

Brod, Garvin; Shing, Yee Lee

## Specifying the role of the ventromedial prefrontal cortex in memory formation

*formal und inhaltlich überarbeitete Version der Originalveröffentlichung in:*

*formally and content revised edition of the original source in:*

*Neuropsychologia 111 (2018), S. 8-15*



Bitte verwenden Sie in der Quellenangabe folgende URN oder DOI /  
Please use the following URN or DOI for reference:

urn:nbn:de:0111-dipfdocs-161012

10.25657/02:16101

<https://nbn-resolving.org/urn:nbn:de:0111-dipfdocs-161012>

<https://doi.org/10.25657/02:16101>

### Nutzungsbedingungen

Dieses Dokument steht unter folgender Creative Commons-Lizenz:  
<http://creativecommons.org/licenses/by-nc-nd/4.0/deed.de> - Sie dürfen das  
Werk bzw. den Inhalt unter folgenden Bedingungen vervielfältigen, verbreiten  
und öffentlich zugänglich machen: Sie müssen den Namen des  
Autors/Rechteinhabers in der von ihm festgelegten Weise nennen. Dieses  
Werk bzw. dieser Inhalt darf nicht für kommerzielle Zwecke verwendet  
werden und es darf nicht bearbeitet, abgewandelt oder in anderer Weise  
verändert werden.

Mit der Verwendung dieses Dokuments erkennen Sie die  
Nutzungsbedingungen an.

### Terms of use

This document is published under following Creative Commons-License:  
<http://creativecommons.org/licenses/by-nc-nd/4.0/deed.en> - You may copy,  
distribute and transmit, adapt or exhibit the work in the public as long as you  
attribute the work in the manner specified by the author or licensor. You are  
not allowed to make commercial use of the work or its contents. You are not  
allowed to alter, transform, or change this work in any other way.

By using this particular document, you accept the above-stated conditions of  
use.



### Kontakt / Contact:

DIPF | Leibniz-Institut für  
Bildungsforschung und Bildungsinformation  
Frankfurter Forschungsbibliothek  
publikationen@dipf.de  
www.dipfdocs.de

Mitglied der

  
Leibniz-Gemeinschaft

# Specifying the role of the ventromedial prefrontal cortex in memory formation

Garvin Brod<sup>a,b</sup> & Yee Lee Shing<sup>a,c</sup>

<sup>a</sup>Max Planck Institute for Human Development, Center for Lifespan Psychology, Berlin, Germany; <sup>b</sup>German Institute for International Educational Research, Frankfurt am Main, Germany; <sup>c</sup>Division of Psychology, University of Stirling, Stirling, UK

1 Correspondence concerning this article should be addressed to Garvin Brod or Yee Lee

2 Shing: [garvin.brod@dipf.de](mailto:garvin.brod@dipf.de); [yee.shing@stir.ac.uk](mailto:yee.shing@stir.ac.uk)

3

4 **Abstract**

5 Recent neuroimaging research suggests that the ventromedial prefrontal cortex (vmPFC)  
6 plays an important role for successful memory formation that takes place in the context of  
7 activated prior knowledge. These findings led to the notion that the vmPFC integrates new  
8 information into existing knowledge structures. However, a considerable number of  
9 neuroimaging studies that have investigated memory formation in the context of prior  
10 knowledge have not found vmPFC involvement. To resolve this inconsistency, we propose a  
11 distinction between knowledge-relevance (the degree to which new information can be linked  
12 to prior knowledge) and knowledge-congruency (the perceived match between prior  
13 knowledge and the to-be-encoded information). We hypothesized that the vmPFC contributes  
14 to successful memory formation only when perceived knowledge-congruency is high,  
15 independent of knowledge-relevance. We tested this hypothesis in a design that varied both  
16 congruency and relevance during memory encoding, which was performed in the MR  
17 scanner. As predicted, the results showed that vmPFC contributions to memory formation  
18 vary as a function of knowledge-congruency, but not as a function of knowledge-relevance.  
19 Our finding contributes to elucidating the seemingly inconsistent findings in the literature and  
20 helps to specify the role of the vmPFC in memory formation.

21

22

23

24

25

26

27

28 **Introduction**

29 In recent years, cognitive neuroscience research on memory has become increasingly  
30 interested in the role of the ventromedial prefrontal cortex (vmPFC) in all stages of memory  
31 processing. Starting with the observation that vmPFC lesions can lead to confabulation  
32 (Moscovitch, 1989; Moscovitch & Melo, 1997), a role for the vmPFC in retrieval monitoring  
33 was proposed in which the vmPFC provides a “feeling of rightness” for memory cues during  
34 retrieval (Moscovitch & Winocur, 2002). Following this account, vmPFC contributions are  
35 not necessary for memory retrieval, but a lack of them leads to the erroneous retrieval of  
36 inappropriate associations. On the contrary, vmPFC contributions can also increase erroneous  
37 retrieval in a situation in which memories have to be rejected that fit well into an activated  
38 knowledge structure (also called schema, Berkers et al., 2016; Warren, Jones, Duff, & Tranel,  
39 2014). This double-edged role of the vmPFC can best be illustrated by its contribution to the  
40 so-called congruency effect, which denotes a memory advantage for knowledge-congruent as  
41 opposed to knowledge-incongruent new information. The congruency effect can be  
42 interpreted as an estimate of the influence of prior knowledge on episodic memory. vmPFC  
43 patients do not show this effect (Spalding, Jones, Duff, Tranel, & Warren, 2015). In line with  
44 this lesion data, recent functional magnetic resonance imaging (fMRI) studies have shown  
45 that the vmPFC displays enhanced activation for successfully retrieved knowledge-congruent  
46 as compared to knowledge-incongruent information (Brod, Lindenberger, Werkle-Bergner, &  
47 Shing, 2015; van Kesteren, Rijpkema, Ruiters, & Fernández, 2010).

48         Concerning the role of the vmPFC in memory formation, results from a patient study  
49 (Ghosh, Moscovitch, Melo Colella, & Gilboa, 2014) suggest that vmPFC lesions lead to  
50 deficient knowledge representation and activation, which is a prerequisite for knowledge-  
51 mediated memory formation. fMRI studies have found enhanced vmPFC activation for  
52 successfully encoded information (van Kesteren et al., 2013; 2014) as well as for successful

53 inference performance during knowledge-related memory encoding (Schlichting & Preston,  
54 2016; Zeithamova, Dominick, & Preston, 2012). Consequently, it has been argued that the  
55 role of the vmPFC during memory encoding is to support the integration of new information  
56 into existing knowledge structures (Gilboa & Marlatte, 2017; Schlichting & Preston, 2015;  
57 van Kesteren, Ruitter, Fernández, & Henson, 2012). Based on findings in animals, it has been  
58 suggested that the mPFC is suited for this role because of its direct anatomical connections to  
59 the hippocampus (Nieuwenhuis & Takashima, 2011).

60         Despite this seemingly clear picture, it has to be acknowledged that a considerable  
61 number of studies that have used memory tasks for which prior knowledge should be  
62 activated and used have not found vmPFC activation that was predictive of later memory  
63 (Bein, Reggev, & Maril, 2014; Brod, Lindenberger, Wagner, & Shing, 2016; van Buuren et  
64 al., 2014; Webb, Turney, & Dennis, 2016). Conversely, other studies that have found  
65 differential vmPFC involvement in successful memory encoding did not use conditions that  
66 clearly differed in prior knowledge activation (e.g., Benoit, Szpunar, & Schacter, 2014;  
67 Reggev, Bein, & Maril, 2016). Therefore, the proposed relationship between prior  
68 knowledge-related memory processing and vmPFC activation is likely more complicated than  
69 initially believed, and there may be several boundary conditions that determine whether or not  
70 the vmPFC is involved.

