-subject factor evidenced a group effect (b=-0.17,95% CI [-0.336,-0.003],p=.046), but no interaction with the blurring degree (p-values >0.05; Fig. 3A) on the discriminability performance. Moreover, the blurring manipulation had an effect on the  $\log d$  measure. The  $\log d$  index for the highest blurring degree was lower than  $\log d$  measures for the non-blurred faces and the lowest blurring degree ( $b_{0px\ vs.\ 4px}=0.03,p=.952;b_{0px\ vs.\ 8px}=0.13,p=.105;b_{0px\ vs.\ 12px}=0.21,p=.001;b_{4px\ vs.\ 8px}=0.10,p=.297;b_{4px\ vs.\ 12px}=0.18,p=.008;b_{8px\ vs.\ 12px}=0.08,p=.453$ ). The LME, including education as a covariate, did not highlight any relevant contribution of this variable to the  $\log d$  performance (b=0.002,95% CI [-0.01,0.02],p=.777).

#### 2.4. Discriminability performance on the PS yes/no recognition task

On the PS Yes/No recognition task,  $A\beta+$  aMCI had a globally lower

performance than the control group (b=-0.21, 95 % CI [-0.38, -0.04], p=.016). In addition, the morphing manipulation affected the log d indexes. Each contrast showed log d differences between morphing levels, except between the non-morphed (new) faces and the morphed faces containing 15% of old (i.e., familiarized) faces, and between the intermediate (morphed faces containing 30% of the original faces) and highest level of similarity with the old faces (morphed faces containing 45% of the original faces;  $b_{0\% \ vs.} \ 15\% = 0.08$ , p=.119;  $b_{0\% \ vs.} \ 30\% = 0.23$ , p<.001;  $b_{0\% \ vs.} \ 45\% = 0.29$ , p<.001;  $b_{15\% \ vs.} \ 30\% = 0.15$ , p<.001;  $b_{15\% \ vs.} \ 45\% = 0.21$ , p<.001;  $b_{30\% \ vs.} \ 45\% = 0.06$ , p=.376). No interaction was observed between the group and the morphing degree on the discriminability performance (p-values > 0.05; Fig. 3B). The LME, including education as a covariate, did not evidence any relevant contribution of this variable to the log d performance (b=0.006, 95% CI [-0.02, 0.03], p=.638).

#### 2.5. Discriminability performance on the PC discrimination task

The log d measure was lower in A $\beta$ + aMCI patients than in the control group (b=-0.15, 95 % CI [-0.29, -0.005], p=.042). There was no interaction between the group and the blurring degree on performance (p-values > 0.05; Fig. 3C). The blurring manipulation influenced the log d measure, the latter being lower for the highest blurring degree compared to the other conditions ( $b_{0px\ Vs.\ 4px}=0.03$ , p=.862;  $b_{0px\ Vs.\ 8px}=0.09$ , p=.156;  $b_{0px\ Vs.\ 12px}=0.23$ , p<.001;  $b_{4px\ Vs.\ 8px}=0.06$ , p=.548;  $b_{4px\ Vs.\ 12px}=0.19$ , p<.001;  $b_{8px\ Vs.\ 12px}=0.14$ , p=.010).

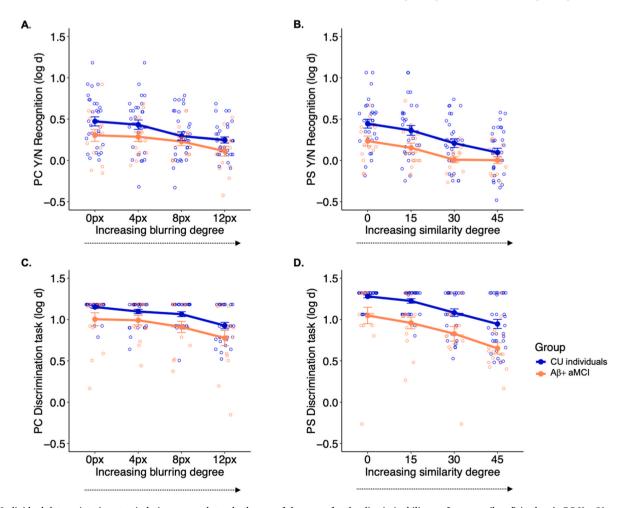


Fig. 3. Individual data points (empty circles), mean and standard error of the mean for the discriminability performance (log d) in the: A. PC Yes/No recognition task, B. PS Yes/No recognition task, C. PC Yes/No discrimination task, and D. PS Yes/No discrimination task, depending on the blurring (i.e., the radius of the added Gaussian blur) or the morphing degree (i.e., morphed faces contained 15/30/45% of the old faces). CU = cognitively unimpaired;  $A\beta + aMCI = amyloid$  positive amnestic Mild Cognitive Impairment.

