

1 **Persistent activity during working memory maintenance predicts**
2 **long-term memory formation in the human hippocampus**

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20 **Abstract**

21 Working Memory (WM) and Long-Term Memory (LTM) are often viewed as separate
22 cognitive systems. Little is known about how these systems interact when forming
23 memories. We recorded single neurons in the human medial temporal lobe while patients
24 maintained novel items in WM and a subsequent recognition memory test for the same
25 items. In the hippocampus but not the amygdala, the level of WM content-selective persist
26 activity during WM maintenance was predictive of whether the item was later recognized
27 with high confidence or forgotten. In contrast, visually evoked activity in the same cells
28 was not predictive of LTM formation. During LTM retrieval, memory-selective neurons
29 responded more strongly to familiar stimuli for which persistent activity was high while
30 they were maintained in WM. Our study suggests that hippocampal persistent activity of
31 the same cell supports both WM maintenance and LTM encoding, thereby revealing a
32 common single-neuron component of these two memory systems.

33 **Introduction**

34 Working Memory (WM) is the ability to hold and manipulate a small amount of information
35 “in mind”, an ability that is fundamental to many aspects of cognition (Baddeley 2012).
36 Since at least the 1960s, when Atkinson and Shiffrin’s first proposed their model of
37 memory (Atkinson and Shiffrin 1968), it has been theorized that WM (then called Short-
38 Term Memory) and Long-Term Memory are two separated but connected systems. This
39 model and later theories of WM suggest that WM acts as intermediary between
40 perception and LTM (Baddeley 2003), a relationship that has been studied extensively
41 for decades. Indeed, in many instances, information held in WM is encoded better into
42 LTM compared to information not held in WM. Behaviorally, this relationship has been
43 shown in many studies (Hartshorne and Makovski 2019). For instance, words which are
44 maintained longer in WM were later recalled better (Souza and Oberauer 2017), and
45 items stored in WM were better remembered in a surprise recognition test compared to
46 items only attended or passively viewed (Daume et al. 2017). A recent meta-analysis and
47 new experiments show that the impact of holding information in WM on the quality of LTM
48 is especially strong in the visual domain (Hartshorne and Makovski 2019).

49 Despite the ubiquity of WM-LTM interactions seen behaviorally, little is known about the
50 mechanisms by which the two memory systems interact. fMRI (Davachi et al. 2001;
51 Schon et al. 2004; Ranganath et al. 2005; Blumenfeld and Ranganath 2006; Axmacher
52 et al. 2008), scalp M/EEG (Khader et al. 2007, 2010; Daume et al. 2017), and intracranial
53 EEG studies (Axmacher et al. 2009, 2010b) indicate that the extent of activation of a given
54 part of the brain as assessed by BOLD-fMRI or oscillatory power during WM maintenance
55 can be predictive of both WM maintenance success and LTM encoding success. Further,
56 in dual task paradigms (Axmacher et al. 2009, 2010b), high WM demands disrupt LTM
57 encoding processes, arguing that they are not independent. Overall, these findings
58 indicate that the neuronal substrate of the two processes are at least partially overlapping
59 or shared, and are located in the same areas of the brain. However, it remains unclear
60 what exactly is shared in terms of the neuronal substrate. One possibility, motivated by
61 theoretical models (see below), is that the two processes of WM encoding and LTM

62 encoding engage the same cells, but this prediction has not been tested experimentally
63 so far.

64 A hypothesis that has motivated a large body of work is that the sustained maintenance
65 of memoranda in WM enables the gradual strengthening of LTM traces through synaptic
66 plasticity (Hebb, 1949). A key prediction from this model is that the stronger the activation
67 of the neurons that represent memory content during WM maintenance, the stronger the
68 resulting LTM. Here we test this hypothesis directly by recording from WM memory-
69 content selective neurons and assess their relationship to LTM encoding in a task with
70 trial-unique novel stimuli for which we later test memory strength. We note that this design
71 is different from most WM studies, in which the items held in WM are re-used throughout
72 an experiment.

73 Neuroimaging, iEEG, and behavioral studies indicate that the medial temporal lobe, and
74 in particular the hippocampus, are strong candidates for shared WM-LTM processes
75 (Squire 2004). Indeed, recent studies indicate that the MTL, particularly the hippocampus,
76 is critical for both WM and LTM in many circumstances as assessed by behavior and
77 neural activity (Nichols et al. 2006; Piekema et al. 2006; Axmacher et al. 2010a; Jeneson
78 and Squire 2012; Libby et al. 2014; Leszczyński et al. 2015). The MTL has therefore
79 emerged as a key candidate for the area where the WM and LTM system might interact.

80 Transient maintenance can only strengthen LTM through synaptic plasticity as proposed
81 by Hebb (Hebb 1949) if the neurons involved in WM maintenance are also part of the
82 circuit that encodes LTM. A candidate substrate that fulfills these criteria is memoranda-
83 selective persistently active neurons. Such cells, which constitute a relatively well
84 understood cellular substrate for maintaining information in WM, have been documented
85 for highly familiar stimuli (Funahashi et al. 1989; Chafee and Goldman-Rakic 1998; Rainer
86 et al. 1998; Kamiński et al. 2017; Kornblith et al. 2017; Daume et al. 2024). In humans,
87 WM-content selective persistently active neurons have been described in the MTL. The
88 activity of these cells is behaviorally relevant and scales with memory load during
89 maintenance of their preferred stimuli (Kamiński et al. 2017; Kornblith et al. 2017; Boran
90 et al. 2019; Daume et al. 2024). We hypothesize that these cells might contribute to both
91 WM maintenance and LTM encoding, thereby allowing the transient maintenance of

92 activity to translate into structural changes through synaptic plasticity. If so, the extent of
93 persistent activity should be indicative of later LTM memory strength as assessed
94 behaviorally and/or neuronally. Here, we used the opportunity to invasively record single
95 neurons in the human MTL in patients undergoing invasive epilepsy monitoring with depth
96 electrodes to test this hypothesis. Patients performed both a WM and an LTM task in the
97 same recording sessions, with a shared stimulus set between the two tasks. This design
98 allowed us to assess whether maintaining a given trial-unique item in WM influences how
99 well that item will later be remembered in a recognition memory test.

100 **Results**

101 41 patients (48 sessions; 1 non-binary; 20 females; 20 males) performed a modified
102 Sternberg WM task with novel images, followed by a subsequent LTM recognition test. In
103 the WM task, patients were asked to hold either one (load 1) or three (load 3) sequentially
104 presented images in their mind until a probe picture appeared 2.5 – 2.8 s later (**Fig. 1a**
105 **top**) (Daume et al. 2024). The task was to indicate whether the probe picture was identical
106 to one of the encoding pictures just presented before the delay period or not. All pictures
107 shown during encoding were novel, i.e. never shown to the subject before. The images
108 shown during the probe were always familiar to the subject, either from having seen them
109 in the current trial during encoding or during a previous trial (an image is shown twice at
110 most, if used as probe; see Methods). Images are drawn from five different picture
111 categories (people, animals, cars (or tools depending on version), food, landscapes).
112 After a delay of 10-30 min, patients performed a LTM recognition task in which half of the
113 images shown were the same as those shown during the WM task (familiar items) and
114 half were novel (**Fig. 1a bottom**). In this part of the task, subjects indicated whether a
115 given picture was “old” (i.e., seen in the earlier performed WM task) or “new”. Patients
116 were also asked to indicate the confidence in their response, i.e., how confident they were
117 that a given item was old or new (“sure”, “unsure”, “guessing”).