71         We (Brod, Werkle-Bergner, & Shing, 2013) have speculated before that the vmPFC  
72 might be involved only when there is a strong congruency dimension in the task, and not  
73 when information is encoded against the backdrop of prior knowledge. In other words, we  
74 proposed that knowledge-congruency can be distinguished from knowledge-relevance.  
75 Knowledge-relevance describes the degree to which the to-be-remembered information can be  
76 linked to a pre-existing semantic network, and, thus, the degree to which prior knowledge can  
77 be used to enable elaborative (i.e., semantic) encoding. By knowledge-congruency, we mean

78 the degree to which the information evokes a sense of fit to the particular, activated  
79 knowledge structures (similar to the “feeling of rightness” notion in memory retrieval by  
80 Moscovitch & Winocur, 2002). Following this terminology, examples of common memory  
81 tasks containing a knowledge-relevance but no knowledge-congruency dimension include  
82 object–place associations in familiar vs. unfamiliar task environments or high vs. low  
83 expertise conditions. Conversely, memory tasks containing a knowledge-congruency but not a  
84 knowledge-relevance dimension include object–place associations in a familiar task  
85 environment in which an object can be expected vs. not expected to occur at a particular  
86 location or event memory for rule-consistent vs. rule-violating chess moves. In short, the  
87 congruency dimension comes into play in the context of expectancies that are confirmed or  
88 violated, whereas the relevance dimension comes into play whenever stimuli make varying  
89 levels of connection to prior knowledge. The two dimensions are not proposed to be mutually  
90 exclusive, i.e., there are situations in which the proposed congruency and relevance  
91 dimensions are positively correlated.

92 In the current study, we sought to include both the knowledge-congruency and the  
93 knowledge-relevance dimension in the same memory encoding task to be able to delineate  
94 vmPFC contributions to prior knowledge-related memory encoding more precisely. We  
95 present new analyses of a previously published data set (Brod et al., 2016) that examined how  
96 real-life gains in knowledge affect the neural correlates of episodic encoding, as measured by  
97 fMRI. Final year medical students were tested on an episodic memory task related to medical  
98 knowledge before and after their final exam. For the current purpose, we only analyzed data  
99 from the first measurement occasion. In the memory task, participants had to memorize either  
100 face–diagnosis (high knowledge-relevance) or face–name (low knowledge-relevance) pairs.  
101 Common names and familiar diagnoses (determined in pilot studies) were used along with  
102 unfamiliar Caucasian faces. The design of the memory task was inspired by previous research

103 showing that remembering face–name associations is much more difficult than remembering  
104 face–personal feature associations, because common names are arbitrary (except for allowing  
105 inferences about gender and, sometimes, nationality) and, thus, lack clear semantic  
106 associations (e.g., Cohen, 1990; McWeeny, Young, Hay, & Ellis, 1987). On the other hand,  
107 personal features (such as, in our case, a known medical diagnosis given to a person) are  
108 linked to a rich semantic network, which facilitates elaborative, semantic encoding (cf.  
109 Cohen, 1990; McWeeny et al., 1987). Thus, the diagnoses and names used in our study are  
110 assumed to differ in the extent to which they evoke a schema that can be applied to elaborate  
111 on a given face (e.g., a person with chronic obstructive pulmonary disease (COPD) will likely  
112 have slightly blue lips and look pale vs. a Michael may have blond hair). In sum, while we do  
113 not imply that prior knowledge cannot be leveraged at all for remembering face–name pairs,  
114 based on previous research we assume that it can be elaborated less effectively than for  
115 remembering face–diagnosis pairs which evoke a rich semantic network in medical exam  
116 candidates. Importantly, we additionally examined subjective congruency ratings during  
117 encoding, which were not explicitly modeled in previous analyses (see Brod et al., 2016).  
118 This gave us leverage to examine both the knowledge-congruency and the knowledge-  
119 relevance dimension within the same memory encoding task.

120 We hypothesized that vmPFC activation would distinguish between knowledge-  
121 congruent and knowledge-incongruent associations, but not between high and low  
122 knowledge-relevance associations. In particular we hypothesized a higher vmPFC activation  
123 for congruent as compared to incongruent information, and an enhanced vmPFC contribution  
124 to successful memory encoding of congruent information. In contrast, we expected the  
125 vmPFC to not display differential activity nor to contribute differentially to successful  
126 memory encoding for high vs. low knowledge-relevance associations. We tested these  
127 hypotheses in two parallel analyses. In one set of analyses, we compared vmPFC activation

128 for congruent and incongruent events as well as for events of high vs. low knowledge-  
129 relevance separately. Next, we tested whether vmPFC regions detected in these contrasts  
130 overlapped with regions contributing to successful memory formation (i.e., remembered >  
131 forgotten contrast). In the other set of analyses, we extracted % signal change from an  
132 independently defined vmPFC cluster and submitted these values to a repeated-measures  
133 ANOVA to directly test whether the vmPFC involvement in successful memory formation  
134 differs as a function of knowledge-congruency and/or knowledge-relevance. This full factorial  
135 analysis was performed on a subset of the full sample to ensure there were sufficient number  
136 of trials within each cell of the factor levels (see Participants).

## 137 **Materials and Methods**

### 138 **Participants**

139 Complete data from forty-nine medical students (29 female, age range = 23–29 years,  
140 mean age = 25.6 years) were collected in the initial study (reported in Brod et al., 2016).  
141 Participants were recruited from Berlin universities and were paid 76 Euro for their  
142 participation. All participants were right-handed, had no history of psychiatric or neurological  
143 disorders, and gave written informed consent. The current analyses were performed on data  
144 from the first measurement occasion of Brod et al. (2016), but go beyond the previously  
145 published data in that they also take into account participants' congruency ratings during  
146 encoding. This was outside the scope of the earlier analyses, which focused on longitudinal  
147 changes in knowledge and how these relate to changes in brain activation patterns. However,  
148 due to the added factor of congruency rating in the current analysis, which led to eight instead  
149 of four within-subject conditions, twenty-four participants had to be excluded for the second  
150 (full factorial) set of analyses because they did not provide enough (>5) valid trials per block  
151 in every condition. Thus, data of twenty-five participants (19 female, age range = 23–29

152 years, mean age = 26.0 years) were analyzed for the current full factorial analysis. Ethics  
153 approval was obtained from the ethics committee of the German Psychological Society  
154 (DGPs).

### 155 **Task and Procedure**

156 The encoding phase was performed after the structural scans and took 20 minutes in total (for  
157 a graphical depiction of the task, see Figure 1). Before entering the MRI scanner, participants  
158 were instructed to memorize face–word pairs, in which half of the words were diagnoses and  
159 the other half were first names. They were told that there would be a memory test later, but no  
160 details were given concerning the nature of the memory test. They were further instructed to  
161 try to memorize both the face–diagnosis and face–name pairs equally well. A total of 140  
162 medical diagnoses and 140 common German first names were used together with 140 neutral  
163 face pictures. Each face was pseudorandomly combined with one diagnosis and one name,  
164 whereby faces and names/diagnoses were matched for gender. Two parallel stimulus lists of  
165 140 face–word pairs each were created and counterbalanced across participants. The stimulus  
166 lists were further subdivided into two experimental blocks, each consisting of 70 trials. The  
167 face stimuli consisted of pictures of Caucasian young adults taken from the Center for Vital  
168 Longevity Face Database (Minear & Park, 2004). Face–word pairs were presented for 5  
169 seconds each in an interleaved fashion (in pseudorandom order). Trials were separated by a  
170 variable fixation cross period of 2–5 seconds (mean: 3.5 seconds). During presentation of the  
171 face–word pairs, participants were asked to indicate whether or not the name / diagnosis fit  
172 with the face (congruency judgment), responding with their left / right index finger. Left /  
173 right response options were counterbalanced across participants.

174 The retrieval phase took place outside of the scanner, about 10 minutes after the end of  
175 the encoding session. Participants were instructed that they would now see all 140 faces again  
176 (in pseudorandom order) and they would see each face together with either 4 first names or 4

177 diagnoses, of which one name/diagnosis had been presented with the face during the encoding  
178 phase (target), whereas the other three were seen with other faces during encoding (lures).  
179 Participants indicated their choice via button press. Afterwards, they were asked to indicate  
180 their decision confidence on a scale of 1 (guess) to 4 (very sure). They were given no time  
181 limit for their responses, but were told to answer as quickly and as correctly as possible.

