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Spatial Binding Impairments in Visual Working Memory following Temporal Lobectomy

1 **Spatial Binding Impairments in Visual Working Memory following Temporal**

2 **Lobectomy**

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Abstract

33

34   Disorders of the medial temporal lobe (MTL) adversely affect visual working

35   memory (vWM) performance, including feature binding. It is unclear whether these

36   impairments generalise across visual dimensions or are specifically spatial. To address this

37   issue, we compared performance in two tasks of thirteen epilepsy patients, who had

38   undergone a temporal lobectomy, and fifteen healthy controls. In the vWM task, participants

39   recalled the color of one of two polygons, previously displayed side by side. At recall, a

40   location or shape probe identified the target. In the perceptual task, participants estimated the

41   centroid of three visible disks. Patients recalled the target color less accurately than healthy

42   controls because they frequently swapped the non-target with the target color. Moreover,

43   healthy controls and right temporal lobectomy patients made more swap errors following

44   shape than space probes. Left temporal lobectomy patients, showed the opposite pattern of

45   errors instead. Patients and controls performed similarly in the perceptual task. We conclude

46   that left MTL damage impairs spatial binding in vWM, and that this impairment does not

47   reflect a perceptual or attentional deficit.

48

49   **Significance Statement**

50   This study examined color recall in temporal lobectomy patients and healthy controls,

51   to determine whether patients show differential impairments binding color and shape vs color

52   and location of memorised objects. Left temporal lobectomy patients were less accurate

53   recalling color, especially when the target object was identified by the location, rather than

54   the shape it had in the initial display. We found no group difference in a task, which required

55   estimating the centroid of three circles, indicating that the memory impairment was not

56   accounted by perceptual or attentional difficulties. Our findings indicate that lateralised

57   medial temporal circuits are crucial for binding visual features to the location where they had

58   appeared, thus ensuring the primacy of space in organising declarative memories.

59

Introduction

60

61   The role of the medial temporal lobe (MTL) in episodic memory is well established

62   (Squire, 2009). Despite initial reports of preserved immediate memory span in temporal

63   lobectomy patients (Drachman and Arbit, 1966), later studies found that MTL lesions also

64   engender substantial working memory (WM) deficits (Olton *et al.*, 1979; Holdstock *et al*,

65   1995; Hannula *et al.*, 2006). Which WM processes are specifically supported by the MTL is,

66   nevertheless, a matter of ongoing investigations.

67   An early, seminal model suggested that visual WM (wWM) contains few discrete

68   "slots", each used to store one and only one object with high fidelity (Luck and Vogel, 1997;

69   Zhang and Luck, 2008). Despite its simplicity, the slot model makes non-trivial predictions.

70   First, the complexity of memorised objects should not affect recall accuracy. Second,

71   recalling feature conjunctions should carry no additional cost over remembering features,

72   since features are stored *ipso facto* as parts of an object into vWM. Wheeler and Treisman

73   (2002) found, instead, that simple objects were recalled more accurately than complex ones,

74   and that recall accuracy was equalised for displays containing the same number of color

75   features rather than the same number of objects. They concluded that memory limitations

76   reflect feature rather than object-based storage mechanisms. Moreover, observers were worse

77   at detecting changes of feature conjunctions than features, indicating that conjunctions are

78   stored or recalled less efficiently than features. Later studies confirmed that changes in

79   feature conjunctions are poorly detected (Allen *et al*., 2006), leading to the suggestion that

80   dimensionally specific registers store features, while an "episodic buffer" is dedicated to

81   holding bound object representations in vWM (Baddeley *et al.*, 2011). The need for binding

82   processes follows logically from the alternative model of vWM which proposes that visual

83   features are stored in dimensionally specific, limited resolution stores (Alvarez and

84   Cavanagh, 2004; Smyrnis *et al.*, 2005; Bays *et al.*, 2009). Clearly, if different feature

85   dimensions are stored separately, then a binding process is required to ensure that features

86   belonging to the same object, but different feature dimensions, are identified as such

87   (Wheeler and Treisman, 2002; Smyrnis *et al.*, 2005).

88   While the idea that conjunctive binding is required to preserve object identity is not

89   unanimously shared (e.g. Luck and Vogel, 2013), there are several proposals regarding its

90   nature. Treisman and Zhang (2006) concluded that binding is automatic, established initially

91   by the features' shared location, but then becomes location independent. Schneegans and

92   Bays (2017) proposed instead that location information is always required, because features

93   from different visual dimensions are stored in separate retinotopic maps.

94   Investigators examining the neurological underpinnings of declarative memory

95   largely embrace the idea that space plays a crucial role in indexing declarative memories.

96   Animal and patient studies (e.g. Chalfonte *et al.*, 1996; Brown and Aggleton, 2001; Eacott

97   and Gaffan, 2005; Piekema *et al.,* 2006; Ranganath, 2010; Libby *et al.*, 2014) documented a

98   functional parcellation of the MTL with separate structures representing respectively the

99   environmental layout, the objects within it, as well as binding the latter to the former.

100   According to this view, space is crucial for recalling events, but not for binding object

101   features. Olson *et al.* (2006) for example, reported that patients with post-anoxic or post-

102   encephalitic MTL pathology had impaired object-location binding in a WM task. This

103   impairment was unaccounted by either diminished recognition or spatial memory. In animals,

104   MTL lesions are also followed by dissociated impairments in object recognition and recall of

105   object-location conjunctions, suggesting that feature and spatial binding depend on distinct

106   MTL processes (Meunier *et al.*, 1993; Murray and Mishkin, 1998; Malkova and Mishkin,

107   2003). Studies in temporal lobe epilepsy (TLE) patients reported deficits in spatial recall,

108   spatial binding and visual recognition (Abrahams *et al.*, 1997; Bohbot *et al.*, 1998;

109   Stepankova *et al.*, 2004), however it remains unclear whether these impairments should be

110   attributed to diminished spatial precision (Kolarik *et al.*, 2016) or a binding deficit (Zokaei *et*

111   *al.*, 2019) and whether binding impairments are dimensionally general (Hannula *et al.*, 2006;

112   Pertzov *et al.*, 2013) or specific.

113   To examine these issues, we tested TLE patients who had undergone temporal

114   lobectomies and healthy controls with two tasks used in a previous investigation of a stroke

115   patient (Dundon *et al.*, 2017). The first requires recalling the color of one of two polygons

116   identified by either a location or a shape probe, thus directly pitting spatial vs. non-spatial

117   binding. The second probes participants' ability to estimate the average position of three

118   visible disks. In this task healthy participants show a pseudo-neglect pattern of leftward static

119   errors (Baud-Bovy and Soechting, 2001), which suggests that centroid estimation is sensitive

120   to attentional biases (Dundon *et al.*, 2017). The centroid task was therefore used to highlight

121   the presence of unilateral neglect, which can follow lesions of the non-dominant

122   parahippocampal cortex (Mort *et a.l*, 2003) as well as the integrity of spatial perception and

123   attention (Drew *et al.*, 2010).