118 Patients performed well in both parts of the task, with an average accuracy of 93.3 ± 7.6
119 % (mean \pm SD) in the WM task and 70.3 ± 9.8 % in the LTM task, respectively (both $p <$
120 0.0001 as compared to 50% chance; permutation-based t-test; 2 sessions from two

121 different patients were excluded from all analyses due to an accuracy of less than 55% in
122 at least one of the tasks; see **Table S1**; see **Fig. S1** for behavior results of 100 healthy
123 participants). In the WM task, patients performed with higher accuracy (**Fig. 1c**; load 1 –
124 load 3: $t(45) = 4.89$, $p < 0.0001$; permutation-based paired t-tests were used throughout
125 the manuscript unless stated otherwise; t-values are provided as reference only; see
126 Methods) and faster (**Fig. 1d**; $t(45) = -4.29$, $p < 0.0001$) in load 1 than load 3 trials. In the
127 LTM task, retrieval was more accurate (**Fig. 1e**; $t(44) = 8.66$, $p < 0.0001$; one patient did
128 not use confidence ratings and was therefore excluded from all confidence-related
129 analyses) and faster (mean RT high: 1.83 ± 0.57 s; mean RT low: 2.62 ± 0.66 s; $t(44) = -$
130 11.13 , $p < 0.0001$) when patients indicated high confidence in their responses. Low
131 confidence was defined as an average of “unsure” and “guessing” responses. Items that
132 were encoded in load 1 trials in the previous WM task were remembered better than items
133 encoded during load 3 trials (**Fig. 1f**; $t(45) = 2.42$; $p = 0.018$). Moreover, items that were
134 also used as the probe and therefore presented twice were remembered better than items
135 not used as the probe (**Fig. 1g**; $t(45) = 7.25$, $p < 0.0001$).

136 We recorded single neuron activity from the hippocampus and the amygdala while
137 patients performed the two tasks (**Fig. 1b**). In total, 883 single units across both brain
138 areas were included in our analyses, 351 from the hippocampus and 532 from the
139 amygdala (see Methods). The same units were recorded for both tasks. The analysis
140 presented here is partly based on a previously published dataset (Daume et al. 2024),
141 but in that report only the WM task was analyzed. Further, more subjects were added in
142 the present manuscript. The LTM part that is the focus of this paper is unpublished. Spike
143 sorting results were assessed quantitatively (**Fig. S2**). We use the terms neuron, unit,
144 and cell interchangeably to refer to a putative single neuron.

145 *Category neurons remain persistently active when their preferred category is held in*
146 *WM*

147 We first selected for neurons whose response following stimulus onset differed
148 significantly between the category of the images shown. We refer to such neurons as
149 ‘category neurons’ throughout (we note that this type of cell is also referred to as visually

150 selective (VS) in other papers (Rutishauser et al. 2015, 2021; Bausch et al. 2021); The
151 two terms are equivalent for purpose of this study). To select category neurons, we
152 assessed whether the firing rate (FR) in a 200 – 1200 ms window following picture onset
153 (encoding 1-3 & probe) was significantly correlated with the five possible picture
154 categories (1x5 ANOVA, followed by a right-sided permutation-based t-test between the
155 category with maximal average spike count and all other categories; if both tests were p
156 < 0.05 , we classified a neuron as a category neuron with the preferred category being the
157 one with maximal average spike count; see Methods). As shown previously, category
158 neurons remain persistently active during the maintenance period of the WM task when
159 their preferred picture is held in WM (Daume et al. 2024). Selecting for category neurons
160 during picture presentation leaves their FRs during the maintenance period of the task
161 independent for subsequent statistical analyses. In the hippocampus, 104 (29.65 %)
162 neurons qualified as category neurons, and in the amygdala 220 (41.35 %) neurons
163 qualified as category neurons (see **Fig. 2a,d** for example neurons from each area).

164 To confirm that category neurons remained persistently active during the maintenance
165 period, we computed a mixed-effects generalized linear model (GLM) using *preferred*
166 *category* (2 levels, true/untrue, categorical) as fixed effect and *neuron ID* nested into
167 *patient ID* as random intercept in each area (these random intercept terms were used for
168 all GLMs; see Methods). We used baseline-normalized FRs from all correct WM trials
169 during the maintenance period (0-2.5 s after last encoding picture offset) for this analysis.
170 In the hippocampus, category neurons remained persistently active throughout the
171 maintenance period (intercept: $\beta = 17.86$, $p = 1.38 \times 10^{-3}$; mixed-effects GLM) and had
172 significantly higher FRs during trials in which images from the preferred category were
173 maintained in WM (**Fig. 2b**; preferred category: $\beta = 12.47$, $p = 8.82 \times 10^{-7}$). Using only
174 preferred trials and modelling WM *accuracy* (2 levels, WM correct/incorrect, categorical)
175 as well as *load* (2 levels, load 1/load 3, categorical) as fixed effects, we further observed
176 that category neurons in the hippocampus had higher FRs in (1) correct than incorrect
177 trials ($\beta = 16.22$, $p = 0.046$) and (2) in load 1 than in load 3 trials (**Fig. 2c**; $\beta =$
178 13.769 , $p = 0.0023$).

179 In the amygdala, category neurons also remained persistently active throughout the
180 maintenance period across all correct trials (intercept: $\beta = 9.78$, $p = 6.76 \times 10^{-4}$) with

181 FRs higher for preferred than unpreferred categories (**Fig. 2e**; preferred category: beta =
182 6.91, $p = 9.38 \times 10^{-7}$). However, unlike in the hippocampus, using only preferred trials
183 category neurons in the amygdala showed a significant main effect only for *load* (**Fig. 2f**;
184 load 1 – load 3; beta = 12.309; $p = 2.46 \times 10^{-7}$), but the effect for WM *accuracy* (correct –
185 incorrect: beta = -6.13; $p = 0.24$) was not significant.

186 *Persistent activity of category neurons in the hippocampus - not the amygdala - predicts* 187 *LTM formation*

188 We next sought to investigate whether the activity of category neurons during the
189 maintenance period of the WM task predicted the success of LTM formation. To that end,
190 we computed a mixed-effects GLM with baseline-normalized FRs from the maintenance
191 period. For a given neuron, we used the subset of trials for which the subject answered
192 the WM question correctly and for which images of the preferred category were tested in
193 the LTM recognition task (not all images seen during WM were shown during the LTM
194 test). We modelled *LTM accuracy* of each image (2 levels, remembered/forgotten,
195 categorical), *confidence* (3 levels, sure/unsure/guessing, continuous), *brain area* (2
196 levels, hippocampus/amygdala, categorical), as well as their interactions as fixed effects.
197 We did not observe any significant main effects nor was the interaction between *LTM*
198 *accuracy* and *confidence* significant (**Fig. 3a**; all $p > 0.26$). However, all interaction terms
199 including *area* showed significant modulations (confidence x area: beta = 16.88, $p =$
200 0.025; LTM accuracy x area: beta = 59.78, $p = 0.0030$; confidence x LTM accuracy x
201 area: beta = -28.64, $p = 0.0029$), suggesting that the relationship between FR and *LTM*
202 *accuracy* and *confidence* differed between the hippocampus and the amygdala. We
203 therefore repeated the analysis in each area separately. This revealed a significant main
204 effect of *confidence* (**Fig. 3b**; beta = 20.30, $p = 4.17 \times 10^{-3}$) and *LTM accuracy* (beta =
205 67.90, $p = 4.43 \times 10^{-4}$), as well as a significant interaction between the two terms (beta =
206 -30.80, $p = 7.74 \times 10^{-4}$) in the hippocampus but not in the amygdala (confidence: beta =
207 1.54, $p = 0.69$; LTM accuracy: beta = -2.27, $p = 0.82$; confidence x LTM accuracy: beta =
208 1.02, $p = 0.83$). These results suggest that activity during the maintenance period of the
209 WM task of category neurons from the hippocampus were higher for later remembered

210 than forgotten trials and therefore predictive of later LTM retrieval performance. This was
211 not the case for persistent WM activity of category neurons from the amygdala.

212 In each area, we next tested FRs across all category neurons from the maintenance
213 period of the WM task between later remembered and forgotten separately for high and
214 low LTM retrieval confidence. In the hippocampus, FRs were higher for remembered than
215 forgotten trials for high confidence (**Fig. 3c**; $t(82) = 2.16$, $p = 0.028$; some neurons were
216 removed due to insufficient data in at least one of the conditions or since they differed ± 3
217 SD from the mean across all neurons and conditions; see Methods), but not low
218 confidence trials ($t(68) = -1.38$, $p = 0.17$). In the amygdala, we neither observed a
219 significant effect for high (**Fig. 3d**; $t(158) = 0.84$, $p = 0.41$) nor low confidence trials ($t(152)$
220 $= 1.15$, $p = 0.26$).

