

UNIVERSITY OF BIRMINGHAM

University of Birmingham
Research at Birmingham

Episodic memory retrieval functionally relies on very rapid reactivation of sensory information

Waldhauser, Gerd T; Braun, Verena; Hanslmayr, Simon

DOI:

[10.1523/JNEUROSCI.2101-15.2016](https://doi.org/10.1523/JNEUROSCI.2101-15.2016)

License:

Creative Commons: Attribution (CC BY)

Document Version

Peer reviewed version

Citation for published version (Harvard):

Waldhauser, GT, Braun, V & Hanslmayr, S 2016, 'Episodic memory retrieval functionally relies on very rapid reactivation of sensory information', *The Journal of Neuroscience*, vol. 36, no. 1, pp. 251-260.
<https://doi.org/10.1523/JNEUROSCI.2101-15.2016>

[Link to publication on Research at Birmingham portal](#)

General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.

The Journal of Neuroscience

<http://jneurosci.msubmit.net>

JN-RM-2101-15R2

Episodic memory retrieval functionally relies on very rapid reactivation of sensory information

Gerd Waldhauser, Ruhr University Bochum
Verena Braun, University of Birmingham
Simon Hanslmayr, University of Birmingham

Commercial Interest:

1 **Title: Episodic memory retrieval functionally relies on very rapid reactivation of sensory**
2 **information**

3 Abbreviated title: Remembering Relies on Rapid Sensory Reactivation

4 Gerd T. Waldhauser^{1,2}, Verena Braun^{1,3}, Simon Hanslmayr^{1,3}

5
6 ¹ Department of Psychology, University of Konstanz, Box 905, 78457 Konstanz, Germany

7 ² Department of Neuropsychology, Institute of Cognitive Neuroscience, Ruhr-University
8 Bochum, Universitätsstr. 150, 44801 Bochum, Germany

9 ³ School of Psychology, University of Birmingham, Edgbaston, B15 2TT, Birmingham, United
10 Kingdom

11
12 **Corresponding author: Dr. Gerd Waldhauser, Department of Neuropsychology, Institute of**
13 **Cognitive Neuroscience, Ruhr-University Bochum, GAFO 05/602, Universitätsstr. 150, 44801**
14 **Bochum, Germany. Phone: +49(0)234-32-28170. Fax: +49(0)234-32-14622. E-mail:**
15 **gerd.waldhauser@rub.de**

16 **Contents:** 38 pages/ 3 tables/ 6 figures/ 163 words in the abstract/ 597 words in the introduction/
17 1421 words in the discussion.

18

19 **Acknowledgments**

20 This research was funded by grants from the Swedish Research Council (VR 435-2011-7163) and
21 the Young Scholar Fund at the University of Konstanz (83946931) awarded to G.W., and the
22 German Research Council awarded to S.H. (DFG HA 5622/1-1). The authors thank Martin Dahl
23 for valuable help during data collection and Tzvetan Popov for assistance with EEG source
24 analysis. The authors declare no competing financial interests.

25

Abstract

26 Episodic memory retrieval is assumed to rely on the rapid reactivation of sensory information
27 that was present during encoding - a process termed 'ecphory'. We investigated the functional
28 relevance of this scarcely understood process in two experiments in human participants. We
29 presented stimuli to the left or right of fixation at encoding, followed by an episodic memory test
30 with centrally presented retrieval cues. This allowed us to track the reactivation of lateralized
31 sensory memory traces during retrieval. Successful episodic retrieval led to a very early (~100-
32 200 ms) reactivation of lateralized alpha/beta (10-25 Hz) electroencephalographic (EEG) power
33 decreases in the visual cortex contralateral to the visual field at encoding. Applying rhythmic
34 transcranial magnetic stimulation (rTMS) to interfere with early retrieval processing in the visual
35 cortex led to decreased episodic memory performance specifically for items encoded in the visual
36 field contralateral to the site of stimulation. These results demonstrate for the first time that
37 episodic memory functionally relies on very rapid reactivation of sensory information.

38

39 **Significance Statement**

40 Remembering personal experiences requires a ‘mental time travel’ to revisit sensory information

41 perceived in the past. This process is typically described as a controlled, relatively slow process.

42 However, by using electroencephalography to measure neural activity with a high time

43 resolution, we show that such episodic retrieval entails a very rapid reactivation of sensory brain

44 areas. Employing transcranial magnetic stimulation to alter brain function during retrieval

45 revealed that this early sensory reactivation is causally relevant for conscious remembering.

46 These results give first neural evidence for a functional, preconscious component of episodic

47 remembering. This provides new insight into the nature of human memory and may help in the

48 understanding of psychiatric conditions that involve the automatic intrusion of unwanted

49 memories.

50

51

52

53 **Introduction**

54 Perceived information can reverberate with stored memory traces (Tulving et al., 1983). This fast
55 and involuntary process is considered a decisive ingredient for the ‘mental time travel’ implied in
56 episodic memory retrieval, reinstating sensory features of study episodes and biasing subsequent
57 retrieval processes leading to the experience of recollection (Tulving, 1983; Tulving et al., 1983).
58 This fundamental memory mechanism, termed ‘ecphory’, has long been described
59 phenomenologically and studied behaviorally (Semon, 1911; Tulving, 1976, 1982).
60 Neurophysiological evidence for such fast reinstatement processes has not emerged until recently
61 (Waldhauser et al., 2012; Wimber et al., 2012; Jafarpour et al., 2014). Using electrophysiological
62 methods, these recent studies show that a reactivation of sensory memory traces can occur very
63 rapidly, within 500 ms after onset of a retrieval cue. However, whether this early reactivation
64 process functionally drives episodic memory retrieval, as assumed in the theoretical idea of
65 ecphory, remains unclear. We employed a visual-half field paradigm to identify the oscillatory
66 signature of early reactivation (Experiment 1) and, moreover, to show that ecphoric reactivation
67 is functionally relevant for episodic memory retrieval (Experiment 2).

68 Retrieval from episodic memory leads to a reactivation of sensory memory traces in the
69 hemisphere contralateral to the visual field of initial presentation (Slotnick and Schacter, 2006;
70 Waldhauser et al., 2012). We made use of this principle in order to track the rapid reactivation of
71 individual memory representations, measuring and modulating brain oscillatory activity by means
72 of electroencephalography (EEG, Experiment 1) and rhythmic transcranial magnetic stimulation
73 (rTMS, Experiment 2). Participants were engaged in instructed or non-instructed encoding of
74 everyday objects presented either in the left or right visual field (LVF/ RVF; Fig. 1). In a
75 subsequent retrieval task, memory cues were presented at the center of the screen and participants
76 engaged in item recognition followed by a source memory task. Source memory was examined to

77 test for the ability to retrieve contextual details of the study episode, which is considered a
78 hallmark of episodic memory (Tulving, 1983).

79 Previous studies were able to localize memory reactivation effects during retrieval to
80 lateralized visual cortical areas active during encoding (Gratton, 1998; Slotnick, 2004; Slotnick
81 and Schacter, 2006) and investigated the timing of lateral reactivation in terms of event-related
82 potential effects (Gratton, 1998; Slotnick and Schacter, 2010). However, it still remains unclear if
83 and how rapid visual cortical reactivation is causally relevant to explicit episodic memory
84 (Slotnick and Schacter, 2010; Thakral et al., 2013), leaving a fundamental question of memory
85 theory unanswered. In order to shed light on these questions we investigated brain oscillations as
86 a highly sensitive, physiologically relevant measure of cortical activity. Following recent ideas
87 (Hanslmayr et al., 2012), a desynchronization of oscillatory power in the alpha/beta frequency
88 bands indicates an increase in the complexity of firing patterns, thereby allowing for higher
89 information coding capacity during memory encoding and retrieval. Thus, we expected a specific
90 decrease of alpha/beta oscillations in the brain hemisphere contralateral to the visual field of
91 encoding as a marker of memory reactivation. In line with the theoretical notion of ecphory, this
92 alpha/beta power decrease was hypothesized to occur very rapidly, i.e. within 500ms (Tulving et
93 al., 1983; Waldhauser et al., 2012; Jafarpour et al., 2014), before the occurrence of signatures of
94 recollection and controlled retrieval processes (Rugg and Curran, 2007). Applying rhythmic
95 transcranial magnetic stimulation (rTMS) at the neural sources, in the time range, and with a
96 frequency as identified in the first experiment was expected to counteract the rapid reactivation of
97 visual cortical areas and lead to disrupt source memory performance. This would give strong
98 evidence for the functional relevance of ecphoric processes for episodic remembering.

99

100

101 **Materials and Methods**

102 **Materials and Procedure**

103 Materials, behavioral task, trial timing, and basic procedure were identical for
104 Experiments 1 and 2 (see Fig. 1). The study was approved by the Ethical Review Board at the
105 University of Konstanz.

106 *Stimulus material.* Two hundred and forty everyday objects (Rossion and Pourtois, 2004)
107 were used in each experiment. Half of these items were presented during encoding, serving as old
108 items during retrieval. Objects subtended a visual angle of $5.6^\circ \times 4^\circ$ and were presented to the left
109 or right visual field (LVF/RVF), 4° below and 6° lateral from central fixation. Items were
110 preselected into 8 sets, so that semantic categories of the depicted objects, frequency of
111 occurrence, vividness, visibility and orientation (portrait vs. landscape) were balanced across
112 conditions.

113 *Procedure.* The experiment was carried out in two blocks, pertaining to the two encoding
114 conditions (instructed and non-instructed encoding). Each block comprised the encoding phase, a
115 distracter task and a final retrieval phase. In the non-instructed encoding condition, participants
116 were supposed to engage in judging the size of each object. In the intentional encoding condition,
117 subjects were simply instructed to intentionally encode each object the best they could for later
118 retrieval. During encoding, participants responded with the index and middle finger of the right
119 hand whether an item was larger or smaller than a shoebox or whether the item was easy or
120 difficult to encode. Allocation of response buttons to index or middle finger was counterbalanced
121 across subjects. The encoding phase was followed by a three-minute distracter task to prevent
122 selective rehearsal, consisting of counting backwards aloud from a three digit number in steps of
123 three. During the subsequent retrieval task, 60 encoded items were presented at the center of the
124 screen as old items together with the same amount of new items. Participants were instructed to

125 first engage in an old/new recognition test and subsequently tested for source memory, indicating
126 whether an item was presented to the left or right visual field during encoding. Participants
127 responded with the index and middle finger of the right hand whether an item was old or new and
128 if the item was endorsed as old, whether the item was initially presented to right or left of
129 fixation. Allocation of response buttons to index or middle finger was counterbalanced across
130 subjects in the old/new task, but the middle finger was always used to indicate source
131 endorsement to the RVF and the index finger was used to indicate LVF presentation. Succession
132 of encoding conditions, old/new status of items and presentation of the old items to the left or
133 right visual field during encoding were counterbalanced across subjects.

134 Presentation of items within encoding phases was randomized so that each VF condition
135 was followed by an item from the same or opposite VF condition with equal probability and
136 under the constraint that the same VF could occur twice in a row. During retrieval, the sequence
137 of items encoded in the left and right VF was also randomized under the same constraint (no
138 more than two items from the same VF condition in a row). Additionally, old items were
139 randomly intermixed with new items so that no more than four old or new items could occur in a
140 row.