Education did not contribute to performance (b = -0.005, 95 % CI [-0.02, 0.01], p = .518).

#### 2.6. Discriminability performance on the PS discrimination task

#### 2.7. Correlational analyses between scores in the experimental tasks

Every two-by-two association between scores in the experimental tasks was positive and globally of weak (0.2  $\leq r <$  0.4) to moderate (0.4  $\leq r <$  0.6) strength, over the entire sample (Fig. 4A). Analyses performed in each group separately evidenced positive moderate to strong (0.6  $\leq r <$  0.8) correlations in A $\beta+$  aMCI patients, while correlations were globally negligeable or weak in CU older individuals (Fig. 4B-C).

## 2.8. Correlational analyses between scores in the experimental tasks and standard cognitive measures

Over the entire sample, performance in the viewpoint-matching task and the PS discrimination tasks were the metrics that correlated the most with standard cognitive measures, including the MMSE and the FCSRT sum of the free and total recalls (Fig. 5A). When analyses were performed within each group, there was no significant association between experimental tasks and standard cognitive measures (Fig. 5B-C).

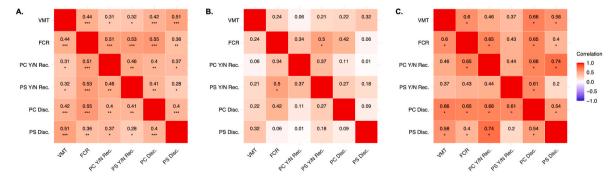
#### 3. Discussion

This study primarily aimed to investigate newly learned FIR abilities in prodromal AD patients, defined as being  $A\beta+$  aMCI, in the light of the PC and PS framework. We used Yes/No recognition and no-delay discrimination tasks with parametrically controlled blurred or morphed facial stimuli. Analyses highlighted a modulation of the behavioral outcomes in response to a parametric alteration of the degree of similarity/degradation of stimuli. This modulation is expected in

tasks assessing PC and PS (K. Y. Liu et al., 2016) and in line with previous studies showing an influence of morphing or blurring on explicit facial identity recognition or discrimination performance (Balas et al., 2019; Campanella et al., 2000; Collishaw and Hole, 2000; Rossion et al., 2001).

FIR is supported by multiple processes along the ventral occipitotemporal cortex (Jacques et al., 2020) and temporal regions are particularly affected by AD pathology from its early stages (Braak and Braak, 1991). Therefore, we hypothesized that newly learned FIR might be impaired in prodromal AD patients compared to controls, especially in PC and PS conditions. Our analyses showed that  $A\beta+$  aMCI patients had lower performance than CU older individuals in the forced-choice recognition task and the Yes/No PC and PS recognition tasks, regardless of the PC and PS demands of the tasks. These results are consistent with previous PS studies in aMCI and/or AD patients (Ally et al., 2013; Stark et al., 2013; Yassa et al., 2010) that documented a general recognition impairment (of objects) coupled with impaired performance in PS conditions in these patients (Ally et al., 2013; Stark et al., 2013). However, contrary to our assumption, no interaction was found between the group and the blurring or morphing degree in the Yes/No PC nor PS recognition tasks. Our hypothesis was based on the finding of Stark et al. (2013), which evidenced a shift in the PS performance curve in MCI patients compared to CU older individuals. This discrepancy could be linked to the methodological differences in the items that were used (objects vs. cropped faces) and/or in the similarity manipulations that were implemented (lure stratification into bins of increasing degrees of "mnemonic" similarity based on the probability of responding "old" to these lures vs. parametrically controlled morphing).

