

Volitional modulation of higher-order visual cortex alters human perception

Article

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1 **TITLE:**

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3 Volitional Modulation of Higher-order Visual Cortex Alters Human Perception

4

5 **AUTHORS:**

6

7 Jinendra Ekanayake^{1,2}, Gerard R Ridgway³, Joel S Winston^{1,2}, Eva
8 Feredoes⁴, Adeel Razi^{1,9}, Yury Koush¹⁰, Frank Scharnowski^{5,6,7}, Nikolaus
9 Weiskopf^{1,8}, Geraint Rees^{1,2}

10

11 **AFFILIATIONS:**

12

13 ¹Wellcome Trust Centre for Human Neuroimaging, UCL Institute of Neurology,
14 London, UK

15 ²UCL Institute of Cognitive Neuroscience, University College London

16 ³Oxford Centre for Functional MRI of the Brain, University of Oxford, Oxford, UK

17 ⁴School of Psychology and Language Sciences, University of Reading, UK

18 ⁵Psychiatric University Hospital, University of Zürich, Lenggstrasse 31, 8032 Zürich,
19 Switzerland

20 ⁶Neuroscience Center Zürich, University of Zürich and Swiss Federal Institute of
21 Technology, Winterthurerstr. 190, 8057 Zürich, Switzerland

22 ⁷Zürich Center for Integrative Human Physiology (ZIHP), University of Zürich,
23 Winterthurerstr. 190, 8057 Zürich, Switzerland

24 ⁸Department of Neurophysics, Max Planck Institute for Human Cognitive and Brain
25 Sciences, Leipzig, Germany

26 ⁹Department of Electronic Engineering, NED University of Engineering and
27 Technology, Karachi, Pakistan

28 ¹⁰Department of Radiology and Biomedical Imaging, Yale University, 300 Cedar
29 Street, New Haven, CT 06519, USA

30

31 **CORRESPONDING AUTHOR:**

32 Jinendra Ekanayake, email: j.ekanayake@ucl.ac.uk

33 **ADDRESS:**

34 Institute of Cognitive Neuroscience,

35 12 Queen Square, WC1N 3AR

36

37 **Conflict of Interest: Nil**

38

39 **Abstract**

40

41 Can we change our perception by controlling our brain activation? Awareness
42 during binocular rivalry is shaped by the alternating perception of different
43 stimuli presented separately to each monocular view. We tested the possibility
44 of causally influencing the likelihood of a stimulus entering awareness. To do
45 this, participants were trained with neurofeedback, using realtime functional
46 magnetic resonance imaging (rt-fMRI), to differentially modulate activation in
47 stimulus-selective visual cortex representing each of the monocular images.
48 Neurofeedback training led to altered bistable perception associated with
49 activity changes in the trained regions. The degree to which training
50 influenced perception predicted changes in grey and white matter volumes of
51 these regions. Short-term intensive neurofeedback training therefore sculpted
52 the dynamics of visual awareness, with associated plasticity in the human
53 brain.

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55 Word count 123 (150 max)

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59 **Highlights**

60

61 • Unconscious biasing of higher-order visual perception with realtime
62 fMRI neurofeedback.

63 • Participants unknowingly modulated two brain regions to control
64 feedback signal

65 • Short-term neurofeedback training over 3 days induced functional
66 plasticity

67 • Neurofeedback may strengthen neural representations and alter prior
68 expectations

69 • Potential avenue for behavioural shaping and therapeutic reduction of
70 aberrant perception