124

125 **Material and Methods**

126   The aim of the present study was to compare non-spatial and spatial binding

127 performance in TLE patients' with medically refractory epilepsy who had undergone

128 temporal lobectomy and healthy controls. Recruitment and testing took place at the

129 Neuropsychology section of the Department of Neurosciences of the Department of

130 Neurosciences of King Faisal Specialist Hospital & Research Centre in Riyadh, Saudi

131 Arabia. The experimental protocol was approved by the local Institutional Review Board.

132 Participants gave written informed consent prior to engaging in any experimental procedure.

133

134 <u>Study participants</u>

135   Over a month period, an opportunity sample of patients attending the Neurology and

136 Neurosurgical Clinics were invited to participate in the study. All had been diagnosed with

137 TLE on the basis of clinical presentation and instrumental diagnostic procedures, inclusive of

138 ambulatory EEG and neuroimaging, and after failing medical therapy, had

139 undergone surgical treatment. All patients had normal or corrected to normal visual

140 acuity. Those with an estimated full-scale IQ of less than 75, as assessed with an Arabic

141 version of the Wechsler Abbreviated Scale of Intelligence – Second Edition (WASI-II, Al-

142 Joudi *et al.*, 2019), were excluded, as well as those with a history of traumatic brain

143 injury or major psychiatric disorders. Patients who suffered a seizure in the preceding 48

144 hours had the testing session postponed. Thirteen patients took part in this study. The

145 study's neurosurgeon identified the anatomical structures involved by the resection on the

146 basis of the surgical record and post-surgical MRI scans.

147   Fifteen healthy participants were concurrently recruited from the local community as

148 controls. Potential participants were excluded if they had a history of a major neurological or

149 psychiatric disorder or an uncorrected visual impairment or an estimated IQ less than 75.

150

151 **Testing protocol**

152   Testing took place in a quiet, dimly lit room. Participants sat comfortably at a distance

153 of approximately 70cm from a MacBook Pro® set at a resolution of 1680x1050

154 pixels. Custom-coded Matlab (Mathworks, Natick, Massachusetts) scripts used a set of freely

155 available routines (Brainard, 1997) to control the timing of the displays. Two tasks were

156 conducted using the computerized set-up.

157

158 <u>Cued color recall</u>

159   In each trial, an equilateral triangle and a square, whose side lengths are 1.29° and

160 0.92° respectively, appear side-to-side in the lower half of the screen, as shown in figure 1A.

161 The shapes are centred at an eccentricity of 2.27° along the main screen diagonals and remain

162 visible for 2.0s. The two shapes are of different colors, either red, blue or green. The sample

163 display is followed by a 0.2s long pattern mask and a 1.3s blank screen. The recall screen

164 contains three colored rectangles, 0.53° wide and 1.59° high, whose lower edges are aligned

165 1.39° above the screen center and spaced horizontally 4.81° apart. A bright cross (location

166 probe) or the outline of one of the polygons (shape probe) identifies the target. The location

167 probe, which also includes a dark cross, appear at the locations occupied by the two

168 shapes. The shape cue appears 3.0° below the screen center. Participants report the

169 target color by placing the cursor over the corresponding colored rectangle and clicking the

170 mouse button. The mouse click prompts the beginning of a new trial after a 1.0s delay during

171 which the screen is blank. Participants practiced the task over 16 trials and then completed

172 two blocks of 96 trials each, including both shape and location cued recalls. Trial order was

173 randomised, minimizing participants' ability to predict whether a shape or location probe

174 would follow the sample display. To ensure that patients had not forgotten the task

175 instructions, at the end of each block they were asked to describe what they had done.

176

177 Centroid estimation

178   This task assesses the accuracy and precision of estimates of the average location of

179 three visible white disks and is illustrated in figure 1B. Each disk's diameter is 0.27°.

180 Participants place a crosshair-shaped cursor at the estimated centroid location and click

181 the mouse. Following a 1.0s interval, a novel set of disks appears and the procedure

182 is repeated. Disks can occupy any three of seven canonical locations, including the screen

183 center and the vertices of a virtual concentric hexagon, with a side length of 3.67°. All

184 permutations of three canonical locations, less any resulting in a collinear configuration, are

185 used as test arrays. Each possible permutation appears twice, for a total of 64

186 trials. Pseudorandom, zero mean, independent circular Gaussian distributions, with a

187 standard deviation of 0.6°, are sampled to jitter each disk's position. Prior to testing,

188 instructions were read to the participants. The centroid was defined as the point where the

189 triangle, whose vertices coincided with the disks' locations, would balance in the horizontal

190 plane (Baud-Bovy and Soechting, 2001). Participants completed 25 practice trials, without

191 feed-back, followed by two blocks of 64 trials each.

192

193 **Neuropsychological tests**

194 Three neuropsychological instruments were used to assess participants: 1) Hopkins Verbal

195 Learning Test – Revised (HVLT-R), 2) Brief Visuospatial Memory Test – Revised (BVMT-

196 R), and 3) Color Trails Test (CTT). The Arabic version of these tests were recently validated

197 (Al-Joudi *et al.*, 2019).

198

199 **Data analysis**

200   In the recall task, participants could either report 1) the color of the target, correct

201 response, 2) the color of the non-target item, that is make a swap error, or 3) the color absent

202 from the sample, that is make a generic error. We approached the group level hypothesis

203 testing as a metanalysis of prevalence data, treating each participant as a separate study. All

204 inferential analysis presented in this study is Bayesian.