141 *Analysis of behavioral data.* Behavioral data during the final memory test were analyzed
142 based on a) hits, i.e. the number of correctly identified old items and b) source hits, i.e. the
143 number of hits for which VF of presentation was correctly identified in addition to correct item
144 recognition. **Number of hits and source hits were each divided by the number of all old items for**
145 **each subject. Arguably, dividing the number of source hits by number of hits would give a**
146 **cleaner measure of pure source memory performance in addition to simple item recognition.**
147 **However, we assumed that source memory performance is already constrained by item memory**
148 **performance in our case, so that a ‘new’ response to an old item (i.e., miss) prevents a correct**

149 source memory judgment, as only an 'old' response prompts a subsequent source memory task.
150 In addition, item recognition performance may already be biased by source memory demands so
151 that only items are endorsed as hits if a correct source memory judgment can be made. As a
152 consequence of our calculation method, source hit rates may appear rather low. Note that chance
153 level for source hits is below 50 %, since the probability to endorse an item as being presented in
154 the LVF or RVF already depends on the probability to endorse an item as old or new (see, e.g.,
155 Cykowicz et al., 2001; Batchelder & Riefer, 1990, for detailed discussion). In addition to the
156 different types of hits, we report c) false alarms, new items that were incorrectly classified as old.
157 For Experiment 2 we also investigated d) source false alarms, new items that were incorrectly
158 endorsed as old and for which a source memory judgment was given. This analysis was
159 conducted to determine whether rTMS affects the tendency to misattribute a new item to the VF
160 contra- or ipsilateral of stimulation. Behavioral data were analyzed in uncorrected repeated
161 measures ANOVAs or uncorrected two-sided paired t-tests.

162

163 **Experiment 1**

164 *Participants.* Sixteen right-handed (Oldfield, 1971) subjects (11 female) with a mean age
165 of 24 years (range 21 – 37), normal or corrected-to-normal vision, and no history of neurological
166 of psychiatric disease participated in this study. Participants received course credit or a monetary
167 reward of 20 € for participating in the experiment. Informed consent was acquired from each
168 participant prior to the experiment.

169 *Data analysis.* EEG was recorded using equidistant 128 Ag/AgCl scalp electrodes (DC-
170 100 Hz, 512 Hz sampling rate) referenced to common average. A time-frequency representation
171 of the EEG signal (1-30 Hz) was derived by means of Morlet wavelets (width 5). Since we had
172 no hypotheses concerning the different encoding tasks and since no statistical differences

173 between encoding tasks were obtained (see Results and Table 1), EEG power was collapsed
174 across encoding tasks. To quantify event-related signal changes on sensor level, poststimulus
175 power change was calculated in relation to a pre-stimulus baseline period (-500 to 0 ms) for both,
176 encoding and retrieval phases. No significant electrode clusters emerged between conditions in
177 the baseline interval in a fieldtrip cluster statistic calculated at all electrodes for the frequency
178 ranges of interest during encoding and retrieval.

179 To identify time-windows and the frequency range of interest, EEG power during
180 encoding was first compared between LVF and RVF conditions in a sliding-time-window
181 fieldtrip cluster statistic (Maris and Oostenveld, 2007). Here, we continuously applied cluster-
182 statistics for time and frequency windows of 200 ms and 2 Hz in steps of 100 ms and 1 Hz to the
183 data from 1 to 30 Hz and from 0 to 1500 ms (Staudigl and Hanslmayr, 2013). Following our
184 hypotheses, we directly compared posterior electrodes over the respective hemisphere
185 contralateral to the VF of presentation between LVF and RVF conditions. We did so by inverting
186 EEG power values in the RVF condition for each time and frequency point at left-hemispheric
187 parieto-occipital sensors through multiplication with -1. Then, we compared the result in each
188 time-frequency window with the corresponding (non-inverted) power values at right-hemispheric
189 sensors for the LVF condition. Each cluster statistic then reveals whether there is a contralateral
190 power decrease, with the highest likelihood of significant effects if there is a strong contralateral
191 decrease in both, LVF and RVF conditions. In order to correct for multiple comparisons, the
192 resulting 630 p-values were adjusted following the false discovery rate procedure (Benjamini and
193 Hochberg, 1995; Benjamini and Yekutieli, 2001). The result of this analysis indicated electrode
194 clusters yielding significant EEG power differences between LVF and RVF conditions over the
195 respective contralateral hemispheres in the alpha/ lower beta range (8-20 Hz), most prominent
196 between 200 and 700 ms after stimulus presentation (see Fig. 3A, top).

197 However, the sliding cluster analyses can only suggest the presence of a statistical
198 difference between VF conditions at the contralateral hemispheres, but it is not able to reliably
199 show the actual topographical clusters that differ between VF conditions and to take into account
200 ipsi- and contralateral sensors. To this end, we subtracted non-inverted data in the RVF from the
201 LVF condition and calculated a fieldtrip cluster statistic in the time (200-700 ms) and frequency
202 (8-20 Hz) window suggested by the sliding analysis, allowing us to identify significant electrode
203 clusters in each hemisphere (Fig. 3A, center). The mean EEG power at these clusters interacted
204 significantly between VF (LVF/RVF) and left and right brain hemispheres (LH/RH, see Fig. 3A,
205 bottom), as indicated by a 2-way ANOVA.

206 In order to investigate lateralized activity during retrieval, EEG power differences
207 between contra- and ipsilateral electrode clusters identified during encoding were averaged over
208 LVF and RVF conditions and compared over time in a frequency range between 1 and 30 Hz.
209 Results were masked by the results of running Wilcoxon signed-rank test applied at each time
210 (~50 ms) and frequency (~0.5 Hz) bin resulting from the Morlet wavelet time-frequency
211 transformation. Since our hypotheses were concerned with rapid contralateral decreases in
212 alpha/beta power, we focused on early (< 500 ms) interaction effects as indicators for ecphoric
213 processes. Negative values in Figure 3B (top) indicate uncorrected significant ($P < .05$)
214 differences between contra- minus ipsilateral electrodes collapsed across both VF conditions.
215 Based on the results of this exploratory analysis, the interaction between VF (LVF/RVF) and left
216 and right brain hemispheres was tested in an uncorrected 2-way repeated-measures ANOVA
217 taking into account mean EEG power (10-25 Hz, 100-200 ms) at the LH/RH clusters identified
218 during encoding (see Fig. 3B, bottom, for mean power depending on condition and hemisphere
219 and Fig. 3B, center, for topographical distribution of mean EEG power). In order to shed light on
220 hemisphere-specificity of these effects (Fig. 4), additional two-sided t -tests were carried out in

221 the 100-200 ms time window, comparing LVF- RVF differences in the hemisphere-specific peak
222 frequencies at the LH and RH electrode clusters.

223 In order to test whether reinstatement strength reflecting in a contralateral alpha/beta
224 power decrease is linked to behavioral performance, we compared the amount of lateralization
225 between source hits and source misses in a two-sided *t*-test. Lateralization was defined as the
226 mean difference between the contra- minus ipsilateral electrode clusters in the 10-25 Hz
227 frequency band from 100 to 200 ms. We expected lateralization to be more negative for source
228 hits than source misses. In a second step, we also investigated whether single trials could be
229 identified as source hits and source misses (i.e. hits that were incorrectly attributed to the VF
230 opposite to the VF of actual presentation) based on the amount of contra- minus ipsilateral
231 lateralization at the electrode clusters in the 10-25 Hz frequency band by means of a contingency
232 table (see Table 2). In this approach, EEG signals were not baseline corrected in order to avoid
233 misclassification of trials due to potentially higher baseline noise in non-averaged single trials.
234 Instead, a lateralization index was estimated for each trial by correcting for the total power at the
235 contra- and ipsilateral electrodes (lateralization index = contralateral – ipsilateral / contralateral +
236 ipsilateral; cf. Händel et al., 2011). A lateralization index < 0 signifies a trial as having a relative
237 power decrease at contralateral electrodes. We hypothesized that such trials would be classified
238 as source hits with a frequency above chance, whereas trials with a lateralization index > 0 would
239 more often be classified as source misses. We tested this assumption by means of a χ^2 -test for all
240 trials from all participants (i.e. fixed effects analysis). In order to make the data more accessible,
241 we also report classification performance in percent ((correctly classified source hits + correctly
242 classified source misses) / all items) * 100). In addition, we also tested whether the mean
243 differences between observed cell frequencies and expected cell frequencies in chi-square tests

244 across all participants were significantly different from zero on the group level by means of a
245 one-sample *t*-test (i.e. random effects analysis).

246 To identify sources of oscillatory activity, we employed the Dynamic Imaging of
247 Coherent Sources (DICS) beamforming approach after calculating the cross-spectral density
248 matrix. We used individual electrode positions as acquired with a sensor digitization tool
249 (Xensor™, www.ant-neuro.com) and the FieldTrip standard MRI. DICS constructs adaptive
250 spatial filters to localize power for each grid point in the entire brain (Gross et al., 2001; Gross et
251 al., 2003). For each individual and the time periods of interest during encoding and retrieval,
252 filters were calculated using activity following the encoding stimulus and the recognition cue,
253 respectively, and baseline periods corresponding to the length of the poststimulus period of
254 interest (Dalal et al., 2008), including the trials from both, LVF and RVF conditions. For
255 encoding data, a baseline period from -500 to 0 ms and poststimulus period from 200 to 700 ms
256 were chosen. For retrieval data, a baseline period of -100 to 0 ms and a poststimulus period of
257 100 to 200 ms were chosen. Cross-spectral density and source power was estimated using
258 frequency analysis with Slepian multitapers as implemented in FieldTrip (Oostenveld et al.,
259 2011) for the frequency range observed at sensor level, i.e. 8-20 Hz for encoding and 10-25 Hz
260 for retrieval. The resulting average source estimate for each condition in the time intervals of
261 interest was corrected for source activity in the baseline interval and subsequently statistically
262 compared with the other condition and interpolated to the standard Montreal Neurological
263 Institute (MNI) brain. In a final step, we aimed at identifying the voxels that differentiated with
264 most sensitivity between conditions across both hemispheres. To this end, we statistically
265 compared the RVF-LVF power difference in the right hemisphere with the corresponding effect
266 in the left hemisphere in a one-sided FieldTrip source cluster statistic. This was done again for
267 both, encoding and retrieval effects. The results were again interpolated to the standard Montreal

268 Neurological Institute (MNI) brain (see Fig. 5). The obtained maximum inter-hemispheric
269 difference between conditions during retrieval was determined at MNI coordinates $\pm 40, -78, 0$.
270 Source localization results were visualized using the Caret software (<http://brainvis.wustl.edu>).

271

272 **Experiment 2**

273 *Participants.* Twenty-four right-handed subjects (14 female) with a mean age of 23 years
274 (range 18 – 27) and normal or corrected-to-normal vision completed the experiment. In addition
275 to a general assessment of history of neurological and psychiatric disease and medication, an
276 additional TMS screening was conducted prior to the experiment (Rossi et al., 2011).

277 Furthermore, a detailed explanation of the TMS method and its risks was provided for the
278 subjects (Rossi et al., 2009). Informed consent was acquired from each participant prior to the
279 experiment. One participant was excluded before the start of the study due to unclear status of
280 inner ear damage and one further person aborted the experiment because of neck pain during
281 phosphene stimulation. Participants received course credit or a monetary reward of 20 € for
282 participating in the experiment and an extra 10 € for taking part in structural MRI assessment.

283 *Procedure.* Behavioral task and procedure were almost identical to Experiment 1.

