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4 **Characterizing the effects of feature salience and top-down attention in the early**
5 **visual system**
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15 *Abbreviated Title:* Salience and Attention in the Early Visual System

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16 Abstract

17   The visual system employs a sophisticated balance of attentional mechanisms:

18 salient stimuli are prioritized for visual processing, yet observers can also ignore such

19 stimuli when their goals require directing attention elsewhere. A powerful determinant of

20 visual salience is local feature contrast: if a local region differs from its immediate

21 surround along one or more feature dimensions, it will appear more salient. Here, we

22 used high-resolution fMRI at 7T to characterize the modulatory effects of bottom-up

23 salience and top-down voluntary attention within multiple sites along the early visual

24 pathway, including visual areas V1-V4 and the lateral geniculate nucleus (LGN).

25 Observers viewed arrays of spatially distributed gratings, where one of the gratings

26 immediately to the left or right of fixation differed from all other items in orientation or

27 motion direction, making it salient. To investigate the effects of directed attention,

28 observers were cued to attend to the grating to the left or right of fixation, which was

29 either salient or non-salient. Results revealed reliable additive effects of top-down

30 attention and stimulus-driven salience throughout visual areas V1-hV4. In comparison,

31 the LGN exhibited significant attentional enhancement but was not reliably modulated by

32 orientation- or motion-defined salience. Our findings indicate that top-down effects of

33 spatial attention can influence visual processing at the earliest possible site along the

34 visual pathway, including the LGN, while the processing of orientation- and motion-

35 driven salience primarily involves feature-selective interactions that take place in early

36 cortical visual areas.

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42   <u>New & Noteworthy:</u> While spatial attention allows for specific, goal-driven enhancement

43   of stimuli, salient items outside of the current focus of attention must also be prioritized.

44   We used 7T fMRI to compare salience and spatial attentional enhancement along the

45   early visual hierarchy. We report additive effects of attention and bottom-up salience in

46   early visual areas, suggesting that salience enhancement is not contingent on the

47   observer's attentional state.

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51   At any given moment, our visual system is presented with far more information

52   than it can process, yet we seldom feel that our visual experience is incomplete or

53   degraded. This reflects a sophisticated balance of attentional mechanisms: the observer

54   can willfully guide attention toward a task-relevant item, but is also predisposed to notice

55   salient stimuli that appear outside of the current focus of attention. Our ability to navigate

56   the dynamic visual environment critically depends on this interplay of top-down guidance

57   of spatial attention and bottom-up processing of visually salient information.

58   The visual salience of an item or portion of the visual field describes the degree

59   to which it can 'grab' attention; this subjective percept is strongly influenced by the local

60   feature differences that occur within the visual scene. Behavioral studies have

61   demonstrated that local differences in color, orientation, size, motion, or other basic

62   features can be rapidly detected in visual search tasks (Nothdurft, 1993). Accordingly,

63   computational models of visual salience have underscored the importance of an initial

64   computation of local feature differences, although models differ on whether feature-

65   selective interactions at early stages of visual processing sufficiently compute a salience

66   map (Li, 2002; Koene and Zhaoping, 2007; Zhang et al., 2012), or whether a summation

67   of various feature-contrast maps occurs at a higher stage of the visual pathway (Itti and

68   Koch, 2001a). These models can predict where people are more likely to look when

69   viewing natural scenes (Itti and Koch, 2001a), though cognitive goals and top-down

70   factors can also exert powerful influence (Henderson, 2003).

71   Neurophysiological studies have found that early visual areas are strongly

72   modulated by local feature contrast. The response of a V1 neuron, for example, is

73   suppressed when a presented stimulus extends beyond the neuron's receptive field and

74   into the surround; this suppression is orientation-tuned, such that greater suppression

75   occurs when the orientation of the surround matches that of the center than when the

76   center and surround orientations are orthogonal (Blakemore and Tobin, 1972; Nelson

77 and Frost, 1978; Cavanaugh, 2002). This form of feature-tuned surround suppression

78 has been shown to emerge for a variety of visual features (Blakemore and Tobin, 1972;

79 Allman et al., 1985; Chao-Yi and Wu, 1994; DeAngelis et al., 1994; Kapadia et al., 1995;

80 Zipser et al., 1996; Jones et al., 2001). Multiple mechanisms likely contribute to feature-

81 tuned surround suppression, including shorter-range interactions arising from horizontal

82 connections between feature-selective neurons within V1 as well as more distal

83 interactions that rely on feedback from higher extrastriate areas (Gilbert and Wiesel,

84 1979; Lamme, 1995; Cavanaugh et al., 2002; Bair et al., 2003; Angelucci and Bressloff,

85 2006a). The computation of local feature contrast can be explained in terms of greater

86 mutual inhibition, or divisive normalization (Carandini and Heeger, 2011), among

87 neurons that share similar feature preferences. Thus, a local region that differs in feature

88 content from its immediate surround should evoke a stronger visual response due to a

89 release from feature-tuned surround suppression.

90   Human neuroimaging studies have investigated the effects of orientation-

91 selective surround suppression and orientation-defined salience, using both simple and

92 more complex displays. Studies employing large target stimuli with immediately abutting

93 surrounds have reported powerful effects of surround suppression (Zenger-Landolt and

94 Heeger, 2003) as well as a more modest feature-selective component of surround

95 suppression (e.g. McDonald et al., 2009). Other studies have tested for effects of

96 orientation-defined salience using more complex displays of multiple spatially separated

97 gratings or lines, akin to the displays commonly used in behavioral investigations of

98 attention and visual search (e.g. Nothdurft, 1993). Results from these neuroimaging

99 studies have been mixed: some studies find that a salient, uniquely oriented item evokes

100 stronger responses in V1 (e.g., Zhang et al., 2012; Schallmo et al., 2016), while others

101 find no reliable differences in early visual areas (Beck and Kastner, 2005; Bogler et al.,

102 2013) or more complex interactions that depend on top-down spatial attention (Hopf et

103   al., 2004; Flevaris and Murray, 2015). Our understanding of visual salience and its

104   neural bases relies critically on testing with multi-item displays, which inform much of our

105   knowledge of the mechanisms of attention and visual search. One factor to consider is

106   that feature-tuned suppression may be more difficult to detect with widely separated

107   items, as surround suppression effects in V1 are known to decrease as a function of

108   retinotopic distance (Bair et al., 2003; Adesnik et al., 2012; Shushruth et al., 2013).

109   Another consideration is that some prior studies have employed more complex visual

110   tasks, raising the possibility that visual attention may interact with the processing of

111   salient visual information.