205

206 Group differences in recall error rates

207   Group level effects were analysed with mixed Bayesian ANOVAs using the JASP

208 software (JASP Team, 2021; jasp-stats.org). The between group variable coded whether the

209 participant was 1) a healthy control, 2) a patient following left or 3) right temporal

210 lobectomy, respectively. The within group variables were probe dimension, i.e., whether a

211 shape or space probe was used to cue recall, and block order, i.e., first or second block. The

212 error rates were normalised with a Friedman-Tukey double arcsine transformation

213 (Barendregt et al., 2013). The transformation stabilizes error rates variances and allows the

214 use of parametric methods to compute group statistics:

215 $$t = \sin^{-1}\sqrt{\frac{c}{n}} + \sin^{-1}\sqrt{\frac{c}{n+1}}$$

216 where c is the number of either swap or generic errors and *n* is the total number of trials for

217 each probe dimension and block. The group average proportions were obtained by applying

218 the following inverse transformation to the transformed proportions group means:

$$\hat{p} = \left[1 - sgn(\cos\hat{t})\cdot\sqrt{1 - \left(\sin\hat{t} - \frac{\sin\hat{t} - 1/\sin\hat{t}}{n}\right)^2}\right]\cdot 0.5$$

219

220 Analysis of centroid task

221   The analysis of the centroid task was carried out by fitting the following regression

222   model to each participants' reports:

$$\begin{pmatrix} \boldsymbol{r}_x \\ \boldsymbol{r}_y \end{pmatrix} = \begin{pmatrix} a_0 \\ b_0 \end{pmatrix} + \begin{pmatrix} a_1 & 0 \\ 0 & b_1 \end{pmatrix} \begin{pmatrix} \boldsymbol{C}_x \\ \boldsymbol{C}_y \end{pmatrix} + \begin{pmatrix} \boldsymbol{N}_x \\ \boldsymbol{N}_y \end{pmatrix}$$

223   where $\boldsymbol{r}_x$ and $\boldsymbol{r}_y$ are the *x-y* screen coordinates of the centroid estimates, $\boldsymbol{C}_x$, $\boldsymbol{C}_y$ are the centroid

224   horizontal and vertical screen coordinates and $\boldsymbol{N}_x$ and $\boldsymbol{N}_y$ are the normal distributions of the

225   respective residuals. Although incenter biases are also known to affect centroid estimates

226   (Baud-Bovy and Soechting, 2001), we did not include them in the model for sake of clarity

227   and because a preliminary analysis did not reveal appreciable group differences. Group and

228   screen coordinates differences in static offsets, i.e. a_0 and b_0, accuracy, i.e. a_1 and b_1, and

229   precision, i.e. the variance of $\boldsymbol{N}_x$ and $\boldsymbol{N}_y$, were assessed with Bayesian mixed ANOVAs.

230 **Results**

231 <u>Participants' demographic, clinical and neuropsychometric characteristics</u>

232   Table 1 reports the demographic and clinical characteristics of the left and right

233 temporal lobectomy patients and healthy controls. The groups were matched on age, gender

234 and educational level. Both patient groups showed a lower full-scale IQ that healthy controls,

235 however all of the variables were more likely to reflect a null effect than a group

236 difference. Table 2 details the sex, education level and neuropsychometric performance of

237 the thirteen patients. Both raw scores as well the values normalised on the basis of a reference

238 sample of healthy controls, whose first language is Arabic (Al-Joudi *et al.*, 2019), are shown.

239 We examined whether patients showed a material specific pattern of lateralized deficits (e.g.

240 Saling, 2009) by comparing performance of the left and right temporal lobectomy patients on

241 the HMVT and the BVMT with Bayesian independent samples t-tests (JASP

242 Team, 2021; <u>jasp-stats.org</u>). There was moderate strength evidence for left temporal

243 lobectomy patients having worse delayed verbal recall on the HVLT than controls ($BF_{10} =$

244 7.99), while there was anecdotal evidence for no group difference in the delayed visuo-spatial

245 recall ($BF_{10} = 0.46$). In Table 3 the MTL structures affected by the surgical excisions are

246 listed, patient by patient, while Table 3-1 (see supplementary material) shows representative

247 postsurgical axial, sagittal and coronal multimodal MRI slices for each patient.

248

249 <u>Cued color recall performance</u>

250   In the cued recall task, participants completed two blocks of 96 trials each. Mixed

251 effect Bayesian ANOVAs were used to examine the influence of three factors on recall: 1)

252 group, namely whether participants were controls, patients following left and right temporal

253 lobectomy, respectively; 2) block and 3) probe dimension. Generic and swap errors were

254 analysed separately.

255   Extended data table 4-1 reports the result of the ANOVA model comparison for swap

256   errors. The model with the highest posterior probability included group, probe dimension and

257   block, as well as the interaction of group by probe dimension. Table 4 summarises the

258   evidence for each predictor. There was moderate evidence for an effect of probe dimension

259   and block. There was very strong evidence for an effect of group and strong evidence for an

260   interaction of group by probe dimension.

261   Extended data table 5-1 summarises the results of the model comparisons for generic

262   errors. The best model was the one which included all three factors, but none of the

263   interactions. Table 5 summarises the analysis of the effects. There was anecdotal evidence for

264   the block and probe dimension affecting the proportion of generic errors. On the other hand,

265   there was anecdotal evidence for a null effect of group.

266   Figure 2 shows the mean proportion of swap and generic errors following space and

267   shape probe, respectively. Controls made fewest swap and generic errors. Controls and

268   patients with right temporal lobectomies made more swap errors following shape than space

269   probes. Patients with left temporal lobectomies made most swap errors and three of them

270   made more swap errors following space than shape probes. Participants made more generic

271   errors following space than shape probe. Participants also made more swap and generic errors

272   in the first than second block (data not shown).

273

274   *Centroid estimation performance*

275   We examined how group and screen coordinates affected three indices of performance in

276   the centroid estimation task: 1) static offsets, 2) accuracy and 3) precision (see Methods). For

277   static offsets the model with the highest posterior probability included the effect of screen

278   coordinates only. In fact, there was strong evidence, $BF_{inc} = 32.13$, that the horizontal and

279   vertical offsets differed. While there was no appreciable horizontal bias, $m = 0.0°$, *95%CI =*

280   [-0.04°, 0.05°], participants showed an upward bias, $m = 0.15°$, *95%CI* = [0.07°, 0.23°].

