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## Human occipital and parietal GABA selectively influence visual perception of orientation and size

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2 **perception of orientation and size**

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58 **ABSTRACT**

59 Gamma-aminobutyric acid (GABA) is the primary inhibitory neurotransmitter in human brain. GABA level  
60 varies substantially across individuals and this variability is associated with inter-individual differences in visual  
61 perception. However, it remains unclear whether the association between GABA level and visual perception  
62 reflects a general influence of visual inhibition, or whether GABA level of different cortical regions selectively  
63 influences perception of different visual features. To address this, we studied how GABA level in parietal and  
64 occipital cortices related to inter-individual differences in size, orientation, and brightness perception, in a group  
65 of healthy young male participants. We used visual contextual illusion as a perceptual assay, since it dissociates  
66 perceptual content from stimulus content and its magnitude reflects the effect of visual inhibition. Across  
67 individuals, we observed selective correlations between GABA level and the magnitude of contextual illusion.  
68 Specifically, parietal GABA level correlated with size illusion magnitude but not with orientation or brightness  
69 illusion magnitude; in contrast, occipital GABA level correlated with orientation illusion magnitude but not with  
70 size or brightness illusion magnitude. Our findings reveal a region- and feature-dependent influence of GABA  
71 level on human visual perception. Parietal and occipital cortices contain, respectively, topographic maps of size  
72 and orientation preference in which neural responses to sizes or orientations are modulated by intra-regional  
73 lateral connections. We propose that these lateral connections may underlie the selective influence of GABA  
74 level on visual feature perception.

75 **SIGNIFICANCE STATEMENT**

76 Gamma-aminobutyric acid (GABA), the primary inhibitory neurotransmitter in human visual system, varies  
77 substantially across individuals and this variability is linked to inter-individual differences in many aspects of  
78 visual perception. The widespread influence of GABA raises the question of whether inter-individual variability  
79 in GABA reflects an overall variability in visual inhibition and has a general influence on visual perception, or  
80 whether GABA level of different cortical regions has selective influence on perception of different visual  
81 features. Here we report a region- and feature-dependent influence of GABA level on human visual perception.  
82 Our findings suggest that GABA level of a cortical region selectively influences perception of visual features  
83 that are topographically mapped in this region through intra-regional lateral connections.

84 **INTRODUCTION**

85 The inhibitory neurotransmitter Gamma-aminobutyric acid (GABA) plays a central role in visual processing  
86 ranging from neural selectivity and neural response gain control, to synaptic plasticity and network oscillation  
87 (Katzner et al., 2011; Lehmann et al., 2012; Priebe et al., 2008). GABA level (measured using Magnetic  
88 Resonance Spectroscopy) varies substantially across human individuals and this variability may contribute to  
89 inter-individual differences in visual processing and visual perception. Indeed, a higher GABA level is  
90 associated with higher visual discrimination ability, lower susceptibility to distraction, stronger surround  
91 suppression and stronger interocular suppression (Edden et al., 2009; Lunghi et al., 2015; Sandberg et al., 2014;  
92 Sandberg et al., 2016; Vanloon et al., 2013; Yoon et al., 2010). Moreover, in neurological disorders such as  
93 attention-deficit / hyperactivity disorder and schizophrenia, both an abnormal level of GABA and an abnormal  
94 performance in perceptual tasks are observed (Edden et al., 2012; Moulton, 2009; Yoon et al., 2010).

95 This wide range of observations raises the question of whether inter-individual variability in GABA reflects an  
96 overall variability in visual inhibition and has a general influence on visual perception, or whether GABA level  
97 of different cortical regions has selective influence on perception of different visual features. One hypothesis is  
98 that, GABA level of each cortical region is uniquely determined in each individual, possibly by a combination  
99 of genetic and environmental factors (Bachtiar et al., 2015; Lunghi et al., 2015; Marengo et al., 2010; Taniguchi  
100 et al., 2011). As such, GABA level of different cortical regions may exhibit dissociable inter-individual  
101 variability and influence perception of different visual features separately. An alternative hypothesis is that,  
102 GABA level of different cortical regions may co-vary as a result of common embryonic origins or shared  
103 subcortical GABAergic projections (Caputi et al., 2013; Chen et al., 2015; Dammerman et al., 2000; Jinno et al.,  
104 2007; Picardo et al., 2011), and may influence perception of different visual features concurrently.