284 Stimulation conditions were applied in a within-subject fashion during the retrieval phase of both
285 blocks. This required pausing the procedure every 40 trials in order to relocate the coil between
286 the hemispheres and change the tilt of the coil according to TMS and sham conditions. Old, new,
287 LVF and RVF items were equally distributed between these segments of 40 trials. Four subjects
288 received only 36 trials per stimulation block due to experimental error, but counterbalancing and
289 matching of condition and stimulus material was preserved. rTMS was applied to the right and
290 left hemisphere during each of the two retrieval phases. Sham was applied to only one
291 hemisphere during a particular retrieval block in order to keep the blocks at reasonable size and

292 length. Succession of rTMS and Sham conditions was counterbalanced across subjects so that
293 stimulation conditions and hemispheres were equally often followed and preceded by the other
294 conditions.

295 TMS was applied with a Magstim Rapid² Transcranial Magnetic Stimulator via a
296 Magstim figure-of-eight coil. At the beginning of an experimental session, phosphene threshold
297 (PT) was identified in each subject, using the modified binary search (MOBS) procedure (Tyrrell
298 and Owens, 1988; Anderson and Johnson, 2006; Romei et al., 2010). To this end, subjects were
299 blindfolded and single TMS pulses were applied with the coil centered midline 2 cm above the
300 inion. Participants had to indicate the presence or absence of a phosphene by answering “yes” or
301 “no”. PT is defined as the percentage of maximum stimulator output above which subjects
302 consistently report seeing phosphenes. PT served as an individual marker of cortical excitability
303 and was used to determine stimulator output during the experiment. rTMS was applied with 90%
304 PT output, which corresponded to a mean stimulator output of 61.3 % ($SD = 7.44$). If no reliable
305 PT could be determined ($n = 3$), a fixed stimulator output of 60 % was used (Romei et al., 2010).
306 No participant reported perception of phosphenes during the experiment.

307 In order to deliver magnetic pulses with high anatomical precision rTMS was guided by a
308 neuronavigation system, which co-registers the individual MRI with the position of the TMS coil
309 using a 3D tracking device (ANTVisor; www.ant-neuro.com). Individual high-resolution T1-
310 weighted MRIs were acquired from a Siemens Skyra 3 T scanner (Flip Angle = 7°; TR =
311 2500ms; TE = 4.06ms) or based on other structural MRI scans from various sources if already
312 existing for the participant. Maximum magnetic field strength was applied to the neural source of
313 alpha/beta oscillatory decreases in the lateral occipital cortex as identified during retrieval in
314 Experiment 1 (MNI coordinates: $\pm 40, -78, 0$). Four TMS pulses were applied with a duration of

315 57 ms between pulses, with application starting at 33.5 ms and lasting until 204.5 ms after cue
316 presentation, corresponding to a frequency of 17.5 Hz (see Fig. 6A).

317 Sham was applied by tilting the TMS coil in an angle of approximately 60° away from the
318 scalp surface, but still touching the head. Thereby, participants still experienced clicking noise
319 and slight vibrating sensation at the scalp surface (Sauseng et al., 2009).

320

321 **Results**

322 **Episodic memory retrieval is accompanied by a rapid decrease of alpha/beta oscillatory** 323 **power**

324 In Experiment 1 (see Fig. 1), high-density EEG was measured during encoding and
325 retrieval to reveal the oscillatory signature of memory reactivation. In a first step, we aimed at
326 identifying encoding-related lateralized brain activity. On a behavioral level, no difference
327 between encoding tasks (instructed vs non-instructed) or visual field conditions (LVF vs RVF)
328 were obtained, neither on item recognition nor on source memory performance (all $t_{15}S < 1.361$,
329 $P_s > 0.05$; see Table 1). In addition, there was no difference between blocks determined by
330 encoding conditions in terms of false alarm rates ($t_{15} = 1.156$, $P = 0.266$; instructed: $M = 11.6\%$,
331 $SD = 8.91\%$; non-instructed: $M = 14.1\%$, $SD = 8.65\%$). This allowed us to collapse the EEG
332 data across encoding instructions to enhance signal-to-noise ratio and to directly compare VF
333 conditions on a neural level. We compared EEG activity between RVF and LVF conditions at the
334 respective left- or right-hemispheric posterior contralateral electrodes in a sliding cluster statistic
335 (see Method section, Fig. 2) to isolate the time and frequency windows most sensitive to the
336 expected contralateral power decreases at encoding. This was achieved by inverting power values
337 for the RVF condition at the left-hemispheric electrodes and comparing them with power at right-
338 hemispheric electrodes for the LVF condition. This analysis indicated maximum power

339 differences at contralateral electrodes between the VF conditions from 200-700 ms in the
340 alpha/beta range (8-20 Hz, $p_{\text{adj}} < 0.05$, FDR corrected; Fig. 3A, top (Genovese et al., 2002)).
341 While this result pinpointed the time-and frequency range of lateral differences between VF
342 conditions, the analysis could neither indicate if the effect is stronger on contra- than ipsilateral
343 electrodes, nor answer exactly which electrodes are most sensitive to hemisphere and VF-specific
344 effects. Thus, we subtracted power in the LVF condition from power in the RVF condition in the
345 identified time-frequency range, such that positive values reflect a stronger alpha/beta power
346 decrease in the RVF condition whereas negative values reflect a power decrease in the LVF
347 condition (Fig 3A, center). We calculated a cluster statistic on all electrodes to identify the
348 clusters most sensitive to VF specific decreases (Maris and Oostenveld, 2007). In line with our
349 hypothesis, this analysis revealed one left- and one right hemispheric electrode cluster (left: $P =$
350 0.038 ; right: $P = 0.006$), each most sensitive to a power decrease in the contralateral VF (see Fig.
351 3A, center). This VF x Hemisphere interaction was supplemented by a 2-way repeated measures
352 ANOVA taking into account mean power at the identified electrode clusters ($F_{1,15} = 62.039$, $P <$
353 0.001), suggesting a significant power decrease at contralateral electrodes differing from
354 ipsilateral activity for each VF condition (see Fig 3A, bottom). Finally, we conducted a
355 beamformer source analysis of the 8-20 Hz alpha/beta oscillatory activity between 200 and 700
356 ms (Gross et al., 2001; Gross et al., 2003). To obtain the maximum inter-hemispheric difference
357 between conditions, we subtracted the interpolated RVF-LVF power difference at source level in
358 the right hemisphere from the effect in the left hemisphere and vice versa. The source analysis,
359 localizing the maximum difference between contra- and ipsilateral hemispheres, revealed neural
360 generators of the EEG effect in the lateral (middle and inferior) occipital gyrus (LOC, BA 18/19;
361 Fig. 5).

362 In order to reveal the neural signature of memory reactivation, we carried out statistical
363 analyses on those electrode clusters showing significant lateralization differences between LVF
364 and RVF at encoding. Following previous EEG studies of memory reactivation (Wimber et al.,
365 2012; Jafarpour et al., 2014; Johnson et al., 2015), and in line with the theoretical notion of
366 ecphory (Tulving et al., 1983), we focused our analysis at retrieval on a time-range preceding the
367 typical timing of recollection effects, before 500 ms after presentation of the retrieval cue. As
368 indicated by a continuous Wilcoxon sign-rank test, a significant difference between ipsi- and
369 contralateral electrode clusters emerged very early, 100-200 ms after cue presentation ($P_s < 0.05$),
370 and in a similar frequency band as during encoding, between 10-25 Hz (see Fig. 3B, top). This
371 difference, again, was due to a power decrease at the electrode cluster contralateral to the VF of
372 presentation during encoding, as indicated by a significant VF x hemisphere interaction ($F_{1,15} =$
373 8.773 , $P = 0.01$, see Figure 3B). This effect appeared to be different between hemispheres in
374 terms of peak frequencies. As shown in Figure 4A, differences between VF conditions were
375 clustered around 20 Hz in the RH cluster whereas the LH cluster displayed a more specific effect
376 at around 10 Hz. Frequency-specificity of the two hemispheres was confirmed in a statistical
377 analysis, showing that only the LH cluster showed a significant VF difference at 10 Hz ($t_{15} =$
378 2.332 , $P = 0.034$) and only the RH cluster showed a significant VF difference at 20 Hz ($t_{15} =$
379 2.616 , $P = 0.02$; Fig. 4B). However, based on our previous studies, and following the idea that we
380 tap into similar oscillatory processes in the two hemispheres, we continued our analyses with data
381 integrated over the whole frequency range showing a mean contra- versus ipsilateral difference
382 (Waldhauser et al., 2012).

383 In order to check whether contra- versus ipsilateral differences in the 10-25 Hz frequency
384 range are indeed due to a poststimulus decrease, and not due to a prestimulus shift of attention,

385 we repeated the same analysis taking into account the raw data from the baseline (-500 to 0 ms)
386 interval. This analysis yielded no significant results ($F_{1,15} < 3.554$, $P_s > 0.05$).

387 According to theories on episodic memory, an ephoric reactivation of trace information
388 is a prerequisite for the recollection of details of an episode. Thus, we expected it to be most
389 pronounced for source hits, for which the source of encoding could be correctly remembered. In
390 line with this idea, the contra- versus ipsilateral alpha/beta power decrease was significantly
391 greater for source hits ($M = -7.13\%$, $SD = 9.631$), when compared to source misses ($t_{15} = 4.061$,
392 $P = 0.001$), the latter actually showing a relative power increase at contralateral electrodes ($M =$
393 7.27% , $SD = 12.534$). The lateralization effects for source hits and source misses were both
394 significantly different from zero (source hits: $t_{15} = -2.962$, $P = 0.01$; source misses: $t_{15} = 2.320$, P
395 $= 0.035$). These results suggest that the laterality of EEG power predicts to which VF an item is
396 attributed to, in a way that subjects tend to attribute an item to the VF that is contralateral to the
397 hemisphere displaying a power decrease. As shown in Table 2, this was also the case on a single-
398 trial level. Source hit trials more often showed a negative lateralization index, i.e., a power
399 decrease at electrodes contralateral to the VF in which the item was actually presented during
400 encoding. Source miss trials more often showed a positive lateralization index, i.e., a power
401 decrease over the ipsilateral hemisphere (see Table 2). A dependency of lateralization and
402 response was confirmed statistically in a fixed effects analysis ($\chi_1^2 = 4.731$, $P = 0.03$), showing
403 that 53 % of all items were classified correctly as source hits and source misses based on EEG
404 lateralization. This statistical dependency was also confirmed in a random effects analysis on
405 group level, with the mean difference between observed and expected cell values being
406 significantly greater than zero ($M = 0.951$, $SD = 1.6374$; $t_{15} = 2.25$, $P = 0.04$). Notably, 11 (out of
407 16) participants numerically showed this classification pattern (i.e. mean differences > 0) on the
408 single trial level. Lateralization and memory performance was independent when taking into

409 account the baseline interval from -500 to 0 ms on a single trial level ($\chi_1^2 = 1.8467$, $P = 0.174$).
410 Classification of source hits and source misses across all subjects based on EEG lateralization
411 was close to chance (49 %). This accorded with a random effects analysis when comparing
412 individual differences between expected and observed frequencies against zero ($M = 0.647$, $SD =$
413 1.317 ; $Z = 1.448$, $t_{15} = 1.885$, $P = 0.079$).

414 Finally, we aimed at localizing the neural generators of alpha/beta power decreases for
415 source hits. Neural generators of this EEG effect corresponded closely to the sources observed
416 during encoding, localized to the middle and inferior LOC (BA 18/19; Fig. 5).