221 To observe when during the maintenance period of the WM task the effect between later
222 remembered and forgotten trials was present, we tested time-resolved FRs between
223 remembered and forgotten trials for all high-confident trials separately for category
224 neurons from hippocampus and amygdala. In the hippocampus, FRs during the beginning
225 of the maintenance period (0 – 650 ms) differed significantly between the two conditions
226 (**Fig. 3e**; cluster- $p = 0.0042$; cluster-based permutation test). In the amygdala, we did not
227 observe any significant cluster throughout the entire maintenance period of the WM task
228 (**Fig. 3f**; cluster- $p = 0.16$).

229 Lastly, we tested whether we observe a relationship between neural activity and LTM
230 formation also for neuronal activity during the maintenance of stimuli from the non-
231 preferred categories of cells (**Fig. 3g**) or for the visually evoked response of neurons when
232 images were shown on the screen during encoding (**Fig. 3h**; encoding 1; 0 – 2s after
233 picture onset; preferred trials only). However, none of the main effects nor interactions in
234 either of the mixed-effects GLMs showed any significant relationship between FR and the
235 factors tested (all $p > 0.06$).

236 *Activity during WM maintenance is linked to subsequent memory signal*

237 During recognition memory tasks, a common observation in the MTL is that ‘memory
238 selective’ (MS) cells differ in their response between novel and familiar images

239 (Rutishauser et al. 2015). These cells are thought to represent a memory strength signal
240 (Rutishauser et al. 2015), with stronger responses associated with stronger memories.
241 We therefore next asked whether MS cells are present in the present experiment, and if
242 so, whether there is a relationship between the activity of MS cells during LTM retrieval
243 and that of category neurons during WM maintenance. Since we only observed a
244 relationship between persistent activity of category neurons and successful LTM
245 formation in the hippocampus, we restricted this analysis to the hippocampus.

246 We selected for MS neurons during all correct trials in the LTM recognition part
247 (permutation-based t-test comparing response between correct familiar and novel
248 images, that is, true positives with true negatives, 200-1200 ms after picture onset, $p <$
249 0.05). Out of the 351 recorded cells, $n = 53$ (15.10 %) were MS cells. Of these, 25 (47%)
250 responded more to familiar than novel items, with the remaining responding more to novel
251 than to familiar items. **Fig. 4a** shows an example neuron that increased its firing rate more
252 for familiar than novel pictures (old > new). To assess whether MS cells, as expected,
253 carry a memory strength signal, we next compared their response strength between trials
254 retrieved with high and low confidence. We used receiver operating characteristics (ROC)
255 analysis to do so (comparing old vs. new trials; see Methods). The response of MS
256 neurons differed significantly more for high- as compared to low-confidence trials (**Fig.**
257 **4b**; $t(40) = 2.89$, $p = 0.0039$; 12 neurons excluded due to insufficient data in either one of
258 the conditions, see Methods). This data shows that MS cells are present and signal
259 memory strength in our experiment.

260 We next examined whether the overlap between the group of category neurons and MS
261 neurons is significantly higher than chance, possibly hinting towards an involvement of
262 category neurons also in LTM retrieval processes. Of the 53 MS neurons and the 104
263 category neurons, 20 neurons (37.8% of MS cells; 19.2 % of category neurons) were part
264 of both groups. We determined whether this overlap is significantly higher than what would
265 be expected by chance. We did so by randomly selecting the same number of neurons
266 as we found for category neurons from the population of all hippocampal cells and
267 determined how many neurons of those randomly selected neurons were also MS cells.
268 This procedure was repeated for 1000 times to obtain a null distribution, used to
269 determine the statistical significance of the originally observed overlap. This revealed that

270 the overlap between category neurons and MS cells was not significantly higher than
271 chance (**Fig. 4c**; $p = 0.11$), suggesting that category and MS cells were statistically
272 independent populations of neurons (as expected (Rutishauser et al. 2015)).

273 To further examine whether, as a group, category neurons carried a memory signal during
274 LTM retrieval, we computed a mixed-effects GLM with FRs of category neurons during
275 all correct trials in the LTM recognition task (0.2 – 1.2 s after picture onset) in which the
276 preferred category of a neuron was shown. We modelled *confidence* (3 levels,
277 sure/unsure/guessing, continuous), *familiarity* (2 levels, old/new, categorical), and their
278 interaction as fixed effects. None of the effects revealed significant modulations of FRs
279 (**Fig. 4d top**; confidence: $\beta = 6.05$, $p = 0.28$; familiarity: $\beta = 4.49$, $p = 0.71$;
280 confidence x familiarity: $\beta = -4.32$, $p = 0.57$). To further confirm this result, we directly
281 compared FRs of category neurons between preferred old and new items and did not
282 observe a significant difference (**Fig. 4d bottom**; $t(94) = -0.28$, $p = 0.78$).

283 Finally, we tested whether the response of MS cells in the recognition task to a given
284 image was correlated with the activity of simultaneously recorded category cells during
285 WM maintenance earlier in the same session while the same picture was held in mind.
286 To do so, we examined all possible pairs of simultaneously recorded MS and category
287 cells ($n = 198$). For each pair, we examined the trials during which images of the preferred
288 category of the category cell were shown both in the WM and in the LTM task (i.e.,
289 preferred familiar trials; see Methods). We split the familiar trials in the LTM recognition
290 task into two groups based on the level of activity of the category cell during WM
291 maintenance for the same images (low vs. high maintenance activity, median split). We
292 used a mixed-effects GLM to model FRs of the MS cells as a function of the fixed effect
293 *Maintenance FR of category cells* (2 levels, high/low, categorical; based on
294 simultaneously recorded FR of category neurons in the earlier WM task). We computed
295 separate models for familiarity-selective (old > new) and novelty-selective (new > old) MS
296 neurons as we hypothesized effects to be specific to neurons signaling familiarity
297 (Rutishauser et al. 2015). This analysis revealed that FRs of familiarity-selective MS cells
298 during LTM retrieval of items that were previously accompanied by high persistent activity
299 in the WM task were higher than those previously accompanied by low persistent activity
300 (**Fig. 4e**; Maintenance FR: $\beta = 14.63$, $p = 1.38 \times 10^{-3}$). No significant relationship was

301 observed for the activity of novelty-selective MS neurons (**Fig. 4f**; Maintenance FR: beta
302 = 14.63, $p = 1.38 \times 10^{-3}$). This result suggests that the strength of category-selective WM
303 maintenance activity is correlated with a neuronal measure of long-term memory strength
304 (the activity of MS cells). This result is in addition to the correlation of WM maintenance
305 activity and later behaviorally assessed long-term memory strength (previous paragraph).

306 **Discussion**

307 Our results reveal that the activity of hippocampal category cells during WM maintenance
308 was predictive of the success of LTM encoding. This relationship was specific for activity
309 during the maintenance period and to trials in which the preferred category of category-
310 selective cells was maintained in WM. In contrast, there was no significant correlation
311 between neural activity of category cells during maintenance of stimuli from the non-
312 preferred categories and LTM strength. There was no correlation between activity of the
313 same category cells during the encoding period with later LTM memory strength,
314 indicating specificity to activity during WM maintenance. Further, this effect was specific
315 to the hippocampus as the activity of category neurons in the amygdala was not predictive
316 of successful memory formation. Together, our findings reveal that the neural code used
317 for maintaining items in WM is at least partially overlapping with the neural code that
318 facilitates LTM encoding.

319 We also observed a relationship with a neuronal measure of LTM memory strength: the
320 stronger the level of persistent activity for a given image, the larger was the response to
321 that same image of memory-selective cells during the recognition memory test (**Fig. 4**).
322 This reveals a direct neuronal-neuronal relationship between activity related to WM
323 maintenance and LTM retrieval. Notably, this neuronal-neuronal relationship was only the
324 case for the MS cells that increased their firing rate to familiar stimuli. In contrast, the MS
325 cells that increased their firing rate to novel stimuli showed no significant correlation (for
326 familiar stimuli). This result further supports the argument that what we observed is a
327 signature of memory, because the activity of memory-selective cells scales with memory
328 strength (and declared confidence) (Rutishauser et al. 2015).

