

1 **Memorability of photographs in subjective cognitive decline and mild cognitive impairment:**
2 **implications for cognitive assessment**

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Abstract

INTRODUCTION: Impaired long-term memory is a defining feature of Mild Cognitive Impairment (MCI). We tested whether this impairment is item-specific, limited to some memoranda whereas some remain consistently memorable.

METHODS: We conducted item-based analyses of long-term visual recognition memory. 394 participants (healthy controls (HC), Subjective Cognitive Decline (SCD), and MCI) in the multicentric DZNE-Longitudinal Cognitive Impairment and Dementia Study (DELCODE) were tested with images from a pool of 835 photographs.

RESULTS: We observed consistent memorability for images in HCs, SCDs, and MCI, predictable by a neural network trained on another healthy sample. Looking at memorability differences between groups, we identified images that could successfully categorize group membership with higher success and a substantial image reduction than the original image set.

DISCUSSION: Individuals with SCD and MCI show consistent memorability for specific items, while other items show significant diagnosticity. Certain stimulus features could optimize diagnostic assessment, while others could support memory.

Keywords: Alzheimer’s disease (AD), subjective cognitive decline (SCD), mild cognitive impairment (MCI), memorability, diagnostic assessment, image analysis

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1. Background

80 Recent work in healthy individuals has found that certain images are intrinsically
81 memorable or forgettable across observers [1,2]; there are images of faces or scenes that most
82 people remember or forget, regardless of their different individual experiences. This
83 *memorability* of an image can be quantified and predicts 50% of the variance in people's
84 performance on a memory test [2]. Viewing memorable images automatically elicits specific
85 neural signatures [3,4], and the memorability score of an image can be predicted by
86 computational models [5,6]. However, image attributes such as aesthetics, emotionality,
87 typicality, or what people believe will be memorable do not fully predict memorability [2,7],
88 and memorability is an automatically processed image property that is resilient to the effects of
89 attention [8]. This means that researchers can predict in advance what images a person is likely
90 to remember or forget, and use such information to create memorable educational materials,
91 or design well-balanced memory tests.

92 While memorability has so far been characterized based on healthy participants'
93 memory behavior, it is unclear if memorability is also consistent in populations with memory
94 impairments at increased risk for Alzheimer's Disease (AD), such as Mild Cognitive Impairment
95 (MCI) or Subjective Cognitive Decline (SCD) [9]. Consistent memorability in SCD and MCI would
96 enable better prediction of what images are likely to be remembered or forgotten.
97 Furthermore, changes in memorability patterns across disease stages could improve cognitive
98 staging and design of cognitive progression markers. By avoiding highly memorable images,
99 cognitive tests could be made more time efficient and more sensitive. Understanding which
100 stimulus features improve or impair memorability could provide insights into the cognitive

101 processes that are impaired. Furthermore, knowledge about memorability could aid in the
102 design of memorable environments, or allow clinicians to focus on aiding memory for
103 forgettable items.

104 In the current study, we analyzed the results of a visual recognition memory test in
105 which each participant had to memorize a randomly selected subset of 88 photographs from a
106 pool of 835. This randomization afforded us the possibility to assess memorability
107 unconfounded by systematic effects of stimulus-selection or stimulus-order effects. Using data
108 from 394 individuals, including those with SCD, MCI, and healthy controls (HC), we identified
109 two meaningful sets of images: 1) images that can consistently predict performance of
110 participant groups, and 2) images that reliably differentiate groups.

111

112 2. Methods

113 **2.1 Study design**

114 Visual memory tests were analyzed from the DZNE-Longitudinal Cognitive Impairment
115 and Dementia Study (DELCODE), an observational, longitudinal memory clinic-based study
116 across 10 sites in Germany. Specific details about this study, the visual memory task, and data
117 handling and quality control are reported in Jessen et al. [10] and Düzel et al. [11]. The data
118 analyzed in this study were from the second data release from the DELCODE study comprising
119 of 700 individuals of which 394 participants with complete datasets were analyzed, including
120 136 participants with SCD, 65 with MCI, and 193 HC. Individuals with SCD and MCI were

121 recruited through referrals and self-referrals, while HC were recruited through public
122 advertisements.

123 The study protocol was approved by all involved centers' institutional review boards and
124 ethical committees, and all participants gave written informed consent. DELCODE is
125 retrospectively registered at the German Clinical Trials Register (DRKS00007966), (04/05/2015).