71

72

73 **Introduction**

74

75 The ability to causally modify how we perceive the world has potential
76 implications in health and disease. Altering perceptual biases, which may be
77 conscious or unconscious, could modify pathological perception such as
78 hallucinations, or provide a means of selective cognitive
79 enhancement(Miranda et al., 2015). Such attempts to deliberately manipulate
80 higher-order sensory perception have, until now, proven to be unsuccessful.
81 For example, attempting to alter perception using mental imagery, a cognitive
82 process which utilises similar neural substrates to perception(O'Craven and
83 Kanwisher, 2000), does not increase the vividness of the imagery. Most
84 importantly, mental imagery training has no effect on perception linked to the
85 imagery strategy used during training, as demonstrated with binocular rivalry
86 (BR) between images specifically associated with the mental imagery
87 training(Rademaker and Pearson, 2012). BR is a unique perceptual
88 phenomenon that has been used to provide a window into the unconscious
89 and conscious processes underlying visual perception. It is produced by
90 simultaneously presenting conflicting monocular stimuli to each eye.
91 Paradoxically, the brain cannot form a stable image. Instead, each image
92 randomly competes for exclusive perceptual dominance. Until now, producing
93 unconscious shifts in higher-order perception by directly modifying brain
94 function has proven to be unsuccessful.

95

96 Neurofeedback training using realtime functional magnetic resonance imaging
97 (rt-fMRI) is an emerging technique which allows participants to control target

98 brain regions by voluntarily modulating online feedback of activity in those
99 regions(Sitaram et al., 2016). Feedback is typically provided via a visual
100 interface during concurrent MR scanning. Online modulation of the Blood
101 Oxygen Level-Dependent (BOLD) signal using neurofeedback involves
102 abstract cognitive strategies, as well as mental imagery that maybe explicitly
103 linked to the brain region-of-interest (ROI). This approach can produce
104 changes in behaviour through the functional modulation of trained brain
105 regions, including low-order visual perception (e.g. grating orientation, colour)
106 by modulating primary retinotopic cortex(Amano et al., 2016; Shibata et al.,
107 2011), pain and craving by modulating anterior cingulate cortex(deCharms et
108 al., 2004; Li et al., 2013), and motor function by modulating supplementary
109 motor area and primary motor cortex(Blefari et al., 2015; Subramanian et al.,
110 2011). We hypothesised that rt-fMRI neurofeedback might prove more
111 powerful than previous approaches, such as mental imagery alone, in
112 enabling participants to modify brain activity associated with higher-order
113 visual perception, and consequently directly influence how they perceive the
114 world.

115

116 To test this hypothesis, we trained human participants using mental imagery
117 *combined* with neurofeedback to voluntarily control the difference in activation
118 between two higher-order visual cortical regions (Fusiform Face Area, FFA
119 and Parahippocampal Place area, PPA). The human FFA responds strongly
120 to faces(Kanwisher et al., 1997; McCarthy et al., 1997), but not to other types
121 of non-face stimuli, while the PPA responds to houses and places, but not
122 faces(Epstein and Kanwisher, 1998). Further, both of these regions activate

123 during mental imagery of faces or places respectively, even in the absence of
124 visual stimuli(O'Craven and Kanwisher, 2000). The differential response
125 properties of these two regions enabled participants in the study to have a
126 visually presented neurofeedback training signal that represented the
127 difference in activation between the two regions i.e. a *differential signal*.

128

129 The use of a differential signal provided an internal control for global brain
130 activation, and helped focus the training effect on the two selected brain
131 regions in a manner that might not occur with mental imagery training only.
132 We tested participants with a BR task, where they were exposed to rivalrous
133 monocular face and house images, before and after neurofeedback training.
134 During BR, participants are consciously aware of only one of the perceptual
135 stimuli at a time, while the other stimulus is temporarily suppressed. The
136 perceptual fluctuation is spontaneous and stochastic, with both top-down (i.e.
137 cognitive modulation) and bottom-up (i.e. salience-based) processes being
138 implicated(Dayan, 1998; Parker and Alais, 2007; Tong et al., 2006). In this
139 study, the ensuing BR, where perception alternated spontaneously between
140 each monocular view, provided a test of whether neurofeedback training had
141 altered the likelihood of either stimuli entering awareness. We investigated
142 whether any perceptual changes were associated with differences in brain
143 activity and structure (see also Supplementary Materials).