105 To test these two alternative hypotheses, we studied how GABA level of parietal and occipital cortices related to  
106 inter-individual differences in size, orientation, and brightness perception. Occipital cortex contains a map of  
107 orientation preference in which individual neurons respond preferentially to specific orientation and neighboring  
108 neurons to adjacent orientations; by contrast, parietal cortex contains a map of size preference in which  
109 individual neuronal populations respond preferentially to specific size of a visually presented object and  
110 neighboring neurons to adjacent sizes (Harvey et al., 2015; Yacoub et al., 2007). Since neurotransmitters are  
111 contained in and released at synapses, GABA level of a cortical region may influence visual feature perception  
112 through lateral connections within the region. These lateral connections link neighboring neurons with similar  
113 feature preferences, and underlie contextual illusions where the perceived feature (e.g., orientation, size) of a

114 visual stimulus is modulated by the stimulus surrounding it (Bosten et al., 2010; Cannon et al., 1996; Kapadia et  
115 al., 1999; Stettler et al., 2002; Song et al., 2013). We therefore used contextual illusion as a perceptual assay,  
116 hypothesizing that selective correlation may be observed between GABA level of a cortical region and  
117 contextual illusion for visual features topographically mapped in this region. Specifically, parietal and occipital  
118 GABA level may correlate selectively with the magnitude of size and orientation illusion.

## 119 **MATERIALS AND METHODS**

### 120 **Participants**

121 Thirty-seven healthy volunteers (aged 20 to 40, all males, females ineligible due to menstrual cycle) gave  
122 written informed consent to participate in this study that was approved by the local ethics committee, De  
123 Videnskabetiske Komitéer for Region Midtjylland, Denmark. All participants had normal or corrected-to-  
124 normal vision, and no neurological or psychiatric history. The Magnetic Resonance Spectroscopy data of four  
125 participants were contaminated by signal from lipids and the psychophysics data of three participants were  
126 outliers of the normal distribution (Shapiro-Wilk test). These data were therefore excluded from further analysis.

### 127 **Magnetic resonance spectroscopy measure of GABA**

128 Neuroimaging took place in a Siemens Trio 3T MRI scanner. Structural MRI data were acquired using a T1-  
129 weighted MPRAGE sequence (TR: 2420 msec; TE: 3.7 msec; resolution: 1 mm isotropic; scanning time: 5.5  
130 min) and were used to guide the voxel placement in Magnetic Resonance Spectroscopy (MRS). Resting GABA  
131 measures were acquired from a 2 cm isotropic voxel in the parietal lobe (TR: 2500 msec; TE: 68 msec; 240 edit  
132 on and edit off averages; scan time: 20 min) and a 3 cm isotropic voxel in the occipital lobe (TR: 2500 msec; TE:  
133 68 msec; 96 edit on and edit off averages; scan time: 8 min), using MEGA-PRESS method (Edden et al., 2007;  
134 Mescher et al., 1998). To compensate for the size differences between the two voxels, the parietal voxel had a  
135 longer scan time (20 min) than the occipital voxel (8 min). An even longer scan time (40 min) could lead to a  
136 better compensation, however the subject motion would be a drawback.

137 We used a standard resting state protocol where participants had their eyes open and faced the insider of the  
138 scanner with no mirrors attached or no visual stimuli presented (Edden et al., 2009; Ogorman et al., 2011). MRS  
139 measure of resting GABA varies little across day or even months (Evans et al., 2010; Near et al., 2014). The

140 high test-retest reliability suggests that the scanning order will not bias the measures. Nevertheless, to minimize  
141 the between-subject variance of no interest, we kept the scanning order identical for all participants, collecting  
142 data for the occipital voxel first and the parietal voxel second. The parietal voxel was placed on the anterior part  
143 of the superior parietal lobe with its anterior border in parallel to the postcentral gyrus. The occipital voxel was  
144 placed to cover the calcarine sulcus bilaterally with its anterior border in alignment with the parietal-occipital  
145 sulcus. Care was taken to avoid the inclusion of the scalp and/or the tentorium cerebelli in the voxels.