329 Lesion studies indicate that the MTL is not necessary to perform simple WM tasks
330 (Jeneson and Squire 2012), which has led to the long-standing idea of parallel memory
331 systems, with the MTL not involved in WM. But if so, why is there persistent activity in the
332 MTL during WM maintenance? One hypothesis is that the purpose of persistent activity
333 is to engage mechanism used in encoding new memories in order be able to utilize
334 synaptic plasticity to recover information in case it drops from the focus of attention
335 (Kamiński and Rutishauser 2020). Under this framework, persistent activity would
336 enhance the strength of items in LTM (Huang and Kandel 1994). This hypothesis is
337 supported by more recent lesion studies, which show that subjects without a functional
338 MTL do exhibit WM deficits in three situations: (1) in the presence of distractors (2), when
339 memory load is high, or (3) when maintenance time is long (Jeneson and Squire 2012).
340 In each of these scenarios, the probability that an item will drop out from the focus of
341 attention is high and thus the network needs a mechanism for recovering this information.
342 Here, we show that the extent of persistent activity in the hippocampus predicts whether
343 items were encoded into LTM, thus revealing a specific example of a neural mechanism
344 within the hippocampus that is engaged by both the WM and LTM system. We
345 hypothesize that the role of persistent activity in the hippocampus is to augment the
346 encoding of new information into LTM through repetition of the firing pattern throughout
347 the maintenance period, thereby strengthening long-lasting long-term potentiation
348 (Huang and Kandel 1994). This hypothesis is supported by theoretical work that indicates
349 that the repetition provided by prolonged activity facilitates the modification of synapses
350 (Jensen and Lisman 1996; Jensen et al. 1996).

351 The response properties of category cells in the amygdala and hippocampus were similar
352 during WM processing but were remarkably different with respect to LTM encoding. In
353 contrast to the hippocampus, activity of category cells from the amygdala did not predict
354 LTM encoding success (**Fig. 3**). The relatively similar tuning properties of neurons in
355 these two areas during encoding is not surprising in the context of prior work. For
356 example, both brain areas contain concept cells (Quiroga et al. 2005, 2009) as well as
357 MS cells (Rutishauser et al. 2008, 2015). Here, we now find that the relationship between
358 short-term memory maintenance and its impact on later LTM is specific to the

359 hippocampus. This is congruent with the fact that the hippocampus is particularly crucial
360 for encoding new memories (Squire et al. 2004).

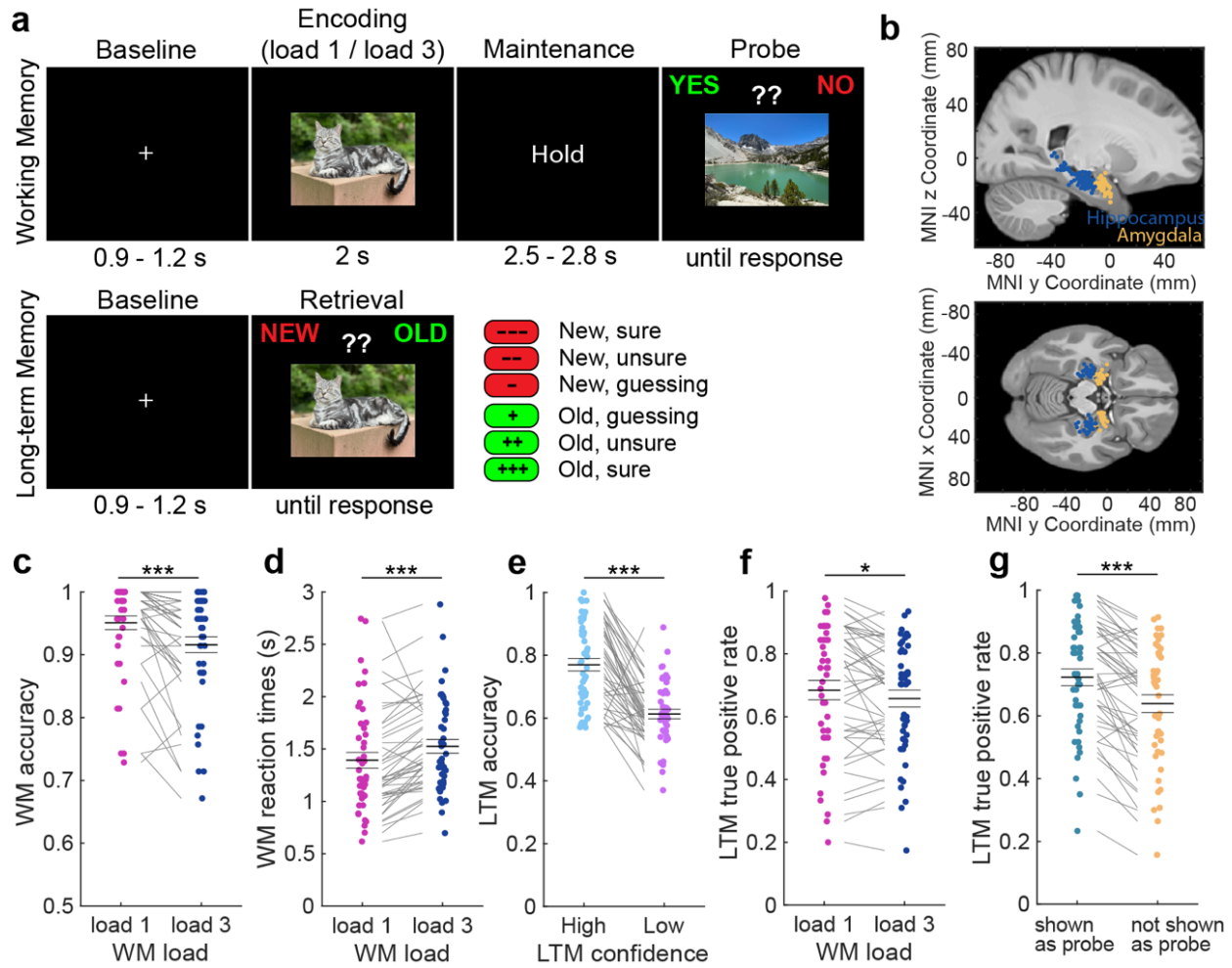
361 Our findings provide evidence for an interaction between WM and LTM where WM
362 maintenance serves as a gating mechanism for LTM formation. In contrast, earlier
363 research has shown that existing long-term memories can also be retrieved to and
364 maintained in WM (Fukuda and Woodman 2017). In the current study, we used complex
365 visual stimuli that are novel to the participants but could have pre-existing LTM
366 associations for a specific person, animal, or object. It is thus possible that in our study
367 such associations have been retrieved into WM to support the successful maintenance
368 of these images. Since we didn't make use of neutral images, such as fractals, without
369 pre-existing associations or haven't measured such associations for the current pictures
370 on an individual basis, it is not possible for us to assess how LTM retrieval supported
371 successful WM maintenance. We note, however, that even if this were the case, this
372 would not explain our effect because regardless of whether WM maintenance engaged
373 retrieval of existing images or not, encoding of a new memory was required to solve our
374 task. We therefore interpret our findings as indicating that WM maintenance supported
375 LTM formation. On a behavioral level, we observed that WM load had an influence on the
376 successful formation of newly stored long-term memories, since images maintained in
377 load 3 trials were less well remembered than images maintained in load 1 trials. Moreover,
378 the strength of persistent activity during the maintenance period predicted successful
379 encoding into LTM, but not the neural activity observed during encoding (see **Fig. 3**).
380 These observations cannot be explained by LTM retrieval processes during the WM
381 maintenance period. Nevertheless, we hypothesize that interactions between the
382 systems likely go in both directions: persistent activity during WM maintenance predicts
383 LTM formation, and, in turn, WM is supported by the retrieval of pre-existing LTM
384 associations, presumably enhancing content-selective persistent activity during WM
385 maintenance. However, future research is needed to shed more light on these interesting
386 questions.