The most significant finding of the present study was that prodromal AD patients demonstrated poorer performance than CU older individuals in the facial matching and no-delay discrimination tasks, which did not imply any FIR demands in episodic memory. Precisely, prodromal AD patients showed lower performance than controls in the familiarization task, which required matching faces across different viewpoints, and in the PC and PS discrimination tasks, which required determining whether two simultaneously presented faces, a proportion of which was manipulated (i.e., blurred or morphed), were identical or not. While initially unexpected, these results agree with behavioral studies that evidenced impaired performance in AD patients in tasks requiring participants to match faces across identical or different viewing conditions (Adduri and Marotta, 2009; Kurth et al., 2015), as in the familiarization task of the present study. Our results are also in line with a study in which 12 aMCI patients and 12 healthy elderly individuals were instructed to indicate which face identity among the three was different, the vertical position of the mouth, inter-ocular distance, or eye brightness being modified in one of these faces (Lim et al., 2011). With limited time presentation (i.e., 2 s), aMCI patients



**Fig. 4.** Correlational matrices between experimental subtasks: A. over the entire sample, B. in CU older individuals, C. in Aβ+ aMCI patients. VMT = Viewpoint-matching task; FRC = Forced-choice recognition task; PC Y/N Rec. = mean log d over the trials involving blurred faces in the PC Yes/No recognition task; PS Y/N Rec. = mean log d over the trials involving morphed faces in the PS Yes/No recognition task; PC Disc. = mean log d over the trials involving blurred faces in the PC discrimination task; PS Disc. = mean log d over the trials involving morphed faces in the PS discrimination task. p < 0.10, p < 0.05; p < 0.01; p < 0.05; p < 0.01 (adjusted p-values using the Benjamini-Hochberg correction).

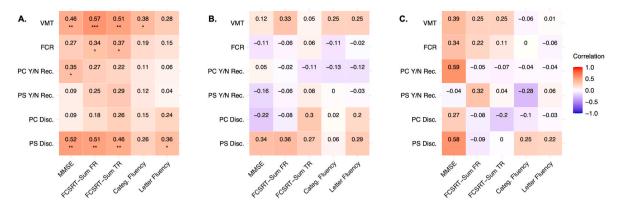


Fig. 5. Correlational matrices between experimental subtasks and standard cognitive measures: A. over the entire sample, B. in CU older individuals, C. in Aβ+ aMCI patients. VMT = Viewpoint-matching task; FRC = Forced-choice recognition task; PC Y/N Rec. = mean log d over the trials involving blurred faces in the PC Yes/No recognition task; PS Y/N Rec. = mean log d over the trials involving morphed faces in the PS Yes/No recognition task; PC Disc. = mean log d over the trials involving blurred faces in the PC discrimination task; PS Disc. = mean log d over the trials involving morphed faces in the PS discrimination task; FCSRT FR = Free and Cued Selective Reminding Test – Sum of Free Recalls; Categ. Flu. = category fluency; Letter Flu. = Letter fluency. p < 0.10, p < 0.05; p < 0.01; p

performed less accurately and less quickly than CU individuals for all three types of face modifications. However, with unlimited time presentation, patients achieved an expected performance level for the configural changes to the mouth but remained impaired for the changes to the eye region.

Interestingly, prodromal AD patients' difficulties in explicit and behavioral discrimination tasks do not appear to be limited to tasks using facial stimuli. Another line of studies using non-facial stimuli showed that individuals with MCI or focal medial temporal lobe (MTL) lesions were impaired in tasks requiring complex discrimination, especially when the visual similarity of the object stimuli was high and created substantial perceptual interference (Barense et al., 2012; Martin and Barense, 2023; Newsome et al., 2012). By nature, faces are characterized by a high intraclass similarity (Werheid and Clare, 2007), as they share a common configuration of features. In the current experiment, facial visual similarity was particularly pronounced as face stimuli were devoid of external features and their physical similarity was even parametrically incremented in the PS conditions. Therefore, the repeated presentation of cropped faces may have generated massive interference in processing these faces and led to poorer performance in prodromal AD patients in the familiarization and no-delay discrimination tasks. In addition, considering the own-age bias in face recognition (i.e., better recognition of faces from people of one's own age; Rhodes and Anastasi, 2012), one may assume that the exclusive use of young faces may also have contributed to increase fine-grained discrimination demands in our sample of older adults.