146 The MEGA-PRESS method measures GABA concentrations through the acquisition of two spectra: one with an  
147 editing pulse targeting the C3-GABA peak at 1.9 ppm (edit on), and one with an editing pulse targeting the  
148 water peak on the symmetrical side at 7.5 ppm (edit off). By averaging the two spectra, the Creatine (Cr) peak at  
149 3.0 ppm was quantified. By subtracting the two spectra, the C4-GABA peak at 3 ppm was quantified. This C4-  
150 GABA peak is often referred to as GABA+, since a coupled macromolecule (MM) resonance at 3 ppm is co-  
151 edited and contributes to the measured signal. Due to the limitation of the MEGA-PRESS sequence, the exact  
152 MM contribution is difficult to estimate or remove. A theoretical model has been proposed to subtract MM  
153 contribution post-hoc (Murdoch et al., 2011). Nevertheless, this technique could introduce additional variability  
154 into the estimated GABA values, and is thus rarely used (see discussion in Mullins et al., 2014). Newer  
155 sequences such as MEGA-SPECIAL (Near et al., 2011) and SPECIAL (Near et al., 2013) aims to remove MM  
156 contribution by editing and modelling, respectively. However, both sequences have other drawbacks such as the  
157 imperfect lipid suppression. The raw GABA value is subject to bias from day-to-day scanner-related variation.  
158 For an unbiased estimate of GABA, a normalization of raw GABA value to Cr is typically applied (Mullins et  
159 al., 2012), since Cr resonates around the same frequency (3 ppm) as GABA and is not affected by disturbances  
160 that depend on the resonance frequency. The ratio GABA+/Cr was calculated to quantify GABA level.

161 The analysis of MRS data was performed by author JUB who was blind to the psychophysics data, and  
162 constituted part of a database that have been reported in previous studies (Near et al., 2014; Sandberg et al.,  
163 2014; Sandberg et al., 2016). The MRS data were first preprocessed in MATLAB with FID-A software for  
164 motion corruption removal, drift correction and phasing, and then analyzed in jMRUI software with AMARES  
165 package (Edden et al., 2007; Mescher et al., 1998; Simpson et al., 2015). Data were visually inspected for noise,  
166 line broadening, voxel misplacement and lipid contamination. Four participants who had spectra with large lipid  
167 contamination failed to pass the visual inspection and were excluded from further analysis. The quality of the  
168 included spectra was evaluated by calculating signal-to-noise ratio (SNR), line width and fit uncertainty.

169 Examples of typical spectra are shown in Fig. 1. SNR was calculated using the difference spectrum following  
170 the phase adjustment such that the N-acetylaspartate (NAA) peak was upright with a phase of 0 degree. Signal  
171 was calculated as the maximal intensity of the NAA peak in the difference spectrum; noise was calculated as the  
172 standard deviation of the noise in the signal-free spectrum, following a baseline correction to remove any 1st  
173 and 2nd order baseline variations. SNR was 108 for the parietal voxel and 226 for the occipital voxel. Line  
174 width was calculated by measuring the full width at half maximum of the NAA peak in the difference spectrum.  
175 Mean line width was 4.8 Hz for the parietal voxel and 5.4 Hz for the occipital voxel. Fit uncertainty was  
176 measured as the SD/amplitude ratio output by jMRUI. Mean SD/amplitude ratio was 0.04 for the parietal voxel  
177 and 0.03 for the occipital voxel.

#### 178 **Psychophysics measure of contextual illusion**

179 Psychophysics took place in a dark room. Visual stimuli were presented on a 17-inch LCD monitor (spatial  
180 resolution: 1024 x 768 pixels; temporal resolution: 60 Hz) and viewed through a chin rest. The magnitudes of  
181 size illusion (Ebbinghaus illusion), orientation illusion (tilt illusion), and brightness illusion (simultaneous  
182 contrast illusion) were measured in separate experiments. The size illusion stimulus comprised two white circles  
183 ( $1^\circ$  diameter), a reference one surrounded by sixteen small white circles ( $0.2^\circ$  diameter) and a test one by seven  
184 large white circles ( $2^\circ$  diameter), presented simultaneously for 500 msec on two sides of the fixation ( $3.85^\circ$   
185 eccentricity) with randomized spatial order. The orientation illusion stimulus comprised two circular gratings  
186 ( $45^\circ$  orientation,  $1.5^\circ$  diameter, 2.5 cycles/ $^\circ$  spatial frequency, 100% contrast), a reference one surrounded by an  
187 annular grating ( $60^\circ$  orientation,  $4.5^\circ$  diameter, 2.5 cycles/ $^\circ$  spatial frequency, 100% contrast) and a test one  
188 with no surround. The brightness illusion stimulus comprised two gray circles (50% luminance,  $1.5^\circ$  diameter),  
189 a reference one surrounded by white annulus ( $4.5^\circ$  diameter) and a test one by black annulus ( $4.5^\circ$  diameter).