112   Prioritization of visual stimuli is determined not only by stimulus-driven factors but

113   also by voluntary selective attention, by which one can enhance the processing of stimuli

114   corresponding to his or her specific goals and needs. While frontal and parietal networks

115   have been implicated in the control of attention (for reviews: Kastner and Ungerleider,

116   2000; Corbetta and Shulman, 2002; Silver and Kastner, 2009; Squire et al., 2013),

117   considerable work has shown that attention strongly modulates responses in early

118   cortical visual areas, and even the lateral geniculate nucleus (LGN; Brefczynski and

119   DeYoe, 1999; Gandhi et al., 1999; O'Connor et al., 2002; Schneider and Kastner, 2009;

120   Ling et al., 2015).

121   Our goal in this fMRI study was to determine how directed spatial attention and

122   feature-defined salience modulate responses at early stages of visual processing. One

123   possibility is that once an item is attended, its salience does not provide any further

124   enhancement. Alternatively, it could be that the effects of top-down attention and

125   feature-based salience are simply summed to determine the overall prioritization of a

126   stimulus in the visual field. We also sought to determine the earliest stages at which

127   salience and top-down attention would lead to reliable modulations of visual activity.

128   Recent work from our lab has demonstrated orientation-selective responses in the

129   human LGN as well as modulatory effects of attention (Ling et al., 2015).

130   Neurophysiological studies in animals suggest the presence of coarse selectivity in LGN

131   (Smith et al., 1990; Xu et al., 2002; Suematsu et al., 2012; Cheong et al., 2013), arising

132   primarily from elongation of the RF (Leventhal and Schall, 1983). Moreover, there is

133   some evidence to suggest that orientation-tuned surround suppression emerges within

134   cat LGN (Jones et al., 2000; Naito et al., 2007). Therefore, it seemed possible that the

135   LGN might be sensitive to orientation-defined salience. However, feature-selective

136   interactions among spatially distributed items require either long-range connections

137   between feature-tuned neurons or feedback from higher visual regions (Nassi et al.,

138   2013; Nurminen and Angelucci, 2014); these effects may be restricted to cortical visual

139   areas, which have larger receptive fields and effective surrounds.

140   We used high-resolution fMRI at 7 Tesla to quantify the effects of top-down

141   spatial attention and feature-defined salience at multiple levels of the visual pathway,

142   including areas V1 through hV4 and the lateral geniculate nucleus (LGN). Observers

143   viewed multi-item displays that contained a single salient grating with a unique

144   orientation or motion direction, and were cued to attend to either the salient or a non-

145   salient grating that was located immediately to the left or right of central fixation. The

146   spatial separation of these elements emphasized longer-range feature-tuned contextual

147   interactions. By testing both orientation- and motion-defined salience, we could evaluate

148   the generality of the effects of feature-defined salience, as most previous research has

149   have focused exclusively on orientation processing (Hopf et al., 2004; McDonald et al.,

150   2009; Zhang et al., 2012; Bogler et al., 2013; Flevaris and Murray, 2015; Schallmo et al.,

151   2016); but see also (Harrison et al., 2007).

152   <u>Materials & Methods</u>

153   *Participants*

154   Six healthy adults (ages 22 to 31, one female) participated in Experiment 1, and

155   six (ages 22 to 33, three females) participated in Experiment 2. Three subjects

156   participated in both experiments. All participants had normal or corrected-to-normal

157   vision, and were compensated for their role. All aspects of the study were approved by

158   the Vanderbilt University Institutional Review Board.

159   *Stimuli & Task: Experiment 1*

160   Our experimental displays, illustrated in Figure 1A, were created using Matlab

161   and Psychophysics Toolbox (Brainard, 1997; Pelli, 1997). Displays consisted of a 3 x 4

162   array of Gabor gratings presented at 100% Michelson contrast, 1.5 cycles/degree, and

163   Gaussian envelope σ= 0.4°. The stimuli measured 3.8° center-to-center. If one

164   considers the effectively visible portions of the Gabor to span 5 standard deviations in

165   width, where the contrast at the edge would dip to 4%, then each Gabor grating can be

166   considered to have an effective width of 1° with a gap of 1.8° between the Gabors.

167   In each block, all gratings except for one appeared with a common orientation,

168   either vertical or horizontal; the other, salient, grating had an orthogonal orientation. The

169   salient grating appeared at one of two possible target locations, immediately to the left or

170   right of the fixation point (0.5° in diameter with a central dot of 0.175°) – we refer to these

171   as the left and right 'target locations' for our region of interest (ROI) analyses. All

172   patches flickered on/off in 200ms intervals (i.e., 2.5 Hz), with the spatial phase of the

173   Gabors randomized on each presentation.

174   In each experimental block, the participant was shown a cue at fixation,

175   instructing them to covertly attend to one of the target gratings while keeping their eyes

176   focused on the central fixation point. The attentional cue consisted of a pair of dots (0.1°)

177   that appeared to the left and right of fixation. One of these dots was black, and the other

178   white; each participant was told to attend to the side marked by one of these two colors

179   throughout the experiment. The spatially balanced design of this fixation cue ensured

180   equivalent stimulus-driven activity in each hemifield and avoided potential effects of

181 exogenous cuing, which could occur with a single lateralized cue (Jehee and Tong,

182 2011; Jehee et al., 2012). The attended cue color was counterbalanced across

183 participants.

184   Participants were asked to perform an attentionally engaging contrast-decrement

185 detection task on the cued stimulus. We chose this task to direct covert spatial attention

186 to the cued grating, and to minimize the potential influences of feature-based attention.

187 In previous work, we have shown that the performance of an attentional task on the

188 orientation of a grating leads to a strong enhancement of orientation-selective responses

189 in V1-V4, while tasks that require attending to the contrast of a grating do not (Jehee and

190 Tong, 2011). Contrast decrements occurred at independent intervals at each of the two

191 target locations throughout the experimental block, but participants were instructed to

192 respond to decrements only at the cued location via a button box. The decrement

193 occurred 8 times per 16s block at randomly determined intervals, lasting for the full

194 200ms duration of that 'on' interval with a minimum 800ms time difference between

195 targets.

196

197 *Stimuli & Task: Experiment 2*

198   The stimulus parameters were similar to those of Experiment 1, except for two

199 key differences: motion direction, rather than orientation, was used to define salience,

200 and the drifting Gabor patches were continuously presented at 30% contrast (see Figure

201 1B). All of the patches were oriented horizontally and phase-randomized, and the

202 gratings drifted either upward or downward at a speed of 5 degrees/second (temporal

203 frequency, 7.5 Hz) within a stationary window. The salient patch moved in the opposite

204 direction relative to the motion of all other Gabor gratings in the array. We chose

205 upward-downward motion directions to minimize the likelihood of inducing involuntary

206 optokinetic nystagmus (OKN; (Honrubia et al., 1968), and to further ensure that if a small

207   eye movement was occasionally induced, it would not be directed toward either of the

208   lateralized target gratings. Participants were asked to perform an attentionally engaging

209   contrast-decrement detection task on the cued stimulus. The contrast decrement lasted

210   for 400ms, and occurred on 20% of these implicit 400ms intervals within each 16s

211   stimulus block.

212   In a separate behavioral eye-tracking session, we confirmed that our participants

213   could maintain stable fixation while viewing these arrays of moving gratings. Participants

214   performed the same experimental task on displays that matched the stimuli and timing

215   (16s blocks) of the fMRI experiment. Overall, our subjects kept their eyes fixed well

216   within the 0.5° fixation dot. Horizontal eye movement deviations (reported as the

217   standard deviation from the true fixation position), ranged from 0.07-0.33° across the 6

218   participants (median 0.15°); vertical deviations ranged from 0.11-0.48° (median 0.23°).