126

127 **2.2 Visual memory test**

128 Participants performed an fMRI scene image encoding and retrieval task [12]. First,
129 while in the fMRI scanner, participants studied 88 novel scene target images (44 indoor and 44
130 outdoor scenes) and 44 repetitions of two pre-familiarized images (one indoor and one outdoor,
131 22 times each). All images were 8-bit gray scale, presented on an MR-compatible LCD screen
132 (Medres Optostim), scaled to 1250 x 750 pixel resolution and matched for luminance, with a
133 viewing horizontal half-angle of 10.05° across scanners. Each image was presented for 2500ms
134 (with an optimized jitter for statistical efficiency), and participants categorized them as “indoor”
135 or “outdoor” with a button press. Outside of the scanner after a 70-minute delay, participants
136 completed a recognition memory task with these 88 images and 44 novel foil images (22 indoor
137 and 22 outdoor). Participants indicated their recognition memory with a 5-point scale: 1) *I am*
138 *sure that this picture is new*, 2) *I think that this picture is new*, 3) *I cannot decide if this picture is*
139 *new or old*, 4) *I think I saw this picture before*, or 5) *I am sure that I did see this picture before*.
140 Results from the fMRI study are reported in [12].

141 While each participant was tested on 88 target images and 44 foil images, these images
142 were randomly sampled from a larger set of 835 scene images, allowing us to conduct image-
143 based analyses on a large set of images (see Figure 1 for example images). This randomization
144 allowed us to avoid confounding effects of image selection and image order on memory
145 performance. On average, each image served as a target image for 20.3 HC, 14.3 SCD, and 6.8
146 MCI individuals.

147

148 **2.3 Analyzing similarity of MCI, SCD, and healthy individuals: Predicting performance**

149 We first asked whether there are consistencies in memory performance for MCI and
150 SCD just as there are for healthy individuals [1]; i.e., whether there are certain images that
151 patients tend to remember or forget, and, if such consistencies exist, to what degree they align
152 with the images that tend to be remembered and forgotten by HCs.

153 To address this question, Spearman's rank correlations of hit rate (HR) performance on
154 images in the visual memory task were calculated between the different patient groups and
155 controls. To assess memorability consistency within patient groups, we conducted a *consistency*
156 *analysis* as described in Isola et al. [1], where participants are split into random halves (across
157 1000 iterations) and their hit rates for all images are calculated, and Spearman's rank
158 correlated between the two halves. We also examined whether a convolutional neural network
159 (CNN) that is significantly able to predict memory performance in healthy individuals [6] could
160 also predict memorability for SCD and MCI groups. MemNet is a CNN with the architecture and
161 pretraining set of Hybrid-CNN [13], a CNN able to classify thousands of object and scene images,

162 then trained to predict the memorability score of an image (i.e., the likelihood for that image to
163 be remembered by any given person). We obtained MemNet scores for each of the 835
164 stimulus images and used Spearman's rank correlations to test the degree to which MemNet-
165 predicted memory scores were correlated with patient group memory scores.

166

167 **2.4 Analyzing dissimilarity of MCI, SCD and healthy individuals: Differentiating patient groups**

168 An equally important question is whether there is a set of images in which consistencies
169 in memory performance reliably differ between patient populations and healthy individuals. If
170 such images exist, then they could form an optimized test to distinguish patients from healthy
171 controls with high efficiency.

172 To explore this question, we conducted an analysis we call the *Iterative Image Subset*
173 (IIS) *Analysis* to compare HC with MCI, and HC with SCD. First, the HC participant pool was
174 randomly downsampled so that the same number of HC were used in the analysis as MCI or
175 SCD individuals. The entire pool of participants was then split into two random halves (Group A
176 and Group B). HR on the memory task was calculated for each image for the HC ($HR_{GroupA,Healthy}$)
177 and for the patients ($HR_{GroupA,Patient}$) in Group A. Using this performance metric, we formed three
178 subsets of images. The number of images used in each subset was selected iteratively for all
179 possible subset sizes, ranging from 0% to 100% of images (835 images) in 1% increments, to
180 determine the optimal image subset size. The three resulting subsets were:

181 1) “H>P”, the top set of images where HC outperformed patients (i.e., maximizing

182 $HR_{GroupA,Healthy} - HR_{GroupA,Patient}$)

- 183 2) “H<P”, the top set of images where patients outperformed HC (i.e., maximizing
184 $HR_{GroupA, Patient} - HR_{GroupA, Healthy}$)
185 3) “H=P”, the top set of images where HC performed most similarly to patients (i.e.,
186 minimizing $|HR_{GroupA, Healthy} - HR_{GroupA, Patient}|$)

187 We then assessed the performance of classifying subjects in Group B using each of the three
188 subsets of images. Specifically, using just the images in a single subset (e.g., H>P), we
189 determined the HR for each of the individuals in Group B (HR_{GroupB}). We then performed a
190 Receiver Operating characteristic (ROC) analysis to determine the diagnostic ability of this
191 subset of images, applying a range of HR cutoffs from 0 to 1 to classify an individual from Group
192 B as either HC or patient, using HR_{GroupB} . We calculated the accuracy of this test based on group
193 membership, and contrasted successful patient diagnosis (true positives) with misclassification
194 of HC (false positives). We assessed classification performance by Area Under the Curve (AUC),
195 where a score of 1 indicates perfect performance, while 0.5 indicates chance performance. This
196 complete analysis was conducted across 100 random participant splits into Group A and B.