417 Together, these data indicate a very rapid reactivation of neural signatures established
418 during encoding, which are visible in a power decrease in the alpha/beta frequency band. Source
419 analysis suggests that alpha/beta decreases can be localized to the LOC, a region that is known to
420 be constitutive for object recognition during perception and encoding (Konen and Kastner, 2008)
421 and that is sensitive to hemisphere-specific retrieval of lateralized visual memory traces
422 (Slotnick, 2004; Slotnick and Schacter, 2006).

423 The very early (~100 ms) re-emergence of alpha/beta oscillatory decreases during
424 retrieval is in line with previous EEG studies of early reactivation (Wimber et al., 2012; Jafarpour
425 et al., 2014; Johnson et al., 2015) and suggests that retrieval correlates with a rapidly occurring
426 ecphoric process. However, it is unclear whether such early reactivations are functionally
427 relevant to successful episodic retrieval. Theoretically, these early reactivation signatures could
428 accompany memory retrieval but they might not be causally relevant to the retrieval process. To
429 investigate this question, we tested whether counteracting early sensory cortical activity with
430 rTMS in the hemisphere contralateral to the site of encoding reduces retrieval of the episodic
431 memory trace.

432

433 **Counteracting early sensory cortical activity through rTMS reduces episodic memory**

434 Behavioral task and procedures in Experiment 2 were identical to Experiment 1 (See Fig.
435 1), except that, instead of measuring EEG, rTMS and Sham stimulation were applied during the
436 retrieval phase of the experiment. Small breaks during the retrieval phases were used to relocate
437 the TMS coil for the stimulation conditions (Sham, TMS) on the different stimulation sites, left
438 hemisphere (LH) or right hemisphere (RH) in each subject. rTMS was applied at the average
439 center EEG frequency observed during retrieval (17.5 Hz) at the neural sources of the EEG
440 retrieval effect obtained in Experiment 1 via a neuronavigation system (ANT-Visor; www.ant-
441 neuro.com). rTMS was centered at the time interval of maximum EEG differences between 100
442 and 200 ms. Driving neural assemblies in the LOC at alpha/beta frequencies with 17.5 Hz rTMS
443 (Thut et al., 2011; Hanslmayr et al., 2014) should counteract the decrease of alpha/beta power
444 observed in Experiment 1 and therefore impair episodic memory retrieval (Waldhauser et al.,
445 2012).

446 As in Experiment 1, encoding condition (instructed vs non-instructed) had no effect on
447 later item recognition or source memory performance, nor did visual field at encoding (all $t_{23S} <$
448 1.686, $P_s > 0.05$, see Table 1). Thus, behavioral data were again collapsed across these encoding
449 conditions. In addition, we collapsed memory performance for items for which TMS was applied
450 to the hemisphere contra- versus ipsilateral to the VF of presentation during encoding. We
451 assumed that rTMS should specifically decrease episodic memory performance for items that
452 were presented contralateral to the hemisphere of stimulation. A 2-way ANOVA on the
453 percentage of correct source hits on all old items revealed a significant interaction between
454 Stimulation (Sham vs. rTMS) and Hemisphere (contralateral vs. ipsilateral to VF of presentation;
455 $F_{1,23} = 4.617$, $P = 0.042$, see Table 3 and Fig. 6B). No main effect for Stimulation or Hemisphere
456 occurred in this analysis ($F_{1,23S} < 3.449$, $P_s > 0.05$). Source memory performance was

457 significantly lower when rTMS was applied at the hemisphere contralateral to the VF of encoding
458 when compared to contralateral source memory performance in the Sham condition ($t_{23} = 2.410$,
459 $P = 0.024$; see Table 3 and Fig. 6B). No difference between rTMS and Sham was found for
460 ipsilateral stimulation ($t_{23} = 0.160$, $P = 0.874$, *ns*; see Table 3 and Fig. 6B). Source hits did not
461 differ between contra- and ipsilateral hemispheres when analyzing rTMS and Sham stimulation
462 data separately ($t_{23s} < 1.973$, $P_s > 0.05$; cf. Table 3).

463 No main or interaction effects were obtained for item recognition as measured in hit rates,
464 regardless of source memory performance ($F_{1,23s} < 2.474$, $P_s > 0.05$, see Table 3), suggesting that
465 rTMS only had an influence on source memory but not item memory. However, there was no
466 significant evidence ($F_{1,23} = 0.013$, $P = 0.911$) that rTMS affected source hits to a larger extent
467 than hits as tested in a 2 x 2 x 2 ANOVA with factors Type (source hits vs. hits), Stimulation
468 (Sham vs. rTMS) and Hemisphere (contralateral vs. ipsilateral), possibly since both measures are
469 not fully independent from each other. To further explore the nature of the rTMS effect on
470 memory several control analysis were carried out. For instance, we investigated in how far rTMS
471 introduced a response bias. To this end, we tested whether rTMS increased false alarm rates and
472 whether a potential effect would be dependent on the hemisphere of stimulation in a two-way
473 repeated measures ANOVA with factors Stimulation (rTMS, Sham) and Hemisphere (LH, RH).
474 There was no significant main or interaction effect differentiating false alarm rates during LH (M
475 $= 9.5\%$, $SD = 9.00$) or RH ($M = 9.1\%$, $SD = 4.28$) rTMS and LH ($M = 8.4\%$, $SD = 8.29$) or RH
476 ($M = 9.0\%$, $SD = 7.15$) Sham stimulation (all $F_{1,23s} < 0.449$, $P_s > 0.05$). Second, we tested
477 whether rTMS increased or decreased the tendency to attribute false alarms to the visual field
478 contralateral to the site of stimulation (see Table 3, source false alarms). Again, no significant
479 main or interaction effect emerged in the two-way repeated measures ANOVA with factors

480 Stimulation (rTMS vs. Sham) and Hemisphere (contralateral vs. ipsilateral; all $F_{1,23} < 3.206$, P_s
481 > 0.05).

482 Taken together, these analyses show that rTMS specifically affects source memory
483 performance for items previously presented in the VF contralateral to the stimulated hemisphere
484 when compared to Sham stimulation. Such an effect could not be observed for hits irrespective of
485 source memory performance, but the reduction in source hit performance was not significantly
486 different from performance for hits in general. Finally, we could rule out any unspecific effect of
487 rTMS on response execution or memory bias by showing that Stimulation had no effect on the
488 endorsement of new items in terms of false alarm rates. This suggests that alpha/beta power
489 decreases are especially relevant for episodic memory through providing rapid sensory
490 reactivation as a basis for later source memory performance.

491

492 **Discussion**

493 We here show that very rapid reactivation of sensory information is functionally relevant for
494 episodic memory retrieval. This conclusion is supported by the results of two independent
495 experiments described above. First, lateralized encoding patterns of alpha/beta power decreases
496 re-emerge rapidly in visual cortical areas during retrieval. Second, interfering with these early
497 reactivation patterns reduces episodic memory retrieval. These findings add to the literature in
498 demonstrating very rapid, context specific memory reactivation, termed ephory (Waldhauser et
499 al., 2012; Wimber et al., 2012; Jafarpour et al., 2014; Johnson et al., 2015) . Our results go one
500 critical step beyond the previous findings in showing that these rapid reactivations of sensory
501 memory traces are functionally relevant for episodic memory retrieval, and directly affect the
502 ability to retrieve contextual details of the study episode. These findings are a major conceptual

503 advance for episodic memory research, providing first evidence that ecphoric processes are
504 causally related to episodic memory retrieval.

505 Ecphory has long been suggested as a prerequisite for the ‘mental time travel’ implied in
506 retrieval from episodic memory (Tulving et al., 1983). It is assumed that incoming sensory
507 information from retrieval cues reverberates with stored memory traces, leading to their
508 immediate and involuntary reactivation (Tulving, 1982). While the theoretical idea has a long
509 tradition in cognitive psychology (Semon, 1911) and is corroborated by behavioral data (Sheldon
510 and Moscovitch, 2010), neural evidence for this process has been sparse. Typically, neural
511 correlates of episodic memory retrieval were identified in a time range not before ~300 ms after
512 onset of a retrieval cue (Rugg and Curran, 2007). However, recent studies showed early
513 reactivation patterns during episodic retrieval that are in line with our results (Waldhauser et al.,
514 2012; Wimber et al., 2012; Jafarpour et al., 2014; Johnson et al., 2015). Albeit using different
515 analysis strategies and stimuli, these studies show that a replay of context information can occur
516 rapidly, well within 500 ms after presentation of a retrieval cue. The exact neural mechanisms of
517 this sensory reactivation and its interaction with controlled retrieval processes are still unclear
518 and deserve further investigation. According to cognitive theories, ecphory is a necessary but not
519 sufficient prerequisite for episodic retrieval (Tulving, 1982, 1983; Moscovitch, 2008). The
520 sensory information needs to be further processed by higher retrieval mechanisms, possibly
521 through hippocampal-neocortical loops (Horner et al., 2012; Staresina et al., 2012) and
522 potentially guided by prefrontal and parietal control (Ranganath and Paller, 1999; Cabeza et al.,
523 2008). As our data suggest, disrupting early sensory reactivation via external stimulation
524 negatively affects the recollection (i.e. retrieval of contextual details) of episodic memories.
525 Interestingly, our results match closely with one of our earlier studies that showed that inhibiting
526 retrieval of interfering information leads to an increase in alpha/beta oscillatory power in the

527 hemisphere housing unwanted memory traces that interfere with the retrieval of a target memory
528 trace (Waldhauser et al., 2012). This suggests that early modulations of alpha/beta power are a
529 decisive ingredient of successful remembering and can already act in concert with retrieval goals
530 and be biased by higher order cognitive control mechanisms.

531 Discussing the possible involvement of prefrontal control processes calls into question
532 whether ‘ecphory’ is the right label for the early sensory reactivation effects observed in the
533 present data. However, as already mentioned in early papers on this topic, higher-order control
534 mechanisms are likely to interact with rapid sensory reactivation during ecphory (Tulving et al.,
535 1983; Johnson, 1992; Lepage et al., 2000; Rugg and Wilding, 2000). Recent neuroscientific
536 studies also suggest that it is difficult to view these processes in separation, even at early stages
537 of memory processing and during involuntary retrieval (Kompus, 2011; Kompus et al., 2011;
538 Waldhauser et al., 2012).

539 In line with our hypothesis, a decrease of alpha/beta oscillatory power at the hemisphere
540 contralateral to the VF of encoding was most pronounced for source hits, to the extent that single
541 trials could be classified as source hits or source misses on the basis of EEG lateralization. In the
542 same vein, rTMS had a selective influence on source memory performance (albeit not to the
543 extent of yielding significant differences between source hits, and hits, i.e. item memory). This
544 pattern of results suggests that alpha/beta power decreases are particularly relevant for source
545 memory performance, which is in accordance with the theoretical notion of ecphory, because
546 correct source memory judgments require the highest amount of ecphoric information (Tulving et
547 al., 1983). Unexpectedly, in the EEG analysis, source misses showed alpha/beta lateralization in
548 the opposite direction compared to source hits. Interpretation of this result has to remain
549 speculative at this point. It appears that visual cortical activity predicted later memory decisions,
550 such that a retrieved memory representation is attributed to the VF contralateral to the

551 hemisphere where a decrease of alpha/beta power occurred. It could be the case that memory
552 representations attributed to the wrong VF were initially stored in the ipsilateral hemisphere
553 during encoding. Alternatively, this misattribution may be due to non-systematic fluctuations in
554 alpha/beta activity that led to illusory recollection of the wrong hemifield (e.g., Lange et al.,
555 2014). Finally, it might be the case that EEG lateralization in general reflects a process of source
556 reconstruction, and not sensory reactivation. However, this possibility seems rather unlikely,
557 since reconstructive processes during memory retrieval are more effortful and typically observed
558 later (> 600 ms) during retrieval processing (Johansson and Mecklinger, 2003; Herron, 2007).
559 Future studies, possibly combining EEG and high-resolution fMRI or using electrophysiological
560 methods that allow for assessing gamma oscillations (see below), might allow to distinguish
561 between true versus false source memories in this paradigm (Slotnick and Schacter, 2004;
562 Sederberg et al., 2007).