219

220   *Experimental Design and Procedure*

221   Apart from differences in the stimuli, the design of both experiments was

222   identical. There were three experimental factors that consisted of: 1) location of the

223   salient grating (left or right of fixation), 2) location to be spatially attended (left or right

224   grating), and 3) the context feature (horizontal or vertical orientation in Experiment 1,

225   upward or downward motion in Experiment 2). This 2 x 2 x 2 factorial design led to 8

226   experimental conditions, which were presented in a randomized order within each run.

227   Each experimental run followed a 16s block design (272s duration), with each of the 8

228   experimental conditions occurring once, interleaved with 16s fixation-rest periods that

229   also occurred at the beginning and end of each run. A fixation circle remained present

230   throughout the experimental run; the spatial attention cue appeared 1s prior to the onset

231   of each stimulus block, informing participants to direct their attention towards the left or

232   right grating. Participants were informed of their performance accuracy at the end of

233   each run, and the magnitude of the contrast decrement was adjusted between runs so

234   that the detection hit rate for each subject fell in a range from approximately 70-90%;

235   across subjects, the magnitude of the contrast decrement ranged from 25% to 40% of

236   the original contrast value.

237   *Behavioral Performance*

238   In Experiment 1, performance at the contrast detection task led to a mean hit rate

239   across individual subjects of 76.4% (st. dev. = 12.1%). Contrast decrements applied to

240   the salient target in the display were detected with 77.4% accuracy, while those applied

241   to non-salient targets yielded 75.4% correct performance. There was no significant

242   difference in performance for salient and non-salient targets across the group ($t(5)$ =

243   0.81, p = 0.45). In Experiment 2, subjects averaged 83.4% hit rate (st. dev. = 7.1%),

244   83.7% correct on salient targets and 82.5% correct on non-salient targets; again, there

245   was no reliable difference in performance for the salient and non-salient targets ($t(5)$ =

246   .59, p = 0.58). Our task, which requires contrast discrimination using supra-threshold

247   contrast changes, was designed to manipulate the locus of spatial attention rather than

248   to assess sensitivity to contrast, which has been shown to be enhanced at salient

249   locations. (e.g. Kapadia et al., 1995; Joo et al., 2012). These behavioral results suggest

250   that participants were able attend selectively to the non-salient grating location when it

251   was the target, and were not distracted by the presence of the salient grating.

252

253   *fMRI Data Acquisition*

254   Data were acquired using a Philips Achieva 7-Tesla MRI scanner at the

255   Vanderbilt University Institute of Imaging Science (VUIIS), with a 32-channel head coil

256   equipped for SENSE imaging. The functional scans employed single-shot gradient-echo

257   echoplanar imaging to measure BOLD activity, and were aligned approximately parallel

258   to the AC-PC line to best capture the LGN and occipital pole. Subjects were scanned

259   using either 1.5 mm isotropic voxel resolution in 20 slices (6 subjects in Experiment 1, 4

260   in Experiment 2) or a 2 mm x 1.875 mm x 1.875 mm voxel resolution in 36 slices (2

261   subjects in Experiment 2). The 1.5 mm thickness scans used the following parameters:

262   2s TR, 26ms TE, 75° flip angle, 192 mm FOV, with no gap. The 2 mm scans used

263   identical parameters, except that the FOV was 210 mm. Twelve to 16 runs of functional

264   data and 2-3 localizer runs were collected for each subject. The spatial extent of our

265   slice prescription allowed us to monitor BOLD activity in the LGN and areas V1, V2, V3

266   and hV4. Area V3A often appeared outside of this slice prescription and was therefore

267   not included in this study.

268

269   *Functional ROI Definition*

270   Cortical visual areas V1-hV4 were demarcated using standard retinotopy

271   procedures, using data acquired from separate scan sessions at 3-Tesla (Engel et al.,

272   1997; Wandell et al., 2007). We used a typical phase-encoded design in which subjects

273   fixated while they viewed flickering checkerboards consisting of rotating wedges to map

274   polar angle and expanding rings to map eccentricity. Retinotopy data was acquired using

275   a Philips 3T Intera Achieva MRI scanner equipped with an 8-channel coil. Subjects were

276   scanned using 3 mm isotropic resolution (TR 2 s, TE 35 ms, flip angle 80˚, 28 slices, 192

277   x 192 FOV). Boundaries between retinotopic areas V1-hV4 were delineated by hand, by

278   identifying reversals in the phase of the polar angle map measurements; the resulting

279   ROIs were aligned to the functional space of the current experiment using FSL and

280   Freesurfer software.

281   In the experimental scan session, we ran 2-3 runs of a visual localizer to identify

282   the target regions of interest corresponding to the spatial extent of the left and right

283   gratings. This involved presenting flickering checkerboards at full contrast within a

284   Gaussian contrast-envelope at each of the two target locations, with alternating 16-s

285   cycles of left or right stimulation, as well as a 16 s fixation period at the beginning and

286   end of each run. Individual checks were 0.75° in width, and contrast-reversed at a rate of

287   5Hz. Subjects did not perform a task during localizer runs, and were instructed to keep

288   their eyes on a central fixation point. Cortical ROIs were selected from the conjunction of

289   retinotopy and a statistical map of the left vs. right contrast of our functional localizer. We

290   report results from the 100 most functionally selective voxels as defined by the t-statistic

291   map in each lateralized ROI in early visual areas.

292   The lateral geniculate nucleus was defined functionally from the same localizer

293   contrast, using a t-value threshold of no less than 2.8; thresholds for each subject were

294   selected to yield distinct, continuous clusters of voxels such that left and right

295   hemisphere nuclei were generally aligned dorsally and were maximally lateralized, so as

296   to avoid the inclusion of the pulvinar region. As the LGN cannot be localized

297   anatomically from T1- or T2-weighted images, we cannot be fully sure that our regions of

298   interest do not include other portions of the thalamus. However, the LGN is more readily

299   activated by visual stimulation than other subcortical regions, and there is evidence to

300   suggest that functional localizers that rely on passive viewing, as ours did, do not

301   activate pulvinar activity as strongly as the LGN (Kastner et al., 2004).

302   In sessions using a 1.5 mm isotropic voxel size, the bilateral LGN region of

303   interest consisted of an average of 72.9 voxels (stdev. = 16.8); in the two participants

304   who were tested using a larger voxel size of 2 mm x 1.875 mm x 1.875 mm voxel size,

305   the LGN region of interest encompassed an average of 42.5 voxels.

306   *fMRI Analysis: Preprocessing*

307   Data were preprocessed using FSL and Freesurfer tools (documented and freely

308   available for download at http://surfer.nmr.mgh.harvard.edu), beginning with 3D motion

309   correction and linear trend removal, followed by a high-pass filter cutoff of 60s.

310   Functional images were registered to a reconstructed anatomical space for each subject;

311   this registration was first automated in FSL and then checked and corrected by hand.

312   This allowed the alignment of the current fMRI data to the retinotopy data, which was

313   collected in a separate session. The functional localizer was spatially smoothed using a

314   1-mm Gaussian kernel; no spatial smoothing was done for the experimental runs.

