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Neural Correlate of Visual Familiarity in Macaque Area V2

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1   **Neural Correlate of Visual Familiarity in Macaque Area V2**

2   *Running title*: Familiarity Suppression in V2

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26   **ABSTRACT**

27   Neurons in macaque inferotemporal cortex (ITC) respond less strongly to familiar than to

28   novel images. It is commonly assumed that this effect arises within ITC because its

29   neurons respond selectively to complex images and thus encode in an explicit form

30   information sufficient for identifying a particular image as familiar. However, no prior

31   study has examined whether neurons in low-order visual areas selective for local features

32   also exhibit familiarity suppression. To address this issue, we recorded from neurons in

33   macaque area V2 with semi-chronic microelectrode arrays while monkeys repeatedly

34   viewed a set of large complex natural images. We report here that V2 neurons exhibit

35   familiarity suppression. The effect develops over several days with a trajectory well fitted

36   by an exponential function with a rate constant of around 100 exposures. Suppression

37   occurs in V2 at a latency following image onset shorter than its reported latency in ITC.

38 **SIGNIFICANCE**

39 Familiarity suppression – the tendency for neurons to respond less strongly to familiar

40 than novel images – is well known in monkey inferotemporal cortex. Suppression has

41 been thought to arise in inferotemporal cortex because its neurons respond selectively to

42 large complex images and thus explicitly to encode information sufficient for identifying

43 a particular image as familiar. No previous study has explored the possibility that

44 familiarity suppression occurs even in early-stage visual areas where neurons are

45 selective for simple features in confined receptive fields. We now report that neurons in

46 area V2 exhibit familiarity suppression. This finding challenges our current

47 understanding of information processing in V2 as well as our understanding of the

48 mechanisms that underlie familiarity suppression.

49 **INTRODUCTION**

50   In macaque inferotemporal cortex (ITC), the population response to an image

51 rendered familiar by long-term experience begins at normal strength but is suppressed

52 shortly after onset, a phenomenon termed familiarity suppression (Meyer et al., 2014).

53 Studies of familiarity suppression typically employ complex natural images rendered

54 familiar by hundreds (Fahy et al., 1993; Sobotka and Ringo, 1993; Xiang and Brown,

55 1998; Freedman et al., 2006; Mruczek and Sheinberg, 2007; Anderson et al., 2008;

56 Woloszyn and Sheinberg, 2012; Meyer et al., 2014) or thousands (Woloszyn and

57 Sheinberg, 2012) of exposures imposed over the course of weeks (Freedman et al., 2006;

58 Meyer et al., 2014) or months (Fahy et al., 1993; Sobotka and Ringo, 1993; Xiang and

59 Brown, 1998; Freedman et al., 2006; Mruczek and Sheinberg, 2007; Anderson et al.,

60 2008; Woloszyn and Sheinberg, 2012). The effect is evident regardless of whether

61 exposure involves active discrimination (Fahy et al., 1993; Sobotka and Ringo, 1993;

62 Xiang and Brown, 1998; Freedman et al., 2006; Mruczek and Sheinberg, 2007; Anderson

63 et al., 2008; Woloszyn and Sheinberg, 2012) or passive viewing (Freedman et al., 2006;

64 Meyer et al., 2014) and irrespective of whether subsequent testing involves active

65 discrimination (Fahy et al., 1993; Sobotka and Ringo, 1993; Xiang and Brown, 1998;

66 Mruczek and Sheinberg, 2007) or passive viewing (Freedman et al., 2006; Mruczek and

67 Sheinberg, 2007; Anderson et al., 2008; Woloszyn and Sheinberg, 2012; Meyer et al.,

68 2014).

69   Three ideas have been put forward with regard to behavioral or perceptual advantages

70 that might arise from familiarity suppression. First, reduction of population response

71 could serve as a signal allowing detection of an image as familiar. Support for this notion

72 has come from experiments requiring monkeys to detect repetition of an image.

73 Suppression is more pronounced when the image is detected as a repeat than when it is

74 not (Meyer and Rust, 2016). Second, reduction of the population response could underlie

75 better discrimination of the familiar image. This is consonant with the observation that

76 familiarity suppression in ITC is especially pronounced for non-preferred images, with

77 the consequence that neuronal tuning is sharper and the population representation is

78 sparser for familiar than for novel images (Freedman et al., 2006; Woloszyn and

79 Sheinberg, 2012). However, behavioral evidence for improved processing has been

80 obtained only under conditions of explicit training as distinct from passive viewing

81 (Rainer and Miller, 2000; Rainer et al., 2004). Finally, familiarity suppression might

82 underlie the reduced salience of familiar as compared to novel images. Monkeys, like

83 humans, spend less time gazing at familiar than at novel images (Jutras and Buffalo,

84 2010; Ghazizadeh et al., 2016). Moreover, familiar distractors are less effective than

85 novel distractors in a visual search task after extensive training requiring monkeys to

86 ignore the distractors (Mruczek and Sheinberg, 2007).