387 Our findings further suggest that the neural mechanisms of successful LTM formation
388 overlap with those of WM maintenance. However, we emphasize that this does not mean
389 that the two processes share exactly the same mechanisms such that the distinction

390 between WM and LTM could eventually be discarded. Instead, our findings should be
391 interpreted within a Hebbian view of two distinct memory systems: a short-term memory
392 system that depends on reverberatory activity of cell assemblies and a long-term storage
393 system that involves strengthening of synaptic connectivity between neurons (Nobre
394 2022). Our findings suggest that processes of LTM formation, which ultimately lead to
395 successful LTM storage, become enhanced through interactions with persistent activity
396 of WM-selective neurons. The exact mechanistic consequences of such interactions,
397 however, remain the subject of future investigations. It also remains unclear whether other
398 forms of WM maintenance, like activity-silent WM (Stokes 2015), interact with LTM
399 formation in the same way as persistent neural activity. Activity-silent WM maintenance
400 has mainly been observed for WM content outside the focus of attention (Rose et al. 2016;
401 Wolff et al. 2017), which is an important difference from our study in which the focus of
402 attention was not manipulated per item. Earlier research, however, indicated that attention
403 to WM items enhances successful LTM formation (Hartshorne and Makovski 2019) which
404 indicates that persistent activity plays a special role in interactions with LTM formation.

405 In conclusion, our study reveals that the activity of hippocampal category-selective cells
406 during WM maintenance is predictive of LTM encoding success. This relationship is
407 unique to the hippocampus and the WM maintenance period, with no similar predictive
408 activity observed in the amygdala or during encoding periods. Our findings suggest that
409 persistent activity of category cells in the hippocampus contributes to the encoding of
410 declarative memories, reinforcing the role of Hebbian-type plasticity. They further show
411 that WM- and LTM-specific neural populations interact on a local level with stronger
412 persistent activity predicting stronger memory-related activity during retrieval. These
413 results provide significant insights into the neural mechanisms involved in interactions
414 between WM and LTM with single-cellular resolution.

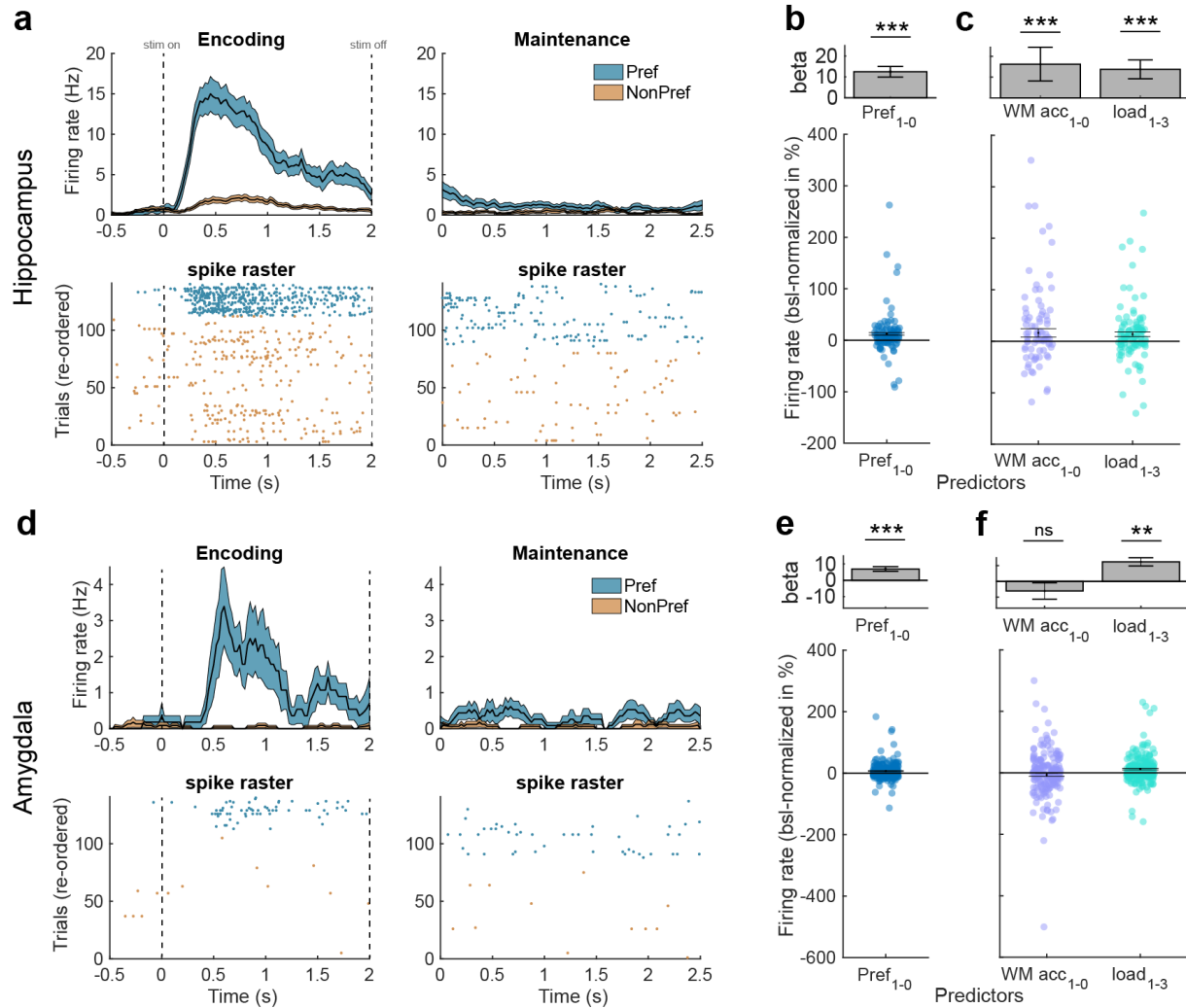
415 **Figure Legends**



416

417 **Figure 1. Experimental design and behavioral analysis.** (a) The study contained a
 418 WM part (top) and a subsequent LTM recognition part (bottom). In the WM task, patients
 419 had to encode either one (load 1) or three (load 3) pictures in their WM and to maintain
 420 these items until a probe picture appeared a few seconds later. Their task was to indicate
 421 whether the probe was part of the encoded items in a given trial or not. All encoding
 422 pictures were novel and drawn from five different picture categories. In the LTM task,
 423 occurring after a 10-30 min break, patients had to answer whether each presented item
 424 on the screen was old (i.e., seen in the previous WM task) or new while indicating their
 425 confidence in their response. (b) We recorded single neuron activity from the
 426 hippocampus and the amygdala of 41 patients across 48 sessions. Each dot is a patient.
 427 (c,d) WM behavior. Patients performed (c) more accurate and (d) faster in load 1