190 To minimize the confounding factors such as decision factors (Gold et al., 2012; Vogels et al., 1986), we kept  
191 the psychophysical procedures identical for all three illusions. Participants first performed a match-to-standard  
192 session in which they manually adjusted the size, orientation, or luminance of the test stimulus till it matched  
193 the perceived size, orientation, or luminance of the reference stimulus, and a visual discrimination session in  
194 which the size, orientation, and luminance discrimination threshold was measured through a standard 2-up-1-  
195 down staircase. The point of subjective equality measured from the match-to-standard session and the visual  
196 discrimination threshold measured from the staircase session were used to guide the choices of stimulus

197 parameters in the subsequent two-alternative-forced choice session. There, participants were asked on 112 trials  
198 to judge which central stimulus was larger (for size illusion), more tilted (for orientation illusion), or brighter  
199 (for brightness illusion). The size, orientation, or luminance of the reference stimulus was kept constant; that of  
200 the test stimulus was varied between seven values (16 trials per value) around the point of subjective equality  
201 acquired from match-to-standard session, with a step size equal to visual discrimination threshold.

202 The data from the two-alternative-forced choice session were fitted with psychometric function to measure the  
203 50% threshold point where the two central stimuli appeared perceptually equal despite their physical difference.  
204 The goodness-of-fitting (R-square) was  $0.963 \pm 0.033$  for orientation illusion,  $0.956 \pm 0.041$  for size illusion,  
205 and  $0.960 \pm 0.033$  for brightness illusion. It did not differ significantly between illusions (size illusion versus  
206 orientation illusion:  $T(29) = 1.03$ ,  $p = 0.313$ ; size illusion versus brightness illusion:  $T(29) = 0.47$ ,  $p = 0.640$ ;  
207 orientation illusion versus brightness illusion:  $T(29) = 0.28$ ,  $p = 0.785$ ), or correlate significantly with GABA  
208 (size illusion and parietal GABA:  $r = -0.194$ ,  $p = 0.304$ ; size illusion and occipital GABA:  $r = 0.143$ ,  $p = 0.451$ ;  
209 orientation illusion and parietal GABA:  $r = 0.244$ ,  $p = 0.194$ ; orientation illusion and occipital GABA:  $r = 0.142$ ,  
210  $p = 0.456$ ; brightness illusion and parietal GABA:  $r = -0.224$ ,  $p = 0.234$ ; brightness illusion and occipital GABA:  
211  $r = 0.174$ ,  $p = 0.359$ ). The physical difference between the two central stimuli at the 50% threshold point was  
212 calculated to quantify the illusion magnitude.

213 To account for the influence of Weber's law (Shen, 2013), we used the log transform of the illusion magnitude  
214 and the semi-log plots (Fig. 3-5) to assess inter-individual differences. Since the magnitude of orientation  
215 illusion is subject to oblique effect (Clifford, 2014), we performed additional control experiments in a group of  
216 twenty healthy volunteers (aged 21 to 35, 11 females) to test the influence of stimulus orientation (cardinal  
217 versus oblique) on the measure of inter-individual differences. We found that although the illusion magnitude  
218 was weaker for cardinal condition than oblique condition ( $t(19) = 20.362$ ,  $p < 10^{-13}$ ), the illusion magnitude were  
219 highly correlated between the two conditions ( $r = 0.866$ ,  $p < 10^{-6}$ ). This observation suggested that inter-  
220 individual differences in orientation illusion magnitude were not biased by oblique effect.