87 Familiarity suppression commonly is assumed to originate in ITC because ITC

88 neurons have large receptive fields capable of encompassing an entire image and exhibit

89 selectivity for particular complex images (Tanaka et al., 1991). Thus they represent in

90 explicit form information that would allow identifying an image as familiar. Familiarity

91 suppression in high-order areas downstream from ITC, including perirhinal cortex (Fahy

92 et al., 1993; Xiang and Brown, 1998), entorhinal cortex (Fahy et al., 1993; Xiang and

93 Brown, 1998), dorsolateral prefrontal cortex (Rainer and Miller, 2000) and the

94 hippocampus (Fahy et al., 1993; Xiang and Brown, 1998), could arise through

95 propagation from ITC. The assumption that familiarity suppression is mediated by

96 neurons selective for complex images is not, however, necessarily justified. Low-order

97 areas upstream from ITC, such as V1 and V2, contain neurons that are individually

98 selective for simple local features and yet, as a population, must uniquely encode the

99 identity of each complex image. It is conceivable that population coding as embodied in

100 these areas is sufficient to support familiarity suppression. To investigate this possibility,

101 we monitored the activity of V2 neurons with semi-chronic electrode arrays while

102 monkeys repeatedly viewed images representing complex artificial and natural objects.

103 **MATERIALS AND METHODS**

104   **Subjects.** Two adult rhesus macaques (*Macaca mulatta*) participated in the study

105 (Monkey G, an 8.5 kg female, monkey L, an 11.1 kg male). All experimental procedures

106 were approved by the Carnegie Mellon University Institutional Animal Care and Use

107 Committee and were in compliance with the guidelines set forth in the United States

108 Public Health Service Guide for the Care and Use of Laboratory Animals.

109   **Images.** The images represented natural and man-made objects against a blank

110 background with a resolution of 150 x 150 pixels. When presented on a CRT monitor at a

111 viewing distance of 57 cm, each image subtended 6.5° of visual angle along whichever

112 axis, vertical or horizontal, was longer.

113   **Task.** Each trial began with attainment of fixation on a central spot. After a delay of

114 300 ms, an image appeared in superimposition on the aggregate receptive field of the

115 recorded V2 neurons. The image was visible for 500-800 ms. After an additional 200 ms,

116 the fixation spot jumped to one of four peripheral locations distributed around the clock

117 at 90° intervals. Liquid reward was delivered upon completion of a saccade to the spot at

118   its new location. Eye position was monitored continuously with an infrared optical eye

119   tracking system sampling at 120 Hz (ISCAN). A trial was aborted without reward if, at

120   any point prior to delivery of reward the monkey failed to maintain fixation within a

121   central window spanning 0.6° to 0.8°. The sequence of images across trials was random

122   except for the constraint that each image appear once in each block of trials. In the typical

123   session using 25 familiar images and 25 session-specific novel images, each block of 50

124   trials contained one instance of each image.

125   **Semi-chronic microelectrode recording.** Recording simultaneously from multiple

126   neurons critical to success of the study. It allowed us to average out noise due to the

127   image selectivity of individual neurons recorded on a given day when comparing

128   responses to familiar and novel images on that day. Averaging across days would

129   likewise have eliminated noise but would have prevented tracking the trajectory with

130   which familiarity suppression developed. We monitored neuronal activity through an

131   SC32-1 array, a modular, replaceable micromanipulator system allowing independent

132   bidirectional control of 32 microelectrodes arranged in a square array with 1.5 mm inter-

133   electrode spacing (Gray Matter Research, MT). The array was implanted over the intact

134   dura above the occipital operculum with its center roughly at the border between areas

135   V2 and V1. A screw-driven mechanism allowed independent bi-directional control of the

136   depth of each electrode over a range of 16 mm with an accuracy of approximately 15 μm.

137   This provided sufficient control to isolate the spiking activity of individual neurons. The

138   location of the tip of each electrode remained relatively stable across multiple days as

139   evidenced by consistency in the pattern of neuronal selectivity for familiar images.

140 However, the precise identity of the recorded neurons probably varied across successive

141 days.

142 **Sequence of sessions.** We carried out six experiments. Each experiment consisted of

143 multiple sessions occupying many but not all days of the full experimental period (Table

144 1, Row 2). The experiments had in common two critical features: (1) during numerous

145 "familiarization" sessions (Table 1, row 3), we exposed the monkey to the 25 images in

146 the experiment-unique familiarization set and (2) during a subset of these sessions which

147 we term "F-N" sessions (Table 1, Row 6), we monitored neuronal responses while

148 presenting, on interleaved trials, not only the 25 familiar images but also 25 session-

149 unique novel images. These critical commonalities allowed us to combine data across

150 experiments to analyze the dependence of familiarity suppression (as measured during

151 each F-N session) on the total number of prior exposures to the familiar images (as

152 received during all preceding familiarization sessions). Other aspects of design varied

153 unavoidably from experiment to experiment. The variability arose from factors

154 impossible to control in a multi-day experiment. The monkey's level of motivation on a

155 given day influenced the number of exposures to the familiar images that could be

156 achieved on that day. Likewise, our estimate of the monkey's level of motivation

157 determined whether, on a given day, we strove to complete a brief session involving

158 exposure just to familiar images or a prolonged session involving interleaved presentation

159 of familiar and novel images together with neuronal data collection. Having established,

160 in early experiments, that familiarity suppression occurred robustly, we introduced, in

161 late experiments, certain manipulations designed to elucidate the dependence of the

162   phenomenon on the properties of the images. These included "aperture/full-view" tests

163   (Table 1, Row 11) and "repeated novel" tests (Table 1, Row 12).