182 Data were analyzed using R (R Core Team, 2014). A repeated-measures ANOVA was  
183 performed with condition (diagnoses / names) and congruency judgment (congruent,  
184 incongruent) as within-subjects factors to test for differences in memory (% correctly  
185 retrieved associations) as a function of knowledge-relevance (high for diagnoses, low for  
186 names) and congruency. A further repeated measures ANOVA was performed to test for  
187 differences in reaction time (RT) between the condition. This ANOVA contained the same  
188 within-subject factors as before plus the additional within-subject factor memory  
189 (remembered, forgotten).

#### 190 *fMRI Data Acquisition and Preprocessing*

191 T2\*-weighted echo-planar images were acquired using a 3T Siemens TIM Trio MRI scanner  
192 (direction = transverse (interleaved ascending), FOV = 216 mm, TR = 2500 ms, TE = 30 ms,  
193 number of slices = 45, slice thickness = 2.5 mm, matrix = 72 x 72, voxel size = 3 x 3 x 2.5  
194 mm, distance factor = 20%, 2 runs with 232 volumes each, including 4 dummy volumes  
195 each). To attenuate signal dropout in orbitofrontal regions, the slice orientation was tilted  
196 upwards vertically by 15 degrees after alignment to the anterior commissure–posterior  
197 commissure plane (Weiskopf, Hutton, Josephs, & Deichmann, 2006). To estimate geometric  
198 distortion and signal loss in the EPI, an additional 53-seconds fieldmap was acquired.  
199 Structural data was acquired using a T1-weighted 3D magnetization-prepared rapid gradient  
200 echo sequence (TR 2500 ms, TE 2500 ms, sagittal orientation, spatial resolution 1 x 1 x 1  
201 mm).

202 Data were preprocessed and analyzed using FEAT in FSL (FMRIB's Software  
203 Library, <http://www.fmrib.ox.ac.uk/fsl>; Smith, Jenkinson, & Woolrich, 2004). Functional data  
204 were corrected for motion (MCFLIRT), slice acquisition times (interleaved), and local field  
205 inhomogeneities (BBR / FUGUE), then high-pass filtered (80 Hz), and spatially smoothed  
206 using a 5-mm full-width half-maximum Gaussian filter. Data were first coregistered with the  
207 structural image and then spatially normalized into a common space (Montreal Neurological  
208 Institute (MNI) 152 standard-space 2 mm<sup>3</sup>).

## 209 **fMRI Analyses**

### 210 *Brain Activation*

211 After preprocessing, first-level analyses were conducted using general linear modeling  
212 (GLM), separately for individual participants and runs (the two experimental blocks).  
213 Regressors were generated by convolving the impulse function related to the onset and length  
214 of encoding events with a Gamma hemodynamic response function (5 seconds boxcar  
215 function). To explore subsequent memory effects (SMEs, i.e. remembered > forgotten  
216 contrasts), encoding trials were sorted according to the retrieval data. The two runs were  
217 combined using a within-subject fixed-effects analysis and normalized into MNI space.  
218 Across-subjects analyses were carried out using a mixed-effects model in the FLAME  
219 framework in FSL. Z-statistic images were thresholded at a voxel-wise threshold of  $z > 2.3$ ,  
220 with a FWE-corrected cluster threshold of  $p < 0.05$ , using FLAME1 in FSL. Based on our a  
221 priori hypothesis about differences in the vmPFC, we created an anatomical mask of the  
222 vmPFC based on FSL's Harvard-Oxford Cortical Structural Atlas, which consisted of the  
223 bilateral frontal medial cortex. In addition, exploratory whole-brain analyses were performed.

224 Two sets of analyses were performed. For the first set of analyses, three separate  
225 GLMs were modeled; one that distinguished high and low knowledge-relevance events, one

226 that distinguished congruent and incongruent events, and another one that distinguished  
227 remembered and forgotten events. The first GLM consisted of separate regressors for  
228 remembered and forgotten face–diagnosis pairs (high knowledge-relevance), respectively, as  
229 well as for remembered and forgotten face–name pairs (low knowledge-relevance), and a  
230 regressor of no interest, which contained all correctly remembered pairs that received a  
231 “guess” rating during retrieval. High and low knowledge-relevance events were then  
232 contrasted, independent of later memory. The second GLM consisted of remembered and  
233 forgotten events that were judged as congruent, remembered and forgotten events that were  
234 judged as incongruent, and the “guess” regressor of no interest. Congruent and incongruent  
235 events were contrasted, independent of later memory. The third GLM consisted of  
236 remembered and forgotten events independent of congruency/relevance and again a “guess”  
237 regressor of no interest. Remembered and forgotten events were contrasted to determine  
238 SMEs. For the across-subject analyses, we tested whether the vmPFC areas revealed in the  
239 first two GLMs (knowledge-relevance and knowledge-congruency, respectively) overlap with  
240 the vmPFC cluster identified in the third GLM (SME, remembered > forgotten). We did so by  
241 using the clusters found in the first two GLMs as a pre-thresholded mask for the SME  
242 analysis.

243 For the second set of analyses, one GLM was constructed that modeled all nine types  
244 of events: remembered congruent diagnoses, forgotten congruent diagnoses, remembered  
245 congruent names, forgotten congruent names, remembered incongruent diagnoses, forgotten  
246 incongruent diagnoses, remembered incongruent names, forgotten incongruent names  
247 forgotten, as well as the “guess” regressor of no interest. For the across-subject analyses, we  
248 extracted percent signal change for the eight main events of interest (against implicit baseline)  
249 from a vmPFC cluster defined based on the SME analysis of those 24 subjects whose data  
250 could only be used for the first set of analyses. This analysis approach was chosen to obtain

251 an unbiased cluster for the percent signal change analyses (due to difficulties in defining  
252 anatomical sub-regions in vmPFC, see Bein, Reggev, & Maril, 2014). The key interest was to  
253 directly test for interactions between memory, congruency, and relevance, in particular the  
254 significance of two interaction terms: congruency x memory and relevance x memory. Due to  
255 the rather low and differing trial counts per cell in this analysis<sup>1</sup>, which might lead to  
256 differences in signal-to-noise ratio between conditions, we controlled for differences in trial  
257 counts by entering trial counts per cell as a covariate in a linear mixed effects analysis. The  
258 linear mixed effects analysis allowed us to deal with interdependence given our within-subject  
259 design and was performed using *lme4* (Bates, Mächler, Bolker, & Walker, 2015) in R. As  
260 fixed effects, we entered congruency, relevance, and memory as interacting regressors into the  
261 model, along with number of trials per cell and encoding RTs as covariates. Subjects were  
262 entered as random effects into the model. Furthermore, a precursory model that tested for  
263 interactions between our covariate and the other regressors revealed a significant memory x  
264 trial count interaction (i.e., more remembered trials than forgotten trials, see Footnote 1).  
265 Therefore, this interaction term was entered into the analysis as an additional fixed effect to  
266 avoid misspecification in the model. To further probe the significance of the main interaction  
267 terms of interest (congruency x memory and relevance x memory), likelihood ratio tests were  
268 performed comparing the goodness of fit between a model with the critical interaction and a  
269 model without this interaction. Statistical significance of the model difference was determined  
270 using  $\chi^2$  (chi-squared) tests with degrees of freedom equal to the difference in dimensionality  
271 of the two models (i.e., 1).

---

<sup>1</sup> High Relevance Congruent Remembered:  $21.6 \pm 5.5$  (M  $\pm$  SD); High Relevance Incongruent Remembered:  $24.2 \pm 6.3$ ; Low Relevance Congruent Remembered:  $23.8 \pm 7.0$ ; Low Relevance Incongruent Remembered:  $14.4 \pm 7.0$ ; High Relevance Congruent Forgotten:  $8.3 \pm 4.1$ ; High Relevance Incongruent Forgotten:  $12.6 \pm 5.3$ ; Low Relevance Congruent Forgotten:  $16.4 \pm 6.0$ ; Low Relevance Incongruent Forgotten:  $15.2 \pm 5.4$ .