The observation of impaired behavioral discrimination of simultaneously presented items in MCI patients aligns with accumulating evidence implicating the perirhinal cortex in behavioral fine-grained discrimination of highly confusable stimuli (see Bastin and Delhaye, 2023; Martin and Barense, 2023 for reviews). This region is vulnerable to age-related alterations (Burke et al., 2011) and represents one of the earliest sites to demonstrate neurofibrillary tangles accumulation in AD, before the hippocampal stage (Braak and Braak, 1991). Therefore, the perirhinal cortex is substantially affected by AD neuropathological changes at the prodromal stage. Located at the apex of the ventral visual stream, this cortical region is thought to represent stimuli in their most integrated form (Bastin and Delhaye, 2023) and to promote stronger orthogonalization within the hippocampus (Amer and Davachi, 2023) that further supports encoding of contextual information through associative processes (Chen et al., 2021).

Nevertheless, it is noteworthy that behavioral no-delay matching and discrimination tasks solicit many different cognitive processes, beyond PS/PC, that are most likely supported by widely distributed cerebral

networks. These tasks require understanding and remembering instructions, visually exploring the displayed stimuli, rapidly building a visual representation of each item, making eve movements between stimuli, maintaining visual information in short-term/working memory while shifting attention between the visual stimuli to compare them, deciding on the answer to give, and producing the answer. In the current study, the PC discrimination task further required completing the blurred facial patterns, while the PS discrimination task required separating highly similar facial patterns. Therefore, the decreased performance highlighted in the familiarization and discrimination tasks in patients could be at least partly linked to a deficit in one or several of these processes. Regarding visual exploration of faces, one study showed that AD patients fixated less on diagnostic regions (i.e., the eyes) and attended more to areas peripheral to the faces than CU older individuals in an emotion identification task (Ogrocki et al., 2000). Another study showed that aMCI patients looked more at the mouth region than CU older individuals in a short-term face memory task (Kawagoe et al., 2017). However, the eye region and the region between the eyes and nose, rather than the mouth region, are the most informative face areas for optimal face identification (Peterson and Eckstein, 2012; Schyns et al., 2002). Regarding the building of visual representations, Tippett (2003) assessed different stages of visual perception by submitting mild-to-moderate AD patients and CU older individuals to a selective test battery. These authors highlighted an impairment in basic shape perception that could account for impairments in higher-level visual tasks (i.e., tasks assessing object shape constancy or stored shape representations) but that felt short of explaining the poorer performance of AD patients in an unfamiliar face identity matching task (i.e., short version of the Benton Facial Recognition Test, Benton & Van Allen, 1968). Compared to other types of visual stimuli, it is well-established that faces are processed qualitatively differently (Yin, 1969), based on specific neural representations (Busigny et al., 2010; Jonas et al., 2016; Kanwisher et al., 1997; Sergent et al., 1992). Specifically, faces are thought to be represented holistically, i.e. with no separate representation of their features ("eyes", "nose", "mouth", etc.; Farah et al., 1998; Rossion, 2013) at a finer grained level of resolution. One study suggested that AD patients had a specific impairment in building holistic visual representations of individual faces by highlighting a reduced face inversion effect in AD patients compared to healthy elderly participants (Lavallée et al., 2016). This finding is in line with AD-related morpho-functional abnormalities in face-selective brain regions (Bokde et al., 2006; Wang et al., 2015) and altered electrophysiological responses to faces (i.e., reduced face-sensitive N170 component) that were evidenced in MCI and AD patients (Feuerriegel et al., 2015; Mazzi et al.,

2020). Thus, a deficit in the holistic processing of faces in prodromal AD patients may also contribute to impaired performance in the familiarization and discrimination tasks. Alternatively, impaired ability to maintain correctly integrated facial representations online to compare them may also contribute to the prodromal AD patients' lower performance in familiarization and discrimination tasks. Future studies will be needed to disentangle the cognitive processes explaining this deficit.

Regarding correlational analyses, scores in all experimental tasks were weakly to moderately positively associated over the entire sample, implying common underlying cognitive processes involved in these different tasks (e.g, processes involved in the building of facial representations, attentional resources, decision-making processes). Correlations appeared mainly driven by the patients' group, as suggested by the correlational analyses performed within each group, likely due to lower variability and/or ceiling effects in some subtasks (e.g., viewpointmatching task, discrimination tasks) in the CU older group. Moreover, over the entire sample, performance in the viewpoint-matching task and the PS discrimination tasks were the measures that demonstrated the highest correlation coefficients with standard cognitive scores compared to the metrics in the other experimental tasks. In particular, the viewpoint-matching task and the PS discrimination performance showed moderate to strong positive associations with the MMSE and the verbal episodic memory measures (FCSRT - sums of free and total recalls). Implemented within each group, these correlation coefficients became globally negligeable or weak. However, the MMSE and the FCSRT metrics were used to define the CU and aMCI status, leading to lower score variability within each group. Correlations over the entire sample may be considered as being representative of how explicit facial identity matching or discrimination abilities evolve along the progressive decline of the global cognitive status and episodic memory occurring from CU stages to the early symptomatic stages of AD.