281   There was moderate evidence in favour of the null and against both an effect of group, BF_{inc}

282   = .22, and its interaction with coordinate, BF_{inc} = .28. For accuracy, the model with highest

283   posterior probability included group. However, there was anecdotal evidence for a null effect

284   of group, BF_{inc} = .76, with moderate evidence in favour of a null effect of coordinate (BF_{inc} =

285   .26), and its interaction with group, BF_{inc} = .28. For precision, namely the variance of the

286   variable errors, the null model had the highest posterior probability. There was anecdotal

287   evidence for a null effect of screen coordinate, $BF_{inc} = 0.4$, anecdotal evidence for a null

288   effect of group, $BF_{inc} = 0.53$, and moderate evidence for a null interaction of group and

289   dimension, $BF_{inc} = 0.15$.

290   **Discussion**

291   In this study we compared performance of healthy controls and temporal lobectomy

292   patients in two tasks, one probing conjunctive binding in vWM, the other perceptual, spatial

293   averaging of disks patterns. The vWM task required the recall of a target's colour, where the

294   target was identified by either a location or a shape probe. The task was thus designed to

295   determine dimensional specificity of working memory conjunctive binding. Controls were

296   more accurate than patients overall. Moreover, they made fewer swap errors following space

297   than shape probes, while left temporal lobectomy patients made more swap errors following

298   space than shape probes. There was no evidence of group differences in static biases,

299   accuracy and precision of perceptual centroid estimates. The implication of these findings for

300   the organization of binding and spatial processes in vWM is discussed in the next paragraph,

301   following a brief overview of prior evidence.

302

303   *MTL lesions specifically disrupt spatial binding in vWM*

304   Previous studies addressed whether MTL pathology is associated with impairments in

305   vWM binding. The ability to recall shape-color, shape-location or item-item conjunctions has

306   been found to be diminished in patients with anoxic/ischemic or infectious pathology

307   involving the MTL as well as neurodegenerative disorders, suggesting an impairment in

308   conjunctive and relational binding (Hannula *et al*., 2006; Olson *et al*., 2006; Parra *et al*.,

309   2009). van Geldorp, Bouman, Hendriks and Kessels (2014) compared patients, who had

310   undergone anterior temporal lobectomies for medically refractory epilepsy, and healthy

311   controls' performance in four match-to-sample tasks. The tasks were difficult and required

312   participants to remember three separate frames presented sequentially. Each frame contained

313   the picture of a face and a building, which differed in location and color. A cue, presented

314   before the sample indicated whether participants should only remember the identity of the

315   items or also their location (spatial binding condition), color (color binding condition) or the

316   item they had been presented with (relational binding condition). Overall, recall was less

317   accurate in patients compared to controls, and particularly so in the relational binding

318   condition. Recall performance in the spatial and color binding conditions were equally

319   affected, suggesting that spatial and non-spatial WM binding were not differentially

320   compromised in these patients. Zokaei *et al*. (2019) found that patients, who had undergone a

321   temporal lobectomy, made more swap errors when recalling the location of fractal patterns,

322   compared to controls. Since neither fractal recognition nor memory for locations were found

323   to be appreciably impaired in these patients, it was inferred that they suffered a primary

324   binding deficit. Using a similar paradigm, Pertzov *et al.* (2013) documented both a spatial as

325   well as a non-spatial binding deficit in individuals recovering from autoimmune encephalitis,

326   suggesting that binding impairments due to MTL dysfunction are not dimensionally specific.

327   Braun *et al.* (2011) concluded instead that TLE patients, who had undergone a right temporal

328   lobectomy, were only impaired when the vWM task required spatial binding, but performed

329   similarly to healthy controls when it required binding of non-spatial features.

330   Our own findings contribute new, crucial evidence for understanding the role of MTL

331   in vWM binding by confirming the association between MTL pathology and spatial binding

332   impairments, unaccounted for by impairments of either spatial vision or feature memory. We

333   found an increase in the proportion of swap errors in the TLE group. Crucially, while healthy

334   participants made significantly more swap errors following the shape probe, left temporal

335   lobectomy patients made more swap errors following the space probe. In healthy participants

336   the results are therefore in keeping with the hypothesis that binding of non-spatial features is

337   mediated by the features' shared location (e.g., Schneegans and Bays, 2017; Treisman and

338   Zhang, 2006). In fact, the likelihood of swap errors should be greater following shape

339   compared to space probes, because in the latter case both target shape and color need to be

340   bound to the target location before they can be bound to each other (Schneegans and Bays,

341   2017). On the other hand, the observation that some patients made significantly more swap

342   errors following space probes than controls may indicate that patients gained the ability to

343   bind non-spatial features directly, without the mediation of a shared location, allowing them

344   to achieve higher accuracies following shape than space probes. Whether this inference is

345   warranted remains to be established. Regardless, the group level pattern of dimensionally

346   specific binding impairments observed in left TLE patients replicates a previous observation

347   in a stroke patient with bilateral MTL damage, found to be impaired only in vWM tasks

348   requiring spatial binding, but not those requiring non-spatial binding (Dundon *et al.*, 2017).

349   These observations thus allow us to draw the following conclusion: MTL pathology can be

350   associated with WM binding impairments that are spatially specific and reverse the spatial

351   advantage characteristic of healthy controls. If processes underlying spatial binding in vWM

352   are independent from processes devoted to binding of non-spatial features, then the role of

353   space in organising vWM may extend beyond providing a common index for the conjunctive

354   binding of visual features.

355

356   <u>Hemispheric lateralization and binding</u>

357   Bohbot *et al.* (1998) found that patients who had undergone thermocoagulation of

358   structures within the right, but not the left MTL were more impaired in a number of spatial

359   WM tasks than those who had not undergone surgery, suggesting that right MTL structures

360   may play an overarching role in spatial memory. Braun *et al.* (2011) compared patients with

361   right temporal lobectomy and healthy controls' performance on a number of single feature

362   and feature conjunction recall tasks and concluded that these patients are specifically

363   impaired in spatial binding. However, the tasks employed memory samples of different

364   complexity to probe recall of features and conjunctions, respectively, thus introducing a load

16

365 confound in the comparison. Our own results are in keeping with the idea that left rather than

366 right MTL structures are specifically involved in spatial binding, since patients who had

367 undergone left temporal lobectomies showed greater spatial binding impairments than

368 patients with right temporal lobectomies. While our results need to be interpreted cautiously,

369 given the small sample size, they agree with the conclusion drawn by Kessels *et al.* (2004),

370 who found that patients who had undergone left, but not right temporal lobectomies were

371 impaired in spatial binding, confirming lateralization effects previously observed by the same

372 group in a sample of patients with cerebrovascular pathology (Kessels *et al.*, 2002). Spiers *et*

373 *al.* (2001) found that left temporal lesion specifically affect object location binding while

374 right temporal lesions affect spatial memory more generally. However, the existing literature

375 remains inconclusive to the relation between laterality and working memory spatial binding.