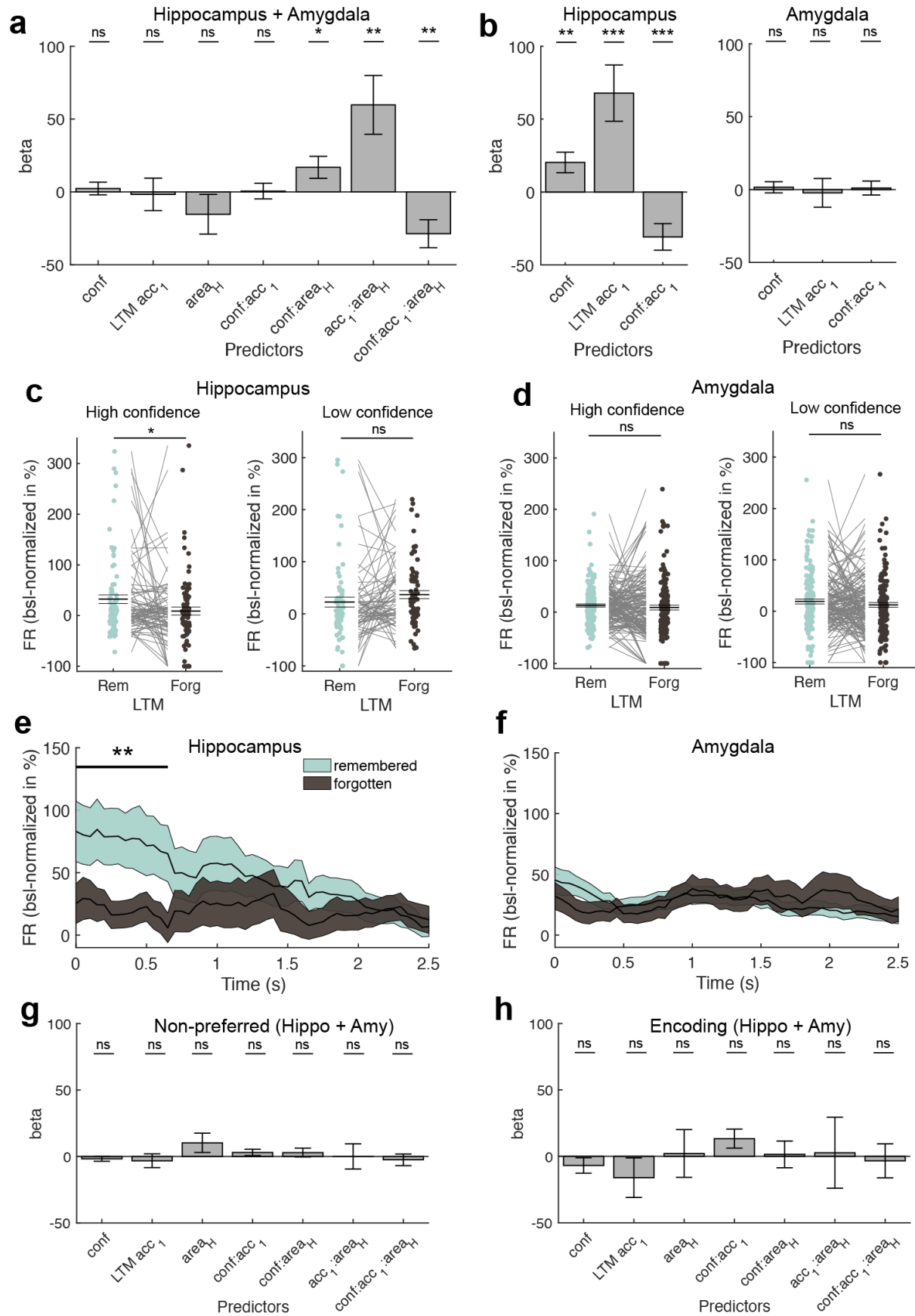
428 compared to load 3 trials. **(e-g)** LTM behavior. **(e)** LTM was more accurate in high than
429 low confidence trials. **(f)** Items previously maintained in load 1 trials were remembered
430 more accurately than when maintained in load 3 trials. **(g)** Pictures that were used as
431 probe and therefore presented twice were remembered better than items not shown as
432 probe. In **(c-g)** we used permutation-based t-tests. Center lines represent mean \pm s.e.m.
433 Each dot is a session. * $p < 0.05$; *** $p < 0.001$.



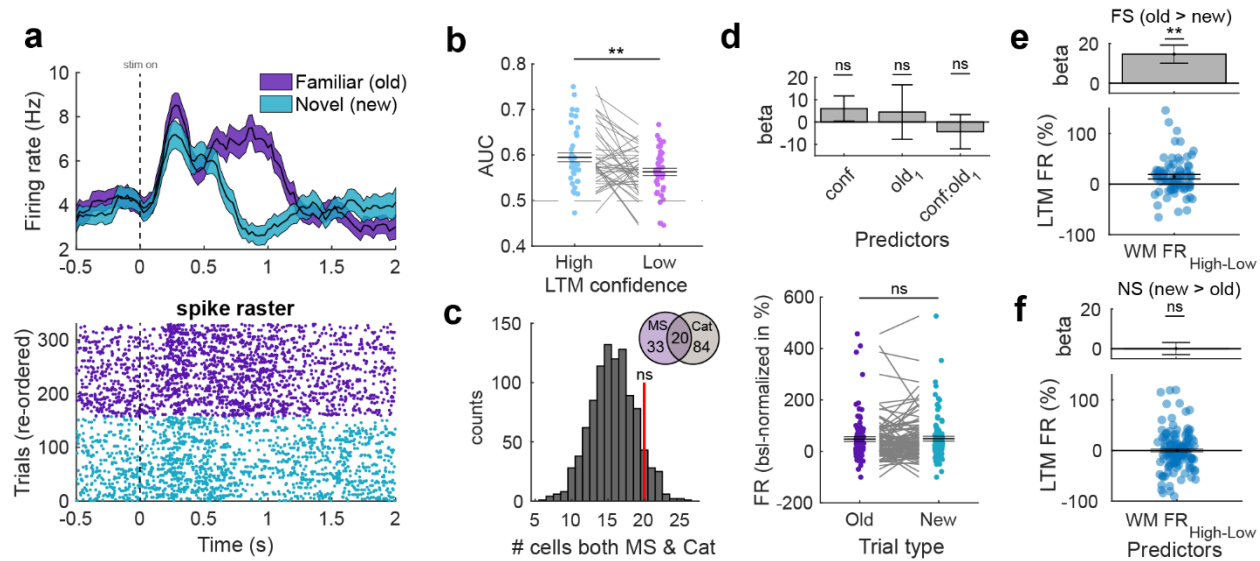
434

435 **Figure 2. Category neurons.** (a-c) Characterization of category neurons in the
 436 hippocampus. (a) Example category neuron. The preferred category of this neuron was
 437 “animals”. Top: Peri-stimulus time histogram (PSTH, bin size = 200 ms, step size = 25
 438 ms) during the first picture in each correct trial. Colored areas represent \pm s.e.m. Bottom:
 439 raster plot with trials re-ordered into preferred and non-preferred categories. Stimulus and
 440 maintenance onset is at $t = 0$ s (left and right, respectively). (b) Firing rates of category
 441 neurons from the hippocampus remained persistently active and were higher for preferred
 442 than unpreferred trials during the WM maintenance period. Top: Beta value extracted
 443 from the GLM for preferred/non-preferred regressor in units of “percent change to
 444 baseline” (-900 – -300 ms before first picture onset). Bottom: Distribution of FR
 445 differences between preferred (pref = 1) and non-preferred (pref = 0) trials across all
 446 hippocampal category neurons (each dot is a neuron, $n = 104$). FRs were baseline-

447 normalized to represent percent change to baseline. **(c)** When the preferred category
448 remained in WM, category neurons in the hippocampus had higher FRs in correct as
449 compared to incorrect and in load 1 as compared to load 3 trials. **(d-f)** Characterization
450 of category neurons in the amygdala. **(d)** Same as in (a) but for an example category
451 neuron from the amygdala. **(e)** Firing rates of category neurons from the amygdala also
452 remained persistently active and were higher for preferred than unpreferred trials during
453 the WM maintenance period (n = 220). **(f)** Their FRs were higher in load 1 as compared
454 to load 3 trials when their preferred category was maintained but there was no difference
455 between correct and incorrect trials. In **(b,c,e,f)** we computed mixed-effects GLMs. Error
456 bars represent standard errors of the coefficient. In **(b,e)** each dot is a neuron. ** p < 0.01,
457 *** p < 0.001, ns = not significant.