## 272 **Results**

### 273 **Memory performance**

274 As can be seen in Figure 2, a repeated-measures ANOVA revealed (a) a main effect of  
275 knowledge-congruency ( $F(1,44) = 46.82, p < .001, \eta^2_G = .10$ ), indicating better memory  
276 performance for face–word pairs judged as congruent as compared to those that were judged  
277 as incongruent; (b) a main effect of knowledge-relevance ( $F(1,44) = 70.41, p < .001, \eta^2_G =$   
278  $.25$ ), indicating better memory performance for high relevance (face–diagnosis) as compared  
279 to low relevance (face–name) pairs; and (c) no interaction ( $F(1,44) = 0.78, p = .383, \eta^2_G =$   
280  $.003$ ).

281 Results were highly similar for the subgroup of subjects used for the full factorial  
282 analysis (i.e., significant main effects of congruency and relevance, non-significant interaction  
283 between the two factors).

284 We also explored RTs to rule out that any interactions in RT confound the interactions  
285 observed in our full factorial fMRI analysis. A repeated-measures ANOVA revealed  
286 significant main effects of relevance ( $F(1,24) = 175.98, p < .001, \eta^2_G = .41$ ), indicating  
287 faster RTs for the low-relevance condition, and memory ( $F(1,24) = 9.55, p = .005, \eta^2_G =$   
288  $.01$ ), indicating faster RTs for remembered events. No main effect of congruency ( $F(1,24) =$   
289  $.84, p = .37, \eta^2_G = .001$ ) and no significant interactions (all  $p > .25$ ) were observed.

## 290 **fMRI Results**

291 In the following, we will report results of two sets of analyses. In the first set of analyses, we  
292 tested whether the vmPFC distinguishes between associations judged as congruent vs.  
293 incongruent and/or associations for which medical knowledge is of high vs. low relevance and  
294 whether these areas overlap with vmPFC areas that show a SME. These analyses were  
295 performed with the full sample ( $n = 49$ ). In the second set of analyses, we tested whether the  
296 vmPFC involvement in successful memory formation interacts with the vmPFC involvement  
297 in knowledge-congruency and/or knowledge-relevance processing. We did so by extracting %  
298 signal change from the vmPFC cluster showing a SME and subjecting these data to a within-  
299 subject ANOVA. The latter analysis was performed in a subgroup ( $n = 25$ ) that provided  
300 enough ( $>5$ ) valid trials in each of the 8 conditions.

### 301 **vmPFC activation as a function of congruency, relevance, and memory**

302 This section reports results from the first set of analyses ( $n = 49$ , anatomical vmPFC mask, for  
303 exploratory whole-brain results see Table 1). Testing for activation that was greater for the  
304 encoding of associations that were judged as congruent as compared to associations judged as  
305 incongruent revealed a cluster in the vmPFC (peak voxel: 6, 42, -16;  $Z = 3.8$ , 208 voxels, see  
306 Figure 3, in green). The opposite contrast, testing for activation that was greater for  
307 associations judged as incongruent, revealed no cluster in the vmPFC.

308 Testing whether the vmPFC was more strongly activated for associations for which the  
309 participants' medical knowledge was of high (i.e. face–diagnosis pairs) vs. low (i.e. face–  
310 name pairs) relevance revealed activation in a cluster in the vmPFC (peak voxel: -2, 36, -16,  
311  $Z = 5.01$ , 121 voxels, see Figure 3, in blue). The opposite contrast, testing for brain regions  
312 that expressed higher activation for low relevance associations also revealed activation in a  
313 cluster in the vmPFC (peak voxel: 4, 52, -4;  $Z = 6.26$ , 190 voxels, see Figure 3, in yellow).

314 Next, we tested whether the vmPFC contributed to successful memory formation,  
315 independent of congruency and relevance. This analysis revealed a large cluster in the vmPFC  
316 (peak voxel: -4, 50, -14;  $Z = 4.6$ , 396 voxels, see Figure 3 in red; see Table 1 for a complete  
317 list of regions that displayed SME). Finally, we sought to test whether this SME cluster  
318 overlaps with the clusters that distinguished congruency and relevance, as revealed in the first  
319 set of analyses. We tested this by using the latter clusters as a pre-thresholded mask for the  
320 SME analysis. These analyses revealed an overlapping cluster with the congruent >  
321 incongruent contrast (peak voxel: -4, 48, -14;  $Z = 4.59$ , 164 voxels see Figure 3 in green), but  
322 not with the high > low relevance or low > high relevance clusters.

323 These results suggest that the vmPFC is indeed sensitive to differences in knowledge-  
324 congruency in that it displays enhanced activation for associations that were judged as  
325 congruent. Concerning the vmPFC's sensitivity to differences in knowledge-relevance, results  
326 were inconclusive in that neighboring clusters within the vmPFC displayed enhanced  
327 activation for both high and low knowledge-relevance associations. Most importantly,  
328 however, both of these clusters did not overlap with the cluster exhibiting a SME. In contrast,  
329 the vmPFC region that was sensitive to knowledge-congruency overlapped with the SME  
330 cluster. This suggests that the vmPFC's involvement in congruency detection might interact  
331 with its role in memory formation.

332 **vmPFC contributions to memory formation vary as a function of knowledge-**  
333 **congruency, but not of knowledge-relevance**

334 We extracted percent signal change from a vmPFC SME cluster (peak voxel: -2, 48, -  
335 14;  $Z = 3.13$ , 236 voxels) that was defined based on those 24 subjects whose data could not be  
336 used for the percent signal change analyses. The goal of the percent signal change analyses  
337 was to directly test whether the vmPFC involvement in successful memory formation differed  
338 between knowledge-congruent and knowledge-incongruent and/or high and low knowledge-

339 relevance associations. Descriptive results are presented in Figure 4. A linear mixed effects  
340 analysis that included trial counts and encoding RTs as covariates revealed a significant  
341 congruency x memory interaction ( $\chi^2(1) = 5.81, p = .016$ ), but no relevance x memory  
342 interaction ( $\chi^2(1) = .23, p = .64$ ) and no congruency x relevance x memory interaction ( $\chi^2(1) =$   
343  $.56, p = .45$ ). To validate the significance of the detected congruency x memory interaction,  
344 we performed an additional likelihood ratio test comparing a model with the congruency x  
345 memory interaction with a model without this interaction. This comparison revealed a  
346 significant difference between the two models ( $\chi^2(1) = 5.70, p = .017$ ), underlining the  
347 significance of the congruency x memory interaction. In contrast, comparing models with and  
348 without the relevance x memory interaction term revealed no significant effect ( $\chi^2(1) = .22, p$   
349  $= .636$ ). Taken together, these findings suggest that the vmPFC contributes more to successful  
350 memory formation when perceived congruency is high than when it is low. In contrast,  
351 vmPFC's contributions to successful memory formation do not vary as a function of  
352 knowledge-relevance.

353

## 354 **Discussion**

355 This study tested the hypothesis that vmPFC contributions to successful memory formation  
356 vary as a function of knowledge-congruency – being strong when an individual perceives a  
357 high fit between activated prior knowledge and new information– but not as a function of  
358 knowledge-relevance.

359 We found evidence for our hypothesis in two sets of analyses. In the first one, we  
360 observed that a cluster in the vmPFC displayed stronger activation for associations perceived  
361 as congruent compared to associations perceived as incongruent, which suggests that the  
362 vmPFC is indeed sensitive to knowledge-congruency. Furthermore, this vmPFC cluster  
363 strongly overlapped with a vmPFC cluster that contributed to successful memory formation

364 (i.e., showed a SME), indicating that the vmPFC's role in congruency detection might interact  
365 with its role in memory formation. In the second analysis, we probed this interaction directly  
366 using a linear mixed effects analysis on the percent signal change data extracted from the  
367 vmPFC SME cluster of those participants whose data were not used for the second analysis.  
368 This analysis revealed a significant congruency x memory interaction in the vmPFC. No  
369 significant interactions involving the knowledge-relevance factor were found. The latter was  
370 true even though memory performance was strongly modulated by knowledge-relevance,  
371 which indicates that prior knowledge was indeed useful for memorizing in our high relevance  
372 condition. These findings indicate that vmPFC contributions to memory formation differ as a  
373 function of knowledge-congruency, but not as a function of knowledge-relevance.