315   Further analyses were conducted using a custom Matlab processing stream. For each

316   ROI-based analysis, data were masked using the labels defined from the retinotopy and

317   functional localizer, which corresponded to the left and right target grating locations in

318   each visual area. Each voxel's intensities were normalized by the mean of the time

319   series, converting to mean percent signal change within each run. Outliers were defined

320   as time points for which the voxel's response measured more than 3 times its standard

321   deviation from its mean, and were Winsorised (Hastings et al., 1947). This condition-

322   blind preprocessing step minimizes the impact of rare spikes in MR intensity while

323   preserving the temporal structure of the responses in each voxel. Only a small fraction of

324   a percentage of data points in the current experiments were marked as outliers (0.26-

325   0.41% across Experiments and ROIs). Further, voxels that left the volume at any time

326   point due to head motion were excluded from that run's analysis. Additionally, we found

327   that during one session in Experiment 1, a combination of slice placement and head

328   motion caused some regions to intermittently clip the edge of the volume. For this

329   subject, we excluded 2 runs from the analysis of bilateral V2 and right hV4, based on

330   drop-out of visually selective responses that was restricted to these ROIs.

331

332   *fMRI Analysis: Mean BOLD*

333   To calculate the average mean BOLD response for each experimental condition,

334   we first converted the MR time series of each voxel from signal intensity units to units of

335   percent signal change. Next, we calculated the average BOLD amplitude for each block,

336   after shifting the response period by 2 TRs to account for hemodynamic lag. To account

337   for baseline differences preceding each condition's onset, the average of the 2 TRs

338   immediately preceding each block was subtracted from its mean. For every stimulus

339   block, we obtained a measure of the mean BOLD response in each ROI, and further

340   calculated the overall BOLD response across all blocks for each experimental condition.

341   Conditions were defined relative to lateralized ROI responses such that, for

342   example, a block in which the left target patch was salient was labeled 'salient' in the

343   right hemisphere and 'non-salient' in the left hemisphere; data were pooled in this way

344   across the left and right hemisphere ROIs. We also combined data across specific

345   feature values (e.g. when the salient target was vertical vs. horizontal in Experiment 1),

346   which were not pertinent to our hypotheses. In each bilateral region, we performed a 2 x

347   2 repeated measures ANOVA to characterize the effects of salience and spatial

348   attention, as well as their interaction.

349   <u>Results</u>

350   *fMRI: Experiment 1*

351   In this experiment, orientation was used to define one salient target location in an

352   array of gratings, while the participant spatially attended to the salient target or to a non-

353   salient target in the contralateral hemifield (see Figure 1A). We compared fMRI

354   responses in early visual areas evoked by the salient grating and by the contralateral

355   non-salient grating across attended and unattended conditions, pooling the data across

356   the left and right ROIs.

357   The time course of mean BOLD responses in the LGN and areas V1-hV4 are

358   shown in the top panel of Figure 2B, while the mean response amplitudes observed in

359   each block are plotted in the bottom panel. Figure 2A shows the modulatory effects of

360   both attention and salience as average difference in BOLD response. Spatial attention

361   led to positive increases in the BOLD response throughout the visual pathway, in both

362   subcortical and cortical regions of interest. We observed reliable effects of top-down

363   attentional modulation in all individual cortical visual areas (V1: $F(1,5) = 7.59$, p < 0.041;

364   V2: $F(1,5) = 8.08$, p < 0.037; V3: $F(1,5) = 23.7$, p < 0.005; hV4: $F(1,5) = 19.2$, p <

365   0.008). This effect was likewise present in the LGN ($F(1,5) = 9.11$, p < 0.030),

366   consistent with previous fMRI reports that the human LGN can be reliably modulated by

367   spatial attention (O'Connor et al., 2002; Schneider and Kastner, 2009; Ling et al., 2015).

368   In contrast, we found that the effect of salience was evident only in the visual

369   cortex. No reliable difference between salient and non-salient items was observed in the

370   LGN ($F(1,5) = 0.028$, p = 0.87). Early visual cortical areas, however, exhibited clear and

371   reliable effects of salience, with higher mean BOLD responses to the salient grating than

372   to the non-salient grating that matched the orientation of the surrounding context (V1:

373    $F(1,5) = 9.47$, p < 0.003; V2: $F(1,5) = 8.53$, p < 0.034; V3: $F(1,5) = 42.8$, p < 0.002;

374   hV4: $F(1,5) = 7.35$, p < 0.043).

375   Interestingly, the main effects of salience and spatial attention did not

376   significantly interact in any of our measured ROIs (V1: $F(1,5) = 1.83$, p = 0.24; V2: $F(1,5)$

377   = 0.14, p = 0.73; V3: $F(1,5) = 2.34$, p = 0.19; hV4: $F(1,5) = 0.12$, p = 0.74). That is, the

378   enhancement of salient items is not contingent on the observer's attentional state or

379   goals. The LGN, which did not show a significant main effect of salience but was reliably

380   modulated by attention, likewise showed no interaction effect ($F(1,5) = 1.07$, p = 0.35).

381   As shown in Figure 2A, comparison of the magnitude of these effects across

382   cortical visual areas reveals a significant difference between regions (ANOVA, $F(3,15) =$

383   5.74; p < .009), suggesting a trend of increasing attention modulation along the visual

384   hierarchy (F-test, $t(2) = 9.00$, p < .013). There appeared to be no difference in the

385   magnitude of salience modulation across visual areas V1 through V4 ($F(3,15) = 1.68$, p

386   = 0.21). Including the LGN in this comparison, however, did yield significant differences

387   across regions of interest ($F(4,29) = 7.8$, p < 8.0×10^{-4}). Specifically, the salience

388   modulation of the LGN was not significantly different from zero ($t(5) = 0.16$, p = 0.87),

389   and significantly weaker than the salience effect observed in V1 ($t(5)$ = 4.7, p < 0.0054).

390   We performed a Bayes factor analysis to estimate the likelihood that the results

391   from the LGN could have arisen from a null effect of salience. We calculated the JZS

392   Bayes Factor (Rouder et al., 2009) applying a scale factor of 1 for the prior on effect size

393   for the alternative hypothesis, and obtained a value of 3.44 in favor of the null

394   hypothesis. It has been suggested that odds factors greater than 3 should be considered

395   as evidence in favor of a hypothesis (Jeffreys, 1961); thus, the LGN data are not strongly

396   conclusive but do tend to favor the null hypothesis.

397   To further test for the possible presence of an interaction effect between salience

398   and spatial attention, we performed an ANOVA on the data of individual subjects, using

399   the fMRI response amplitudes observed on individual fMRI blocks for each participant

400   (Figure 6). Consistent with our group-analysis results, we observed statistically

401   significant main effects of salience and top-down attention in early visual areas for the

402   majority of individual subjects. However, the interaction between salience and attention

403   did not reach statistical significance in any ROI for any subject. To illustrate the quality of

404   data collected, as well as the differences between measurements of the LGN and of

405   cortex, representative single-subject data from this Experiment is shown in Figure 3A/B.