376 A distinct view of lateralization of binding impairments is that the latter reflect attention

377 deficits which follow cortical strokes, especially involving the non-dominant right

378 hemisphere. For example. Cohen-Dallal *et al.* (2021) reported that patients with unilateral

379 attentional neglect show delay-dependent decrements in spatial binding performance. In light

380 of the fact that parahippocampal damage is associated with unilateral neglect (Mort *et al.*,

381 2003), Cohen-Dallal *et al.*'s finding raises the possibility that lateralized attentional deficits

382 may also contribute to the binding impairments observed in our study. However, performance

383 in a centroid estimation task did not show group differences in lateralized static biases,

384 suggesting that lesion in our sample was not associated with unilateral neglect. Moreover,

385 patients showed neither diminished accuracy nor lower precision in the centroid task

386 compared to controls, indicating that spatial perception and attention were not compromised

387 (Drew *et al.*, 2010).

388   A further concern is that uncontrolled verbal strategies may have confounded the

389 interaction of lesion laterality and probe dimension. We found in pilot studies that healthy

17

390   participants maintain a spatial advantage in WM binding under condition of articulatory

391   suppression and therefore concluded that the spatial advantage in WM binding does not

392   depend on verbal strategies (unpublished data). However, we cannot rule out the possibility

393   that left temporal lobectomy patients used a verbal strategy and thus managed to selectively

394   improve binding of shape and color.

395   It is important to note, with regard to the issue of localization and the nature of cognitive

396   impairments encountered in TLE patients, that group level results belie substantial inter-

397   individual differences (see Figure 2). Previous electrophysiological recordings from the left

398   MTL indicated that trial by trial changes in the amplitude of low-frequency oscillations,

399   obtained during encoding episodes, predict subsequent recall accuracy of object/place

400   conjunctions in TLE patients (Miller et al., 2018), in keeping with our own conclusion that

401   spatial binding is dependent on left lateralized processes. Interestingly, this was not the case

402   in all suggesting that spatial binding processes are not universally left lateralised in these

403   patients. Unfortunately, the study did not report whether the lateralization of spatial binding

404   processes was affected by the laterality of the seizure focus, precluding firmer conclusion

405   regarding the relation between the two. Other studies have, however, demonstrated

406   anomalous lateralization in high proportion of TLE patients, as memory processes often shift

407   to the contra-lesional hemisphere both pre (Bellgowan *et al.*,1998; Golby *et al.*, 2002;

408   Janszky *et al.*, 2004) and postoperatively (Sidhu *et al.*, 2016). These findings may provide

409   one possible interpretation of the interindividual differences highlighted above, namely that

410   neural plasticity in some TLE patients modifies the lateralization of memory processes

411   usually encountered in healthy controls. An alternative explanation, initially born out of

412   observations in non-human primates with focal lesions (Browning *et al.*, 2010; Croxson et al.,

413   2012), is that effects of MTL functional and structural damage in postsurgical TLE patients

414   may be attenuated by non-lateralized recruitment of neocortical areas (Sidhu *et al.*, 2013). To

415   determine whether either or both of these hypotheses can account for interindividual

416   differences in spatial binding impairments and to what extent other factors, like age of seizure

417   onset, severity and frequency of seizures, neuropsychiatric complications and antiepileptic

418   medications, known to affect neural plasticity and degree of cognitive impairment (Bell *et al.*,

419   2011), also contribute to hemispheric lateralization in TLE patients will require new

420   experimental evidence.

421   Despite the potential confound listed above, the present study indicates that following

422   left temporal lobectomy, vWM binding is diminished in a dimensionally specific manner in

423   the absence of appreciable perceptual, attentional or visual-spatial memory deficits.

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578

26

579 **Legends**

580 **Figure 1. Tasks' structure.** Panel A shows the event sequence in the color recall task.

581 Participants had to remember the color of a triangle and a square displayed side by side. The

582 sample display was followed by a pattern mask and a blank screen. The recall target was

583 identified either by a space probe, consisting a bright cross displayed at the location.

584 previously occupied by the target, or by a shape probe, consisting of the outline of the target

585 shape. The color was reported by placing the cursor over the corresponding rectangle and

586 clicking the mouse button. Panel B shows the centroid estimation task. The visual display

587 contained 3 bright dots and the participant had to indicate the location of the center of mass

588 of the imaginary triangle whose vertices corresponded to the dots location, by dragging the

589 cursor and clicking.

590

591 **Figure 2. Recall error rates.** The bar graph on the left shows the group averaged proportions

592 of swap errors, while the bar graph on the right shows the group averaged proportions of

593 generic errors, following space and shape probes, respectively. Overall patients made more

594 swap errors than controls. Moreover, patients with left temporal lobectomies made more

595 swap errors following space than shape probes, suggesting a specific impairment of spatial

596 binding in this group only. For generic errors, group differences were marginal and were not

597 further affected by probe dimension. For sake of clarity, the data are averaged over the two

598 blocks. Circles are individual participants' error rates. Continuous lines join swap error rates,

599 following space and shape probes respectively, of each left temporal lobectomy patient.

600 Broken lines join the swap error rates of each right temporal lobectomy patient. Error bars

601 are standard errors of the mean.

602

603   **Table 1. Demographic and clinical sample characteristics.** Group frequencies were

604   compared using a Bayesian contingency table. Continuous variables were compared with

605   Bayesian ANOVAs or Bayesian independent samples t-test. The values in parenthesis are

606   standard deviations. None of the demographic or clinical variables showed appreciable group

607   differences since the Bayes factor (BF_{10}) was less than 1.0 for all comparisons.