164   **Receptive field mapping.** At the outset of each multi-day experiment, after having

165   advanced the electrodes to the desired depth, we plotted the receptive fields of the newly

166   isolated neurons. We first manually delineated the receptive fields of neurons recorded

167   through each electrode while the monkey maintained fixation on a central spot. Having

168   thus approximately located all receptive fields, we proceeded to plot them automatically

169   by presenting long narrow horizontal and vertical bars for a duration of 250 ms at

170   locations staggered to span the region of collective visual sensitivity. Each bar was 0.1°

171   wide and was either 4° or 8° long as dictated by the need to span the region of collective

172   visual sensitivity. The horizontal (or vertical) bar was presented at twelve vertical (or

173   horizontal) locations evenly spaced at intervals of 0.33° (in the case of the 4° bar) or 0.5°

174   (in the case of the 8° bar). Independently for vertical and horizontal bars, we determined

175   the center of the receptive field and its diameter at half-height. In plots representing the

176   receptive field as a circle, the diameter of the circle is the average of the horizontal and

177   vertical diameters. These stimuli, although not matched to the preferences of neurons at

178   any individual site, nevertheless did elicit responses from neurons at all V2 sites and so

179   did allow receptive field mapping. It is possible that use of long bars, as required for

180   automatic mapping of multiple receptive fields, led to a slight underestimation of

181   receptive field size due to the fact that the bars extended into the receptive field surround.

182   The dimensions of the plotted receptive fields are, however, consistent with results

183   obtained by more precise mapping procedures. V2 neurons representing the portion of the

184 visual field on which this study is focused (Figure 1, *A*) have receptive fields with an

185 average diameter of 1.5° (Shushruth et al., 2009).

186   **Decoding.** To decode image identity from single-trial population activity we

187 employed a support vector machine. We trained 300 binary classifiers on all possible

188 pairwise discriminations of the 25 images in the set. To prevent training and testing on

189 the same data, we used a tenfold cross-validation design, running ten sessions in each of

190 which one tenth of the trials was held in reserve for testing. At voting time, the image that

191 got the highest number of votes was taken as the output of the combined classifier. The

192 reported accuracy scores are averages across all ten sessions.

193   **Experimental Design and Statistical Analysis.** All statistical analyses were carried

194 out in Matlab (https://www.mathworks.com/). Individual analyses are described in

195 Results. The statistical tests used in these analyses, including the Wilcoxon signed rank

196 test, the χ^2 test and linear regression with a large sample size, do not assume normality in

197 the data.

198 **RESULTS**

199 We monitored neuronal visual responses through multiple electrodes implanted semi-

200 chronically in area V2 during six experiments in three hemispheres of two monkeys

201 (Table 1, Row 1). At the outset of each experiment, we advanced the electrodes so as to

202 obtain well isolated neuronal activity. We then plotted the receptive fields of neurons at

203 all recording sites. We identified recording sites as being in V2 on the basis of well

204 established patterns of receptive field size and topography (Gattass et al., 1981). The

205 number of electrodes yielding V2 data ranged from 7 to 26 across experiments (Table 1,

206 Row 5). The number of differentiable action potentials recorded from an electrode was

207   typically one or two. All neurons had receptive fields centered in the lower contralateral

208   quadrant of the visual field (Figure 1, *A*). At the beginning of each experiment, we

209   selected 25 images to serve as the familiarization set and adjusted the location of the 6.5°

210   x 6.5° image frame to encompass the receptive fields of the newly isolated neurons

211   (Figure 1, *B*). Each experiment consisted of multiple familiarization sessions spread out

212   over a period of 1-5 weeks (Table 1, Rows 2-4). Each session was divided into trials

213   during each of which the monkey maintained central fixation while a single image was

214   presented for 500-800 ms. The number of exposures per familiar image per day ranged

215   from 8 to 45 with a mean of 17. During most sessions, the monkey viewed not only the

216   25 images in the familiarization set but also, on an equal number of interleaved trials, 25

217   session-unique novel images (Figure 1, *C*).

218   To determine whether V2 neurons exhibited familiarity suppression, we compared

219   population visual responses elicited by 25 familiar and 25 novel images presented during

220   interleaved trials on the same day (Table 1, Row 6). We averaged the visual responses of

221   all neurons recorded on a given day so as to minimize the influence of inter-neuronal

222   differences in image selectivity. We averaged the visual responses across all images in a

223   given category so as to minimize the influence of inter-image differences in salience. We

224   tested for a reduction in familiar-image response strength relative to novel-image

225   response strength, rather than for a reduction in absolute familiar-image response

226   strength, so as to factor out day-to-day fluctuations in the firing rates of the recorded

227   neurons. On inspecting population histograms representing responses to familiar and

228   novel images, we discovered that familiarity suppression emerged in V2 over the course

229   of the first few familiarization sessions. For example, in experiment 2, suppression was

230 not evident during sessions 1-2 whereas it was consistently present from session 3

231 onward (Figure 1, *D*). The histograms representing "novel " and "familiar " responses on

232 day 1 provide an example of noise arising from stochastic variability in response strength

233 and differential image efficacy because, on day 1, both sets of images were being viewed

234 for the first time.