406   All preceding analyses were performed on the mean activations of the functional

407   ROIs; in the cortex, these were selected from individual retinotopic regions, and defined

408   as the 100 most selective voxels in each hemisphere based on independent localizer

409   runs. We assessed whether this ROI size criteria had a meaningful effect on the pattern

410   of our results by calculating the magnitude of attentional and salience-based modulation

411   for a wide range of ROI sizes. Figure 4 plots the magnitude of attention and salience-

412   based enhancement as a function of the number of voxels selected from each ROI. As

413   can be seen, these effects are broadly consistent across a wide range of ROI sizes.

414   The results of Experiment 1 suggest that effects of orientation-defined salience

415   emerge in the primary visual cortex, with a similar degree of enhancement observed in

416   higher extrastriate visual areas. Although orientation-specific responses have recently

417   been demonstrated in the human LGN (Ling et al., 2015), here we find no evidence of

418   enhanced responses to orientation-defined salience at this subcortical site. However, we

419   do find that spatial attention reliably modulates responses in the LGN, in agreement with

420   previous fMRI studies (O'Conner et al., 2002; Ling et al., 2015). The finding that

421   modulatory effects of visual salience and top-down attention emerged at different levels

422   of the visual pathway provides support for the proposal that these mechanisms operate

423   independently and are functionally distinct. Consistent with this proposal, the modulatory

424   influences of spatial attention and orientation-defined salience appeared to be separable

425   and additive in early visual areas of interest.

426

427   *fMRI: Experiment 2*

428   Do the effects of orientation-based salience generalize to other feature domains?

429   Most studies that find salience enhancement in early visual areas have focused on

430   orientation as the defining feature (Li, 2002; Joo et al., 2012; Zhang et al., 2012;

431   Schallmo et al., 2016); however, direction-selective contextual interactions in V1 have

432   been reported for spatially separated moving stimuli (Harrison et al., 2007). In

433   Experiment 2, we were motivated to test whether motion-defined salience would also

434   yield similar effects of top-down attention and stimulus-driven salience across the visual

435   hierarchy. In this experiment, one Gabor grating drifted in a direction opposite to that of

436   all other gratings in the display and was deemed salient. Meanwhile, observers

437   performed an attentionally demanding task on either the salient item or on a non-salient

438   item, as illustrated in Figure 1B.

439   As can be seen in Figure 5, mean BOLD responses were consistently greater for

440   attended than unattended items. A repeated-measures ANOVA indicated that this

441   modulatory effect of attention was statistically significant in all regions of interest,

442   including the lateral geniculate nucleus (LGN: $F(1,5) = 27.5$, $p < .004$; V1: $F(1,5) = 47.9$,

443    $p < 9.7 \times 10^{-4}$; V2: $F(1,5) = 44.0$, $p < 0.0013$; V3: $F(1,5) = 37.6$, $p < 0.002$; hV4: $F(1,5)$

444    $= 96.6$, $p < 1.9 \times 10^{-4}$). While absolute BOLD amplitudes in the LGN were variable

445   across subjects, as evidenced by the size of the error bars in Figure 5B (which

446   correspond to +/- 1 S.E.M. across the six subjects), the within-subject effect of attention

447   was statistically reliable in the LGN. Moreover, the effect of attention appeared highly

448   consistent in both LGN and visual cortex, with every participant showing attentional

449   modulations in the predicted direction. This is illustrated in Figure 5A, which depicts

450   individual subjects' effect amplitudes as grey dots overlaid on the mean effect across

451   ROIs; representative individual subject data for Experiment 2 is shown in Figure 3C/D.

452   In the visual cortex, we again observed significant modulation by salience: non-

453   salient gratings that drifted in the same direction as the contextual gratings elicited

454   weaker mean BOLD responses than did items that drifted in the opposite direction.

455   Significant enhancement of salient items was observed in each of the cortical regions of

456   interest, beginning in V1 ($F(1,5) = 33.7$, $p < .003$) and persisting through V2-hV4 (V2:

457    $F(1,5) = 10.0$, $p < 0.026$; V3: $F(1,5) = 42.5$, $p < 0.002$; hV4: $F(1,5) = 18.1$, $p < .009$).

458   However, this motion-defined salience did not significantly modulate activity in the LGN

459   ($F(1,5) = 0.14$, $p = 0.72$).

460   Critically, the enhancements of BOLD activity elicited by attention and salience

461   did not appear to interact in this experiment. Analysis of variance indicated that salience

462   and attention conditions did not lead to a significant interaction effect in any of the

463   cortical regions of interest (V1: $F(1,5) = .015$, $p = 0.91$; V2: $F(1,5) = 4.4$, $p = 0.09$; V3:

464    $F(1,5) = 0.083$, $p = 0.78$; hV4: $F(1,5) = .62$, $p = 0.47$), nor in the LGN $F(1,5) = 1.90$, $p =$

465   0.23). Thus, the degree of enhancement observed for salient items appeared

466   comparable under conditions of attention and inattention.

467   Figure 5A shows the modulatory effects of spatial attention and of salience in

468   Experiment 2 for each region of interest. Similar to the results of the first experiment, we

469   see a trend toward increasing attentional modulation as one ascends from V1 to V4

470   (ANOVA $F(3,15) = 4.26$, $p = 0.023$; F-test $t(2) = 7.19$, $p < .019$). Salience modulations

471   appear similar in magnitude across areas V1-hV4, and no reliable difference was found

472   among these cortical ROIs ($F(3,15) = .38$, $p = 0.77$). A difference emerged across brain

473   areas when data from the LGN was included in the analysis of variance ($F(4,29) = 7.46$,

474    $p < 9.0 \times 10^{-4}$) and paired comparisons indicated that salience modulation was

475   significantly weaker in the LGN than in V1 ($t(5) = 4.88$, $p < .0046$). As in the previous

476   experiment, salience modulation in the LGN did not significantly differ from zero ($t(5) =$

477    $.38$, $p = 0.72$). In this case, a Bayes factor analysis indicated a value of 3.25, in

478   moderate favor of the null hypothesis. We again note the difficulty in interpreting a null

479   effect in the LGN: small effect sizes, when present, are difficult to detect, and the

480   increased physiological noise when measuring subcortical activity can impede the

481   reliability of fMRI measures. However, the magnitude of salience modulation appears

482   clustered around zero for the majority (5/6) of our individual subjects (Figure 5A), in

483   contrast with individual effects of attention in the LGN or of salience in cortex.

484   Overall, the two experiments yielded very similar patterns of results,

485   demonstrating that both orientation- and motion-defined salience lead to common effects

486   of enhancement in the early visual cortex. These effects did not significantly interact in

487   any region of interest, neither in the group analysis nor in analysis results for any

488   individual subject, suggesting that stimulus-driven salience and top-down attention

489   provide independent sources of modulatory influence at early stages of the visual

490   system.