459 **Figure 3. Relationship between WM maintenance activity and LTM formation. (a)**
460 Mixed-effects model using the FR obtained during the WM maintenance period in correct
461 and preferred trials of all category cells across both regions, modelling *confidence*,
462 subsequent *LTM accuracy* (remembered vs forgotten), *area*, and their interactions as
463 fixed effects and *neuron ID* nested into *patient ID* as random intercepts. We found
464 significant modulations of FR by interactions of *confidence* and *LTM accuracy* with *area*,
465 suggesting differences in FR modulations by LTM accuracy and confidence per area. **(b)**
466 Mixed-effects GLM results separately for the hippocampus (left) and the amygdala (right).
467 Only in the hippocampus, we observed that persistent activity during the WM
468 maintenance period predicted later LTM accuracy as well as confidence. **(c,d)**
469 Comparison of FRs during the maintenance period between later remembered and
470 forgotten images, separately for high (left) and low confidence trials (right) for category
471 neurons from **(c)** the hippocampus and **(d)** the amygdala. Statistics are permutation-
472 based t-tests, each dot is a neuron. FRs differed significantly between remembered and
473 forgotten images in the hippocampus for high but not low confidence trials. **(e,f)** Time-
474 resolved FR differences between later high-confident remembered and forgotten trials in
475 (e) the hippocampus and (f) the amygdala for the maintenance period. FR differences
476 between remembered and forgotten trials in the hippocampus were strongest in the first
477 section of the WM delay period (0 – 650 ms). Cluster-based permutation t-test. Colored
478 areas represent \pm s.e.m. $t=0$ marks the onset of the maintenance period. **(g)** Mixed-effects
479 model results using the WM maintenance period FRs of non-preferred trials across all
480 category neurons from both regions. **(h)** Mixed-effects model results using the FRs during
481 the first picture presentation (encoding 1; 0-2 s after picture onset; preferred images and
482 correct trials only) across all category neurons from both regions. In **(a,b,g,h)** error bars
483 represent standard errors of the coefficients. Betas are shown in units of baseline-
484 normalized FRs (percent change to baseline, -900 – -300 ms before first picture onset).
485 In **(c,d)** center lines represent mean \pm s.e.m. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, ns =
486 not significant.



487

488 **Figure 4. Relationship between memory-selective and category-selective neurons**

489 **in the hippocampus. (a)** Example of a memory-selective cell that had significantly higher

490 FRs during correct old than new trials in the LTM recognition task. Colored areas in the

491 PSTH plot (top) represent \pm s.e.m. t=0 is stimulus onset. **(b)** ROC analysis comparing

492 neuronal response of MS cells between new and old trials separately for low and high

493 confidence. AUC was significantly higher for high than low confidence trials. Permutation-

494 based t-test. Each dot is a neuron. **(c)** Null distribution of randomly selecting the same

495 number of cells from the entire hippocampal population as category neurons for 1000

496 times and determining the overlap with MS cells. The overlap between category cells and

497 MS cells (red bar) was not significantly higher than expected by chance. **(d)** Top: Mixed-

498 effects GLM model testing for a relationship between FR of category neurons and

499 confidence or familiarity ("old₁₋₀"). FR is estimated during picture presentation in the LTM

500 task and only trials of the preferred category of a given cell are used. Bottom:

501 Permutation-based t-test comparing FRs of category neurons during picture presentation

502 between old and new items (preferred category only). Category neurons neither coded

503 for familiarity nor novelty in the LTM task. **(e)** Response of familiarity-selective (FS) MS

504 cells during familiar trials in the LTM task was stronger if maintenance activity for the

505 same image was high during WM maintenance. Mixed-effects GLM. Top: Beta extracted

506 from GLM result. Bottom: Distribution of FR differences between high and low

507 maintenance trials. Each dot is a FS-category cell pair (n = 76). **(f)** Same as (e), but for

508 novelty-selective (NS) MS cells (n = 122). The response of novelty-selective MS cells to
509 familiar images did not differ significantly between whether the WM maintenance activity
510 was low or high for an image. In **(b,d,e,f)** each dot is a neuron. In **(b,d(bottom))** we used
511 permutation-based t-tests. Center lines represent mean \pm s.e.m. In **(d(top),e,f)** error bars
512 represent standard error of the coefficients. MS = memory-selective; Cat = category-
513 selective; FS = familiarity-selective; NS = novelty-selective; ** $p < 0.01$, ns = not
514 significant.

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524 **Author contributions**

525 Conceptualization, J.D., J.K. and U.R.; Writing – Original Draft, J.D., J.K., and U.R.;
526 Writing – Review & Editing, all authors. Investigation: J.D., J.K., Y.S.; Formal analysis:
527 J.D. and U.R.; Methodology, J.D., J.K., and U.R.; Funding Acquisition, Resources, and
528 Supervision, J.D., U.R. and A.N.M.; Performed surgery, A.N.M., T.A.V., and W.A.

529 **Declaration of interests**

530 The authors declare no competing interests.

531 **STAR Methods**

532 **Resource availability**

533 *Lead Contact and Materials Availability*

534 Further information and requests for resources should be directed to the Lead Contact,
535 Ueli Rutishauser (ueli.rutishauser@cshs.org).

536 *Data and Code Availability*

537 Data will be made available publicly upon acceptance in the NWB format, similar to
538 DANDI #673 (which contains only the WM part; we will add the LTM part). Example code
539 will accompany the data release.

540 **Experimental Model and Study Participant Details**

541 41 patients (48 sessions; 1 binary; 20 females; 20 males; age: 39.9 ± 12.9 years; **Table**
542 **S1**; note of these, 38 sessions are also included in (Daume et al. 2024) and 10 were
543 added here), undergoing invasive monitoring to assess treatment options for drug-
544 resistant epilepsy, participated in the study. Two patients with task performance lower
545 than 55% correct in either the WM or the LTM task were excluded from further analyses
546 (see **Table S1**). All patients had Behnke-Fried hybrid electrodes (AdTech Inc.) implanted
547 for intracranial seizure monitoring, gave their informed consent, and participated
548 voluntarily. This study was part of an NIH Brain consortium between three institutions
549 (Cedars-Sinai Medical Center, Toronto Western Hospital, and Johns Hopkins Hospital)
550 and approved by the Institutional Review Board of the institution at which the patient was
551 enrolled. Electrode localization was performed using a pre-operative MRI together with
552 either MRI or CT post-operative images and Freesurfer as previously described (Minxha
553 et al. 2020). Electrode positions are plotted on the CITI168 Atlas Brain (Tyszka and Pauli
554 2016) in MNI152 coordinates for the sole purpose of visualization (**Fig. 1b**). Coordinates

555 appearing in white matter or outside of the target area is due to usage of a template brain.
556 Electrodes that were localized outside of the target area in native space were excluded
557 from analysis (4 out of a total of 149 recording sites).

558 **Method Details**

559 *Task*

560 The study consisted of two separate tasks: a modified Sternberg WM task followed by a
561 subsequent LTM recognition task. The WM task has been described elsewhere (Daume
562 et al. 2024). It consisted of 140 trials and 280 novel pictures. In each trial, the onset of a
563 fixation cross presented for 0.9 to 1.2 s (see **Fig. 1a top**) indicated the start of the trial.
564 The fixation cross was followed by either one (load 1; 70 trials) or three (load 3; 70 trials)
565 consecutively presented pictures, each presented for 2 s. A maintenance period of 2.55
566 to 2.85 s length followed the picture presentation, during which only the word “HOLD” was
567 shown on the screen. Then, a probe picture was presented, which was either one of the
568 pictures shown earlier in the same trial (match) or a picture already presented in one of
569 the previous trials (non-match). The task was to indicate whether the probe picture
570 matched one of the pictures shown earlier *in the same trial* or not. Note that the probe
571 image shown was always one that had been shown before and thus familiar, with the
572 answer ‘Yes’ if the image was shown in this particular trial and ‘No’ if it was shown in a
573 previous trial. For trials where the correct answer was ‘No’ (i.e. the probe image was not
574 shown during encoding in this trial), we used images that were presented in a previous
575 trial to assure that all probe images were equally familiar, thereby preventing the use of
576 novelty as a signal to answer the probe question. Probe images in the ‘No’ category were
577 chosen from one of the categories for which no images were shown during encoding in a
578 given trial. The probe picture was shown until patients provided their response via button
579 press. All pictures shown during encoding were novel (i.e., the patient had never seen
580 this particular image) and were drawn from five different visual categories: faces, animals,
581 cars (or tools depending on the version), fruits, and landscapes. In load 3 trials, each
582 image shown during encoding was from a different category.

583 After a brief delay (lasting 10 - 30min), patients completed a LTM recognition task. During
584 this task, 400 images were shown one at a time. 200 of these images were new (not used
585 in the WM task), whereas 200 were old (previously shown in the WM task). Each trial
586 started with a fixation cross (**Fig. 1a, bottom**), followed by a single image for which the
587 subject was asked to decide whether they had seen this image before (during the WM
588 task) and to indicate the confidence in their response (sure, unsure, guessing). The image
589 stayed on the screen until a response was given (no timeout). The 'new' images (foils)
590 were chosen from the same 5 visual categories as the 'old' images. Note that due to this
591 design, solving the recognition memory task required remembering the specific stimuli
592 seen because the new images used were similar to the old images.