144

145 To anticipate our findings, following neurofeedback training, there was a
146 sustained influence on the perceptual dynamics of BR, suggesting functional
147 plasticity. This effect was additionally observed when participants performed

148 concurrent modulation of brain activity during BR. Further, a multivariate
149 analysis of changes in brain structure produced by neurofeedback training
150 predicted changes in BR dynamics.
151

152 **Methods**

153

154

155 **Main experiment:**

156

157 **Participants**

158

159 Ten neurologically normal adult volunteers (24–35 years of age; mean age 28
160 years; 8 females) with normal or corrected-to-normal visual acuity participated
161 in the experiment. Each participant gave written informed consent. The study
162 was approved by the local ethics committee (UCL Ethics Committee code:
163 09/H0716/14).

164

165 **Stimuli and Materials**

166

167 All visual stimuli were generated and displayed via scripts in MATLAB created
168 with the Cogent 2000 toolbox (http://www.vislab.ucl.ac.uk/cogent_2000.php),
169 on a viewing screen with a visual angle of 23 degrees by 17 degrees, (30 x 26
170 LCD projector (LT158; NEC). The mirror-mounted viewing screen was set on
171 the top of the scanner bore (optical distance 52 cm). During the
172 neurofeedback sessions, participants saw a fluctuating thermometer bar at
173 the centre of the screen. During the BR sessions only, participants wore a pair
174 of prism glasses. Additionally, a black cardboard divider was placed between
175 the forehead and the screen to ensure that each eye could see one side of
176 the screen only, and provide a stable base for fixation. Two identical box
177 stimuli were displayed side-by-side on the monitor, each with a central white
178 fixation cross (0.68 visual angle) and tile frame surround (11.78 visual angle),

179 upon a uniform grey background (background luminance $\frac{1}{4}$ 65 Cd/m²).
180 Optimal perceptual fusion of the two box stimulus images was confirmed with
181 the participant prior to commencing each BR session. Face or house stimuli
182 were presented (20 exemplars each). Responses for durations were obtained
183 via a pair of custom-built, MR-compatible, response boxes.

184

185 **FMRI Scanning**

186

187 Scanning was performed on a 3T Allegra head-only scanner (standard
188 transmit-receive head coil). Functional data was acquired with a single-shot
189 gradient echo planar imaging sequence (matrix size, 64x64; field of view,
190 192x192mm; isotropic in-plane resolution, 3x3 mm; 32 slices with ascending
191 acquisition; slice thickness, 2 mm; slice gap, 1 mm; echo time (TE), 30 ms;
192 repetition time (TR), 1920 ms; flip angle, 90°; receiver bandwidth, 3551
193 Hz/pixel). Although the nominal slice thickness was 2mm, the effective slice
194 profile achieved in practice is typically larger such that the effective slice
195 thickness is closer to 3mm. Allowing a gap additionally minimised any risk of
196 saturation effects upon excitation of the subsequent slice (again due to
197 imperfect slice profiles). This is particularly important in the case of ascending
198 acquisition order, as used here. Ascending acquisition order was chosen to
199 minimise the impact of any participant motion, which again could lead to
200 saturation effects if the motion resulted in any part of the previously excited
201 slice being re-excited in a time shorter than the TR.

202

203 Within each scanning session, double-echo fast, low-angle shot sequence

204 (FLASH) field maps (TE1, 10 ms; TE2, 12.46 ms; resolution, 3 x 3 x 2 mm;
205 slice gap, 1 mm) were acquired and used to correct geometric distortions.

206

207 **High Resolution Structural Scans**

208

209 A whole brain high-resolution T1-weighted structural scan was performed
210 before and after training. This was in addition to structural scans performed on
211 each neurofeedback training day. The scan was a 3D-modified, driven
212 equilibrium Fourier transform (MDEFT) scan (1mm isotropic resolution; matrix
213 size, 256x240 mm; field of view, 256x240 mm; 176 sagittal partitions; TE, 2.4
214 ms; TR, 7.92 ms; inversion time, 910 ms; flip angle, 15°; readout bandwidth,
215 195 Hz/pixel; spin tagging in the neck with flip angle 160° to avoid flow
216 artifacts for superposition of functional maps(Deichmann et al., 2004)).