491

492   <u>Discussion</u>

493   In two experiments, we used high-field fMRI to characterize the effects of top-

494   down attention and feature-defined salience at multiple levels of the visual hierarchy. We

495   found that orientation- and motion-defined salience consistently enhanced responses to

496   stimuli in areas V1 through hV4, implying a common mechanism for detecting local

497   feature differences across spatially disparate stimuli. These feature-tuned contextual

498   interactions are critical for the computation of the local salience of a region, as predicted

499   by modeling work (Itti and Koch, 2001b; Li, 2002). Additionally, we found that directed

500   spatial attention enhanced responses in all regions of interest, including the LGN; our

501   findings add to a growing number of studies indicating that activity in the LGN can be

502   altered by top-down attentional goals (O'Connor et al., 2002; McAlonan et al., 2008;

503   Schneider and Kastner, 2009; Ling et al., 2015). In contrast, we did not find evidence

504   that LGN activity is reliably modulated by feature-defined salience. Although one must

505   be cautious about the interpretation of null effects, the absence of a statistically reliable

506   effect of salience in the LGN is consistent with the proposal that long-range feature-

507   selective interactions depend on cortical mechanisms (Bair et al., 2003; Shushruth et al.,

508   2009; Nassi et al., 2013; Shushruth et al., 2013). Our results support the proposal that at

509   the earliest stages of visual processing, salience is distinct from mechanisms of top-

510   down attention.

511   Consistent with this view, we found that the effects of salience did not lead to

512   significant interactions with the effects of attention in any of our regions of interest. Our

513   findings suggest that the effects of top-down attention and bottom-up salience are

514   summed in a simple additive manner, such that both mechanisms distinctly inform the

515   prioritization of items within a visual scene. These results concur with a recent fMRI

516   study by Schallmo et al. (Schallmo et al., 2016) though it should be noted that more

517   complex interactions between bottom-up mechanisms and top-down attention may occur

518   if attention is allowed to spread to other neighboring items. For example, feature-based

519   attention may counteract the influence of feature-tuned suppression with certain stimulus

520   configurations and tasks. Flevaris and Murray (2015) found that an attended target

521   grating evoked greater responses when flanked by orthogonally oriented gratings than

522   when the target and flankers were iso-oriented. When participants attended to one of the

523   flanking gratings, however, attention appeared to spread to the target if the gratings

524   shared a common orientation. This reported interaction presumably emerged due to the

525   spatial spreading of feature-based attention (Saenz et al., 2002). In the present study,

526   attention was cued to shift between target locations in separate hemifields, thereby

527   minimizing the spread of attention between the lateralized target regions. Under these

528   conditions, we observed separate additive effects of top-down attention and salience at

529   each of the target locations. We should note, however, that the limited range of contrast

530   levels in the current experiments may bias us toward finding additive effects if the neural

531   response function is saturated (Carrasco, 2006).

532   Our results support the view that processing of feature-defined salience in V1

533   relies on horizontal interactions within the region (Stettler et al., 2002; Adesnik et al.,

534   2012) as well as more long-range effects of feedback from higher extrastriate areas to

535   V1 (Bair et al., 2003; Angelucci and Bressloff, 2006b; Nassi et al., 2013). Such feature-

536   selective interactions are believed to underlie a variety of early contextual effects

537   (Stettler et al., 2002) including tilt repulsion (Dragoi et al., 2001; Jin et al., 2005),

538   collinear enhancement (Kapadia et al., 1995), and figure-ground processing (Lamme,

539   1995); the current experiments considered how these early visual interactions may

540   function over spatially disparate elements in a scene, which is critical toward building a

541   behaviorally relevant representation of salience. Of course, further processing of

542   salience occurs in higher-level extrastriate and parietal regions as the observer orients

543   his or her attention during visual search (Melloni et al., 2012), integrates many features

544   in a naturalistic environment (Bogler et al., 2011), shifts attention (Kincade et al., 2005), or

545 plans eye movements (Gottlieb et al., 1998; Mazer and Gallant, 2003; Fecteau and

546 Munoz, 2006). The current work informs the wider study of salience by investigating the

547 early cortical stages involved in these processes, and by demonstrating that the

548 representation of this information is unaffected by the observer's attentional focus.

549   Our results in the LGN suggest that feature-selective surround effects in this

550 region are either negligible or too weak to be reliably detected in the current paradigm,

551 which relied on spatially separated gratings to manipulate salience. Existing

552 neurophysiological work is consistent with these views. Studies of the LGN in cats and

553 monkeys have demonstrated size-tuned responses to gratings due to strong

554 suppression from the immediate surround, which likely arises from mechanisms

555 originating from the retina (Alitto and Usrey, 2008) as well as effects of cortical feedback

556 (Jones et al., 2012). While some orientation bias has been reported in LGN neurons in

557 several species (e.g. cat: Suematsu et al., 2012; owl monkey: Xu et al., 2002; Cheong et

558 al., 2013; and macaque: Smith et al., 1990), positive effects of feature-tuned

559 suppression in this structure have been predominantly reported in the cat (Cudeiro and

560 Sillito, 1996; Jones et al., 2000; Naito et al., 2007). Given the known anatomical

561 differences between cat and primate LGN, our null effect could reflect a lack of feature-

562 tuned surround suppression in the region. It is also possible that feature-tuned

563 suppression in the LGN may operate at a more local spatial scale than our Gabor array

564 displays were designed to probe (Angelucci and Bressloff, 2006b), as suggested by our

565 group's positive report of modulatory effects of orientation masking in this structure (Ling

566 et al., 2015). Alternatively, it may be that particular elements of our experimental design

567 precluded us from detecting modulatory effects: we were limited in testing only one

568 contrast level in each experiment, and using a constant spatial frequency (1.5cpd)

569 throughout the study.

570   These findings contribute to a broader understanding of how surround

571   suppression functions toward a behaviorally relevant representation of the visual scene.

572   The effects of surround suppression have been shown to fall off with distance; however,

573   modulations in apparent contrast of a central stimulus can be detected even with spatial

574   separation of several degrees between the center and surround (Cannon and

575   Fullenkamp, 1991; Petrov and McKee, 2006). While the generalization of surround

576   suppression to natural image or movie inputs has posed a challenge in vision research,

577   recent work has suggested that the suppression may be gated by the degree of

578   redundancy in a natural image (Coen-Cagli et al., 2015). Homogeneity in a natural

579   image was found to elicit stronger suppression, which may act to reduce redundancy in

580   visual input and code natural input more efficiently (Vinje and Gallant, 2000). fMRI

581   studies of perceptual grouping report effects of global configuration, consistent with this

582   view of redundancy reduction (Joo et al., 2012). Given the visual system's adaptive

583   nature, sensitivity to the statistics of natural input may provide a bridge from fundamental

584   mechanisms of suppression and contextual interactions to behaviorally relevant

585   representations of salience in the environment (Kayser et al., 2004; Coen-Cagli et al.,

586   2012), especially as these mechanisms function across different spatial scales

587   (Nurminen and Angelucci, 2014). By representing the influences of visual salience and

588   top-down attention at the earliest stages of cortical visual processing, the visual system

589   is able to achieve a balance between automatic prioritization of local regions throughout

590   the visual field and voluntary guidance based on current goals and tasks.