## 221 **Statistics**

222 Pearson's correlation can capture the linearity in the relation between two variables, whereas Spearman's rank  
223 correlation can only reflect whether two variables are monotonically related or not. For example, Spearman's



224 correlation coefficient will return the same result of 1 for two variables that both monotonically increase,  
225 regardless of whether their rates of increase are linearly or non-linearly correlated; by contrast, Pearson's  
226 correlation coefficient can capture the difference between these two conditions. As such, Pearson's correlation  
227 coefficient is a more suitable test for studying the difference in correlation coefficient between conditions (e.g.,  
228 between size illusion and parietal versus occipital GABA). Application of Pearson's correlation requires the  
229 data to satisfy normal distribution. Shapiro-Wilk test failed to refute the assumption of normality for parietal  
230 GABA level ( $W = 0.952$ ,  $p = 0.187$ ), occipital GABA level ( $W = 0.962$ ,  $p = 0.295$ ), size illusion magnitude ( $W$   
231  $= 0.937$ ,  $p = 0.072$ ), orientation illusion magnitude ( $W = 0.985$ ,  $p = 0.942$ ), or brightness illusion magnitude ( $W$   
232  $= 0.960$ ,  $p = 0.314$ ). Therefore, Pearson's correlation was used throughout the study to test the relations between  
233 variables, with age regressed out.

## 234 RESULTS

235 We found that GABA level in parietal cortex ( $0.252 \pm 0.035$ ) and GABA level in occipital cortex ( $0.299 \pm 0.042$ )  
236 exhibited dissociable inter-individual variability (Fig. 2;  $r = -0.066$ , 95% C.I. of  $r = [-0.372, 0.250]$ ,  $p = 0.730$ ,  $N$   
237  $= 30$ ). Subsequently, we studied how parietal GABA level versus occipital GABA level contributed to inter-  
238 individual differences in size illusion (Ebbinghaus illusion), orientation illusion (tilt illusion), and brightness  
239 illusion (simultaneous contrast illusion).

240 Across individuals, we observed a positive correlation between the magnitude of size illusion and parietal  
241 GABA level (Fig. 3;  $r = 0.395$ , 95% C.I. of  $r = [0.117, 0.610]$ ,  $p = 0.031$ ,  $N = 30$ ). By contrast, we did not  
242 observe any significant correlation between the magnitude of size illusion and occipital GABA level (Fig. 3;  $r =$   
243  $-0.038$ , 95% C.I. of  $r = [-0.317, 0.250]$ ,  $p = 0.841$ ,  $N = 30$ ). Moreover, compared to occipital GABA level,  
244 parietal GABA level showed a significantly higher correlation with size illusion magnitude ( $t(27) = 2.369$ ,  $p =$   
245  $0.018$ ). These results suggest a selective correlation between size illusion and parietal GABA.

246 Conversely, across individuals, the magnitude of orientation illusion exhibited a positive correlation with  
247 occipital GABA level (Fig. 4;  $r = 0.367$ , 95% C.I. of  $r = [0.042, 0.599]$ ,  $p = 0.046$ ,  $N = 30$ ), but not with parietal  
248 GABA level (Fig. 4;  $r = 0.002$ , 95% C.I. of  $r = [-0.363, 0.355]$ ,  $p = 0.990$ ,  $N = 30$ ). Moreover, occipital GABA  
249 level correlated with orientation illusion magnitude significantly higher than parietal GABA level did ( $t(27) =$   
250  $1.990$ ,  $p = 0.047$ ). These results suggest a selective correlation between orientation illusion and occipital GABA.

251 For the brightness illusion, we did not observe any significant correlation across individuals between the illusion  
252 magnitude and parietal GABA level (Fig. 5;  $r = -0.149$ , 95% C.I. of  $r = [-0.456, 0.163]$ ,  $p = 0.431$ ,  $N = 30$ ) or  
253 occipital GABA level (Fig. 5;  $r = -0.017$ , 95% C.I. of  $r = [-0.377, 0.391]$ ,  $p = 0.927$ ,  $N = 30$ ). Accordingly, the  
254 correlation between parietal GABA level and brightness illusion magnitude was not significantly different from  
255 the correlation between occipital GABA level and brightness illusion magnitude ( $t(27) = 0.690$ ,  $p = 0.490$ ).  
256 These results suggest that GABA level does not influence all types of contextual illusion, and its correlation  
257 with size or orientation illusion may relate with the way how stimulus size or orientation is cortically processed.