374         Our results contribute to a better understanding of the role of the vmPFC in memory  
375 formation. They suggest that the vmPFC's involvement in memory encoding is not modulated  
376 by prior knowledge of the stimulus material per se, but that its contributions are modulated by  
377 the perceived congruency between prior knowledge and the to-be-encoded information. These  
378 findings emphasize the subjective nature of congruency, which can be high even when overall  
379 knowledge-relevance is low (such as when associating names with faces). They also provide  
380 empirical support for our claim that knowledge-relevance and knowledge-congruency can be  
381 distinguished and might help to explain why a number of published experiments that  
382 examined prior knowledge effects on memory encoding have not found vmPFC activation  
383 (Bein, Reggev, & Maril, 2014; Brod, Lindenberger, Wagner, & Shing, 2016; van Buuren et  
384 al., 2014). All of these studies contrasted high and low knowledge-relevance associations (in  
385 the case of Bein et al., 2014, semantically related and unrelated word pairs), which did not  
386 involve a congruency dimension. We, thus, propose an amendment to the existing models of  
387 the vmPFC's role in memory encoding (Gilboa & Marlatte, 2017; Schlichting & Preston,  
388 2015; van Kesteren et al., 2012). We suggest that the vmPFC's contributions to memory

389 encoding are dependent on the subjectively perceived congruency between prior knowledge  
390 and new information (i.e., stronger when congruency is high), but that they seem not to be  
391 dependent on how well the new information can be linked to a pre-existing semantic network.  
392 This claim resonates well with the idea of the vmPFC's role in memory retrieval as providing  
393 a "feeling of rightness", which was based on work with confabulating patients (Moscovitch &  
394 Winocur, 2002). It is also in line with the vmPFC's role in self-referential processing  
395 (Macrae, Moran, Heatherton, Banfield, & Kelley, 2004; Northoff & Bermpohl, 2004) and in  
396 providing affective value information in decision making, such as the correctness of a  
397 prediction (Kumaran, Summerfield, Hassabis, & Maguire, 2009; Roy, Shohamy, & Wager,  
398 2012). All of these different lines of research highlight the subjective dimension of vmPFC  
399 recruitment, and we believe that this common role of the vmPFC extends to the memory  
400 domain.

401         Several limitations of our study and of the proposed model revision have to be  
402 discussed. First, even though our proposed distinction between knowledge-congruency and  
403 knowledge-relevance is able to explain why several recent memory studies have not observed  
404 vmPFC involvement despite being knowledge-related, it is challenged by one study that  
405 found differential vmPFC involvement although its conditions did not seem to differ in  
406 knowledge-congruency. In this study (van Kesteren et al., 2014), students of biology and  
407 education had to encode new facts that were related to either biology or education. Successful  
408 encoding of facts from their own discipline (i.e. of high knowledge-relevance) led to  
409 enhanced vmPFC activation as compared to facts from the other discipline. Although the  
410 strength of the activation difference was modest (27 voxels), this finding seems difficult to  
411 reconcile with our model. One could speculate that, even though the two conditions did not  
412 differ in congruency per se, the participants generally perceived higher congruency for facts  
413 related to their own subject as compared to the other one. Evidence for this speculation comes

414 from data of the encoding task, in which the participants had to indicate whether they will  
415 remember the fact or not. For their own subject, participants indeed more often expected to  
416 remember the new fact as compared to for the other subject (cf. van Kesteren et al., 2014).  
417 This points to a more general issue, which is that a congruency decision may also entail a  
418 difficulty decision because associations that are easier to encode may be deemed congruent.  
419 This leads to a second limitation of our model, which is that knowledge-congruency and  
420 knowledge-relevance are often not completely independent. Nevertheless, our data suggest  
421 that knowledge-congruency and associated vmPFC activation can be high even though overall  
422 knowledge-relevance is low. This suggests that the subjective congruency dimension can be  
423 independent of the experimental condition manipulation. A further concern is that the  
424 reported lack of a relevance x memory interaction in the vmPFC has to be interpreted with  
425 caution due to its null-effect nature. This finding does not preclude the possibility that the  
426 vmPFC is sensitive to differences in knowledge-relevance. In fact, two clusters in the vmPFC  
427 were sensitive to differences in knowledge-relevance, albeit in opposite directions (i.e.,  
428 greater activation for high vs. low in one cluster, and vice versa for the other cluster).  
429 Critically, however, their involvement was not predictive of successful memory formation.

430 Future studies are necessary to determine whether making an explicit decision is  
431 actually necessary for the vmPFC to be involved. Our study, along with most of the studies  
432 reported thus far, included explicit congruency judgments performed by the participants and  
433 sorted trials based on these judgments. Knowledge-relevance, on the other hand, was content-  
434 based (diagnoses vs. names) and defined by the experimenters. Nevertheless, making a  
435 decision that something is congruent could trigger reward-related processes that have been  
436 shown to lead to vmPFC activation as well (Rushworth, Noonan, Boorman, Walton, &  
437 Behrens, 2011), as has been shown for information rated as self-related (Gutchess, Kensinger,  
438 & Schacter, 2007). Thus, it is currently unclear whether a task in which there is a clear

439 congruency dimension would be enough to trigger vmPFC activation even when the  
440 participants are not asked to give a response. Further studies are also needed to determine  
441 whether vmPFC contributions to memory encoding differ by sub-region. As an example, a  
442 study on memory-based decision-making has reported distinctive contributions of subcallosal  
443 vmPFC and posterior orbitofrontal cortex to monitoring and control processes, respectively  
444 (Hebscher, Barkan-Abramski, Goldsmith, Aharon-Peretz, & Gilboa, 2016, for a proposal on  
445 sub-regional organization of the vmPFC, see Hebscher & Gilboa, 2016).

446         To conclude, we have shown that the vmPFC contributions to memory encoding differ  
447 by knowledge-congruency, but not by knowledge-relevance. We reported evidence for a  
448 theoretical distinction according to which the vmPFC is not involved in memory encoding in  
449 the context of prior knowledge per se, but that its contributions are modulated by the  
450 perceived congruency between prior knowledge and the to-be-encoded information. We  
451 believe that this revision to the emerging model of the vmPFC's role in knowledge-based  
452 memory encoding can be helpful to advance research in the field because it is easily  
453 falsifiable and it allows to derive clear hypotheses about when the vmPFC can be expected to  
454 be involved in memory encoding.

455

456

457 **Funding**

458 This work was funded by the Max Planck Society and a Heinz Maier Leibnitz prize awarded  
459 to YLS by the German Research Foundation. Garvin Brod was supported by a doctoral  
460 fellowship of the International Max Planck Research School on the Life Course (LIFE;  
461 [www.imprs-life.mpg.de](http://www.imprs-life.mpg.de)), and a scholarship of the German Academic Exchange Service  
462 (DAAD).

463

464 **Acknowledgments**

465 This study was conducted within the “Cognitive and Neural Dynamics of Memory across the  
466 Lifespan” (CONMEM) project at the Center for Lifespan Psychology, Max Planck Institute  
467 for Human Development. GB was supported by a fellowship of the International Max Planck  
468 Research School on the Life Course (LIFE; [www.imprs-life.mpg.de](http://www.imprs-life.mpg.de)). We thank Ulman  
469 Lindenberger and Anthony Wagner for their comments and support for this project.