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794

795

796   *Figure 1.* Annotated sample displays for both experiments. Feature-contrast salience is

797   defined by orientation in A and by drifting motion direction in B (indicated by arrows,

798   which were not present during the experiment). Dotted circles (likewise not present

799   during the experiments) indicate the two locations at which the salient patch could

800   appear and to which spatial attention could be directed. While the task-relevant contrast

801   decrement occurred at both of these locations, the observer was instructed to only

802   perform the detection task on one patch, as indicated throughout each block by a small

803   cue. In these examples, if the participant was cued to attend to the black cue (as

804   labeled), in A the left patch is attended/salient, while the right patch is unattended/non-

805   salient; in B, the left patch is attended/salient, and the right patch is unattended/salient.

806   Gabor patch edges were Gaussian blurred and also spatially separated by a gap of 0.8°,

807   yielding an effective spatial separation of approximately 1.8°.

808

809   *Figure 2.* Results of Experiment 1 for the four salience/attention conditions. A)

810   Magnitude of the attention and salience effects across ROIs, computed as difference in

811   percent signal change. Dots show the effect in individual subjects, and error bars depict

812   one standard error (across subjects). In the LGN, only attention significantly modulated

813   BOLD responses; neither the main effect of salience nor the interaction effect were

814   significant. A significant effect of salience first emerges in V1 and is evident in each

815   cortical ROI. Attention also modulated BOLD responses in V1 through hV4, but the two

816   effects do not reliably interact in any region. B) The top panel shows mean ROI time-

817   courses time-locked to the beginning of each experimental block, which lasted 8 TRs

818   and is demarcated by dotted lines. The bottom panel shows the same data averaged

819   across the block, offset to account for hemodynamic lag, and normalized by subtracting

820   the mean response of the 2 TRs immediately preceding the block. Error bars on block

821   averages depict one standard error in the mean BOLD response across subjects.

822

823 *Figure 3.* Examples of average fMRI time courses from representative subjects in

824 Experiment 1 (A, B) and Experiment 2 (C, D). Error bars depict +/- 1 SEM for each

825 experimental condition, and each of the four panels shows data from a different

826 individual. As expected, there is some variability between subjects; fMRI responses in

827 the LGN are also more variable than those in early visual areas, partly because of the

828 LGN's smaller size and the presence of greater physiological noise in midbrain

829 structures.

830

831 *Figure 4.* Magnitude of attention and salience effects plotted as a function of ROI size.

832 We calculated the difference in BOLD response for attended minus unattended

833 conditions and salient minus non-salient conditions, for a wide range of ROI sizes,

834 ranging from 2-60 maximum voxels per hemisphere in the LGN and from 10-350 voxels

835 per hemisphere in individual cortical visual areas. Error bars indicate one standard error

836 across subjects. Our findings of positive salience and attention effects in each cortical

837 ROI are highly consistent across a wide range of ROI sizes.
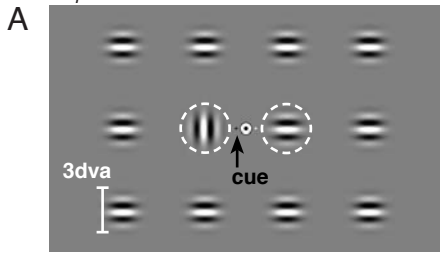
838

839 *Figure 5.* Mean BOLD amplitudes in Experiment 2, in which salience was defined by the

840 direction of drifting motion of Gabor patches. A) Attention and salience effects (percent

841 signal change difference) across ROIs, with dots plotting individual subjects' results and

842 error bars showing one standard error across subjects. B) Results in each condition are

843 averaged across the stimulus block and normalized by a pre-stimulus window for each

844 condition. The pattern of results follows that of the first experiment: attentional

845 enhancement is evident in each ROI, including the LGN, while salience modulated only

846 cortical mean BOLD responses. In every region studied, the effects of attention and

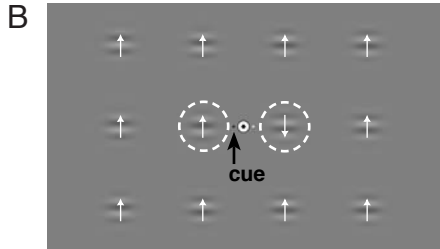847 salience did not significantly interact.

848

849 *Figure 6.* Individual subject ANOVA results for Experiments 1 (left) and 2 (right). Here,

850 each experimental session was analyzed independently, with experimental run as the

851 repeated measure. Filled circles indicate significant effects of attention (black), salience

852 (grey), or their interaction (cross) at $p < 0.05$ level. Subject labels (S1-S6) are arbitrary

853 and unmatched between the two experiments. While many subjects exhibit significant

854 main effects of attention and salience, the interaction of these two factors is not
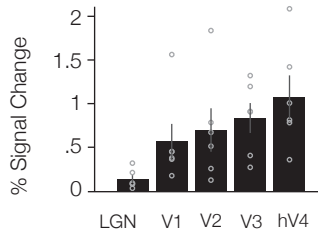
855 significant in any ROI in any subject.
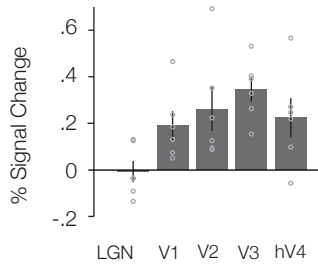
Experiment 1: Orientation
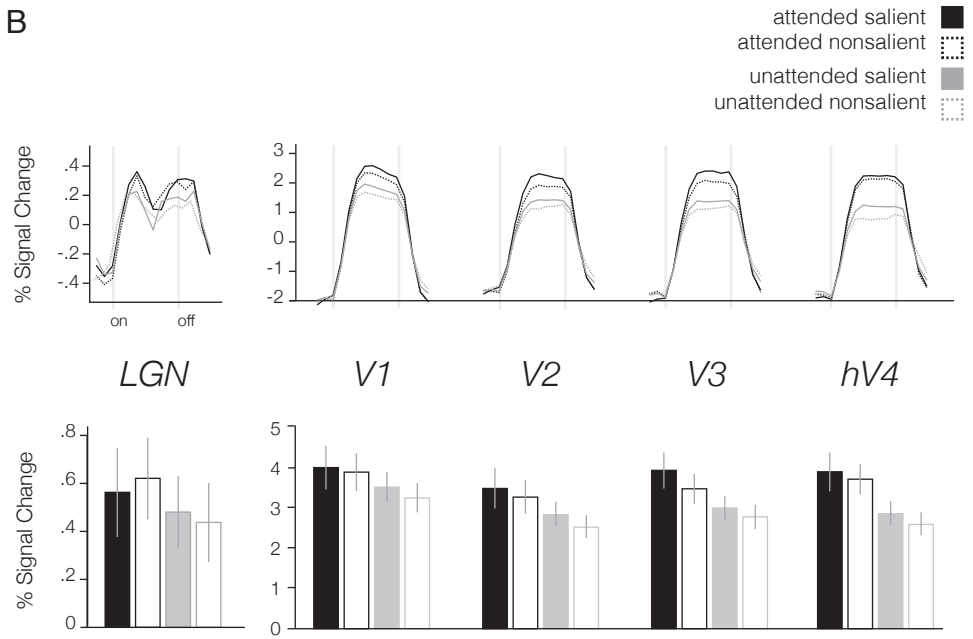
A