197

198 **2.5 Finding image attributes that distinguish these image sets**

199 To see what aspects of the images may determine their membership into different
200 image sets, we conducted an experiment using the online crowd-sourcing platform Amazon
201 Mechanical Turk (AMT). For each of the 835 images, 12 online participants rated the scene in
202 the image on five relevant properties identified in previous scene perception and memorability
203 research [7,14] using a 5-point Likert scale: size (of the portrayed scene), clutter, aesthetics,

204 interest, and whether they think they would remember the image (subjective memorability).
205 They also indicated whether the image showed a natural or manmade scene and if there was a
206 person present. 450 people anonymously participated in the study and provided consent, and
207 this study was approved by the National Institutes of Health (NIH) Office of Human Subjects
208 Research Protections. Two main comparisons were tested for each attribute, using paired
209 samples t-tests: 1) forgettable versus memorable images with similar performance between HC
210 and patients, 2) diagnostic versus non-diagnostic images, where HC and patients differed in
211 their performance. Forgettable and memorable images were identified as the top set of images
212 where both HC and patients had average performance below or above (respectively) median
213 performance, and the difference between groups was minimized (i.e., H=P). Diagnostic and
214 non-diagnostic images were selected from the sets resulting from the IIS analysis (Section 2.4),
215 e.g., H>P and H<P image sets, respectively. The number of images in each set was taken as the
216 optimal number of images identified from the IIS analysis.

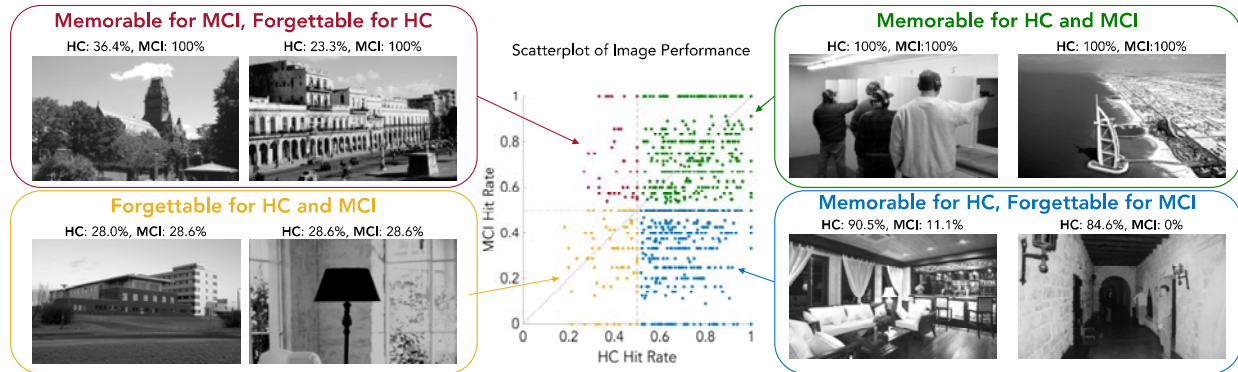
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3. Results

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Figure 1: Example images and group performance. The scatterplot shows the distribution of memory performance

(hit rate) for all 835 images for healthy controls (HC) versus individuals with Mild Cognitive Impairment (MCI). The

diagonal line indicates the points at which performance is equal between both groups. Based on performance,

images can be conceptually sorted into four quadrants: 1) images that are memorable to both HC and MCI

individuals (green), 2) images that are memorable to HC but forgettable to MCI (blue), 3) images that are

forgettable to both groups (yellow), and images that are memorable to MCI but forgettable to HC (red). Example

images and performances at the extreme ends for each quadrant are arranged around the scatterplot. In the work

that follows, we analyze these four groups of images and determine if they can be used meaningfully to predict