## 258 **DISCUSSION**

259 Taken together, our study reveals a region- and feature-dependent influence of neurotransmitter level on human  
260 visual perception. We show that inter-individual variability in parietal GABA level correlated with size illusion  
261 magnitude but not with orientation or brightness illusion magnitude; in contrast, inter-individual variability in  
262 occipital GABA level correlated with orientation illusion magnitude but not with size or brightness illusion  
263 magnitude. Our findings suggest that inter-individual variability in GABA does not reflect a general variability  
264 in visual inhibition; instead, GABA level of different cortical regions has selective influence on perception of  
265 different visual features. This influence is likely to be exerted through lateral connections within the cortical  
266 region and is observed specifically for visual features mediated by such connections.

267 In occipital cortex, neurons exhibit orientation preference such that their response is the strongest for a preferred  
268 orientation and gradually decays as the stimulus orientation deviates from this preferred orientation (Ringach et  
269 al., 2002). Neurons preferring adjacent orientations are cortically adjacent to one another and are connected by  
270 intra-regional lateral connections (Bock et al., 2011; Li et al., 2012; Yacoub et al., 2007). This topographical  
271 organization of lateral connections allows the orientation preference of neurons to be modulated by the activity  
272 of their adjacent neurons, and the level of occipital GABA to affect the degree of modulation (Burr et al., 1981;  
273 Chavane et al., 2011; Eysel et al., 1990; Fitzpatrick, 2000; Gilbert et al., 1996; Morrone et al., 1987; Smith et al.,  
274 2006; Stettler et al., 2002). This neural-level modulation may then give rise to perceptual-level modulation,  
275 where the perceived orientation of a stimulus is modulated by the orientation of the stimulus surrounding it  
276 (Schwartz et al., 2007; Song et al., 2013). If so, the correlation between orientation illusion magnitude and  
277 occipital GABA level could be a perceptual reflection of the link between neural-level modulation and GABA.

278 Whereas orientation preference is topographically mapped in occipital cortex with neurons preferring more  
279 similar orientations being more highly connected, there is no topographic map of size preference in occipital  
280 cortex (Chklovskii et al., 2004; Swindale, 2000). As such, a local GABA influence, exerted through lateral  
281 connections within occipital cortex, is likely to be specific to orientation illusion and not generalizable to size  
282 illusion. Just as the topographic map of orientation preference is prominent in occipital cortex (Kaschube et al.,  
283 2010; Wolf et al., 1998; Yacoub et al., 2007), a topographic map of size preference exists in parietal cortex  
284 where individual neuronal populations respond preferentially to specific size and adjacent neurons to adjacent  
285 sizes (Harvey et al., 2015). By contrast, there is no map of orientation preference in parietal cortex. Therefore, a  
286 local GABA influence, exerted through lateral connections within parietal cortex, would be specific to size  
287 illusion and not generalizable to orientation illusion. Similar to the topographical maps of orientation preference  
288 and size preference in visual cortices, neurons in the retina exhibit preference for stimulus luminance and are  
289 topographically connected by their luminance preference. Possibly, the inter-individual differences in brightness  
290 illusions may associate with inter-individual variability in retinal GABA (Lukasiewicz et al., 1998; Wu, 2010).  
291 Moreover, since neural responses to visual features are modulated not only by intra-regional lateral connections  
292 but also by inter-regional feedback connections (Fitzpatrick, 2000; Smith et al., 2006), the lack of correlation  
293 between brightness illusion and occipital or parietal GABA could also indicate a predominant contribution of  
294 inter-regional (as opposed to intra-regional) modulation to this illusion (Kinoshita, 2001; Perna et al., 2005).

295 This account, that GABA level of a cortical region influences perception of visual features topographically  
296 mapped in this region, would be able to explain the reported correlations between occipital GABA level and  
297 orientation discrimination threshold (Edden et al., 2009). The intra-regional modulation exerted through lateral  
298 connections may not only shift the orientation preference of neurons, and give rise perceptual shifts in  
299 orientation illusion, but also sharpen the orientation tuning of neurons, and give rise perceptual sharpenings in  
300 orientation discrimination (Benyishiai et al., 1995; Orban et al., 1998; Somers et al., 1995; Song et al., 2013;  
301 Song et al., 2015). As such, the influence of occipital GABA level on orientation illusion could be mirrored in  
302 orientation discrimination (Song et al., 2013). In addition to orientation preference, ocular preference is also  
303 topographically mapped in occipital cortex, where individual neurons respond preferentially to stimulus from a  
304 specific eye, and adjacent neurons to opposite eyes (Adams et al., 2007; Dechent et al., 2000; Menon et al.,  
305 1997). There, lateral connections would link neurons with opposite ocular preference, allowing the influence of  
306 occipital GABA on orientation perception to generalize to binocular perception. This would explain the reported  
307 decrease in both occipital GABA and interocular suppression after monocular deprivation (Lunghi et al., 2015).