3dva

cue

Experiment 2: Motion Direction

B

cue

A

Attention Effect

% Signal Change

LGN V1 V2 V3 hV4

Salience Effect

% Signal Change

LGN V1 V2 V3 hV4

B

attended salient
attended nonsalient
unattended salient
unattended nonsalient

% Signal Change

on   off
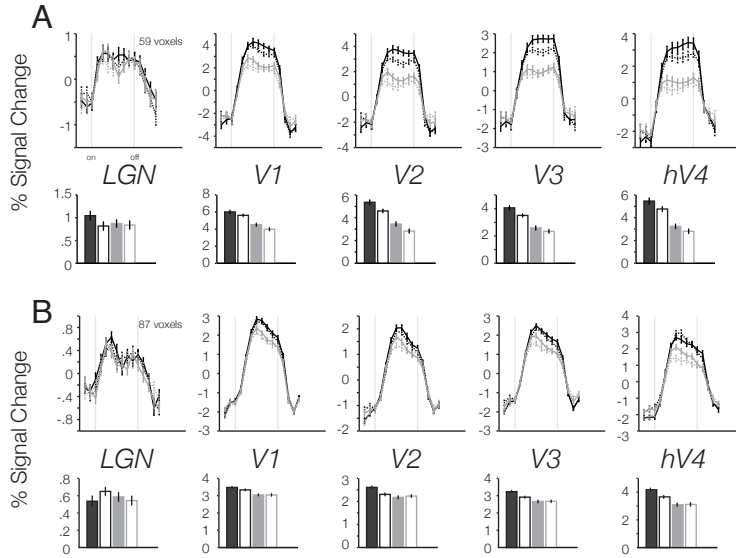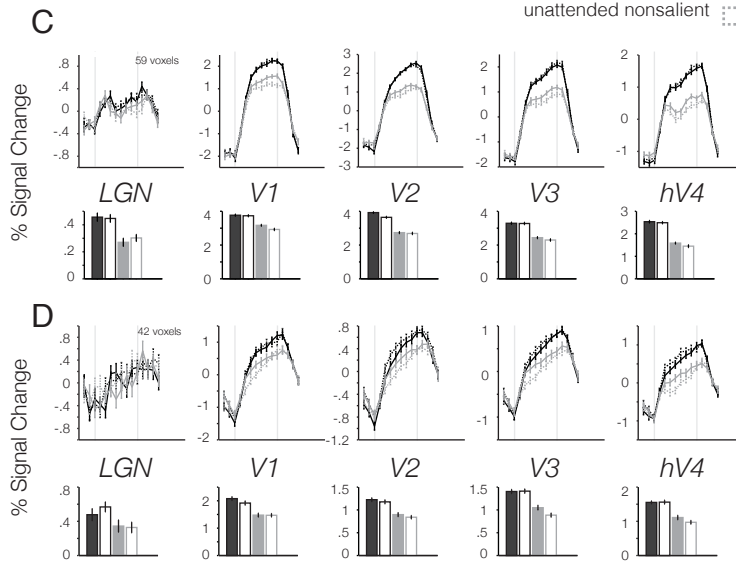
LGN   *V1*   *V2*   *V3*   *hV4*

% Signal Change

Experiment 1: Orientation

attended salient ■
attended nonsalient ▦
unattended salient ■
unattended nonsalient ▦

A

% Signal Change

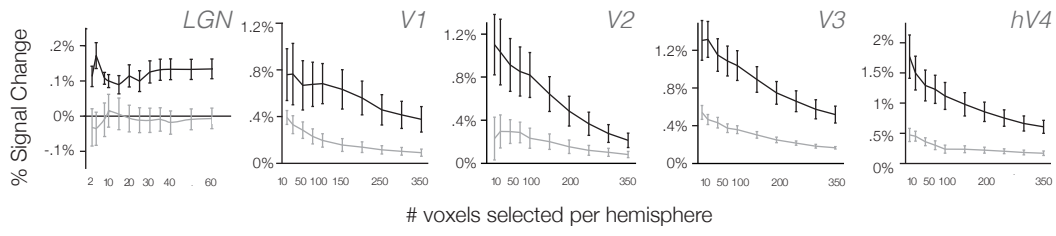LGN   V1   V2   V3   hV4
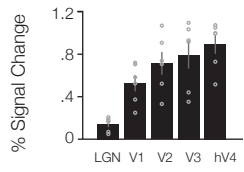
B

% Signal Change

LGN   V1   V2   V3   hV4

Experiment 2: Motion

attended salient ■
attended nonsalient ▦
unattended salient ■
unattended nonsalient ▦

C

% Signal Change

LGN   V1   V2   V3   hV4

D

% Signal Change

LGN   V1   V2   V3   hV4

% Signal Change

LGN

.2%
.1%
0%
-.1%

2 10 20 30 40 . 60

V1

1.2%
.8%
.4%
0%

10 50 100 150   250   350

V2

1.2%
.8%
.4%
0%

10 50 100   200   350

V3

1.2%
.8%
.4%
0%

10 50 100   200   350

hV4

2%
1.5%
1%
.5%
0%

10 50 100   200   350

voxels selected per hemisphere

A

Attention Effect

% Signal Change

Salience Effect

% Signal Change

B

% Signal Change
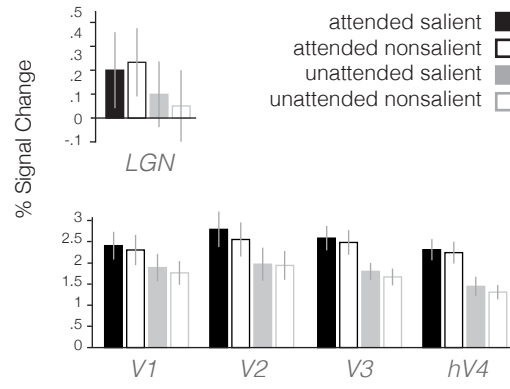
- attended salient ■
- attended nonsalient □
- unattended salient ▪ (gray)
- unattended nonsalient □ (light gray)

LGN

V1 *V2* *V3* *hV4*

Expt 1: Orientation *Expt 2: Motion*

	LGN	V1	V2	V3	V4
S1	○○○	●○○	●○○	●○○	●○○
S2	○○○	●○○	○●○	●●○	●○○
S3	●○○	●○○	●○○	●○○	●○○
S4	○○○	●●○	●●○	●○○	●●○
S5	○○○	●●○	●●○	●●○	●●○
S6	●○○	●○○	●●○	●●○	●○○

	LGN	V1	V2	V3	V4
S1	○○○	●●○	●●○	●●○	●○○
S2	●○○	●●○	●●○	●●○	●●○
S3	●○○	●●○	●●○	●●○	●○○
S4	○○○	●○○	●○○	●○○	●○○
S5	○○○	●○○	●●○	●●○	●●○
S6	●○○	●●○	●○○	●○○	●○○

● attention   ● salience   ⊗ interaction