217

218 **Realtime fMRI Set-up for Neurofeedback**

219

220 Turbo Brain Voyager(Goebel et al., 2006) was used, with custom realtime
221 image export tools programmed in ICE VA25 (Siemens Healthcare)(Weiskopf
222 et al., 2004), and custom MATLAB based scripts. Participants were shown
223 visual representations of BOLD signal changes in brain regions previously
224 identified with a functional localiser scan (i.e. target ROIs). Realtime data
225 preprocessing encompassed 3D motion correction, smoothing, and
226 incremental linear detrending of time series. The ROI time course(s) were
227 extracted from the prescribed ROI masks, averaged and exported. Signal
228 drift, spikes and high frequency noise were further removed in realtime from

229 the exported time courses with custom MATLAB scripts(Koush et al., 2012).
230 The feedback signal (a ‘fluctuating’ thermometer bar) was displayed to the
231 participants with a delay of 2 s from the acquisition of the image.

232

233 **Binocular Rivalry Set-up and Behavioural data acquisition**

234

235 Inside the scanner, participants, wearing custom-made prism glasses, were
236 shown two stimuli equidistant from a central viewing screen divider. During
237 the viewing blocks, a face stimulus and a house stimulus were presented in
238 the left and right hemi-fields respectively. The stimuli were pseudorandomised
239 with regards to which eye received the face or house stimuli. Each viewing
240 block (40 s followed by rest 20 s) was performed with a new pair of stimuli
241 from the pool of 20 stimuli. Six blocks were performed per session, for three
242 sessions.

243

244 During the BR sessions, participants pressed one of three buttons to record
245 their percept of ‘face’, ‘house’ or ‘mixed’. The participants were instructed to
246 switch as accurately and rapidly as possible between the three possible
247 button presses linked to the three percepts. This was the only instruction
248 given during pre-training BR and post-training BR, which were identical save
249 for being performed either side of neurofeedback training. Additional
250 instructions were given for two further post-training BR conditions (see below,
251

252 **Day 5: Post-training BR).**

253

254 Cumulative dominance durations were calculated, which were equal to the
255 total amount of time each monocular stimulus was perceived, and averaged
256 across blocks. The three percepts were then pooled as follows: (1) **strategy-**
257 **related percept** e.g. face percept for the neurofeedback group advised to use
258 face mental imagery ('Face' group) or house percept for the neurofeedback
259 group advised to use house mental imagery ('House' group) (2) **strategy-**
260 **unrelated percept**' e.g. house percept for the 'Face' group, face percept for
261 the 'House' group); and (3) **'mixed percept'**.

262

263 **Experimental Outline**

264

265 The experiment was divided into multiple days, with each participant attending
266 five consecutive scanning days (Figure 1). The participants were split into two
267 groups, with five participants in the 'face' group and five participants in the
268 'house' training group.

269

270 **Day 1: Pre-training BR and Localiser**

271 A **Pre-training BR** scan was performed as described above for all
272 participants. They then underwent a **functional localiser** scan to identify FFA
273 and PPA regions (12 minutes, 16 blocks of face stimuli, 16 blocks of house
274 stimuli, and 20 different exemplars per block). Each stimulus was presented
275 for 600 ms (400 ms interstimulus interval). A one-back task was performed (3
276 targets per block), requiring a button press upon detection of the same
277 stimulus. Two contrasts were used; Houses vs. Faces and Faces vs. Houses.
278 Using the Juelich histological atlas to provide an anatomical

279 landmarks(Eickhoff et al., 2006, 2005), voxel selection for the ROIs were
280 defined along the ventral and lateral surfaces of the temporal lobe in proximity
281 to the fusiform gyrus for FFA, and lateral to the collateral sulcus in the
282 parahippocampal region for PPA respectively.

283

284 **Day 2-4: Neurofeedback Sessions**

285 Each neurofeedback training day comprised three scanning sessions, each
286 six blocks of 60 s with an 'upregulate' period (40 s) followed by 'rest' (20 s).