563 Our findings are in line with the idea that alpha/beta power decreases reflect sensory
564 information of episodic memory traces (Hanslmayr et al., 2012). However, we cannot conclude
565 that these are the only frequency bands that are involved in ephoric processing since we
566 restrained analyses to low frequencies up to 30 Hz because EEG is not ideally suited to pick up
567 the presumably very local high-frequency activities in the gamma range (da Silva, 2013).
568 Furthermore, we restrained rTMS to the center frequency of the alpha/beta range observed in
569 Experiment 1 but did not apply stimulation with another frequency. Thus, although we have
570 strong reason to assume that alpha/beta power in visual cortex plays a decisive role for ephoric
571 processes, we cannot conclude that ephory is specific to the alpha/beta range. It might be that
572 gamma together with theta and alpha oscillations also play a decisive role in ephoric processes
573 (Osipova et al., 2006; Osipova et al., 2008). These are important questions that are beyond the
574 scope of our study and should be addressed by future studies using techniques that allow for

575 investigating these high-frequency activities (MEG or intracranial EEG) and applying different
576 control frequencies in stimulation protocols (using TMS or transcranial alternating current
577 stimulation). Another interesting question that is beyond the scope of our study is the role of
578 hippocampal-neocortical interactions during early retrieval processes. For instance, does the rapid
579 reactivation of sensory information depend on the hippocampus or is it a purely cortical or
580 thalamo-cortical phenomenon (Staudigl et al., 2012; Headley and Weinberger, 2015; Ketz et al.,
581 2015)? Our results add an important angle to this research topic by suggesting that the earliest
582 interactions between sensory information and stored memory traces may occur in the alpha/beta
583 oscillatory band, beyond the long-discussed role of theta and gamma oscillations for memory
584 processing. Finally, another open question is whether similar results would be observed in
585 different sensory modalities, or with different visual stimuli. Future studies, together with past
586 research using different stimulus material and different experimental manipulations are required
587 to generalize our findings (Gratton et al., 1997; Wheeler and Buckner, 2003; Slotnick and
588 Schacter, 2006; Waldhauser et al., 2012).

589 Together, our results show that retrieval from episodic memory leads to a very rapid
590 reactivation of encoding activity which is visible in alpha/beta power decreases in visual brain
591 regions. Affecting the cortical generators of the alpha/beta power decrease with rTMS in the
592 same frequency range hampered episodic memory retrieval. These observations suggest that
593 episodic memory retrieval relies on ephoric processes. A deeper understanding of ephory and
594 its manipulation with cortical stimulation techniques potentially offers new perspectives for the
595 treatment of neuropsychiatric disorders (McNamara et al., 2001). For example, patients suffering
596 from posttraumatic stress disorder suffer from the rapid intrusive reactivation of sensory
597 memories pertaining to their traumatic experiences (Reynolds and Brewin, 1999). Treating

598 memory intrusion through the external induction of oscillatory activity could be an important
599 future therapeutic mean to assist patients in controlling unwanted memories.

600

References

- 601
- 602 Anderson AJ, Johnson CA (2006) Comparison of the ASA, MOBS, and ZEST threshold
603 methods. *Vision Res* 46:2403-2411.
- 604 **Batchelder, W. H., & Riefer, D. M. (1990). Multinomial processing models of source monitoring.**
605 ***Psychol Rev*, 97:548-564.**
- 606 Benjamini Y, Hochberg Y (1995) Controlling the false discovery rate: A practical and powerful
607 approach to multiple testing. *J R Stat Soc B* 57:289-300
- 608 Benjamini Y, Yekutieli D (2001) The control of the false discovery rate in multiple testing under
609 dependency. *Ann Stat* 29:1165-1188.
- 610 Cabeza R, Ciaramelli E, Olson IR, Moscovitch M (2008) The parietal cortex and episodic
611 memory: An attentional account. *Nat Rev Neurosci* 9:613-625.
- 612 **Cycowicz, Y. M., Friedman, D., Snodgrass, J. G., & Duff, M. (2001). Recognition and source**
613 **memory for pictures in children and adults. *Neuropsychologia* 39:255-267.**
- 614 da Silva FL (2013) EEG and MEG: relevance to neuroscience. *Neuron* 80:1112-1128.
- 615 Dalal SS, Guggisberg AG, Edwards E, Sekihara K (2008) Five-dimensional neuroimaging:
616 Localization of the time–frequency dynamics of cortical activity. *Neuroimage* 40:1686-
617 1700.
- 618 Genovese CR, Lazar NA, Nichols T (2002) Thresholding of statistical maps in functional
619 neuroimaging using the false discovery rate. *Neuroimage* 15:870-878.
- 620 Gratton G (1998) The contralateral organization of visual memory: A theoretical concept and a
621 research tool. *Psychophysiology* 35:638-647.
- 622 Gratton G, Corballis PM, Jain S (1997) Hemispheric organization of visual memories. *J Cogn*
623 *Neurosci* 9:92-104.
- 624 Gross J, Timmermann L, Kujala J, Salmelin R, Schnitzler A (2003) Properties of MEG
625 tomographic maps obtained with spatial filtering. *Neuroimage* 19:1329-1336.
- 626 Gross J, Kujala J, Hamalainen M, Timmermann L, Schnitzler A, Salmelin R (2001) Dynamic
627 imaging of coherent sources: Studying neural interactions in the human brain. *Proc Natl*
628 *Acad Sci USA* 98:694-699.
- 629 Händel BF, Haarmeier T, Jensen O (2011) Alpha oscillations correlate with the successful
630 inhibition of unattended stimuli. *J Cogn Neurosci* 23:2494-2502.
- 631 Hanslmayr S, Staudigl T, Fellner MC (2012) Oscillatory power decreases and long-term
632 memory: The information via desynchronization hypothesis. *Front Hum Neurosci* 6.

- 633 Hanslmayr S, Matuschek J, Fellner M-C (2014) Entrainment of prefrontal beta oscillations
634 induces an endogenous echo and impairs memory formation. *Curr Biol* 24:904-909.
- 635 Headley DB, Weinberger NM (2015) Relational associative learning induces cross-modal
636 plasticity in early visual cortex. *Cereb Cortex* 25:1306-1318.
- 637 Herron JE (2007) Decomposition of the ERP late posterior negativity: Effects of retrieval and
638 response fluency. *Psychophysiology* 44:233-244.
- 639 Horner AJ, Gadian David G, Fuentemilla L, Jentschke S, Vargha-Khadem F, Duzel E (2012) A
640 rapid, hippocampus-dependent, item-memory signal that initiates context memory in
641 humans. *Curr Biol* 22:2369-2374.
- 642 Jafarpour A, Fuentemilla L, Horner AJ, Penny W, Duzel E (2014) Replay of very early encoding
643 representations during recollection. *J Neurosci* 34:242-248.
- 644 Johansson M, Mecklinger A (2003) The late posterior negativity in ERP studies of episodic
645 memory: Action monitoring and retrieval of attribute conjunctions. *Biol Psychol* 64:91-
646 117.
- 647 Johnson JD, Price MH, Leiker EK (2015) Episodic retrieval involves early and sustained effects
648 of reactivating information from encoding. *Neuroimage* 106:300-310.
- 649 Johnson MK (1992) MEM: Mechanisms of recollection. *J Cogn Neurosci* 4:268-280.
- 650 Ketz NA, Jensen O, O'Reilly RC (2015) Thalamic pathways underlying prefrontal cortex-medial
651 temporal lobe oscillatory interactions. *Trends Neurosci* 38:3-12.
- 652 Kompus K (2011) Default mode network gates the retrieval of task-irrelevant incidental
653 memories. *Neurosci Lett* 487: 318–321.
- 654 Kompus K, Eichele T, Hugdahl K, Nyberg L (2011) Multimodal imaging of incidental retrieval:
655 The low route to memory. *J Cogn Neurosci* 23:947-960.
- 656 Konen CS, Kastner S (2008) Two hierarchically organized neural systems for object information
657 in human visual cortex. *Nat Neurosci* 11:224-231.
- 658 Lange J, Keil J, Schnitzler A, van Dijk H, Weisz N (2014) The role of alpha oscillations for
659 illusory perception. *Behav Brain Res* 271:294-301.
- 660 Lepage M, Ghaffar O, Nyberg L, Tulving E (2000) Prefrontal cortex and episodic memory
661 retrieval mode. *Proc Natl Acad Sci USA* 97:506-511.
- 662 Maris E, Oostenveld R (2007) Nonparametric statistical testing of EEG- and MEG-data. *J*
663 *Neurosci Methods* 164:177-190.

- 664 McNamara B, Ray J, Arthurs O, Boniface S (2001) Transcranial magnetic stimulation for
665 depression and other psychiatric disorders. *Psychol Med* 31:1141-1146.
- 666 Moscovitch M (2008) The hippocampus as a "stupid", domain-specific module: Implications for
667 theories of recent and remote memory, and of imagination. *Can J Psychol* 62:62-79.
- 668 Oldfield RC (1971) The assessment and analysis of handedness: The Edinburgh inventory.
669 *Neuropsychologia* 9:97-113.
- 670 Oostenveld R, Fries P, Maris E, Schoffelen J-M (2011) FieldTrip: Open source software for
671 advanced analysis of MEG, EEG, and invasive electrophysiological data. *Comput Intell*
672 *Neurosci* 2011:1.
- 673 Osipova D, Hermes D, Jensen O (2008) Gamma power is phase-locked to posterior alpha
674 activity. *PLoS ONE* 3:e3990.
- 675 Osipova D, Takashima A, Oostenveld R, Fernandez G, Maris E, Jensen O (2006) Theta and
676 gamma oscillations predict encoding and retrieval of declarative memory. *J Neurosci*
677 26:7523-7531.
- 678 Ranganath C, Paller KA (1999) Frontal brain potentials during recognition are modulated by
679 requirements to retrieve perceptual detail. *Neuron* 22:605-613.
- 680 Reynolds M, Brewin CR (1999) Intrusive memories in depression and posttraumatic stress
681 disorder. *Behav Res Ther* 37:201-215.
- 682 Romei V, Gross J, Thut G (2010) On the role of prestimulus alpha rhythms over occipito-parietal
683 areas in visual input regulation: Correlation or causation? *J Neurosci* 30:8692-8697.
- 684 Rossi S, Hallett M, Rossini PM, Pascual-Leone A (2011) Screening questionnaire before TMS:
685 An update. *Clin Neurophysiol* 122:1686.
- 686 Rossi S, Hallett M, Rossini PM, Pascual-Leone A, Grp STC (2009) Safety, ethical
687 considerations, and application guidelines for the use of transcranial magnetic stimulation
688 in clinical practice and research. *Clin Neurophysiol* 120:2008-2039.
- 689 Rossion B, Pourtois G (2004) Revisiting Snodgrass and Vanderwart's object pictorial set: The
690 role of surface detail in basic-level object recognition. *Perception* 33:217-236.
- 691 Rugg MD, Wilding EL (2000) Retrieval processing and episodic memory. *Trends Cogn Sci*
692 4:108-115.
- 693 Rugg MD, Curran T (2007) Event-related potentials and recognition memory. *Trends Cogn Sci*
694 11:251-257.