The strengths of the present study include the combined investigation of both old/new face identity recognition and simultaneous facial discrimination, and patients' inclusion based on both AD biomarker and cognitive criteria. However, the cognitively unimpaired individuals did not undergo any amyloid examination. Therefore, we cannot ascertain that these participants did not present an underlying AD pathology at an asymptomatic stage. Another limitation relates to the small sample size of prodromal AD patients. Nevertheless, the group effect was medium to large in specific subtasks (i.e., viewpoint-matching task, forced-choice recognition task). In addition, participants were white Caucasian and had high educational levels, limiting the results' generalizability. Moreover, in the current design, every participant completed the PC and PS recognition and discrimination tasks in the same order. This choice was made as we considered that the morphing manipulation might have led to excessive interference in face representation rather than blurring but a balanced design was not tested. Furthermore, this study specifically focused on behavioral facial identity discrimination and recognition performance, which likely rely on processes analogous to PS/PC. Neural evidence supporting this hypothesis could be explored through functional neuroimaging and/or electrophysiology.

Despite the mentioned limitations, the current study highlighted that prodromal AD patients were impaired in tasks requiring no-delay matching and discrimination of facial patterns, in addition to a general FIR deficit. Further research is needed to disentangle the cognitive processes that might be responsible for poor performance in newly learned FIR and facial discrimination tasks. One avenue could be to use implicit measures of face identity discrimination with electroencephalography (EEG), in particular the highly sensitive tests developed over the past decade with fast periodic visual stimulation (FPVS), providing objective, implicit, and directly quantifiable responses of unfamiliar face discrimination (Liu-Shuang et al., 2014; Rossion et al., 2020 for review) and its impairment (Fisher et al., 2020; Liu-Shuang et al., 2016).

Furthermore, future work should investigate whether an isolated behavioral PC or PS impairment could be identified earlier in the course of AD and serve as a preclinical marker. Indeed, a dissociation between preserved general memory recognition and impaired PS abilities was reported in CU individuals identified as "at-risk" of cognitive decline (i. e., because they were in the bottom third of normal ranked scores on an episodic memory test), suggesting that isolated behavioral PS impairment could be identified at a pre-symptomatic stage (Stark et al., 2013). The hemodynamic responses in a PS recognition task involving objects were even found altered in young adults carrying the APOE allele e4 (H. Lee et al., 2020), one of the most critical AD genetic risk factors (C.-C. Liu et al., 2013).

#### CRediT authorship contribution statement

Lisa Quenon: Writing – original draft, Visualization, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. Bruno Rossion: Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Methodology, Investigation, Conceptualization. Lara Huyghe: Writing – review & editing. Justine David: Writing – review & editing. John L. Woodard: Writing – review & editing, Validation, Formal analysis. Laurence Dricot: Writing – review & editing, Resources. Renaud Lhommel: Writing – review & editing, Resources. Bernard Hanseeuw: Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Methodology, Funding acquisition, Conceptualization. Adrian Ivanoiu: Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Methodology, Funding acquisition, Conceptualization.

#### Acknowledgements

During the design of the experiment and data acquisition, this research was supported by the Belgian Foundation for Scientific Research (FNRS) with grants awarded to L.Q. (ASP10975961) and B.H. (SPD28094292). At the time of data analysis and manuscript drafting, L. Q. and B.H. had support from the Belgian Foundation for Alzheimer's Research (grant P16008). B.H. was also funded by the FNRS (grant CCL40010417) and the FRFS-WELBIO (grant 40010035). L.H. was supported by the Belgian Foundation for Scientific Research (grant ASP40016560), and J.D. was funded by an ANRT CIFRE PhD fellowship (n°2021/0405). We are grateful to GE Healthcare Ltd. for providing [18F]Flutemetamol for the amyloid-PET imaging, per a convention with our clinic. We also thank Benvenuto Jacob for programming the experimental tasks, and Clémence Lefèvre and Jennifer Hoyaux for their assistance with data collection. The authors declare no potential conflicts of interest.

#### Data availability

Data will be made available on request.

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