470

471

472

473

474 **References**

- 475 Bates, D., Mächler, M., Bolker, B. M., & Walker, S. C. (2015). Fitting linear mixed-effects  
 476 models using lme4. *Journal of Statistical Software*, *67*(1), 1–48.  
 477 <http://doi.org/10.18637/jss.v067.i01>
- 478 Bein, O., Reggev, N., & Maril, A. (2014). Prior knowledge influences on hippocampus and  
 479 medial prefrontal cortex interactions in subsequent memory. *Neuropsychologia*, *64*, 320–  
 480 330. <http://doi.org/10.1016/j.neuropsychologia.2014.09.046>
- 481 Benoit, R. G., Szpunar, K. K., & Schacter, D. L. (2014). Ventromedial prefrontal cortex  
 482 supports affective future simulation by integrating distributed knowledge. *Proceedings of*  
 483 *the National Academy of Sciences*, *111*(46), 16550–16555.  
 484 <http://doi.org/10.1073/pnas.1419274111>
- 485 Berkers, R. M. W. J., van der Linden, M., de Almeida, R. F., Müller, N. C. J., Bovy, L.,  
 486 Dresler, M., ... Fernández, G. (2016). Transient medial prefrontal perturbation reduces  
 487 false memory formation. *Cortex*. <http://doi.org/10.1016/j.cortex.2016.12.015>
- 488 Brod, G., Lindenberger, U., Wagner, A. D., & Shing, Y. L. (2016). Knowledge Acquisition  
 489 during Exam Preparation Improves Memory and Modulates Memory Formation. *Journal*  
 490 *of Neuroscience*, *36*(31), 8103–8111. <http://doi.org/10.1523/JNEUROSCI.0045-16.2016>
- 491 Brod, G., Lindenberger, U., Werkle-Bergner, M., & Shing, Y. L. (2015). Differences in the  
 492 neural signature of remembering schema-congruent and schema-incongruent events.  
 493 *NeuroImage*, *117*, 358–366. <http://doi.org/10.1016/j.neuroimage.2015.05.086>
- 494 Brod, G., Werkle-Bergner, M., & Shing, Y. L. (2013). The Influence of Prior Knowledge on  
 495 Memory: A Developmental Cognitive Neuroscience Perspective. *Frontiers in*  
 496 *Behavioral Neuroscience*, *7*(October), 1–13. <http://doi.org/10.3389/fnbeh.2013.00139>
- 497 Cohen, G. (1990). Why is it difficult to put names to faces? *British Journal of Psychology*. *81*,  
 498 287–297. <http://doi.org/10.1111/j.2044-8295.1990.tb02362.x>
- 499 Ghosh, V. E., Moscovitch, M., Melo Colella, B., & Gilboa, A. (2014). Schema Representation  
 500 in Patients with Ventromedial PFC Lesions. *Journal of Neuroscience*, *34*(36), 12057–  
 501 12070. <http://doi.org/10.1523/JNEUROSCI.0740-14.2014>
- 502 Gilboa, A., & Marlatte, H. (2017). Neurobiology of Schemas and Schema-Mediated Memory.  
 503 *Trends in Cognitive Sciences*, *21*(8), 618–631. <http://doi.org/10.1016/j.tics.2017.04.013>
- 504 Hetscher, M., Barkan-Abramski, M., Goldsmith, M., Aharon-Peretz, J., & Gilboa, A. (2016).  
 505 Memory, decision-making, and the ventromedial prefrontal cortex (vmPFC): the roles of  
 506 subcallosal and posterior orbitofrontal cortices in monitoring and control  
 507 processes. *Cerebral Cortex*, *26*(12), 4590–4601. <https://doi.org/10.1093/cercor/bhv220>
- 508 Hetscher, M., & Gilboa, A. (2016). A boost of confidence: The role of the ventromedial  
 509 prefrontal cortex in memory, decision-making, and schemas. *Neuropsychologia*, *90*, 46–  
 510 58. <https://doi.org/10.1016/j.neuropsychologia.2016.05.003>
- 511 Kumaran, D., Summerfield, J. J., Hassabis, D., & Maguire, E. a. (2009). Tracking the  
 512 emergence of conceptual knowledge during human decision making. *Neuron*, *63*(6),  
 513 889–901. <http://doi.org/10.1016/j.neuron.2009.07.030>
- 514 Loftus, G. R., & Masson, M. E. J. (1994). Using confidence intervals in within-subject  
 515 designs. *Psychonomic Bulletin & Review*, *1*(4), 476–490.  
 516 <http://doi.org/10.3758/BF03210951>
- 517 Macrae, C. N., Moran, J. M., Heatherton, T. F., Banfield, J. F., & Kelley, W. M. (2004).  
 518 Medial prefrontal activity predicts memory for self. *Cerebral Cortex*, *14*(6), 647–654.  
 519 <http://doi.org/10.1093/cercor/bhh025>
- 520 Maril, A., Avital, R., Reggev, N., Zuckerman, M., Sadeh, T., Sira, L. Ben, & Livneh, N.  
 521 (2011). Event congruency and episodic encoding: A developmental fMRI study.  
 522 *Neuropsychologia*, *49*(11), 3036–3045.

- 523 <http://doi.org/10.1016/j.neuropsychologia.2011.07.004>
- 524 McWeeny, K. H., Young, A. W., Hay, D. C., & Ellis, A. W. (1987). Putting names to faces.  
525 *British Journal of Psychology*, 78, 143–149. <http://doi.org/10.1111/j.2044->  
526 8295.1987.tb02235.x
- 527 Minear, M., & Park, D. C. (2004). A lifespan database of adult facial stimuli. *Behavior*  
528 *Research Methods, Instruments, & Computers*, 36(4), 630–633.  
529 <http://doi.org/10.3758/BF03206543>
- 530 Moscovitch, M. (1989). Confabulation and the Frontal Systems: Strategic versus Associative  
531 Retrieval in Neuropsychological Theories of Memory. In H. L. Roediger & F. I. M.  
532 Craik (Eds.), *Varieties of memory and consciousness: essays in honour of Endel Tulving*  
533 (pp. 133–161). Hillsdale, NJ: Lawrence Erlbaum.
- 534 Moscovitch, M., & Melo, B. (1997). Strategic retrieval and the frontal lobes: Evidence from  
535 confabulation and amnesia. *Neuropsychologia*, 35(7), 1017–1034.  
536 [http://doi.org/10.1016/S0028-3932\(97\)00028-6](http://doi.org/10.1016/S0028-3932(97)00028-6)
- 537 Moscovitch, M., & Winocur, G. (2002). The frontal cortex and working with memory. In D.  
538 T. Stuss & R. T. Knight (Eds.), *Principles of Frontal Lobe Function* (pp. 188–209). New  
539 York, NY: Oxford University Press.
- 540 Nieuwenhuis, I. L. C., & Takashima, A. (2011). The role of the ventromedial prefrontal  
541 cortex in memory consolidation. *Behavioural Brain Research*, 218(2), 325–334.  
542 <http://doi.org/10.1016/j.bbr.2010.12.009>
- 543 Northoff, G., & Bermpohl, F. (2004). Cortical midline structures and the self. *Trends in*  
544 *Cognitive Sciences*, 8(3), 102–107. <http://doi.org/10.1016/j.tics.2004.01.004>
- 545 R Core Team. (2014). R: A Language and Environment for statistical computing. Vienna,  
546 Austria: R Foundation for Statistical Computing.
- 547 Reggev, N., Bein, O., & Maril, A. (2016). Distinct neural suppression and encoding effects  
548 for conceptual novelty and familiarity. *Journal of cognitive neuroscience*, 28(10). 1455–  
549 1470. [http://doi.org/10.1162/jocn\\_a\\_00994](http://doi.org/10.1162/jocn_a_00994)
- 550 Roy, M., Shohamy, D., & Wager, T. D. (2012). Ventromedial prefrontal-subcortical systems  
551 and the generation of affective meaning. *Trends in Cognitive Sciences*, 16(3), 147–156.  
552 <http://doi.org/10.1016/j.tics.2012.01.005>
- 553 Rushworth, M. F. S., Noonan, M. P., Boorman, E. D., Walton, M. E., & Behrens, T. E.  
554 (2011). Frontal Cortex and Reward-Guided Learning and Decision-Making. *Neuron*,  
555 70(6), 1054–1069. <http://doi.org/10.1016/j.neuron.2011.05.014>
- 556 Schlichting, M. L., & Preston, A. R. (2015). Memory integration: neural mechanisms and  
557 implications for behavior. *Current Opinion in Behavioral Sciences*, 1, 1–8.  
558 <http://doi.org/10.1016/j.cobeha.2014.07.005>
- 559 Schlichting, M. L., & Preston, A. R. (2016). Hippocampal–medial prefrontal circuit supports  
560 memory updating during learning and post-encoding rest. *Neurobiology of Learning and*  
561 *Memory*, 134(Part A), 91–106. <http://doi.org/10.1016/j.nlm.2015.11.005>
- 562 Smith, S., Jenkinson, M., & Woolrich, M. (2004). Advances in functional and structural MR  
563 image analysis and implementation as FSL. *Neuroimage*, 23, 208–219.
- 564 Spalding, K. N., Jones, S. H., Duff, M. C., Tranel, D., & Warren, D. E. (2015). Investigating  
565 the Neural Correlates of Schemas: Ventromedial Prefrontal Cortex Is Necessary for  
566 Normal Schematic Influence on Memory. *Journal of Neuroscience*, 35(47), 15746–  
567 15751. <http://doi.org/10.1523/JNEUROSCI.2767-15.2015>
- 568 van Buuren, M., Kroes, M. C. W., Wagner, I. C., Genzel, L., Morris, R. G. M., & Fernández,  
569 G. (2014). Initial investigation of the effects of an experimentally learned schema on  
570 spatial associative memory in humans. *The Journal of Neuroscience : The Official*  
571 *Journal of the Society for Neuroscience*, 34(50), 16662–70.  
572 <http://doi.org/10.1523/JNEUROSCI.2365-14.2014>