- 695 Sauseng P, Klimesch W, Heise KF, Gruber WR, Holz E, Karim AA, Glennon M, Gerloff C,
696 Birbaumer N, Hummel FC (2009) Brain oscillatory substrates of visual short-term
697 memory capacity. *Curr Biol* 19:1846-1852.
- 698 Sederberg PB, Schulze-Bonhage A, Madsen JR, Bromfield EB, Litt B, Brandt A, Kahana MJ
699 (2007) Gamma oscillations distinguish true from false memories. *Psychol Sci* 18:927-932.
- 700 Semon RW (1911) *Die Mneme als erhaltendes Prinzip im Wechsel des organischen Geschehens*.
701 Leipzig: Engelmann.
- 702 Sheldon SA, Moscovitch M (2010) Recollective performance advantages for implicit memory
703 tasks. *Memory* 18:681-697.
- 704 Slotnick SD (2004) Visual memory and visual perception recruit common neural substrates.
705 *Behav Cogn Neurosci Rev* 3:207-221.
- 706 Slotnick SD, Schacter DL (2004) A sensory signature that distinguishes true from false
707 memories. *Nat Neurosci* 7:664-672.
- 708 Slotnick SD, Schacter DL (2006) The nature of memory related activity in early visual areas.
709 *Neuropsychologia* 44:2874-2886.
- 710 Slotnick SD, Schacter DL (2010) Conscious and nonconscious memory effects are temporally
711 dissociable. *Cogn Neurosci* 1:8-15.
- 712 Staresina BP, Fell J, Do Lam ATA, Axmacher N, Henson RN (2012) Memory signals are
713 temporally dissociated in and across human hippocampus and perirhinal cortex. *Nat*
714 *Neurosci* 15:1167-1173.
- 715 Staudigl T, Hanslmayr S (2013) Theta oscillations at encoding mediate the context-dependent
716 nature of human episodic memory. *Curr Biol* 23:1101-1106.
- 717 Staudigl T, Zaehle T, Voges J, Hanslmayr S, Esslinger C, Hinrichs H, Schmitt FC, Heinze H-J,
718 Richardson-Klavehn A (2012) Memory signals from the thalamus: Early thalamocortical
719 phase synchronization entrains gamma oscillations during long-term memory retrieval.
720 *Neuropsychologia* 50:3519-3527.
- 721 Thakral PP, Slotnick SD, Schacter DL (2013) Conscious processing during retrieval can occur in
722 early and late visual regions. *Neuropsychologia* 51:482-487.
- 723 Thut G, Veniero D, Romei V, Miniussi C, Schyns P, Gross J (2011) Rhythmic TMS causes local
724 entrainment of natural oscillatory signatures. *Curr Biol* 21:1176-1185.
- 725 Tulving E (1976) Euphoric processes in recall and recognition. In: *Recall and recognition* (Brown
726 J, ed), pp 37-73. Oxford: John Wiley & Sons.

- 727 Tulving E (1982) Synergistic ephory in recall and recognition. *Can J Psychol* 36:130-147.
- 728 Tulving E (1983) *Elements of episodic memory*. Oxford: Oxford University Press.
- 729 Tulving E, Le Voi ME, Routh DA, Loftus E (1983) Ecphoric processes in episodic memory [and
730 discussion]. *Phil Trans R Soc B* 302:361-371.
- 731 Tyrrell RA, Owens DA (1988) A rapid technique to assess the resting states of the eyes and other
732 threshold phenomena: The modified binary search (MOBS). *Behav Res Meth Ins* 20:137-
733 141.
- 734 Waldhauser GT, Johansson M, Hanslmayr S (2012) Alpha/Beta oscillations indicate inhibition of
735 interfering visual memories. *J Neurosci* 32:1953-1961.
- 736 Wheeler ME, Buckner RL (2003) Functional dissociation among components of remembering:
737 Control, perceived oldness, and content. *J Neurosci* 23:3869-3880.
- 738 Wimber M, Maaß A, Staudigl T, Richardson-Klavehn A (2012) Rapid memory reactivation
739 revealed by oscillatory entrainment. *Curr Biol* 22:1482-1486
- 740
- 741
- 742

743

Table Legends

744 **Table 1.** Percentages of hits and source hits ($M \pm SEM$) did not differ between VF (LVF and
745 RVF) or Instruction (Instructed vs. Non-instructed) at encoding (see Results).

746 **Table 2.** Contingency between lateralization index (contra- minus ipsilateral power; LI) and
747 source memory performance as observed absolute frequencies across all single trials of all
748 subjects (expected values calculated in a χ^2 -test are given in parentheses). $LI < 0$ signifies an
749 alpha/beta power decrease at the electrode cluster contralateral to the VF of encoding, as
750 hypothesized for source hits, whereas $LI > 0$ signifies an ipsilateral decrease in the 100-200 ms
751 time window.

752 **Table 3.** Percentages of hits, source hits and source false alarms ($M \pm SEM$) depending on
753 Stimulation (Sham vs. rTMS) and Hemisphere (Contra- vs. Ipsilateral).

754

755

Figure Legends

756 **Figure 1.** Posterior electrodes selected for analysis at encoding. Lateral electrodes selected for
757 the initial sliding cluster statistic are depicted in large broken (LH) and dotted (RH) circles. In the
758 topographical cluster analysis comparing LVF and RVF condition, central electrodes (large solid
759 black) were also included.

760 **Figure 2.** Experimental procedure for Experiments 1 and 2. Pictures of everyday objects were
761 presented to the left or right of fixation at encoding, followed by a response task according to
762 encoding condition (instructed versus non-instructed). Instructed encoding required participants
763 to intentionally encode the presented object and to judge the difficulty to do so. For non-
764 instructed encoding, participants were requested to estimate whether the depicted object would fit
765 into a shoebox or not. During retrieval, all previously shown old items were presented together
766 with the same amount of previously unseen new items. All pictures were shown at the center of

767 the screen to isolate lateralized cortical activity to the reactivation of sensory memory traces
768 established during encoding. An old/new item recognition task was followed by a source memory
769 task, asking for the VF at presentation. The whole procedure was carried out twice in each
770 subject, once with instructed, once with non-instructed encoding. In Experiment 1, EEG was
771 measured throughout the experiment. In Experiment 2, rTMS and Sham was applied to the left or
772 right cortical hemisphere during retrieval, switching between these stimulation conditions every
773 40 trials.

774 **Figure 3.** EEG activity in Experiment 1 at sensor level. **A:** Encoding effects. Top: FDR-corrected
775 results of the sliding cluster statistic, thresholded at $P_{\text{adj}} < 0.05$, indicating significant power
776 differences between LVF and RVF conditions at respective posterior contralateral sensors (cf.
777 Fig. S2) between 200-700 ms and 8-20 Hz (boxed white). Center: LVF-RVF power differences in
778 the selected time-frequency window. Significant electrode clusters interacting with VF condition
779 indicated by black (left hemisphere) and white (right hemisphere) circles. Bottom: Mean power at
780 the left-hemispheric (LH) and right-hemispheric (RH) electrode clusters interaction with VF
781 condition (LVF and RVF). Error bars signify \pm SEM. **B:** Retrieval effects. Top: Mean difference
782 between contra- and ipsilateral EEG power for both VF conditions at the LH and RH electrode
783 clusters identified at encoding, showing a contralateral power decrease between 100-200 ms and
784 10-25 Hz, thresholded at $P < 0.05$ (Wilcoxon sign rank test). The analysis focused on the time
785 window preceding recollection effects (< 500 ms; post-recollection time window masked grey).
786 Center: LVF-RVF power differences in the selected time-frequency window. Black (left
787 hemisphere) and white (right hemisphere) circles represent electrode clusters identified during
788 encoding. Bottom: Mean power at the left-hemispheric (LH) and right-hemispheric (RH)
789 electrode clusters identified at encoding, interacting with VF condition (LVF and RVF). Error
790 bars signify \pm SEM.

791 **Figure 4.** Hemisphere-specific effects for the LVF-RVF comparison: **A:** Time-frequency
792 representation of the LVF-RVF difference for left (red circles) and right (blue circles)
793 hemispheric electrode clusters. The 100-200 ms time-window selected on the basis of the running
794 Wilcoxon-Test (Fig. 3B, top) is boxed black (LH) or white (RH). **B:** Mean difference between
795 LVF and RVF conditions at left and right hemispheric clusters between 100-200 ms at the
796 hemisphere-specific peak frequencies (10 and 20 Hz). Note that only the LH cluster shows a
797 significant difference between VF conditions at 10 Hz, whereas effects for the RH cluster are
798 more pronounced at higher frequencies, peaking at 20 Hz. Error bars signify \pm SEM. Significant
799 ($P < 0.05$) differences are marked by asterisks.

800 **Figure 5.** Cortical sources of EEG power differences between LVF and RVF conditions and
801 between contra- and ipsilateral hemispheres at encoding (8-20 Hz, 200-700 ms, green) and
802 retrieval (10-25 Hz, 100-200 ms, blue). Interhemispheric differences are backprojected to the
803 cortical hemispheres, reflecting corresponding voxels in each hemisphere. Depicted t -values are
804 thresholded at $P < 0.01$, with maximum values reflecting interhemispheric LVF-RVF differences
805 at $P < 0.0005$.

806 **Figure 6. A:** Schematic depiction of rTMS stimulation in the retrieval trial procedure of
807 Experiment 2 at the left (red) and right (green) maximum cortical source (MNI coordinates: ± 40 ,
808 -78 , 0) of 10-25 Hz (100-200 ms) interhemispheric LVF-RVF differences at retrieval as
809 identified in Experiment 1. **B:** Behavioral results from Experiment 2, showing the difference
810 between TMS-Sham condition effects on source memory performance for items presented in the
811 contra- and ipsilateral VF during encoding. Error bars signify \pm SEM. Significant ($P < 0.05$)
812 effects are marked by asterisks.