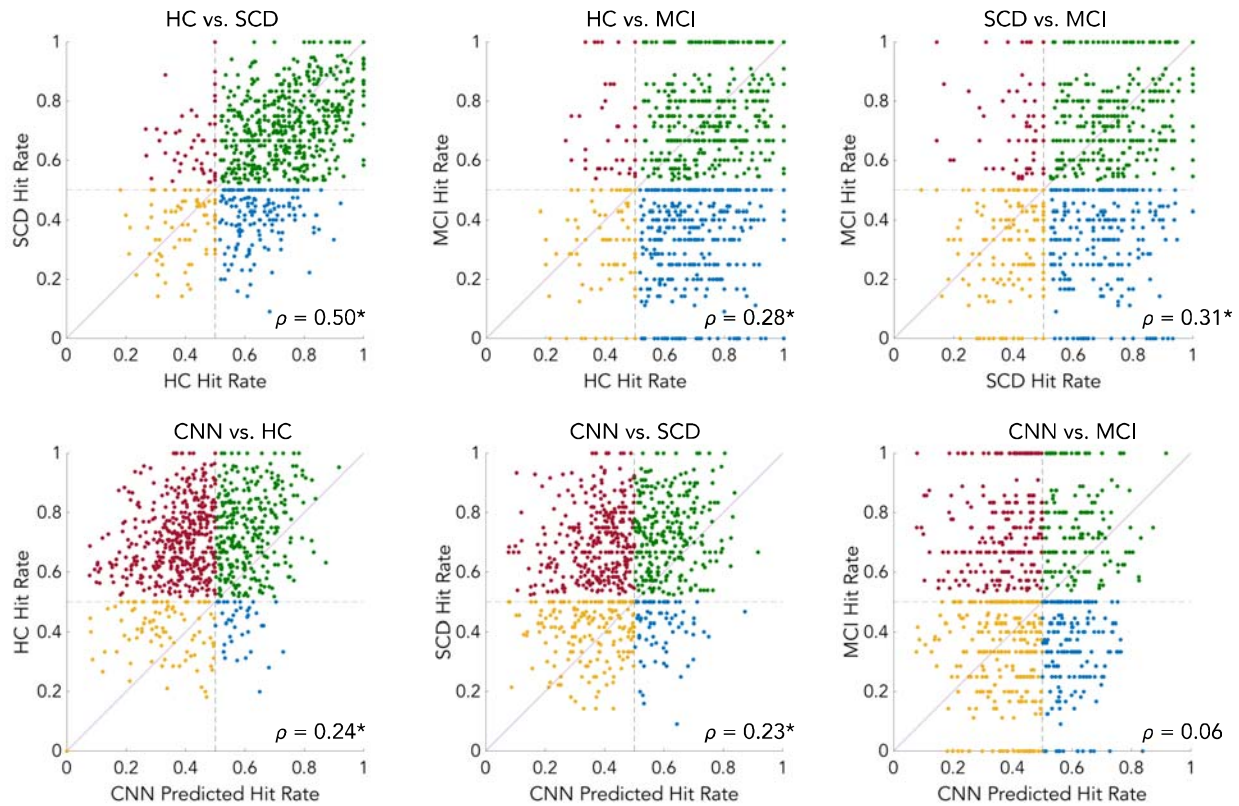
memory performance.

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232 3.1 Consistencies in the memories of patient groups

Scatterplots of Image Performance



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234 **Figure 2: Consistencies across groups and neural networks.** The scatterplots show a comparison of hit rates for
235 each of the 835 images between all pairings of the experimental groups (Healthy Controls, HC; Subjective Cognitive
236 Decline, SCD; Mild Cognitive Impairment, MCI), as well as predicted hit rate from a convolutional neural network
237 (CNN) trained to predict memorability scores. Asterisks (*) indicate significant Spearman's rank correlations.
238 Scatterplot points are colored by quadrant (as in Figure 1), and the diagonal line indicates points where both
239 groups show equal performance.

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241 As expected, patient groups of increasing memory impairment showed decreases in
242 average memory performance (HC: M=0.68, SD=0.17; SCD: M=0.62, SD=0.18; MCI: M=0.53,