287 During an upregulation period, participants viewed a fluctuating red bar and a
288 fixed horizontal black bar. The latter was placed towards the top of the screen,
289 and the participants were asked to push the red bar above it. Participants
290 were told that the fluctuating red bar was linked to their brain activity, and that
291 they should drive the red bar up to the level of the black bar using a mental
292 imagery strategy. They were advised to maintain the red bar at that level, for
293 as long as possible, during the 'upregulate' period. Participants were told that
294 there was a delay related to the training signal (produced by the
295 hemodynamic response function, HRF) of approximately 6-8 s. During rest,
296 participants were instructed to perform a mental arithmetic task (serial
297 subtraction of 7 from 100).

298

299 ***Controlling the Neurofeedback Training Signal***

300

301 Participants were pseudorandomised into two groups – a 'Face' group and a
302 'House' group. Each group was instructed to use mental imagery strategies.
303 They were given examples of what might work (Figure 1), although the

304 participants could use their own interpretation. Specific examples for the
305 house group were ‘think about your house, or a building you are familiar with
306 such as a school or church’, or ‘think about walking down the road looking at
307 buildings’. Specific examples for the face group were ‘think of faces of people
308 you know’, ‘think of celebrity faces’, or ‘think of memorable faces you have
309 seen recently’. Both groups were instructed to pay close attention to the
310 fluctuating red bar, and to find the best way of pushing the bar up for as much
311 and as long as possible. Both groups were instructed to use whatever
312 strategy worked best, including their own, and to vary the strategy to ensure
313 continuous control of the fluctuating red bar.

314

315 Each group was unaware of the precise nature of their feedback signal.
316 During neurofeedback training, the fluctuating red bar was driven by brain
317 activity in which the signal from PPA was subtracted from FFA for the ‘Face’
318 group, and the reverse subtraction (PPA – FFA) for the ‘House’ group.
319 Participants were trained to modulate a *differential* training signal. Therefore,
320 the ‘Face group’ learned to voluntarily increase the difference in BOLD
321 between FFA and PPA. In contrast, the ‘House group’ learned to voluntarily
322 increase the difference in BOLD between PPA and FFA.

323

324 For each group there was a *strategy-related ROI* (e.g. FFA for the Face group
325 and a *strategy-unrelated ROI* (e.g. PPA for the Face group, and vice versa for
326 the House group, Figure 2A).

327

328 **Day 5: Transfer Session**

329 After the final neurofeedback training session, there were two transfer
330 sessions, each comprising six blocks. Each block lasted 60 s and consisted of
331 an 'upregulate' period (40 s) followed by 'rest' (20 s). During upregulation,
332 participants were required to drive their brain activity 'up', using the mental
333 imagery strategies successfully used to drive the bar during neurofeedback
334 training, but now in the absence of a feedback signal.

335

336 **Day 5: Post-training BR**

337 All participants then performed post-training BR, with the same set-up
338 described for pre-training BR. Three different BR conditions were performed
339 (2 sessions each) pseudorandomised and counterbalanced across all
340 participants: (1) **Post-training BR**. The instruction was identical to the pre-
341 training BR; (2) **Post-training BR with 'concurrent trained upregulation'**.
342 Both groups were instructed to use their trained mental imagery strategies
343 that had worked best during the training sessions while simultaneously
344 performing BR; and (3) **Post-training BR with 'concurrent non-trained**
345 **mental imagery'**. Participants were instructed to use mental imagery related
346 to either houses if in the 'Face group', or faces if in the 'House group'. Mental
347 imagery was to be performed while concurrently performing BR.

348

349 **Brain Imaging**

350

351 Functional data was analysed using SPM12 (<http://www.fil.ion.ucl.ac.uk/spm>).
352 To allow for T1 equilibration the first five images of each session were
353 discarded. Preprocessing involved bias correction, realignment of each EPI to
354 the mean EPI, unwarping, and co-registration of the functional data to the

355 structural image. Normalisation was not performed, as initial analyses were
356 performed in native space. Data was smoothed with a 6 mm FWHM Gaussian
357 kernel and high-pass filtered (128s cut-off) to remove low-frequency noise,
358 while at the same time preserving as many of the spontaneous fMRI
359 fluctuations as possible(Cordes et al., 2001). Session-specific grand mean
360 scaling was applied with no global normalisation.