235   To characterize the rate at which suppression developed, we considered data from all

236 56 sessions in which monkeys viewed interleaved familiar and novel images (Table 1,

237 Row 6). For each session, we computed an index of familiarity suppression: (N-F)/(N+F)

238 where N (or F) was the mean across all recorded neurons of the spike rate elicited by

239 novel (or familiar) images in a window 120-540 ms after stimulus onset. Upon plotting

240 this index as a function of the number of times the monkey had viewed each familiar

241 image prior to the session in question, we found that the index was positive, indicating

242 the occurrence of familiarity suppression, in all sessions conducted after the monkey had

243 viewed each image 50 or more times (Figure 2, *A*). The zero-intercept exponential

244 function yielding the best fit to the data had an asymptote of 0.13 and a rate constant of

245 130 prior exposures. This function yielded a significantly better fit than a zero-intercept

246 line (F-test, $p = 0.017$, $F = 6.07$, $n = 58$). Basing the analysis on the number of prior

247 training days rather than the number of prior exposures to the familiar images yielded

248 qualitatively similar results. The zero-intercept exponential function yielding the best fit

249 to the data had an asymptote of 0.11 and a rate constant of 8 days. This function yielded a

250 significantly better fit than a zero-intercept line (F-test, $p = 0.00033$, $F = 14.61$, $n = 58$).

251 Thus there was a significant tendency, whether the analysis was based on exposures or

252 days, for suppression not only to increase but also to saturate over the course of an

253 experiment.

254   The apparent increase in familiarity suppression over the course of the experiment

255 might have been an artifact of our using more effective novel-image sets later in the

256 experiment. To rule out this interpretation, we dedicated several late sessions to repeat

257 presentation of images, both familiar and novel, presented during a session early in the

258 experiment (Table 1, Row 12). We found that familiarity suppression was stronger during

259 the late sessions than during the early sessions even when the novel images use for

260 comparison were physically identical (Figure 2, *B*). The tendency for familiarity

261 suppression to be stronger during the late session, as revealed by the preponderance of

262 points beneath the identity line, was statistically significant (Wilcoxon signed rank test,

263 early mean = 0.017, late mean = 0.047, p = 0.0014, n = 17). This finding is especially

264 striking because the repeated novel images, having been viewed during an early session,

265 were no longer strictly speaking novel. We conclude that the familiarity suppression

266 measured late in the main experiment was not an artifact of the accidental properties of

267 the session-unique novel images selected for use late in the main experiment.

268   Familiarity suppression in V2 could have been a product of feedback from ITC. If so,

269 then suppression in V2 should have appeared at relatively long latency after image onset.

270 To measure the latency of suppression, we considered data from 46 sessions following

271 establishment of the effect (Table 1, Row 7). Upon plotting the difference between the

272 novel-image response and the familiar-image response as a function of time following

273 image onset, we found that suppression appeared at around 100 ms following image onset

274 (Figure 3). To characterize the timing of the effect precisely, we smoothed the data from

275   each session by convolution with a 5-ms-standard-deviation half-Gaussian kernel

276   encompassing past but not future time-points. We then identified the first sequence of

277   five consecutive bins in each of which the number of sessions with observations greater

278   than zero significantly exceeded the number of sessions with observations less than zero

279   (χ^2 test with Yates correction, $\alpha = 0.05$, n = 46). We took the first bin of this string as

280   marking the time of onset of suppression. The latency as measured thus was 110 ms.

281   Following its onset, suppression exhibits an intriguing dynamic pattern, first ramping up

282   over the course of around 100 ms and then declining somewhat (Figure 3, *B*). The slow

283   onset of suppression (Figure 3,*B*) stands in contrast to the rapid onset of the population

284   visual response (Figure 3, *A*). It suggests dependence on multi-synaptic recurrent or

285   feedback connections and involvement of attractor dynamics.

286   Inasmuch as the images used in this experiment were larger than the receptive fields

287   of the V2 neurons, it is natural to wonder whether V2 neurons were sensitive to the

288   familiarity of the entire image or only that part of the image within their receptive fields.

289   To resolve this issue, we dedicated 13 sessions during the late stage of data collection to

290   testing whether familiarity suppression was diminished by blocking off parts of the image

291   around the periphery of the frame and therefore outside the receptive fields of most of the

292   recorded neurons (Table 1, Row 11). We presented either the full image or only that part

293   of the image visible through a 3° square aperture centered on the image frame. If only

294   image content inside the neuronal receptive field mattered, then, for neurons with

295   receptive fields confined to the aperture, familiarity suppression should have been of

296   equal strength under the two conditions. We found instead that familiarity suppression

297   was reduced under the aperture condition as compared to the full-view condition (Figure

298   4, *A-C*). The aperture manipulation reduced familiarity suppression in all 13 such

299   sessions (Figure 4, *D*), with the collective effect attaining statistical significance

300   (Wilcoxon signed rank test, full-view mean = 0.033, aperture mean = 0.011, p = 0.0039,

301   n = 13). The reduction might have occurred because some neurons had receptive fields

302   extending beyond the 3° aperture and so were deprived of visual stimulation when

303   images were confined to the aperture. In accordance with this interpretation, the

304   population firing rate was slightly reduced under the aperture condition (Figure 4, *B*) as

305   compared to the full-view condition (Figure 4, *A*). To resolve this issue, we repeated the

306   analysis on subpopulations of sites selected to minimize the distance between the

307   receptive-field center and the aperture center. As we confined analysis to sites with

308   receptive fields closer and closer to the center of the aperture, the aperture-induced

309   reduction in familiarity suppression persisted (Figure 4, *E-F*). We conclude that

310   familiarity suppression depended not only on parts of the image within the classic

311   receptive field but also on image content in the near or far surround.