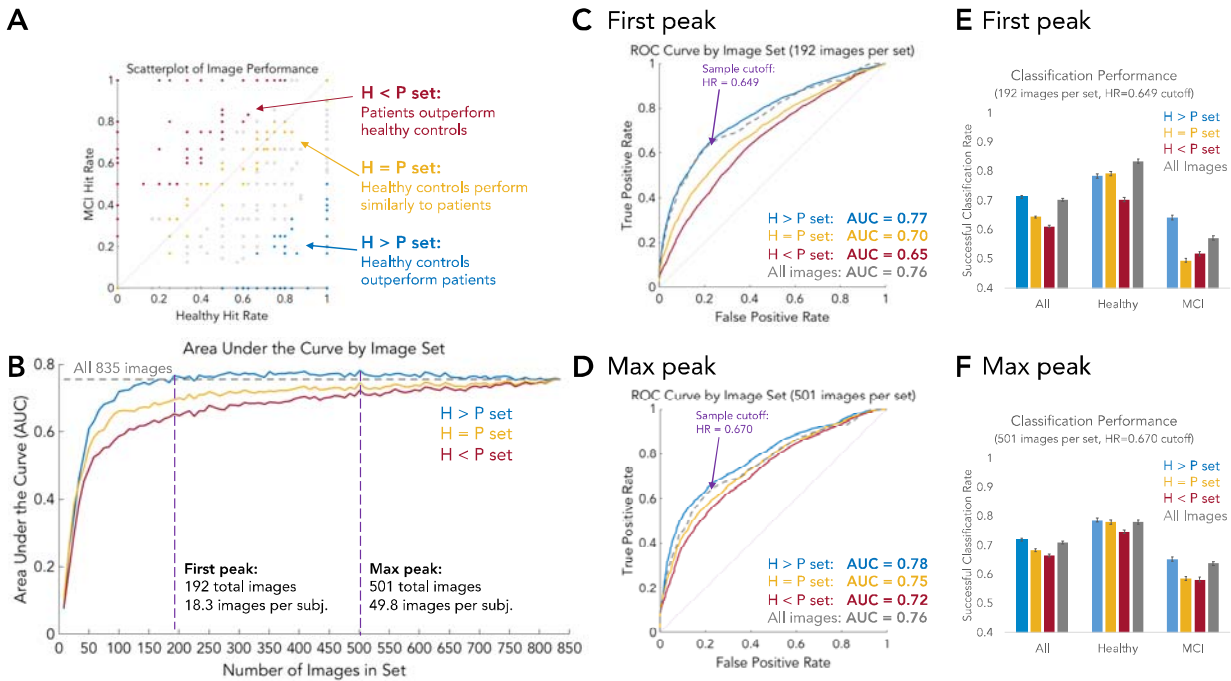
243 SD=0.26). However, there were also impressive correlations across groups in the images they
244 remembered best or worst (Figure 2). HC and SCD had a significant Spearman's rank correlation
245 of $\rho=0.50$ ($p=1.03 \times 10^{-54}$), while HC and MCI had a significant correlation of $\rho=0.28$ ($p=1.34 \times$
246 10^{-16}), and SCD and MCI had a significant correlation of $\rho=0.31$ ($p=2.12 \times 10^{-19}$). HC performance
247 was significantly more similar to SCD performance than MCI performance ($Z=6.13$, $p \sim 0$), and
248 SCD performance was significantly more similar to HC performance than MCI performance
249 ($Z=5.42$, $p \sim 0$). These results indicate that patient groups and healthy elderly individuals tended
250 to remember the same images as each other. All groups were also internally consistent (HC:
251 $\rho=0.42$; SCD: $\rho=0.32$; MCI: $\rho=0.22$; all $p < 0.0001$), meaning a patient will tend to remember
252 similar images to someone else with the same diagnosis.

253 The MemNet CNN trained to predict image memorability showed significant
254 correlations with HC ($\rho=0.24$, $p=3.29 \times 10^{-12}$) and SCD behavior ($\rho=0.23$, $p=1.84 \times 10^{-11}$), while
255 MCI behavior correlations did not pass significance thresholds ($\rho=0.06$, $p=0.080$).

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258 3.2 Differentiating patient groups from healthy controls



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260 **Figure 3: Finding the optimal number of images to diagnose MCI.** A) This scatterplot of image performance shows
 261 an example of the three possible subsets the images can be divided into: H<P (red), H=P (yellow), and H>P (blue).
 262 B) Area Under the Curve (AUC) by image set and number of images in the set. Testing each of these subset types at
 263 different set sizes, we find that the H>P set (blue line) consistently outperforms the other image subsets at all set
 264 sizes. Importantly, the H>P set also outperforms the all-image set (gray dotted line) at a surprisingly small number
 265 of images, first overtaking the all-image set at only 192 images versus the 835 images used in the all-image set.
 266 From this set of 192 images, each participant saw on average only 18.3 images. C & D) Receiver Operating
 267 Characteristic (ROC) curves for two peaks – the first peak where H>P overtakes the all-image set, and the max peak
 268 where H>P has the largest difference from the all-image set. E & F) Participant classification performance,
 269 averaged across 100 iterations of participant split-halves, at a sample cutoff (determined as the point where the
 270 *true positive rate + (1 - false positive rate)* is at its maximum), broken down by participant type for the different
 271 image sets. Error bars indicate standard error of the mean across the 100 iterations. Note that the optimized H>P
 272 image subset particularly shows a boost in patient diagnosis sensitivity overall other image sets.

273

274 As a first test, we examined the ability to differentiate HC and MCI individuals. The IIS
275 analysis shows that the H>P image subset consistently outperforms the H=P and H<P image
276 subsets at all subset sizes, in diagnosing individuals as MCI versus HC (Figure 2). This means that
277 images that are highly memorable to healthy controls but highly forgettable to patients are
278 best able to distinguish these two groups. Surprisingly, H>P image subsets as small as 23% of
279 the original image set were able to surpass the original image set in diagnostic ability. With only
280 192 total images (or 18.3 images seen per participant), the diagnosis AUC was 0.77, while using
281 the full set of 835 images resulted in an AUC of 0.76. At this 192-image subset size, the
282 difference between subsets is also clear: the H=P set only reaches an AUC of 0.70, while the
283 H<P set performs worse with an AUC of 0.65.

284 Differentiating HC from SCD individuals shows similar results, even though the two
285 groups have more similar memory performance. The AUC of the H>P set is higher than those of
286 H=P and H<P at all image subset sizes, and the H>P subset first overtakes performance of the
287 full image set at only 92 images in the subset. The AUC for the full image set is 0.59, while with
288 the 92-image subset, the AUC of H>P is also 0.59. In regard to the other image subsets, the AUC
289 for H=P is 0.57, and for H<P it is 0.55. H>P reaches a maximum of performance at a subset size
290 of 367 images, with an AUC of 0.61.