361

362 **Offline ROI Analysis: *Fusiform Face Area and Parahippocampal Place*** 363 ***Area***

364

365 **Neurofeedback**

366 BOLD signals across the 9 training sessions (acquired on Days 2-4) were
367 modeled using a GLM, with regressors for each of the 9 sessions. Boxcar
368 functions were created for the six upregulation blocks, convolved with the
369 canonical HRF. Six regressors for movement and a global constant were
370 included. Beta values from the GLM were averaged across all the voxels in
371 the ROI masks (FFA and PPA ROIs based on the functional localiser). Mean
372 percentage signal change (PSC) was then calculated. For each participant,
373 the differential mean PSC between the two ROIs (i.e. strategy-related ROI
374 minus strategy-unrelated ROI) was calculated across sessions. From this, the
375 average mean PSC across participants over the training was calculated.

376

377 **Transfer Sessions**

378 Two transfer sessions were performed, with participants performing six blocks
379 of upregulation of brain activity as trained, but now in the absence of a

380 neurofeedback signal. In a similar manner to the neurofeedback sessions
381 (see above), the differential mean PSC between the two ROIs (i.e. strategy-
382 related ROI minus strategy-unrelated ROI) was calculated across sessions,
383 and from this, the average mean PSC across participants over transfer was
384 calculated.

385

386 **Binocular Rivalry**

387 Boxcar functions were created to model the onset of the BR block, convolved
388 with the canonical HRF, for each BR condition. A GLM was performed at the
389 single participant level. Beta values for each of the trained ROIs were
390 averaged for each condition and adjusted for the global brain signal. Mean
391 percentage signal change (PSC) was then calculated.

392

393 For inferential statistical analyses, SPSS 21 (IBM Corp. Armonk, USA) was
394 used to perform ANOVAs and follow-up planned paired sample t-tests, which
395 were two-tailed unless otherwise stated.

396

397 **Control Experiment- Mental Imagery:**

398

399

400 **Experimental outline**

401

402 Ten different participants (age range = 22-39 years, mean age 30. years, 8
403 females) were recruited for a control BR experiment. They viewed a Dell LCD
404 monitor (width: 43.5 cm; resolution: 1600 900; refresh rate: 60 Hz) from a
405 distance of 43 cm (fixed using a chin rest) through a mirror stereoscope. The
406 stereoscope reflected the left and right sides of the screen into the

407 participants' left and right eyes, so that each eye was presented with only one
408 of the two images (house or face). In order to ensure robust fusion of
409 binocular images, prior to the start of BR task, fusion was achieved for each
410 participant by slowly moving two grey squares from the edge toward the
411 centre of the screen. At the beginning of this process the participants would
412 see two squares. By the end of this process the participants would report
413 when they were seeing one square. All testing took place in a darkened room.
414 During the viewing blocks, a face stimulus and a house stimulus were
415 presented in the left and right hemi-fields respectively. The stimuli were
416 pseudorandomised with regards to which eye received the face or house
417 stimuli. Each viewing block (40 s followed by rest 20 s) was performed with a
418 new pair of stimuli from the pool of twenty stimuli. Six blocks were performed
419 per session, for three sessions. Participants were instructed to indicate a
420 perceptual shift only if the whole exemplar was perceived; any combination or
421 'patchwork' percept regardless of the predominance of the exemplar category
422 was reported as a 'mixed' percept. The participants were instructed to switch
423 as accurately and rapidly as possible between three possible button presses
424 linked to the three perceptual states (face percept, house percept, mixed
425 percept). This resulted in measures of the cumulative duration of the percept
426 throughout the BR measurement period.