308 This account, that GABA level of a cortical region influences perception of visual features topographically  
309 mapped in this region, further predicts a correlation between parietal GABA level and numerosity perception.  
310 Just as occipital cortex is crucial for processing low-level visual features and contains maps of orientation  
311 preference and ocular preference, parietal cortex is important for processing high-level visual features and  
312 contains maps of size preference and numerosity preference (Buetti et al., 2009; Chklovskii et al., 2004; Dehaene  
313 et al., 2007; Dormal et al., 2008; Harvey et al., 2013; Harvey et al., 2015; Kadosh et al., 2009; Nieder et al.,  
314 2009; Pinel et al., 2004; Roitman et al., 2007; Roitman et al., 2012; Walsh, 2003). The lateral connections in  
315 parietal cortex are likely to link neighboring neurons with similar numerosity preference, which would allow  
316 parietal GABA to influence numerosity discrimination and numerosity illusion (Almeida et al., 2007; Bosten et  
317 al., 2010; Dormal et al., 2008; Pinel et al., 2004). While the posterior (e.g., occipital, parietal) part of the cortex  
318 is involved in sensory processing, a topographic map of conceptual knowledge was discovered in prefrontal  
319 cortex, suggesting a potential role of frontal GABA in conceptual categorization (Constantinescu et al., 2016). It  
320 would be of interest for future studies to test the links between parietal GABA and numerosity perception, as  
321 well as between frontal GABA and conceptual categorization.

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- 489

490 **FIGURE LEGENDS**

491 **Figure 1. MRS Spectra.** MRS measure of resting GABA was acquired in separate experiment runs, from a  
492 parietal voxel (blue) placed on the anterior part of the superior parietal lobe with its anterior border parallel to  
493 the postcentral gyrus, and a occipital voxel (red) placed to cover the calcarine sulcus bilaterally with its anterior  
494 border in alignment with the parietal-occipital sulcus. Examples of MRS spectra from ten randomly selected  
495 participants are shown. The GABA peak is seen at 3 ppm and the inverted NAA peak at around 2 ppm.

496 **Figure 2. Parietal and occipital GABA.** Parietal and occipital GABA levels were plotted against each other,  
497 illustrating a lack of inter-individual correlation between these two variables. Each data point represents a  
498 participant. Statistics are Pearson's correlation and bootstrap results.

499 **Figure 3. GABA and size illusion.** In the Ebbinghaus illusion, two physically identical central circles appear to  
500 have different perceived size as a result of the surrounding context of either smaller or larger circles. The  
501 magnitude of Ebbinghaus illusion for each participant was plotted in semi-log graph against their parietal or  
502 occipital GABA level, illustrating a positive correlation between size illusion magnitude and parietal GABA  
503 level, as well as a lack of significant correlation between size illusion magnitude and occipital GABA level.  
504 Each data point represents a participant. Statistics are Pearson's correlation and bootstrap results.

505 **Figure 4. GABA and orientation illusion.** In the tilt illusion, two physically identical central gratings appear to  
506 have different perceived orientation as a result of their immediate surroundings. The magnitude of tilt illusion  
507 for each participant was plotted in semi-log graph against their parietal or occipital GABA level, illustrating a  
508 positive correlation between orientation illusion magnitude and occipital GABA level, as well as a lack of  
509 significant correlation between orientation illusion magnitude and parietal GABA level. Each data point  
510 represents a participant. Statistics are Pearson's correlation and bootstrap results.

511 **Figure 5. GABA and brightness illusion.** In the simultaneous contrast illusion, two physically identical central  
512 circles appear to have different brightness as a result of their immediate surroundings. The magnitude of  
513 simultaneous contrast illusion for each participant was plotted in semi-log graph against their parietal or  
514 occipital GABA level, illustrating a lack of significant correlation between brightness illusion magnitude and  
515 either parietal or occipital GABA level. Each data point represents a participant. Statistics are Pearson's  
516 correlation and bootstrap results.