291 We also determined if the image subsets generalized across groups. We performed the
292 IIS analysis by training on MCI data to determine the image subsets, but then testing those
293 images with SCD data. We find these subsets generalize to each other: the H>P image subset

294 shows higher performance than the other image subsets (H=P, H<P), and first overtakes
295 performance of all images (AUC=0.60) at a subset size of only 100 images (H>P: AUC=0.60; H=P:
296 AUC=0.50; H<P: AUC=0.55). The H>P image subset reaches its peak in performance at 417
297 images, at an AUC of 0.63.

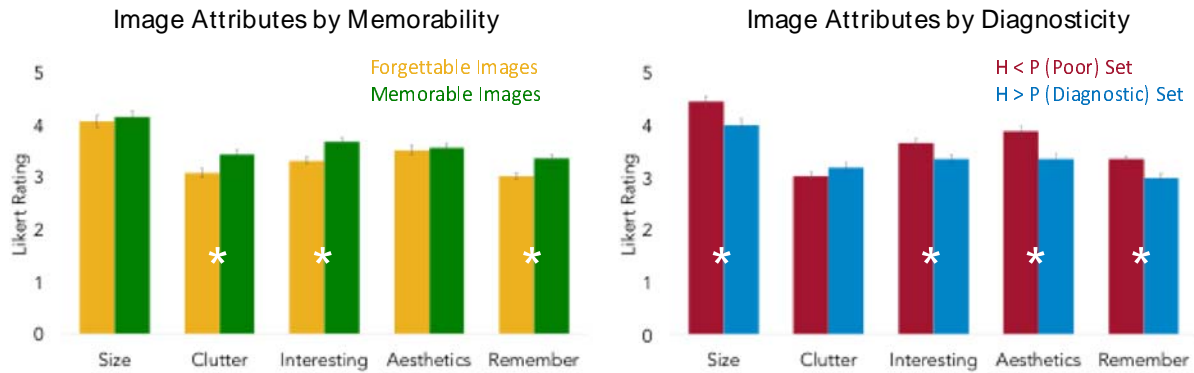
298 These results show that using a small, honed subset of images results in higher
299 diagnostic performance than a large, exhaustive set of images, for both SCD and MCI
300 populations. Additionally, using a poor set of images (e.g., H<P) could result in a high diagnosis
301 failure rate. We also find that diagnostic images can successfully transfer across groups; using
302 images that identify MCI can also successfully identify SCD. Since all of the above tests use
303 separate halves of the participants to determine the diagnostic images and to predict group
304 membership, this image diagnosticity is likely to translate to other participant samples as well
305 as other experimental contexts.

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3.3 Image attributes that distinguish these image sets

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311 **Figure 4: Average attribute ratings based on image set.** (Left) Comparison of average attribute ratings between
312 images that are forgettable versus memorable to both HC and individuals with MCI or SCD. (Right) Comparison of
313 average attribute ratings between images from the poorly diagnostic image set (H<P) versus highly diagnostic set
314 (H>P). (Both) All attributes are rated on a Likert scale of 1 (low) to 5 (high). “Remember” is a rating of how likely
315 participants believed they’d be able to remember the image. Asterisks indicate significant differences in a paired
316 samples t-test ($p < 0.05$). Error bars indicate standard error of the mean.

317

318 Finally, we investigated image attributes related to why an image is memorable to both
319 groups, or why it is diagnostic (Figure 4). Focusing on images that have highly correlated
320 performance between patients and healthy controls, memorable scene images tended to
321 contain more clutter ($t(191)=2.84, p=0.005$), appeared more interesting ($t(191)=3.30, p=0.001$),
322 and were subjectively more memorable to healthy controls ($t(191)=3.59, p=4.17 \times 10^{-4}$).
323 However, they were not different in scene spatial size ($p=0.567$) nor aesthetics ($p=0.752$). In
324 terms of content, memorable versus forgettable images tended to be manmade rather than
325 natural (forgettable: 76.6% manmade, memorable: 87.0%; $Z(191)=2.64, p=0.008$), but were

326 equally likely to be indoors (forgettable: 52.1% indoors; memorable: 50.5%; $p=0.76$) and
327 contain people (forgettable: 7.8% contained people; memorable: 13.0%; $p=0.09$).