312   In ITC, image familiarization has been reported to sharpen neuronal selectivity for the

313   familiar images and possibly to make them more discriminable from each other on the

314   basis of population activity (Freedman et al., 2006; Woloszyn and Sheinberg, 2012). To

315   investigate whether sharpening occurred in V2, we carried out an analysis based on

316   responses to familiar and novel images presented during late sessions (Table 1, Row 7).

317   We ranked images from best to worst for each neuron, computed mean population firing

318   rate as a function of image-rank and characterized the resulting population tuning curve

319   with a standard sparseness index (Vinje and Gallant, 2000):

320                                       $1-[(\Sigma r_i/n)^2/ \Sigma(r_i^2/n)]/(1-n^{-1})$

321   where r_i is the firing rate elicited by image i and n is the number of images. The

322   sparseness index was slightly greater for familiar images (0.27) than for novel images

323   (0.25) but the difference was not significant (Kolmogorov-Smirnov test comparing

324   curves normalized to rank 1 firing rate, $p = 0.96$, $n = 25$). To assess whether population

325   activity encoded familiar image identity more efficiently than novel image identity, we

326   carried out a decoding analysis. This was based on data collected in experiments 3-6

327   during sessions in which familiarity suppression was demonstrably present (Table 1, Row

328   7). We focused on experiments 3-6 because the average number of neurons per session

329   (15 or higher) was sufficiently large to support meaningful decoding. For each of 26

330   sessions, independently for familiar and session-unique novel images, we trained a linear

331   support vector machine to report image identity on the basis of single-trial population

332   activity. The mean classification accuracy was 42% for novel images and 39% for

333   familiar images as compared to chance expectation of 4%. The difference between the

334   accuracies achieved for the two image categories achieved statistical significance (signed

335   rank test, $p = 0.0027$, $n = 26$). Thus decoding was actually less efficient for familiar than

336   for novel images.

337   **DISCUSSION**

338   The key finding of this study is that neurons of macaque area V2 exhibit familiarity

339   suppression. Previous studies of visual plasticity in low-order visual areas of the adult

340   monkey have concerned primarily subtle shifts of stimulus tuning that develop during the

341   performance of tasks requiring difficult visual discriminations and that are evident

342   specifically in the context of task performance (Schoups et al., 2001; Ghose et al., 2002;

343   Lee et al., 2002; Li et al., 2004; Gilbert and Li, 2012, 2013; Liang et al., 2017).

344   Familiarity suppression has been demonstrated previously only in inferotemporal cortex

345   (ITC) and areas of higher order to which it projects (Fahy et al., 1993; Sobotka and

346   Ringo, 1993; Xiang and Brown, 1998; Freedman et al., 2006; Mruczek and Sheinberg,

347   2007; Anderson et al., 2008; Anderson and Sheinberg, 2008; Woloszyn and Sheinberg,

348   2012; Meyer et al., 2014). In ITC, familiarity suppression could arise from fatigue of

349   neurons selective for the particular complex images or from fatigue of synapses to which

350   those neurons give rise. In V2, however, neurons are selective for local features (Hegde

351   and Van Essen, 2003; Freeman et al., 2013). Any given feature is unlikely to have been

352   represented with excessive strength in the 25 images of the arbitrarily selected

353   familiarization set. Thus the nature of the mechanism that underlies familiarity

354   suppression in V2 is unclear.

355   One possibility is that familiarity suppression in V2 is fed back from ITC. This idea is

356   concordant with the principle that top-down feedback plays a critical role in the control of

357   neuronal visual responsiveness in V1 and V2 (Riesenhuber and Poggio, 1999; Lamme

358   and Roelfsema, 2000; Hochstein and Ahissar, 2002; Lee and Mumford, 2003; Li et al.,

359   2004; Friston, 2005; Gilbert and Li, 2013; Wokke et al., 2013) and fits with studies

360   demonstrating that top-down effects appear in V1 and V2 at latencies of 100 ms or more

361   following visual onset (Lamme and Roelfsema, 2000; Lee and Nguyen, 2001; Lee, 2002;

362   Lee et al., 2002; Super et al., 2003; Poort et al., 2012; Chen et al., 2014). If the

363   suppressive signal in V2 were simply a duplicate of the suppressive signal in ITC,

364   conveyed through top-down transmission, then it would necessarily appear at a longer

365   latency in V2 than in ITC. The only previous report explicitly describing suppression

366   latency in ITC indicated relatively late onset, at 120 ms, 118 ms and 158 ms, in three

367   monkeys (Anderson et al., 2008). The reported values are, however, based on a statistical

368   criterion different from ours. To level the playing field between studies and to allow for

369   comparison to a broader range of studies, we took measurements directly from population

370   histograms depicted in figures illustrating familiarity suppression (Freedman et al., 2006;

371   Mruczek and Sheinberg, 2007; Anderson et al., 2008; Woloszyn and Sheinberg, 2012;

372   Meyer et al., 2014). First, we measured the latency of the visual response itself. We found

373   visual latency to be longer by around 30 ms in ITC than in V2 (Table 2, Visual Latency)

374   in general agreement with previous reports (Lamme and Roelfsema, 2000; Self et al.,

375   2017). The difference in latencies presumably corresponds to the feedforward

376   transmission delay between V2 and ITC. If feedback involves a comparable transmission

377   delay, then familiarity suppression fed back from ITC to V2 should appear in V2 at a

378   delay of around 30 ms relative to its appearance ITC. To assess whether this was so, we

379   compared the latency of familiarity suppression in V2 in the present study to its latency

380   in ITC in previous studies. We found that familiarity suppression, far from occurring later