608

609   **Table 2. Demographics and neuro-psychometric performance of TLE patients.** Raw

610   scores are reported for each test and participant (see methods). The corresponding normalised

611   values are shown in parenthesis. Normalised z-scores values were computed by subtracting

612   the mean score and dividing by the standard deviation of a reference sample (Al-Joudi et al.,

613   2019). To facilitate inspection of the table scores corresponding to better than mean

614   performance are underlined. HVLT-R = Hopkins Learning Test – Revised; BVMT-R = Brief

615   Visuospatial Memory Test – Revised; CTT = Colour Trails Test.

616

617   **Table 3. Patients' lesion anatomy.** The table lists the pathology and regions affected by the

618   lobectomy for each patient. Table 3-1 of the extended data shows representative MRI slices

619   through the medial temporal lobes. GG, ganglioglioma; MG, meningioma; MTS, medial

620   temporal sclerosis; HIP, hippocampus; ERC, entorhinal cortex; PRC, perirhinal cortex; PHC,

621   parahippocampal cortex; ITC, inferotemporal cortex; MTG, Middle temporal gyrus; ATP,

622   anterior temporal pole; STG, superior temporal gyrus; AMG, amygdala. ''0'' indicates an

623   unaffected subregion, ''+'' a rostro-caudal lesion extent up to 20 mm, and ''++'' up to 40

624   mm.

625

626   **Table 3-1 (Extended data). Post-surgical MRI scans for thirteen patients.** The images

627   were obtained with T1 weighted, T2 weighted, Fluid-attenuated Inversion Recovery and

628   Gradient Recalled Echo sequences. Legend: ERC, Entorhinal Cortex; PHC, Parahippocampal

629   Cortex; PRC, Perirhinal Cortex; Hipp, Hippocampus; AMG, Amygdala; Temporal pole, TP;

630   antSTG, anterior Superior Temporal Gyrus; antMTG, anterior Middle Temporal Gyrus.

631

632   **Table 4. Swap errors – analysis of effects.** The table lists each factor and interaction for

633   swap error rates. Table 4-1 of the extended data lists the models and associated prior and

634   posterior probabilities from which the values in the present table are computed. P(incl) is the

635   prior probability of the effect; P(incl|d) is the posterior probability of the effect; BF_{incl} is

636   Bayes factor. A BF greater than 1.0 favours the effect, a BF less than 1.0 favours a null

637   instead. Values of the BF greater than 3.0 are in bold, to highlight those effects that have at

638   least moderate evidence in their favour. Block, probe dimension, group and the interaction of

639   group by probe dimension all have at least moderately strong evidence in their favour.

640

641   **Table 4-1 (Extended data). Best model comparisons for swap errors.** The table presents

642   each of the model comparisons from the Bayesian ANOVA. The within factors are block (B)

643   and probe dimension (D). The between factor is group G. P(M) is the a-priori model

644   probability, P(M|d) is the posterior model probability. BF_M is the Bayes factor of the model,

645   BF_{10} is the Bayes factor of the model relative to the best one. The best model contained all

646   three factors and the interaction of group by probe dimension.

647

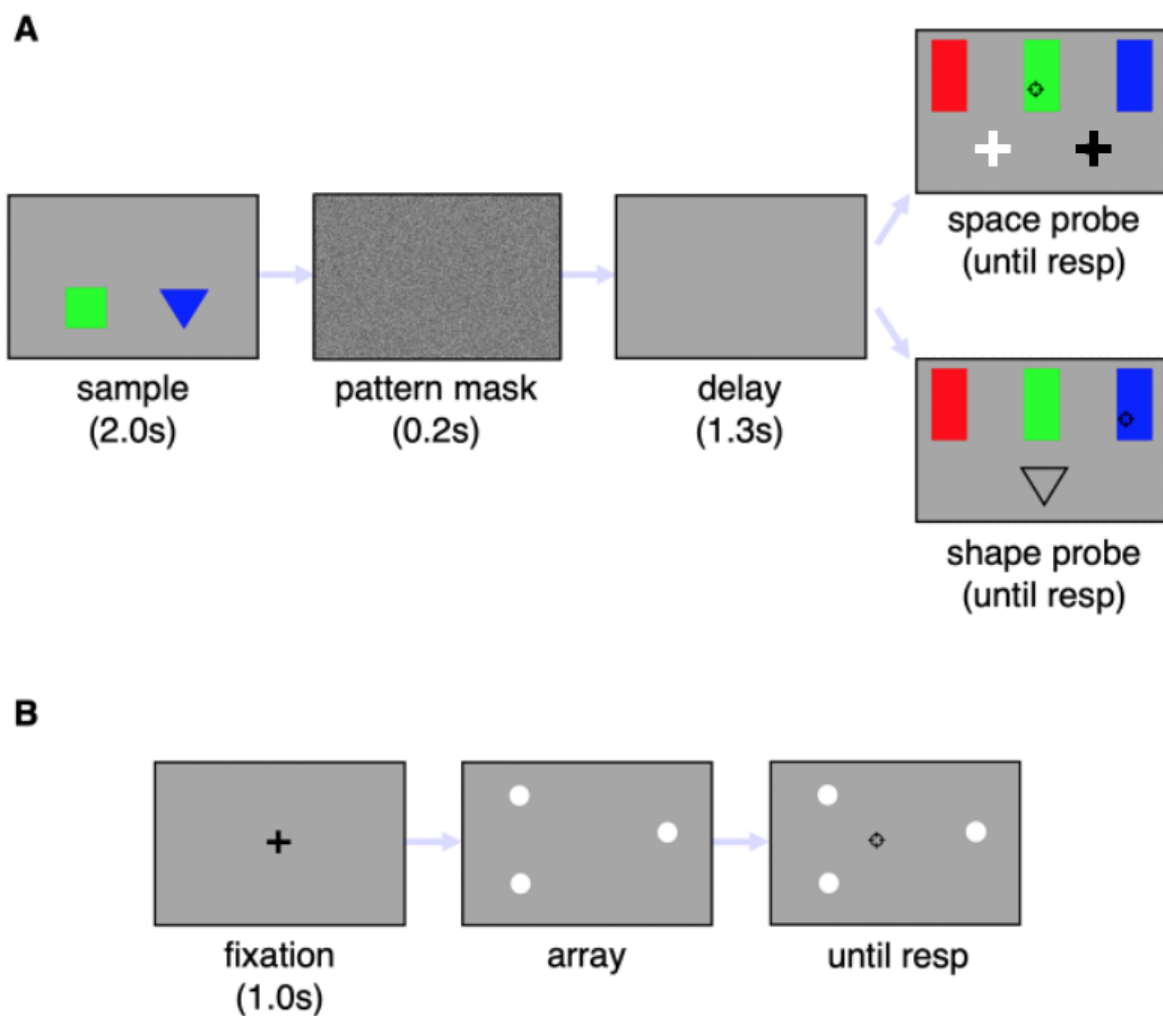648   **Table 5. Generic error – analysis of effects.** The table lists each factor and interaction for

649   generic error rates. Table 5-1 of the extended data lists the models and associated

650   probabilities, used to compute the effects. P(incl) is the prior probability of the effects;

651   P(incl|d) is the posterior probability of the effect; BF_{incl} is Bayes factor. A BF greater than 1.0

652 favours the effect, a BF less than 1.0 favours a null effect instead. The only predictors with

653 favourable evidence, albeit of very modest entity, are block and probe dimension.