328 Focusing on images that show large differences between healthy controls and patients,
329 successfully diagnostic images versus non-diagnostic images tended to be of smaller spaces
330 ($t(191)=3.05$, $p=0.003$), were less interesting ($t(191)=2.81$, $p=0.005$), less aesthetic ($t(191)=4.04$,
331 $p=7.70 \times 10^{-5}$), and were judged to seem more forgettable by healthy controls ($t(191)=3.79$,
332 $p=2.05 \times 10^{-4}$), but showed no difference in clutter ($p=0.153$). In terms of content, diagnostic
333 images tended to be manmade (non-diagnostic: 72.4%; diagnostic: 83.9%; $Z(191)=2.72$,
334 $p=0.007$), indoors (non-diagnostic: 37.5%; diagnostic: 55.7%; $Z(191)=3.58$, $p=3.40 \times 10^{-4}$), and
335 contained people (non-diagnostic: 5.2%; diagnostic: 17.7%; $Z(191)=3.85$, $p=1.20 \times 10^{-4}$).
336 Memorable images were significantly more interesting ($t(191)=2.80$, $p=0.006$) and seemed
337 subjectively more memorable ($t(191)=3.55$, $p=4.86 \times 10^{-4}$) than diagnostic images. This shows
338 that diagnostic images that patients forget but healthy controls remember tend to be those
339 that are generally less aesthetic or interesting, yet are manmade, indoor scenes containing
340 people.

341

342 4. Discussion

343 While individuals with SCD and MCI have decreased memory performance in
344 comparison to HC, there is a considerable overlap in the images that they remember and forget.
345 Thus, there are images that are highly memorable and forgettable to everyone regardless of
346 diagnosis. These consistencies in memorability exist not only between patient groups and

347 healthy controls, where consistencies in memorability are already well-established for controls
348 [1,2], but also within patient groups themselves. Our questionnaire-based assessment of image
349 attributes revealed that this common memorability is not related to aesthetics or spaciousness,
350 but to being manmade scenes that contain more objects, and are subjectively more memorable
351 and interesting. While previous work has reported that ratings of interestingness, subjective
352 memorability, and aesthetics are ultimately not predictive of scene memorability at a fine-
353 grained scale for healthy populations [7], such attributes may be important for guiding the
354 selection of images that are broadly memorable across population types.

355 Additionally, we show that a publicly available convolutional neural network (MemNet
356 [6]) trained to predict image memorability also aligns with performance of HC as well as those
357 with SCD and marginally with MCI. This raises the possibility that computational methods may
358 guide the selection of images for diagnostic or therapeutic tools on the basis of memorability.
359 Such tools may assist in creating or adapting environments to ease memory burdens on
360 patients by avoiding low memorability items, or focusing strategies on rehearsing particularly
361 forgettable information.

362 While memorability is generally consistent across HC, SCD, and MCI groups, we have
363 also identified a specific set of images that significantly differ between groups. Namely, we find
364 that there are images that are highly memorable to HC, yet highly forgettable to patients, and a
365 certain subset of these images can be used to best determine if an individual is likely to be
366 healthy or have MCI or SCD. The images generalize across impairments; images that
367 differentiate MCI also successfully differentiate SCD, indicating that SCD may show similar
368 cognitive impairments to those developed in MCI. This image set results in as much as a 10%

369 improvement in diagnostic performance in comparison to a poorly chosen set of images (e.g.,
370 images memorable to patients but forgettable to healthy controls). Further, this optimized
371 image set reaches peak diagnostic performance with as few as 18.3 images seen per participant,
372 classifying as well as the original set with 88 images per participant. This means that individuals
373 with MCI or SCD can be identified with higher certainty, and in a quicker, easier test. In terms of
374 content, these diagnostic images tended to be manmade, indoor scenes that contained people.
375 However, in contrast to memorable images, they tended to be less aesthetic, less interesting,
376 and seem subjectively less memorable. Scenes containing people tend to be the most
377 memorable [7], however it is perhaps the combination of memorable image content (e.g.,
378 people, manmade objects) yet lack of memorable qualities (e.g., interestingness, aesthetics)
379 that causes these images to be remembered by healthy controls but forgotten by patients.

380 Functional neuroimaging work with healthy individuals has found that viewing
381 memorable images results in automatic, stereotyped activity patterns in the visual cortex and
382 medial temporal lobe [3,4]. In future work, investigating the neural fate of memorable and
383 forgettable images in older individuals and those with SCD or MCI may aid in understanding
384 how patients may differentially process images at different processing stages of perception and
385 memory encoding. In the DELCODE study, we have indeed obtained fMRI data alongside the
386 behavioral data reported here [11] and will be able to address this question in the future. A
387 related question is how Alzheimer's pathology is related to memorability. For instance, we have
388 previously shown that increasing levels of CSF total-tau are related to decreasing novelty
389 responses in the amygdala and the hippocampus [11]. These functional consequences of tau-
390 pathology could influence memorability patterns in MCI or SCD. Indeed, activity in medial

391 temporal lobe regions shows early and automatic sensitivity to the memorability of an image in
392 healthy individuals [3]. Image diagnosticity as calculated in this study could also be related to
393 the biomarker status of individuals, a possibility that we will be able to address in the future
394 with larger sample sizes. It will also be important to better understand the features of an image
395 that drive it to be forgettable, memorable, or diagnostic. While the current work uses a CNN
396 trained on healthy participant memory data, as larger-scale patient data is collected, a CNN
397 could learn to identify images that would be particularly effective in diagnosing patients.