- 573 van Kesteren, M. T. R., Beul, S. F., Takashima, A., Henson, R. N., Ruiter, D. J., & Fernández,  
574 G. (2013). Differential roles for medial prefrontal and medial temporal cortices in  
575 schema-dependent encoding: From congruent to incongruent. *Neuropsychologia*, *51*(12),  
576 2352–9. <http://doi.org/10.1016/j.neuropsychologia.2013.05.027>
- 577 van Kesteren, M. T. R., Rijpkema, M., Ruiter, D. J., & Fernández, G. (2010). Retrieval of  
578 associative information congruent with prior knowledge is related to increased medial  
579 prefrontal activity and connectivity. *The Journal of Neuroscience : The Official Journal*  
580 *of the Society for Neuroscience*, *30*(47), 15888–94.  
581 <http://doi.org/10.1523/JNEUROSCI.2674-10.2010>
- 582 van Kesteren, M. T. R., Rijpkema, M., Ruiter, D. J., Morris, R. G. M., & Fernández, G.  
583 (2014). Building on prior knowledge: Schema-dependent encoding processes relate to  
584 academic performance. *Journal of Cognitive Neuroscience*, *26*(10), 2250–2261.  
585 [http://doi.org/10.1162/jocn\\_a\\_00630](http://doi.org/10.1162/jocn_a_00630)
- 586 van Kesteren, M. T. R., Ruiter, D. J., Fernández, G., & Henson, R. N. (2012). How schema  
587 and novelty augment memory formation. *Trends in Neurosciences*, *35*(4), 211–219.  
588 <http://doi.org/10.1016/j.tins.2012.02.001>
- 589 Warren, D. E., Jones, S. H., Duff, M. C., & Tranel, D. (2014). False Recall Is Reduced by  
590 Damage to the Ventromedial Prefrontal Cortex: Implications for Understanding the  
591 Neural Correlates of Schematic Memory. *Journal of Neuroscience*, *34*(22), 7677–7682.  
592 <http://doi.org/10.1523/JNEUROSCI.0119-14.2014>
- 593 Webb, C. E., Turney, I. C., & Dennis, N. A. (2016). What’s the gist? The influence of  
594 schemas on the neural correlates underlying true and false memories. *Neuropsychologia*,  
595 *93*(September), 61–75. <http://doi.org/10.1016/j.neuropsychologia.2016.09.023>
- 596 Weiskopf, N., Hutton, C., Josephs, O., & Deichmann, R. (2006). Optimal EPI parameters for  
597 reduction of susceptibility-induced BOLD sensitivity losses: A whole-brain analysis at 3  
598 T and 1.5 T. *Neuroimage*, *33*(2), 493–504.
- 599 Zeithamova, D., Dominick, A. L., & Preston, A. R. (2012). Hippocampal and ventral medial  
600 prefrontal activation during retrieval-mediated learning supports novel inference.  
601 *Neuron*, *75*(1), 168–79. <http://doi.org/10.1016/j.neuron.2012.05.010>

602  
603

604

605

606

607

608

609

610

611

612

613

614

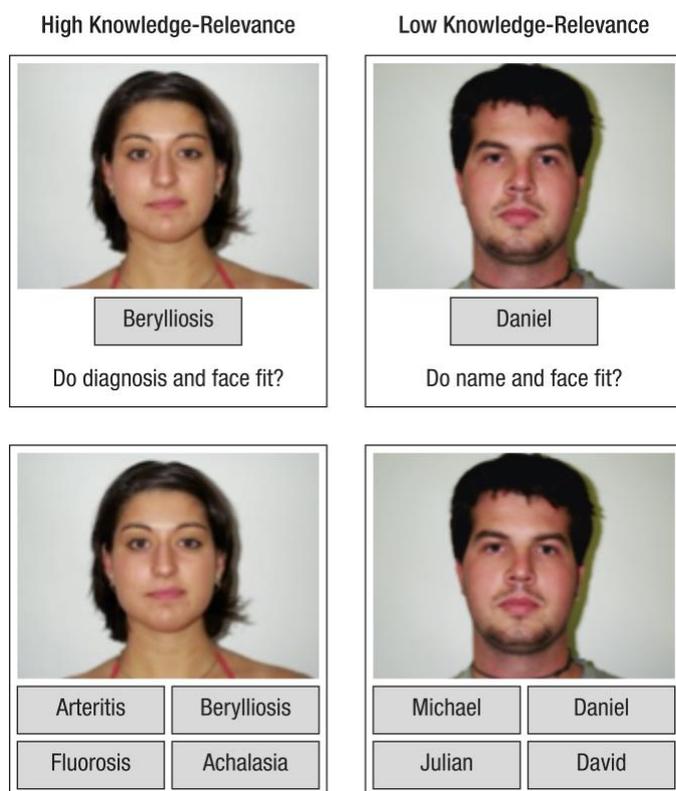
615 **Tables**

616 Table 1. Regions exhibiting stronger activation for high vs. low and low vs. high knowledge-  
 617 relevance pairs as well as for subsequently remembered vs. forgotten pairs. To better capture  
 618 the involved brain regions, local maxima are presented in addition to cluster maxima for very  
 619 large clusters.