381   in V2 than in ITC, actually appeared earlier by around 20 ms (Table 2, Suppression

382   Latency). In both V2 and ITC, suppression of the familiar-image response accompanies a

383   brief post-peak upward inflection of firing rate (arrows in Figure 5, *A-C*), but the

384   inflection and the suppression alike are earlier in V2 than in ITC. These observations do

385   not, however, absolutely rule out the idea that familiarity suppression in V2 depends on

386   top-down input from areas of higher order. The measurements of latency in V2 and ITC

387   were made in different animals. Even if they were replicated in the same animal, they

388   might be reconciled with a mechanism whereby familiarity suppression is fed back to V2

389   from areas less hierarchically elevated than ITC. There are, indeed, preliminary

390 indications that neurons in V4 do indeed exhibit familiarity suppression (Guan et al.,

391 2017). Finally, it is possible that familiarity suppression in V2 depends in some way on

392 feedback from ITC during the earliest phase of the visual response, beginning at around

393 70 ms, when ITC neurons encode image identity but do not yet exhibit familiarity

394 suppression and when a few ITC neurons highly selective for the familiar image respond

395 especially strongly to it (Woloszyn and Sheinberg, 2012).

396 An alternative possibility is that familiarity suppression in V2 arises at least in part

397 from a mechanism intrinsic to the area. This raises the question: How could neurons

398 selective for local features detect a global image as familiar? Our thoughts on this subject

399 begin with the fact that a familiar image is represented in V2 by simultaneous activity of

400 an ensemble of neurons selective for its local features. Familiarity suppression might

401 occur in V2 at an ensemble-specific rather than a neuron-specific level. For example, if

402 the late phase of the response to an image depended on lateral interactions among the

403 neurons responsive to it, and if repeated exposure to the image induced weakening of

404 excitatory interactions or strengthening of inhibitory interactions among co-active

405 neurons (Barlow and Földiák, 1989; Lim et al., 2015), then the result would be ensemble-

406 specific familiarity suppression. Such an effect would run counter to the classic idea that

407 synapses between co-active neurons undergo Hebbian strengthening but would be

408 consistent with a scheme in which efficient coding arises from redundancy reduction

409 (Lewicki, 2002; Olshausen and Field, 2004; King et al., 2013). Two observations in the

410 present study are compatible with this model. First, we have found that parts of the image

411 outside the classic receptive field contribute to familiarity suppression. Lateral

412 interactions among V2 neurons could explain the impact of these features. Second, we

413 have found that the onset of familiarity suppression is coincident with a post-peak

414 upward inflection in the population firing rate (Figure 5, *C*). This inflection could reflect

415 the arrival of indirect inputs relayed from other V2 neurons via lateral connections. The

416 possibility that familiarity suppression in V2 depends in part or in whole on a mechanism

417 intrinsic to V2 has direct implications for our understanding of the phenomenon in all

418 areas. It suggests regarding familiarity suppression as a general manifestation of

419 principles of statistical learning operative at all levels of ventral stream processing rather

420 than as a product of definitive recognition such as one might assume to occur only at a

421 late stage of visual processing.

422   Familiarity suppression develops rapidly in V2. It is well established after the

423 monkey has viewed each image as few as 50 times over the course of several days. The

424 fact that familiarity suppression develops rapidly in V2 is in harmony with previous

425 reports on ITC indicating that experience-dependent effects are evident after as little as a

426 few hours (Li and DiCarlo, 2010) or a single day (Erickson et al., 2000). The rate at

427 which familiarity suppression develops in ITC is not known. In addition to establishing

428 that familiarity suppression develops rapidly in V2, we have also found that it tends to

429 level out over the course of a few hundred exposures. This is indicated by the fact that an

430 exponential function relating effect strength to exposure number affords a significantly

431 better fit to the data than a linear function. We caution, however, that the asymptote of

432 the best-fit exponential function, $(N-F)/(N+F) = 0.13$, may not represent a true limit on

433 the process. In ITC, familiarity suppression appears to increase gradually over the course

434 of thousands of exposures (Mohan and Freedman, 2017). The same could be true in V2.

435 This is one possible explanation for the fact that familiarity suppression in V2 in our

436   study is of relatively small magnitude as compared to familiarity suppression in ITC in

437   previous studies involving more numerous exposures.

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553

554   **TABLE LEGENDS**

555   **Table 1.** Summary of five experiments. **Row 1**. This indicates in which of two monkeys

556   the experiment was conducted (G or L) and in which hemisphere (LH: left or RH: right).

557   **Row 2**. This indicates the duration of the entire period during which exposure and

558   recording were carried out. **Row 3**. This indicates the number of daily sessions in which

559   the monkey was given exposure to the familiar images up to and including the final F-N

560   session (row 6). **Row 4**. This indicates the number of times the monkey saw each familiar

561   image across all days indicated in row 3. **Row 5**. This indicates the number of electrodes

562   yielding V2 activity at some point during the experiment. **Row 6**. This indicates the

563   number of sessions in which neuronal activity was monitored during interleaved exposure

564   to the familiar image set and a session-unique novel image set. **Row 7**. This indicates the

565   number of F-N sessions (row 6) in the phase of each experiment consisting of the first

566   session in which familiarity suppression was statistically significant ($p < 0.05$, signed

567   rank test, with number of observations in each category equal to number of neurons

568   recorded during the session) and all subsequent sessions. Data from these blocks formed