398 In sum, we show the importance of images themselves in predicting what patients are
399 likely to remember and differentiating patients from healthy individuals. Such insights will have
400 a meaningful impact in how we design cognitive assessment tools and tests for early diagnosis
401 of memory impairments, and in understanding how and why we process and remember certain
402 images over others in our complex, visual world.

403

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410 **Conflicts of Interest**

411 E. Düzel and D. Berron are co-founders of neotiv GmbH.

412

5. References

413 [1] P. Isola, J.X. Xiao, A. Torralba, A. Oliva, What makes an image memorable? 24th IEEE Comput
414 Soc Conf Comput Vis Pattern Recognit 2011;145-152.

415 [2] W.A. Bainbridge, P. Isola, A. Oliva, The intrinsic memorability of face photographs. J Exp
416 Psychol Gen 2013;142:1323-1334.

417 [3] W.A. Bainbridge, D.D. Dilks, A. Oliva, Memorability: A stimulus-driven perceptual neural
418 signature distinctive from memory. Neuroimage 2017;149:141-152.

419 [4] W.A. Bainbridge, J. Rissman, Dissociating neural markers of stimulus memorability and
420 subjective recognition during episodic retrieval. Sci Rep 2018;8:8679.

421 [5] A. Khosla, W.A. Bainbridge, A. Torralba, A. Oliva, Modifying the memorability of face
422 photographs. Proc IEEE Int Conf Comput Vis 2013.

423 [6] A. Khosla, A.S. Raji, A. Torralba, A. Oliva, Understanding and predicting image memorability
424 at a large scale. Proc IEEE Int Conf Comput Vis 2015:2390-2398.

425 [7] P. Isola, J. Xiao, D. Parikh, A. Torralba, A. Oliva, What makes a photograph memorable? IEEE
426 Trans Pattern Anal Mach Intell 2014;36:1469-1482.

427 [8] W.A. Bainbridge, The resiliency of memorability: A predictor of memory separate from
428 attention and priming. arXiv 2018.

429 [9] C.R. Jack, D.A. Bennett, K. Blennow, M.C. Carrillo, B. Dunn, S.B. Haeberlein, D.M. Holtzman,
430 W. Jagust, F. Jessen, J. Karlawish, E. Liu, NIA-AA Research Framework: Toward a biological
431 definition of Alzheimer's disease. Alzheimers Dement 2018;14:535-562.

- 432 [10] F. Jessen, A. Spottke, H. Boecker, F. Brosseron, K. Buerger, C. Catak, K. Fließbach, C. Franke,
433 M. Fuentes, M.T. Heneka, D. Janowitz, I. Kilimann, C. Laske, F. Menne, P. Nestor, O. Peters, J.
434 Priller, V. Pross, A. Ramirez, A. Schneider, O. Speck, E.J. Spruth, S. Teipel, R. Vukovich, C.
435 Westerteicher, J. Wiltfang, S. Wolfsgruber, M. Wagner, E. Düzel, Design and first baseline data
436 of the DZNE multicenter observational study on predementia Alzheimer’s disease (DELCODE).
437 *Alzheimers Res Ther* 2018;10:15.
- 438 [11] E. Düzel, D. Berron, H. Schütze, A. Cardenas-Blanco, C. Metzger, M. Betts, G. Ziegler, Y.
439 Chen, L. Dobisch, D. Bittner, W. Glanz, M. Reuter, A. Spottke, J. Rudolph, F. Brosseron, K.
440 Buerger, D. Janowitz, K. Fließbach, M. Heneka, C. Laske, M. Buchmann, P. Nestor, O. Peters, D.
441 Diesing, S. Li, J. Priller, E.J. Spruth, S. Altenstein, A. Ramirez, A. Schneider, B. Kofler, O. Speck, S.
442 Teipel, I. Kilimann, M. Dyrba, J. Wiltfang, C. Bartels, S. Wolfsgruber, M. Wawgner, F. Jessen, CSF
443 total tau levels are associated with hippocampal novelty irrespective of hippocampal volume.
444 *Alzheimers Dement (Amst)* 2018;10:782-790.
- 445 [12] E. Düzel, H. Schütze, A.P. Yonelinas, H.-J. Heinze, Functional Phenotyping of Successful
446 Aging in Long-Term Memory: Preserved Performance in the Absence of Neural Compensation.
447 *Hippocampus* 2011;21:803-814.
- 448 [13] B. Zhou, A. Lapedriza, J. Xiao, A. Torralba, A. Oliva, Learning deep features for scene
449 recognition using places database. *Adv Neural Inf Process Syst* 2014;487-495.
- 450 [14] S. Park, T. Konkle, A. Oliva, Parametric coding of the size and clutter of natural scenes in
451 the human brain. *Cereb Cortex* 2015;25:1792-1805.