654

655 **Table 5-1 (Extended data). Best model comparisons for generic errors.** The table presents

656 the model comparisons obtained from a Bayesian ANOVA. The within factors are block (B)

657 and probe dimension (D). The between factor is group G. P(M) is the a-priori model

658 probability, P(M|d) is the posterior model probability. BF_M is the Bayes factor of the model,

659 BF_{10} is the Bayes factor of the model relative to the best one. The best model included the

660 three main factors, namely block (B), probe dimension (D) and group (G).
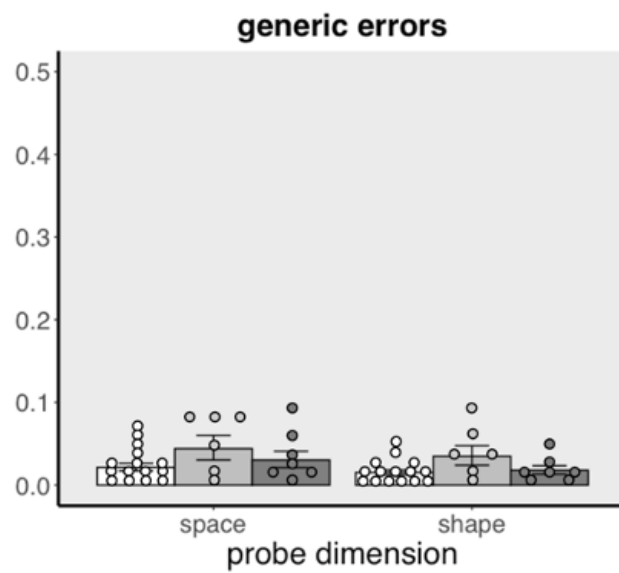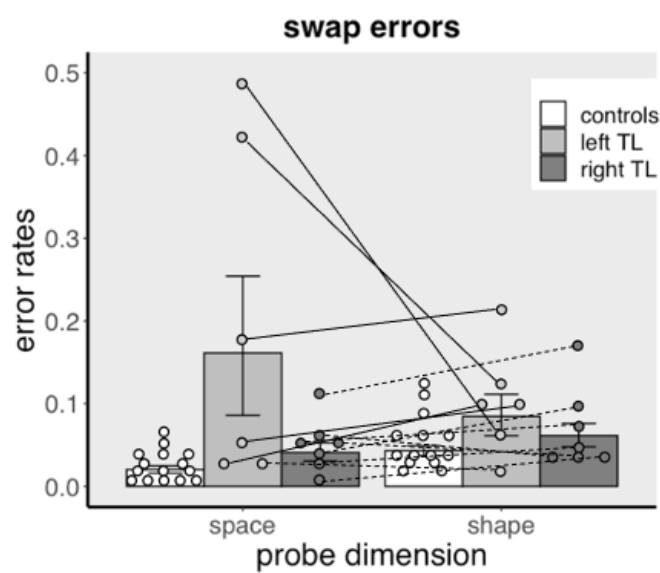
A

sample
(2.0s)

pattern mask
(0.2s)

delay
(1.3s)

space probe
(until resp)

shape probe
(until resp)

B

fixation
(1.0s)

array

until resp

Table 1. Demographic and clinical sample characteristics.

	left TLE (n=6)	right TLE (n=7)	controls (n=15)	BF_{10}
Sex (%males)	83.3	100	93.3	.64
Age (years)	35.2 (±7.9)	33.08 (±8.9)	33.3 (±7.8)	.29
Education (highest grade)	15.3 (±1.6)	14.3 (±1.9)	14.3 (±2.4)	.5
Full Scale IQ	92.0 (±11.7)	87.3 (±9.9)	99.5 (±15.5)	.9
Epilepsy onset age (years)	11.1 (±10.2)	22.1 (±17.2)	—	.84

Frequency group differences were compared using a Bayesian contingency table. Continuous variables were compared with Bayesian ANOVAs or Bayesian independent samples t-test. The values in parenthesis are standard deviations. None of the demographic or clinical variables showed appreciable group differences since the Bayes factor (BF_{10}) was less than 1.0 for all comparisons.