813

814 **Table 1**815 *Memory Performance Depending on Encoding Condition in Experiments 1 and 2.*

	Experiment 1				Experiment 2			
	Instructed	Non- instructed	LVF	RVF	Instructed	Non- instructed	LVF	RVF
Hits	67.9 ±	71.3 ±	71.2 ±	68.0 ±	69.7 ±	72.0 ±	69.4 ±	73.3 ±
	3.35	1.45	2.25	2.76	2.48	2.81	2.71	2.51
Source	55.7 ±	50.3 ±	53.1 ±	52.9 ±	56.8 ±	52.0 ±	54.0 ±	55.9 ±
Hits	4.01	2.31	2.95	2.96	2.90	3.03	2.85	2.91

816

817

818 **Table 2**819 *Contingency between Source Memory Performance and EEG Lateralization in All Single Trials*

	LI < 0	LI > 0
Source hits	470 (454)	427 (443)
Source misses	123 (139)	151 (135)

820

821 **Table 3**822 *Memory Performance Depending on Stimulation and Hemisphere in Experiment 2.*

	rTMS		Sham	
	Contralateral	Ipsilateral	Contralateral	Ipsilateral
Source Hits	51.7 ± 2.82	54.6 ± 2.61	58.8 ± 3.22	54.9 ± 3.07
Hits	69.2 ± 2.61	70.5 ± 2.43	75.3 ± 3.34	70.3 ± 3.15
Source FA	4.0 ± 0.55	4.1 ± 0.53	5.3 ± 0.97	3.4 ± 0.52

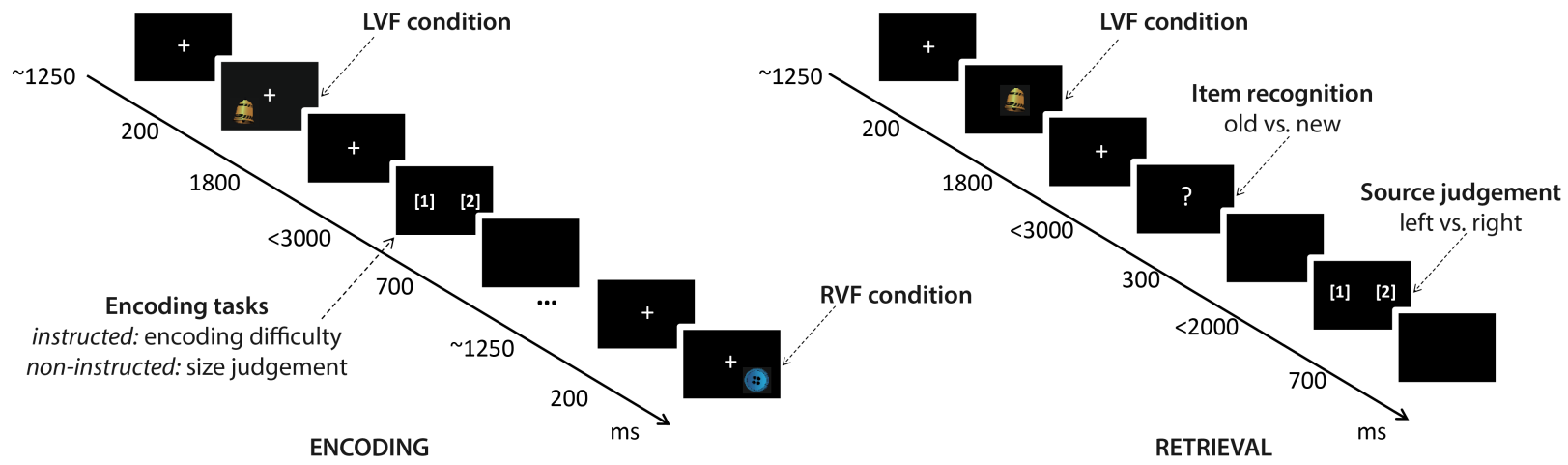
823

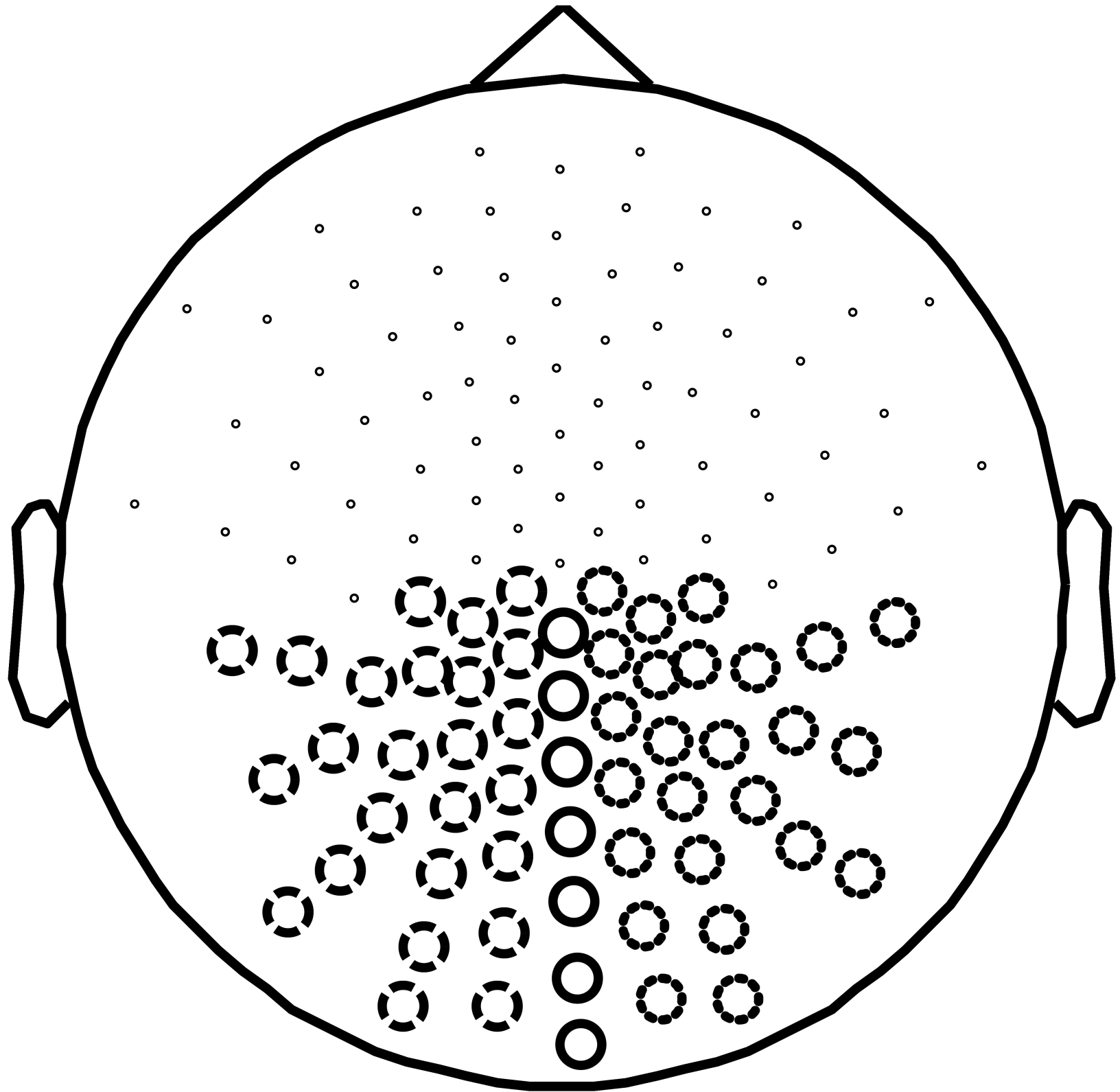
824

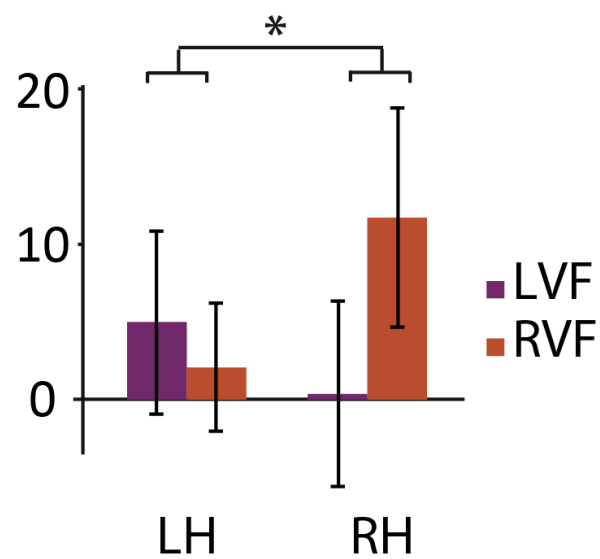
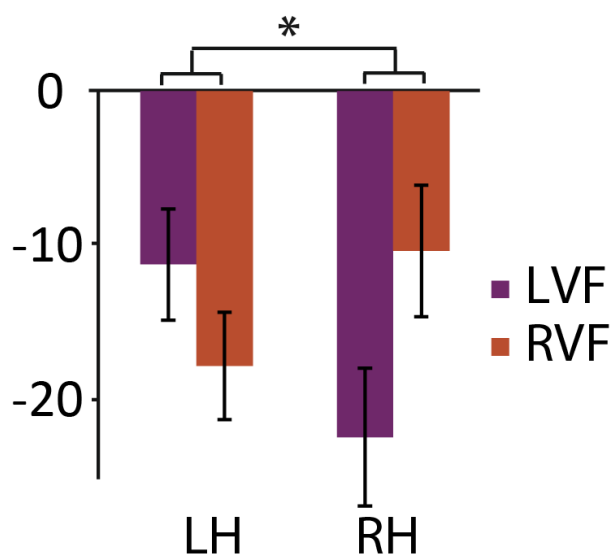
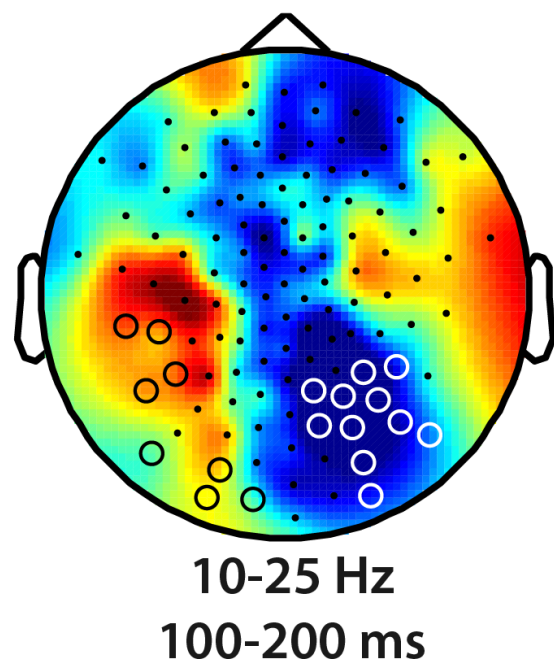
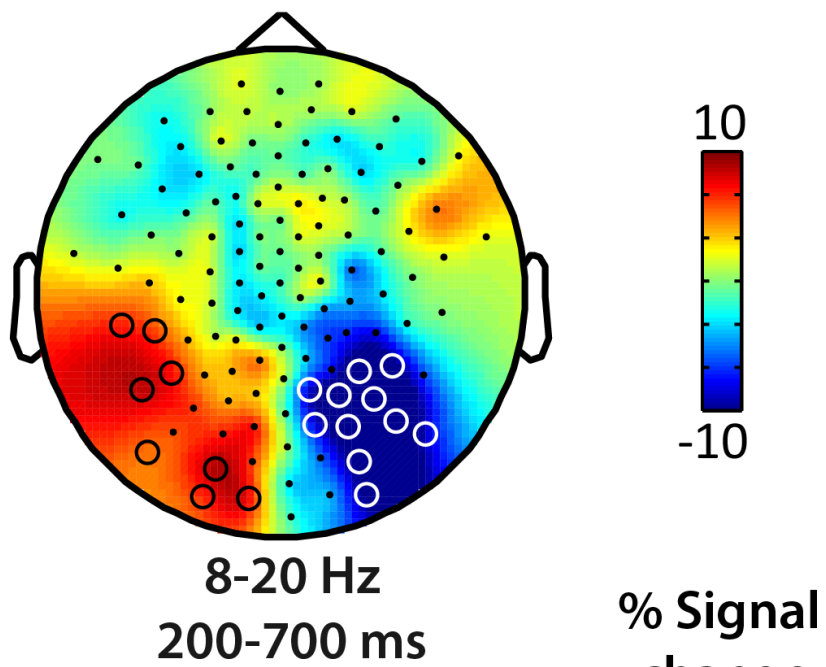
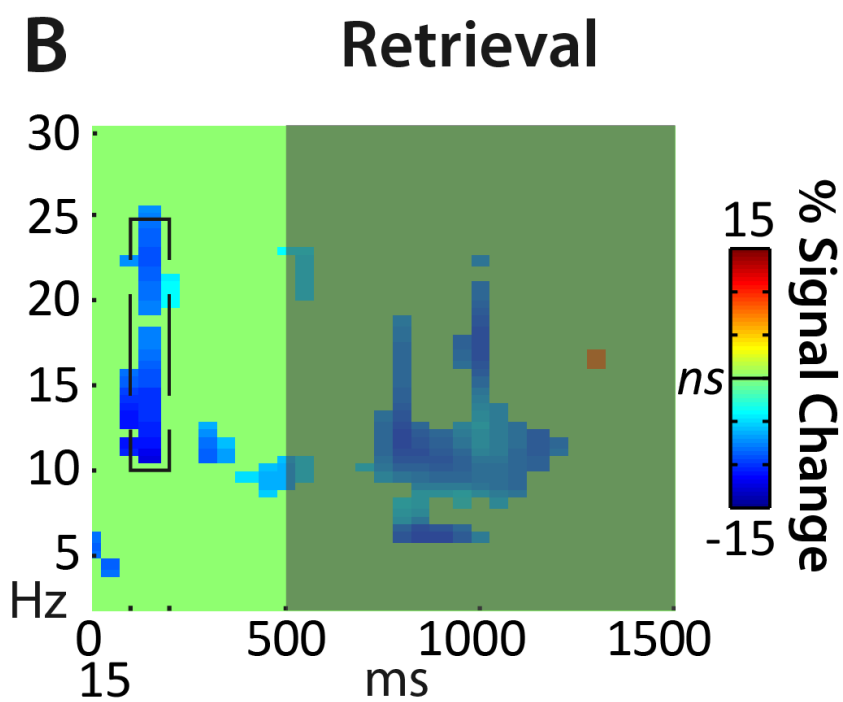
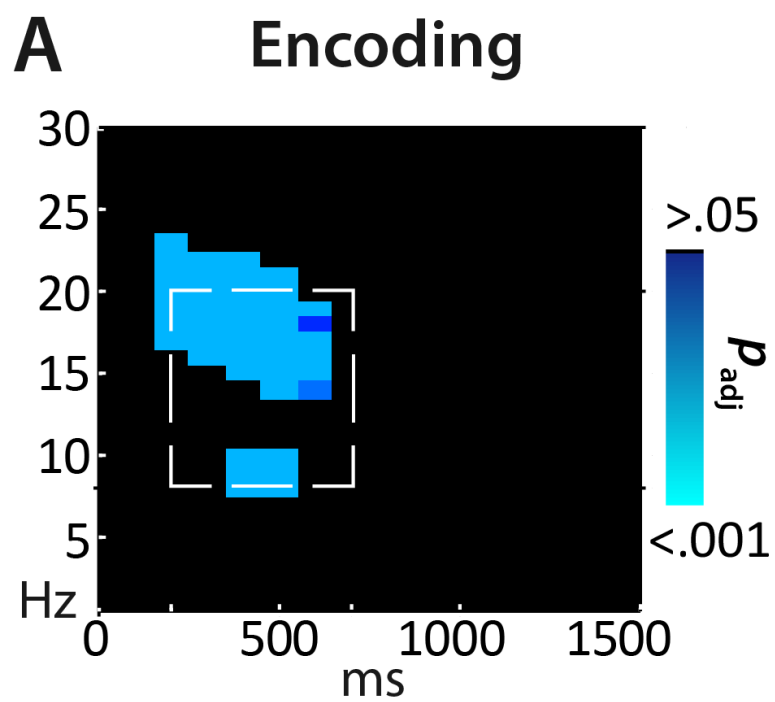
825