593 **Quantification and Statistical Analysis**

594 *Spike sorting*

595 For each hybrid depth electrode, we recorded the broadband LFP signal between 0.1 and
596 8,000 Hz at a sampling rate of 32 kHz (ATLAS system, Neuralynx Inc.; Cedars-Sinai
597 Medical Center and Toronto Western Hospital) or 30 kHz (Blackrock Neurotech Inc.;
598 Johns Hopkins Hospital) from a total of eight microwires. All recordings were locally
599 referenced within each recording site by using either one of the eight available micro
600 channels or a dedicated reference channel with lower impedance provided in the bundle,
601 especially when all channels contained recordings of neuronal spiking. We used the
602 semiautomated template-matching algorithm OSort (version: 4.1) (Rutishauser et al.
603 2006) to detect and sort spikes from putative single neurons in each wire. Spikes were
604 detected after bandpass filtering the raw signal in the 300 – 3,000 Hz band (see **Fig. S2**
605 for single cell quality metrics). The two tasks (WM and LTM) were acquired in a single
606 recording and all neurons were jointly sorted for both tasks. In total, we isolated 950
607 neurons across both areas of the MTL. Neurons with a firing rate lower than 0.1 Hz in
608 either the WM or the LTM tasks were excluded from analysis (67 neurons (7.1%)).
609 Analyses are based on 351 isolated neurons in the hippocampus and 532 in the amygdala
610 (a total of 883 neurons across both areas).

611 *Selection of neurons*

612 To select for category neurons whose firing rate differed systematically between the
613 picture categories during image presentation (encoding) in the WM task, we counted the
614 number of spikes a given neuron fired in a window between 200 to 1,200 ms after picture
615 onset across all trials in each category (all encoding periods and the probe period). We
616 then then computed a 1x5 permutation-based ANOVA with visual category as the
617 grouping variable. In addition, we computed a post-hoc right-sided permutation-based t-
618 test between the category with maximum spike count and all other categories combined.
619 We classified a given neuron as a category neuron if both tests were significant (both $p <$
620 0.05) (Daume et al. 2024). We refer to the category with the maximum average spike
621 count as the preferred category of the cell. We note that category cells are selected only
622 using spiking activity from the encoding period, leaving the firing rates during the
623 maintenance period independent for later analyses.

624 In the recognition task, we selected for neurons that were memory-selective by comparing
625 the number of spikes fired following image onset (window of 0.2-1.2 seconds after image
626 onset) between correct familiar and novel trials using a permutation-based t-test ($p < 0.05$,
627 two-sided). Neurons with higher firing rates for familiar than novel items (old $>$ new) were
628 classified as familiarity-selective, the other way round (new $>$ old) as novelty-selective.

629 *Relating WM maintenance activity to LTM formation*

630 We tested whether category-selective WM maintenance activity predicted LTM formation
631 using a mixed-effects GLM across all category-selective cells. The analysis was
632 performed on baseline-normalized firing rates during the maintenance period (0-2.5 s) of
633 the WM task in trials in which the preferred category of a given neuron was held in WM.
634 We only considered WM trials for which the probe question was answered correctly, and
635 which contained an image that appeared in the subsequent LTM recognition test. We
636 used LTM *accuracy* (2 levels, correct (remembered)/forgotten (wrong), categorical), LTM
637 *confidence* (3 levels, high/medium/low, continuous), and *area* (2 levels, hippocampus /
638 amygdala, categorical) as fixed effects and neuronID nested into patientID as random
639 intercepts.

640 $FR \sim 1 + acc * conf * area + (1 | patientID) + (1 | patientID:neuronID)$

641 We hypothesized that firing rates during the WM maintenance period should be lower for
642 pictures that were later forgotten (i.e., rated by mistake as “novel”) with high confidence
643 (that is, “high-confidence wrong” trials) than those forgotten with low confidence (“low-
644 confidence wrong” trials). The reason for this hypothesis is that for items that were
645 forgotten with high confidence, there should be a weaker memory trace than for items for
646 which patients were unsure whether they have seen the image before. We therefore
647 labeled the confidence ratings for forgotten trials as high = 1, medium = 2, low = 3. This
648 way the confidence labeling was consistent with our hypothesis. For remembered trials,
649 in turn, we hypothesized that firing rates should be higher for high compared to low
650 confidence trials, so we used the confidence labels high = 3, medium = 2, low = 1. To test
651 whether category-selective activity predicted LTM formation during the encoding window,
652 we based our GLM analysis on firing rates determined during the picture 1 window of
653 preferred images (0-2 s).

654 *Single-neuron AUC analysis*

655 For MS neurons, we performed ROC analysis to assess how well the firing rate of
656 individual cells distinguished between novel and familiar trials (Rutishauser et al. 2015).
657 Spike counts between 200 and 1,200 ms after stimulus onset in the LTM recognition task
658 were used for each neuron’s ROC analysis. We varied the detection threshold between
659 the minimal and maximal spike count observed, linearly spaced in 25 steps. Only neurons
660 with at least ten correct novel and familiar trials each were included. A separate ROC
661 analysis was performed for high and low confidence trials. Only one of the two groups
662 used for the ROC analysis was modified according to confidence while the other was kept
663 constant. For familiarity-selective neurons, the fixed group was all true-negative trials
664 (regardless of confidence) which was compared with high-confident true-positive and low-
665 confident true-positive trials separately. For novelty-selective neurons, the fixed group
666 was all true-positive trials which were compared with high-confident true-negative and
667 low-confident true-negative trials separately.

668 *Interaction between simultaneously recorded category- and memory-selective neurons*

669 We determined whether MS neurons were more active during LTM retrieval of a familiar
670 picture when the persistent activity of a simultaneously recorded category-selective
671 neuron for that same picture was also high during the earlier WM maintenance period in
672 the same session. To do so, we median-split the FRs of each category neuron during the
673 maintenance period of correct trials that contained a preferred picture later tested in the
674 LTM task into low and high FR trials (separately for load 1 and 3 trials to avoid a bias in
675 FRs across loads). We then tested FRs of simultaneously recorded MS cells during LTM
676 retrieval (determined during 0.2-1.2s after picture onset) between items that have been
677 previously maintained with high vs low persistent activity. For that we used a mixed-
678 effects GLM with *Maintenance FR* (2 levels, high vs low, categorical) as fixed effect and
679 *neuronID* nested into *patientID* as random intercept.

680
$$FR_{Retrieval} \sim 1 + Maint. FR + (1 | patientID) + (1 | patientID:neuronID)$$

681 We performed this analysis separately for familiarity-selective (old > new) and novelty-
682 selective (new > old) cells.

683 *Statistics*

684 For all statistical tests, we use (cluster-based) non-parametric permutation tests
685 (statcond.m as implemented in EEGLab, using option 'perm', or ft_freqstatistics.m in
686 FieldTrip), i.e., tests that do not make assumptions about the underlying distributions, or
687 mixed-effects GLMs (fitglme.m in MATLAB) to assess statistical differences between
688 conditions. Before each test, we removed neurons that differed ± 3 SD from the mean
689 across all neurons and all tested conditions. In the permutation-based tests, random
690 permutations of condition labels were performed to estimate an underlying null
691 distribution, which was then used to assess the statistical significance of the effect. All
692 permutations statistics used 10,000 permutations, and t-tests were tested two-sided
693 unless stated otherwise. The corresponding t estimates, which are computed based on a
694 normal distribution, are provided as reference only. Cluster-based permutation statistics
695 were performed as implemented in FieldTrip (Maris and Oostenveld 2007) with 10,000

696 permutations and an alpha level of 0.025 for each one-sided cluster. Lastly, error bars
697 shown in figures reflect standard errors of the mean for permutation-based t-tests or
698 standard errors of the coefficient for mixed-effect GLM results.

699 **Key Resources Table**

700 See separate file.

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