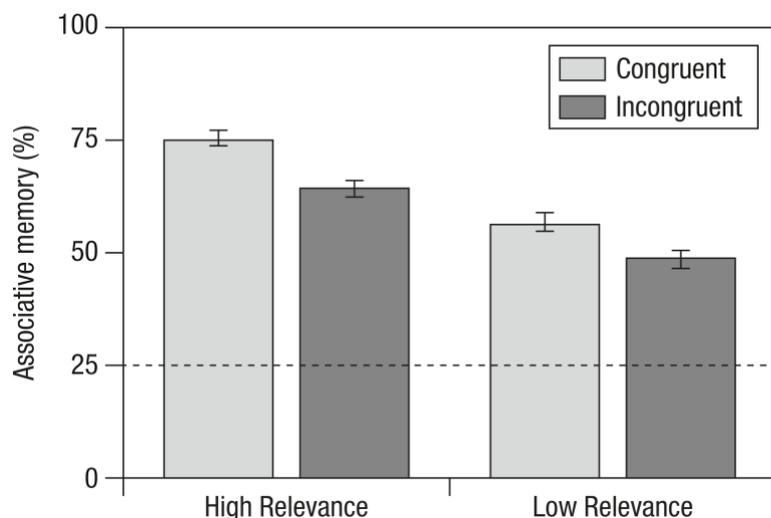
Region	x	y	z	Z-Max	# voxels
<b>High vs. Low Knowledge-Relevance</b>					
Left Inferior Temporal Gyrus	-46	-54	-16	8.23	42790
Left Temporooccipital Fusiform Cortex	-40	-46	-18	8.18	"
Left Lateral Occipital Cortex	-48	-68	-14	8.11	"
Left Inferior Temporal Gyrus	-42	-52	-14	6.72	"
Left Superior Frontal Gyrus	-54	-52	-12	8.07	"
Left Inferior Temporal Gyrus	-52	-56	-12	7.99	"
Paracingulate Gyrus / Superior Frontal Gyrus	-6	16	48	8.34	3629
Insular Cortex	32	26	2	7.38	717
Right Middle / Inferior Frontal Gyrus	48	14	32	4.6	667
<b>Low vs. High Knowledge-Relevance</b>					
Right Supramarginal / Angular Gyrus	60	-42	38	7.24	50504
Paracingulate Gyrus	2	48	2	3,31	"
Right Supramarginal Gyrus	54	-40	30	7.17	"
Cingulate Gyrus	-2	38	6	6.99	"
Right Supramarginal Gyrus	62	-32	36	6.89	"
Cingulate Gyrus	-2	36	12	6.83	"
<b>Subsequent Memory Effect (Rem &gt; Forg)</b>					
Right Lateral Occipital Cortex	42	-72	-6	4.65	4093
Left Temporooccipital Fusiform Cortex	-40	-56	-14	4.61	2906
Left Inferior Frontal Gyrus / Frontal Pole	-54	32	14	4.86	2715
Frontal Pole	-8	54	42	4.62	2560
Left Amygdala / Hippocampus	-18	-6	-14	4.9	1009
Left Lateral Occipital Cortex	-48	-70	36	4.11	796
Right Amygdala / Hippocampus	20	-6	-16	4.77	630
Bilateral Ventromedial Prefrontal Cortex	-4	50	-14	4.61	575
Right Inferior Frontal Gyrus	56	34	12	3.96	571
<b>Congruent vs. Incongruent</b>					
Bilateral Ventromedial Prefrontal Cortex	2	62	16	4.19	580
Bilateral Caudate	-8	16	0	4.35	401
<b>Incongruent vs. Congruent</b>					
Right Middle Frontal Gyrus	48	28	36	3.81	555

620

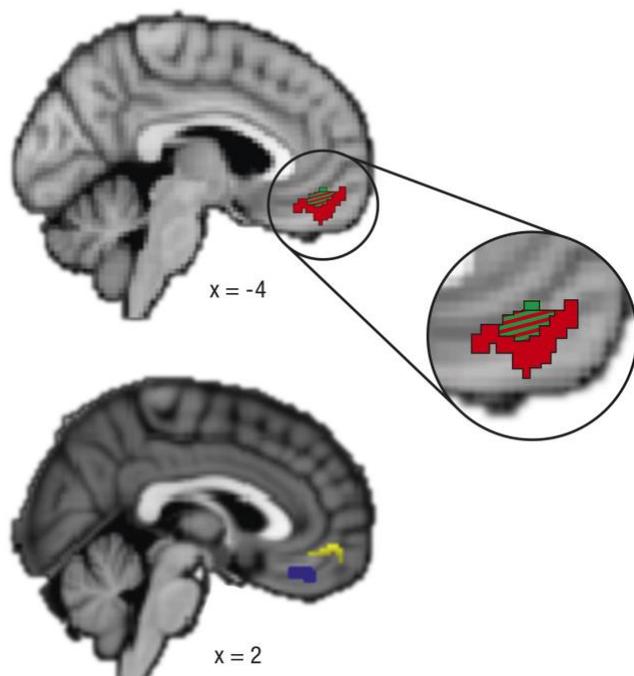
621 **Figures**



622  
623 *Figure 1. Memory task. Participants were instructed to memorize face–word pairs in the MRI*  
624 *(upper part) and to indicate whether the face fits the word or not (congruency judgment). Half*  
625 *of the words were diagnoses (high knowledge-relevance, left example) and half were first*  
626 *names (low knowledge-relevance, right example). Retrieval took place outside of the scanner*  
627 *(lower part). All of the studied faces were presented again, together with four first names or*  
628 *four diagnoses, of which only one had been presented with the face during the encoding*  
629 *phase. Participants had to indicate the word with which the face was presented during*  
630 *encoding. The three lures were names or diagnoses that had been paired with other faces*  
631 *during the encoding phase.*

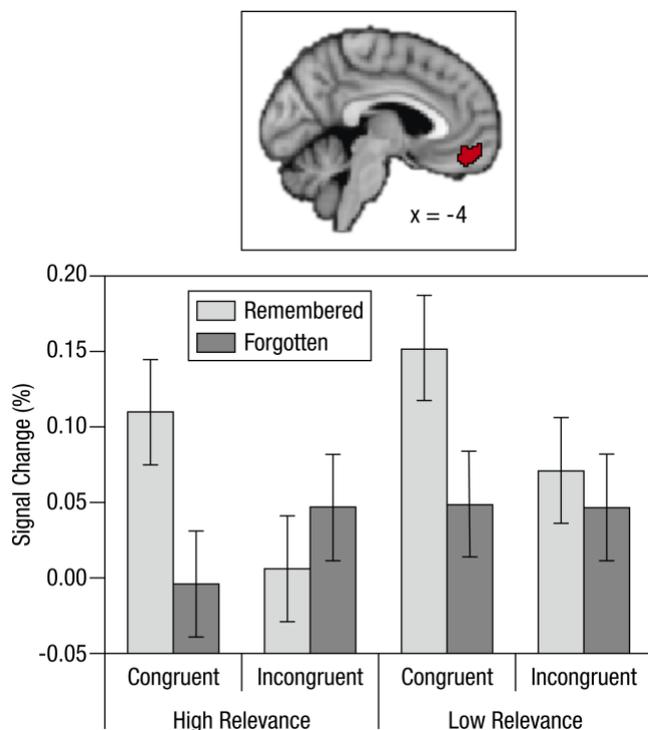


632  
633 Figure 2. Memory performance was higher for associations that were rated as congruent and  
634 that had high knowledge-relevance (i.e., face–diagnosis pairs), with no interaction between  
635 congruency and relevance. Chance level was 25%. Error bars are within-subject standard  
636 errors (Loftus & Masson, 1994).



637  
638 Figure 3. Effects of memory, congruency, and relevance within our vmPFC anatomical mask.  
639 Upper part: the vmPFC was more strongly activated for associations that were judged as

640 congruent as compared to associations judged as incongruent (peak voxel: 6, 42, -16; Z = 3.8,  
 641 208 voxels, in green). This cluster overlaps (overlap = 208 voxels, striped) with the vmPFC  
 642 cluster distinguishing associations that were later remembered vs. forgotten (i.e. SME) (peak  
 643 voxel: -4, 50, -14; Z = 4.6, 396 voxels, in red). Lower part: Nearby regions of the vmPFC  
 644 displayed more activation for associations for which the participants' medical knowledge was  
 645 of high vs. low relevance (peak voxel: -2, 36, -16, Z = 5.01, 121 voxels, in blue) and of low  
 646 vs. high relevance (peak voxel: 4, 52, -4; Z = 6.26, 190 voxels, in yellow).  
 647



648  
 649 Figure 4. Congruency x memory interaction in the vmPFC. Signal change (%) was extracted  
 650 from a vmPFC SME cluster (peak voxel: -2, 48, -14; Z = 3.13, 236 voxels, in red) that was  
 651 defined in an independent sample. A linear mixed effects analysis revealed a significant  
 652 congruency x memory interaction ( $\chi^2(1) = 5.81, p = .016$ ), but no relevance x memory  
 653 interaction ( $\chi^2(1) = .23, p = .64$ ). Error bars are within-subject standard errors (Loftus &  
 654 Masson, 1994).  
 655