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Human occipital and parietal GABA selectively influence visual 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 modualted 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; Moult, 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; Marenco 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　Videnskabsetiske 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° diameter), a reference one surrounded by sixteen small white circles (0.2° diameter) and a test one by seven

184   large white circles (2° diameter), presented simultaneously for 500 msec on two sides of the fixation (3.85°

185   eccentricity) with randomized spatial order. The orientation illusion stimulus comprised two circular gratings

186   (45° orientation, 1.5° diameter, 2.5 cycles/° spatial frequency, 100% contrast), a reference one surrounded by an

187   annular grating (60° orientation, 4.5° diameter, 2.5 cycles/° spatial frequency, 100% contrast) and a test one

188   with no surround. The brightness illusion stimulus comprised two gray circles (50% luminance, 1.5° diameter),

189   a reference one surrounded by white annulus (4.5° diameter) and a test one by black annulus (4.5° 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 ± 0.033 for orientation illusion, 0.956 ± 0.041 for size illusion,

205 and 0.960 ± 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 ± 0.035) and GABA level in occipital cortex (0.299 ± 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.

9

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 topogrpahical 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 (Bueti 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.

322

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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.

Parietal Voxel

Occipital Voxel

Participant 1
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 6
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 1
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 6
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 2
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 7
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 2
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 7
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 3
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 8
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 3
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 8
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 4
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 9
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 4
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 9
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 5
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 10
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 5
GABA
NAA
5 4 3 2 1
Frequency (ppm)

Participant 10
GABA
NAA
5 4 3 2 1
Frequency (ppm)

r = -0.066 [-0.372 0.250], p = 0.730, N = 30

diameter: 2.0 deg of visual angle

diameter: 0.2 deg of visual angle

diameter: 1.0 deg of visual angle

r = 0.395 [0.117 0.610], p = 0.031, N = 30

r = -0.038 [-0.317 0.250], p = 0.841, N = 30

r = 0.002 [-0.363 0.355], p = 0.990, N = 30

r = 0.367 [0.042 0.599], p = 0.046, N = 30

luminance: 100%

luminance: 0%

luminance: 50%

r = -0.149 [-0.456 0.163], p = 0.431, N = 30

r = -0.017 [-0.377 0.391], p = 0.927, N = 30

Brightness Illusion Magnitude (%)

32.7

12.3

4.66

1.76

0.20 0.24 0.28 0.32

Parietal GABA (GABA+/Cr Ratio)

Brightness Illusion Magnitude (%)

32.7

12.3

4.66

1.76

0.22 0.28 0.34 0.40

Occipital GABA (GABA+/Cr Ratio)