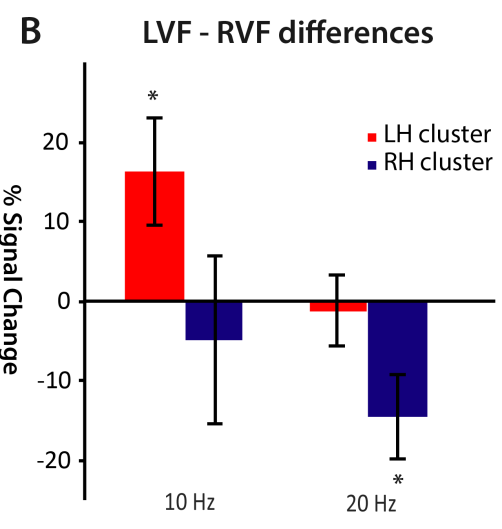
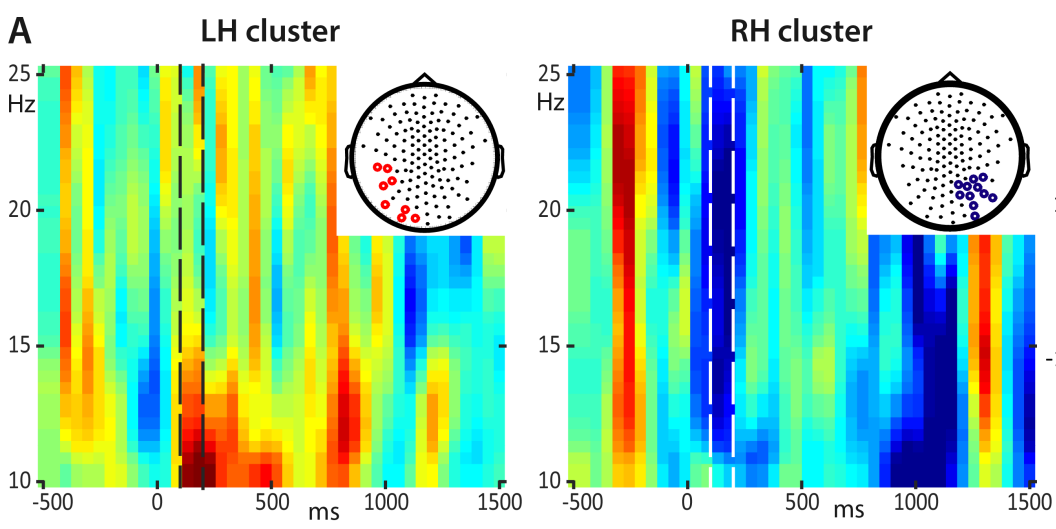
826

Procedure Experiments 1 and 2

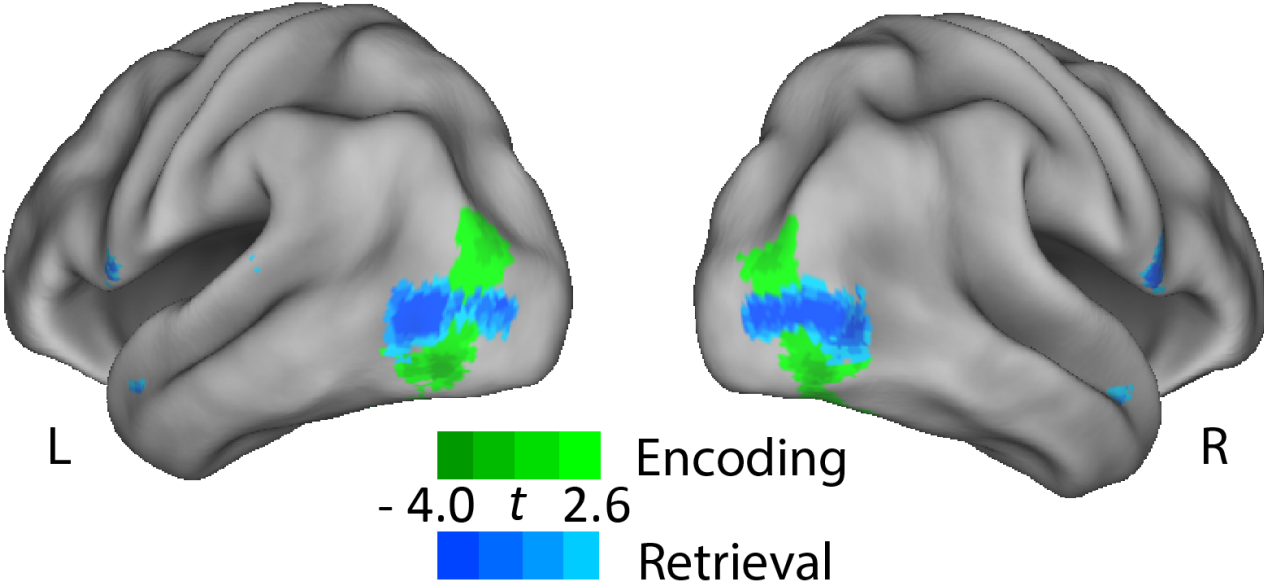




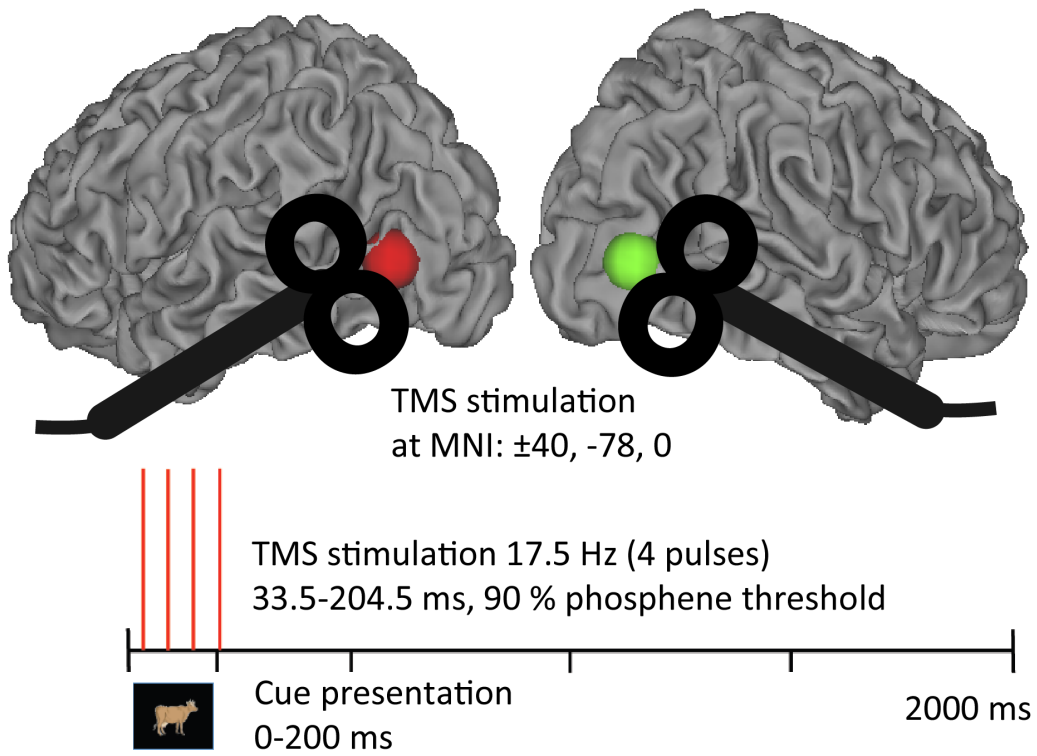




Source localization results



A TMS stimulation



B TMS results