Table 2. Demographics and neuro-psychometric performance of TLE patients

Patient	Gender	Education (years)	WAIS II				HVLT			BVMT			CTT	
			Block Design	Vocab	Matrix Reasoning	Similar	Immediate	Delayed	Discrimin	Immediate	Delayed	Discrimin.	CTT1 (sec)	CTT2 (sec)
P1	M	16	16 (-.59)	18 (-1.6)	12(-.41)	24 (-.77)	19 (-1.43)	6 (-1.47)	9 (-1.9)	12 (-1.01)	4(-1.22)	4 (-1.4)	85 (1.24)	160 (2.0)
P2	M	14	18 (-.46)	27 (-.83)	12 (-.41)	23 (-.88)	26 (.36)	9 (.11)	12 (1.1)	10 (-1.28)	4 (-1.22)	4 (-1.4)	97 (1.74)	166 (2.22)
P3	F	16	12 (-.88)	25 (-1.0)	18 (.53)	28 (-.31)	24 (-.15)	7 (-.95)	10 (-.9)	9 (-1.41)	6 (-.58)	5 (-.4)	65 (.41)	130 (.92)
P4	M	14	16 (-.59)	26 (-.91)	14 (-.09)	26 (-.54)	22 (-.67)	7 (-.95)	11 (.1)	14 (-.75)	5 (-.9)	4 (-1.4)	66 (.45)	191 (3.12)
P5	M	12	14 (-.74)	28 (-.74)	10 (-.72)	25 (-.66)	24 (-.15)	8 (-.42)	8 (-2.9)	7 (-1.68)	3 (-1.55)	3 (-2.4)	65 (.41)	135 (1.1)
P6	M	16	24 (-.0)	20 (-1.48)	16 (.22)	22 (-1.0)	24 (-.15)	7 (-.95)	11 (.1)	21 (.19)	7 (-.26)	5 (-.4)	75 (.82)	150 (1.65)
P7	M	16	14 (-.74)	28 (-.74)	8 (-1.03)	25 (-.66)	19 (-1.43)	5 (-2.0)	7 (-3.9)	12 (-1.01)	5 (-.9)	4 (-1.4)	87 (1.33)	154 (1.79)
P8	M	16	39 (1.09)	45 (.71)	21 (1.0)	30 (-.08)	27 (.62)	10 (.63)	12 (1.1)	13 (-.88)	9 (.39)	5 (-.4)	32 (-.97)	85 (-.7)
P9	M	14	27 (.21)	32 (-.4)	18 (.53)	26 (-.54)	21 (-.92)	8 (-.42)	11 (.1)	21 (.19)	7 (-.26)	5 (-.4)	52 (-.13)	105 (.02)
P10	M	14	19 (-.37)	22 (-1.26)	9 (-.88)	24 (-.77)	18 (-1.69)	7 (-.95)	10 (-.9)	17 (-.35)	7 (-.26)	4 (-1.4)	94 (1.62)	165 (2.19)
P11	M	11	26 (.14)	22 (-1.26)	16 (.22)	24 (-.77)	20 (-1.18)	7 (-.95)	10 (-.9)	15 (-.61)	6 (-.58)	4 (-1.4)	80 (1.03)	151 (1.68)
P12	M	12	13 (-.81)	23 (-1.17)	12 (-.41)	22 (-1.0)	19 (-1.43)	5 (-2.0)	8 (-2.9)	12 (-1.01)	5 (-.9)	4 (-1.4)	86 (1.28)	153 (1.75)
P13	M	16	17 (-.52)	28 (-.74)	11 (-.56)	28 (-.31)	21 (-.92)	8 (-.42)	10 (-.9)	14 (-.75)	6 (-.58)	4 (-1.4)	83 (1.16)	158 (1.94)

Raw scores are reported for each test and participant (see methods). The corresponding normalised values are shown in parenthesis. Normalised z-scores values were computed by subtracting the mean score and dividing by the standard deviation of a reference sample (Al-Joudi et al., 2019). To facilitate inspection of the table, scores better than mean reference performance are underlined. HVLT-R = Hopkins Learning Test – Revised; BVMT-R = Brief Visuospatial Memory Test – Revised; CTT = Colour Trails Test.

1

Table 3. Patients' lesion anatomy

	Age	Pathology	Lesion laterality	Temporal lobe structures								
				HIP	ERC	PRC	PHC	ITG	MTG	TP	STG	AMG
P1	25	GGs	L	0	+	+	0	0	0	+	0	0
P2	25	MTS	R	++	0	0	0	0	0	+	0	++
P3	50	MG	L	0	0	+	0	0	+	+	0	0
P4	41	GGs	R	0	+	+	0	0	0	+	0	0
P5	31	MTS	R	++	+	0	+	0	+	+	+	++
P6	27	MTS	L	++	0	0	0	0	0	0	0	0
P7	40	MG	L	0	0	0	0	0	+	+	0	0
P8	32	MTS	R	++	0	0	0	+	0	++	0	+
P9	33	MTS	R	++	+	0	++	+	0	0	+	+
P10	22	MTS	L	+	+	0	0	++	0	0	+	0
P11	25	MTS	R	++	+	0	0	0	0	0	+	++
P12	47	GGs	L	0	+	0	0	0	++	++	+	0
P13	32	MTS	R	+	+	0	+	+	0	0	+	0

The table lists the pathology and regions affected by the lobectomy for each patient. Table 3-1 of the extended data shows representative MRI slices through the medial temporal lobe. GG, ganglioglioma; MG, meningioma; MTS, medial temporal sclerosis; HIP, hippocampus; ERC, entorhinal cortex; PRC, perirhinal cortex; PHC, parahippocampal cortex; ITC, inferotemporal cortex; MTG, Middle temporal gyrus; ATP, anterior temporal pole; STG, superior temporal gyrus; AMG, amygdala. ''0'' indicates an unaffected subregion, ''+'' a rostro-caudal lesion extent up to 20 mm, and ''++'' up to 40 mm.

Table 4. Swap errors - analysis of effects

Effects	P(incl)	P(incl|d)	BF$_{incl}$
B	0.737	0.941	**5.673**
D	0.737	0.925	**4.414**
G	0.737	0.997	**119.755**
B·D	0.316	0.206	0.563
G·B	0.316	0.188	0.500
G·D	0.316	0.891	**17.629**
G·B·D	0.053	0.017	0.317

The table lists each factor and interaction for swap error rates. In the extended data table 4-1 lists the models and associated prior and posterior probabilities from which the values in the present table are computed. P(incl) is the prior probability of the effect; P(incl|d) is the posterior probability of the effect; BF$_{incl}$ is Bayes factor. A BF greater than 1.0 favours the effect, a BF less than 1.0 favours a null instead. Values of the BF greater than 3.0 are in bold, to highlight those effects that have at least moderate evidence in their favour. Block, probe dimension, group and the interaction of group by probe dimension all have at least moderately strong evidence in their favour.

Table 5. Generic errors - analysis of effects

Effects	P(incl)	P(incl|d)	BF$_{incl}$
B	0.737	0.804	1.463
D	0.737	0.815	1.571
G	0.737	0.641	0.637
B·D	0.316	0.142	0.360
G·B	0.316	0.085	0.202
G·D	0.316	0.087	0.206
G·B·D	0.053	7.157e -4	0.013

The table lists each factor and interaction for generic error rates. Table 5-1 of the extended data lists the models and associated probabilities, used to compute the effects. P(incl) is the prior probability of the predictors; P(incl|d) is the posterior probability; BF$_{incl}$ is Bayes factor. A BF greater than 1.0 favours the predictor, a BF less than 1.0 favours a null effect instead. The only predictors with favourable evidence, albeit of very modest entity, are block and probe dimension.