569   the database for the analysis of the latency of familiarity suppression. **Row 8**. This

570   indicates the number of neurons recorded in late F-N sessions (row 7). Neurons recorded

571   on the same electrode on successive days counted as different. **Row 9**. This indicates the

572   population familiarity suppression index computed on the basis of all late F-N sessions

573   according to the formula $(N-F)/(N+F)$ where N and F were the mean firing rates elicited

574   by novel and familiar images 120-540 ms after stimulus onset. **Row 10**. This indicates

575   whether the tendency for the novel-image firing rate to exceed the familiar-image firing

576   rate achieved significance at the level $p < 0.0001$ (Wilcoxon rank sum test with n equal to

577   the number of neurons indicated in row 7). **Row 11**. This indicates the number of

578   sessions in which familiarity suppression was compared between a condition in which the

579   full view was presented and a condition in which only that portion of the image visible

580   through a 3° square aperture centered on the image frame was presented. These sessions

581   do not contribute to counts in previous rows. **Row 12**. This indicates the number of

582   sessions conducted late in the experiment, after familiarity suppression had developed, in

583   which a novel image set used during an early session was employed again. These

584   sessions do not contribute to counts in previous rows.

585   **Table 2.** Latency of the visual response and of repetition suppression in ITC and V2 as

586   estimated by taking measurements from population histograms in the indicated figures.

587   **Visual latency**: time following image onset at which firing rate rose above baseline.

588   **Suppression latency**: time at which novel-image-minus-familiar-image difference rose

589   above zero. **Suppression half-height**: Time of attainment of half-peak height by the

590   novel-image-minus-familiar-image signal. The approach of taking measurements from

591   population histograms was necessary as a means for including multiple studies (since

592   most do not provide numeric latencies) and for equating the latency criterion across

593   studies (because subtle variations in criterion can produce substantial changes in latency).

594   Where a numeric estimate based on a statistical criterion is available, it is provided

595   parenthetically after the estimate based on direct measurement. Note that attainment of

596   statistical criterion is generally delayed relative to signal onset visible in population

597   histograms.

598   **FIGURE LEGENDS**

599   **Figure 1.** Experimental design. *A*, Receptive fields of area V2 neurons from all six

600   experiments superimposed on a map of the inferior contralateral visual field. Receptive

601   fields from experiment 6, the only experiment involving the left hemisphere, are mirror-

602   reflected across the vertical meridian. *B*, The same receptive fields are shown in relation

603   to the image frame. Their relative arrangement is altered because the location of the

604   frame was shifted at the beginning of each experiment so as to center it on currently

605   recorded neuronal receptive fields. *C,* On each exposure day, the monkey viewed 25

606   images from a familiarization set that remained the same throughout the experiment. On

607   most exposure days, the monkey also viewed 25 images from a session-unique novel set.

608   *D*, Example from experiment 2. Familiarity suppression was first evident on day 3 and

609   persisted thereafter until the end of the experiment on day 8. Yellow fill indicates

610   suppression of the familiar-image response (dashed curve) relative to the novel-image

611   response (solid curve) for each day on which the effect was statistically significant ($p <$

612   0.05, signed rank test, with number of observations in each category equal to number of

613   neurons recorded during the session). Each curve represents the instantaneous population

614   firing rate as averaged across all V2 neurons recorded on the indicated day for all images

615   in a given category (25 familiar images or 25 novel images). Smoothing was

616   accomplished by convolution with a Gaussian kernel having a standard deviation of 10

617   ms. Firing rates on each day were normalized according to the formula $R' = (R-B)/(P-B)$

618   where B was the baseline firing rate at time zero and P was the peak firing rate, with both

619   measures based on mean population activity in data combined across novel-image and

620   familiar-image trials.

621   **Figure 2.** Development of familiarity suppression. *A*, Familiarity suppression developed

622   as a saturating monotonic function of the number of prior exposures to the images in the

623   repeating set. This graph plots familiarity suppression as a function of the number of

624   times the monkey had seen each image in the familiarization set prior to the recording

625   day. Each point represents results from one recording day in one experiment. The six

626   symbols represent six experiments as identified in the inset. The index of familiarity

627   suppression was (Nov-Fam)/(Nov+Fam) where Nov was the population mean firing rate

628   elicited by novel images and Fam was the population mean firing rate elicited by familiar

629   images, with both measures based on an epoch 120-540 ms after image onset. The curve

630   and formula represent the best-fit zero-intercept exponential function. *B*, Familiarity

631   suppression was independent of the accidental properties of the images as indicated by

632   the outcome of 17 "repeated novel" sessions (Table 1, Row 12). In these sessions, we

633   recorded neuronal responses late in the experiment (day 7-22) to 25 images in the

634   familiar set and 25 images in a novel set previously used early in the experiment (day 1-

635   4). For each of the 17 cases, we plot the index of familiarity suppression obtained during

636   the early session against the index of familiarity suppression obtained during the late

637   session. Symbols indicate the training day on which the first use of the novel image set

638   occurred. Points below the identity line derive from 11/13 tests in monkey L and 4/4 tests

639   in monkey G.

640   **Figure 3.** Latency of familiarity suppression. *A*, Population mean firing rate as a function

641   of time following image-onset during 46 sessions in which familiarity suppression was

642   demonstrably present (Table 1, row 7). Solid and dashed curves indicate responses to

643   familiar and novel images respectively *B*, Difference in firing rate between novel-image

644 trials and familiar-image trials as a function of time following stimulus onset. Ribbons

645 indicate standard error of the mean. Curves in *A* and *B* were smoothed by convolution

646 with a Gaussian function with a standard deviation of 5 ms.