427

428 BR was performed in this manner prior to and after 3 days of consecutive
429 mental imagery training (see below).

430

431 **Mental Imagery Training over 3 Days**

432

433 Participants returned to perform mental imagery training. Participants were
434 pseudorandomised into two equal groups, and were explicitly advised to use
435 mental imagery strategies that involved faces ('Face group') or house/places
436 ('House group'). Mental imagery was undertaken while viewing a LCD monitor
437 screen with a fixed horizontal black bar. They were told to imagine pushing a
438 bar above the fixed black bar, while performing their mental imagery
439 strategies. Each mental imagery training session comprised three sessions,
440 each including six blocks of 60 s with a 'perform mental imagery' period (40 s)
441 followed by 'rest' (20 s).

442

443 **Brain Structural Analysis**

444

445 The structural analysis was performed using Tensor Based Morphometry
446 (TBM), an emerging computational analysis technique(Ceccarelli et al., 2009;
447 Farbota et al., 2012; Li et al., 2009; Wang et al., 2013; Welch et al., 2013),
448 which is better suited to studies with smaller participant samples. TBM
449 enables longitudinal quantitative assessment by identifying regional structural
450 differences from the gradients of the deformation fields that nonlinearly warp
451 each individual image to the template.

452

453 For each participant, high-resolution T1 structural images were reoriented
454 placing the anterior commissure at the MNI origin. Longitudinal nonlinear
455 registration(Ashburner and Ridgway, 2012) was performed to align the two
456 time-points (before and after training) to their within-subject average,

457 characterising the relative volumetric expansion or contraction (as the
458 divergence of a velocity field) of each voxel in each time-point with respect to
459 the average. The within-subject average images were then segmented to
460 produce grey and white matter segmentations for each participant (Ashburner
461 and Friston, 2005). These segmentations were nonlinearly aligned to their
462 group-wise average using DARTel (Ashburner, 2007), and the final DARTel
463 average template was affinely registered to MNI space. The resultant
464 between-subject transformations were then used to spatially normalise the
465 divergence maps of the velocity fields, which were finally smoothed with a
466 6mm FWHM Gaussian kernel.

467

468 Divergence measures for each participant were then extracted within
469 spherical ROIs for FFA and PPA (6 mm). The spheres were centered on
470 coordinates that demonstrated the highest functional activity within the
471 localiser ROIs across training. A t-test was then performed to establish if a
472 specific brain region had changed significantly before versus after training.

473

474 **Canonical Variate Analysis**

475

476 We used a Canonical Variate Analysis (CVA) to demonstrate that measures
477 of change in brain activation and brain structure following neurofeedback
478 training predicted changes in behavioural measures. Also known as a
479 multivariate analysis of variance, or ManCova (Friston et al., 2014, 1995),
480 CVA enables statistical inferences to be made about associations between
481 the imaging data, and behavioural data that are distributed over variables. It

482 was chosen for analysis of this dataset because it can accommodate
483 statistical dependencies between multivariate predictor variables (behavioural
484 changes) and multivariate outcome variables (functional or structural
485 measures). Neither the behavioural nor imaging data had to be examined in
486 isolation, which had the advantage that distributed changes could be
487 identified, while minimising the multiple comparisons problem. The
488 behavioural changes for each participant was the change in dominance
489 duration of each the three percepts (e.g. *strategy-related* percept, *strategy-*
490 *unrelated* percept, *mixed* percept) between the pre-training BR condition and
491 post-training BR (Figure S3), and between the pre-training BR condition and
492 post-training BR with concurrent trained up-regulation (Figure S3). As the
493 behavioural and structural measures were taken prior to and immediately after
494 neurofeedback training, the functional measures for each participant were the
495 change in the different signal between the first and the last training run (e.g.
496 run 1 and run 9). The structural measures for each participant were the
497 divergence measures for each ROI, FFA and PPA (6 mm).

498

499 The objective of the CVA was to find the linear combination of outcome
500 variables that was best predicted by a linear mixture (contrast) of structural or
501 functional components. The weights of these linear combinations are called
502 canonical vectors. The canonical variates of the outcome and predictor
503 variables are the expression of each canonical vector in each subject. Other
504 quantities generated by the CVA include Bartlett's approximate chi-squared
505 statistic for Wilks' Lambda and its associated significance, or p-value, which
506 test for the significance of a linear mapping or correlation between the

507 canonical variates (in other words, if one or more pairs of canonical variates
508 show a significant statistical dependency).