647 **Figure 4.** Familiarity suppression depended in part on image content in the periphery of

648 the image frame. *A*, Population responses to novel and familiar images presented in full

649 view in the 6.5° x 6.5° image frame. *B*, Population responses to the same images cropped

650 down to the parts visible through a 3° x 3° square aperture centered on the image frame.

651 *C*, Familiarity suppression was reduced on aperture trials compared to full-view trials. *D*,

652 This effect occurred in all 13 such tests. *E*, Familiarity suppression might have been

653 reduced on aperture trials because the receptive fields of some neurons lay outside the

654 aperture with the consequence that they were not effectively stimulated. To control for

655 this possibility, we repeated the analysis on subsets of neurons in which the receptive

656 field center was displaced by no more than a stipulated distance from the center of the

657 image frame. As the stipulated distance was reduced in 0.5° decrements, the tendency for

658 familiarity suppression to be muted on aperture trials as compared to full-view trials

659 persisted, in support of the interpretation that familiarity suppression depended on image

660 content outside the classic neuronal receptive field. Horizontal axis: upper threshold on

661 distance of receptive-field center from image-frame center. Vertical axis: (N-F)/(N+F)

662 where F and N are mean responses to familiar and novel images respectively. *F*,

663 Receptive fields of neurons with receptive-field centers no more than 1° from the image-

664 frame center. This most tightly constrained set of neurons yielded the values represented

665 by the leftmost points on the curves in *E*.

666 **Figure 5.** The latency of familiarity suppression is shorter in V2 than in ITC. *A*,

667 Responses elicited in ITC by novel images (black) and familiar images (gray) in a

668 previous study from the Miller laboratory. Adapted from Figure 8 of that report

669 (Freedman et al., 2006). *B*, Responses elicited in ITC by novel images (magenta) and

670 familiar images (green) in a previous study from the Sheinberg laboratory. Adapted from

671 Figure 9A of that report (Mruczek and Sheinberg, 2007). *C*, Responses elicited in V2 by

672 novel images (solid curve) and familiar images (dashed curve) in the present study (same

673 data as in Figure 2, *C*). The red vertical line marks 100 ms following image onset. Each

674 arrow indicates a post-peak upward inflection of the firing rate. Each vertical scale

675 indicates firing rate in Hz. The comparatively high firing rate in *B* is due to recording of

676 multi-unit activity.

677 **Table 1**

Experiment	1	2	3	4	5	6
1. Monkey	G_{RH}	L_{RH}	L_{RH}	L_{RH}	L_{RH}	G_{LH}
2. Duration in days	30	35	10	20	32	15
3. Number of familiarization days	12	22	9	10	15	11
4. Number of familiarization exposures	285	282	195	147	248	191
5. Number of V2 electrodes	7	10	23	26	25	30
6. Number of F-N sessions	6	17	8	7	10	9
7. Number of late F-N sessions	5	15	6	5	8	7
8. Number of neurons in late F-N sessions	21	110	125	133	194	197
9. Mean suppression index in late sessions	0.068	0.13	0.073	0.050	0.056	0.028
10. Suppression significant at $p < 0.0001$	yes	yes	yes	yes	yes	yes
11. Number of aperture/full-view sessions	--	--	3	4	1	5
12. Number of repeated novel sessions	--	5	2	3	3	4

678

679

680   **Table 2**

	Visual Latency (ms)	Suppression Latency (ms)	Suppression Half-height (ms)
ITC: Freedman 2006 (Freedman et al., 2006) Figure 8	76	109	152
ITC: Mruczek 2007 (Mruczek and Sheinberg, 2007) Figure 9A	56	131	154
ITC: Anderson 2008 (Anderson et al., 2008) Figure 4M	82	106 (*120*)	121
ITC: Anderson 2008 (Anderson et al., 2008) Figure 4J	55	116 (*118*)	158
ITC: Anderson 2008 (Anderson et al., 2008) Figure 4S	63	133 (*158*)	154
ITC: Woloszyn 2012 (Woloszyn and Sheinberg, 2012) Figure 4A	80	142	164
ITC: Meyer 2015 (Meyer et al., 2014) Figure 5A	57	110	182 (*180*)
ITC: Average across Studies	67	121	155
V2: Current Study Figure 2, *C*	30 (*45*)	100 (*110*)	113 (*116*)

681

682

A

0.25

$y = 0.13(1-e^{-x/130})$

(Nov-Fam)/(Nov+Fam)

0.20

0.15

0.10

0.05

0.00

-0.05

○ Expt 1   ● Expt 4
□ Expt 2   ■ Expt 5
△ Expt 3   ▲ Expt 6

50   100   150   200   250   300

B

First use:
■ Day 1
▲ Day 2
● Day 3
▼ Day 4

0.12

Early (Nov-Fam)/(Nov+Fam)

0.08

0.04

0.00

-0.04

-0.04   0.00   0.08   0.12

Late (Nov-Fam)/(Nov+Fam)

A

B

A

Image Onset

ITC: Freedman et al. (2006)

Firing rate (Hz)

15

0

B

200

ITC: Mruczek and Sheinberg (2007)

Firing rate (Hz)

0

C

30

V2: Present study

Firing rate (Hz)

0

0   100   200   300   400   500

Time (ms)