509

510

511

512

513 **Results**

514

515 We first examined the effect of neurofeedback training on behaviour using
516 three comparisons. We compared perceptual dynamics, specifically
517 cumulative dominance durations, performed during BR before and after
518 training. We then examined the effects of learned upregulation on BR by
519 comparing pre-training BR versus post-training BR with concurrent ‘learned’
520 upregulation of brain activity. For the final comparison, we examined the non-
521 trained mental imagery on BR, by comparing perceptual dynamics during pre-
522 training BR versus post-training BR with concurrent non-trained mental
523 imagery. The effects of trained mental imagery were additionally examined
524 separately – see Mental Imagery Control Experiment and Figure S1
525 (Supplementary Materials).

526

527 As the durations of the three percepts were dependent on each other, a
528 change in one percept occurred linked to changes in one or both of the other
529 percepts.

530

531 **Within Condition Comparisons:**

532 ***Comparison 1. Pre-training BR vs. Post-training BR***

533 Comparing behavioural measures of pre-training BR and post-training BR
534 indicated an effect of training (Figure 3). Paired t-tests revealed a significant
535 reduction in the cumulative dominance durations (i.e. how long a percept type
536 was perceived) for the strategy-unrelated percept ($t(9)=2.88, p=0.02$), and a
537 significant increase in mixed percept durations ($t(9)=2.74, p=0.02$), with no

538 significant change in the dominance duration of the strategy-related percept
539 ($t(9)=0.46, p=0.66$).

540

541 ***Comparison 2. Pre-training BR vs. Post-training BR with Concurrent***
542 ***Trained Upregulation***

543 Paired t-tests revealed a significant reduction in the duration of the strategy-
544 unrelated percept ($t(9)=4.76, p=0.001$), and a significant increase in the
545 duration of the mixed percept ($t(9)=2.68, p=0.03$). There was no significant
546 change in the dominance duration of the strategy-related percept
547 ($t(9)=0.53, p=0.61$) (Figure 3). The changes in BR dynamics were similar to
548 those observed with pre-training BR vs. post-training BR (Comparison 1).

549

550 ***Comparison 3. Pre-training BR vs. Post-training BR with concurrent***
551 ***Non-trained Mental Imagery***

552 Paired t-tests indicated a significant reduction in the duration of the strategy-
553 related percept ($t(9)=2.41, p=0.04$), and a significant increase in the duration
554 of the mixed percept ($t(9)=2.68, p=0.03$). There was no significant change in
555 the dominance duration of the strategy-unrelated percept ($t(9)=0.12, p=1.74$).

556

557 We further examined differences between conditions.

558

559 **Between Condition Comparisons:**

560

561 ***1. Post-training BR vs. Post-training BR with Concurrent Trained***
562 ***Upregulation (Comparison 1 vs. Comparison 2)***

563 There was a significantly greater reduction in the dominance duration of the
564 strategy-unrelated percept ($t(9)=2.40$, $p=0.04$) in Comparison 2 as compared
565 with Comparison 1 (Figure 3B). There were no other significant differences
566 between the two comparisons (strategy-related percept: $t(9)=0.95$, $p=0.37$;
567 mixed percept: $t(9)=0.90$, $p=0.39$).

568

569 ***2. Post-training BR vs. Post-training BR with Non-trained Mental Imagery***
570 ***(Comparison 1 vs. Comparison 3)***

571 There was a significantly greater reduction in the dominance duration of the
572 strategy-related percept ($t(9)=3.12$, $p=0.01$) (Figure 3B). There was also a
573 significantly greater increase in the dominance duration of the mixed percept
574 ($t(9)=2.62$, $p=0.03$). There were no significant changes in the strategy-
575 unrelated percept ($t(9)=0.09$, $p=0.93$)

576

577 ***3. Post-training BR with Concurrent Trained Upregulation vs. Post-***
578 ***training BR with Non-trained Mental Imagery (Comparison 2 vs.***
579 ***Comparison 3)***

580 There was a trend towards reduction in the dominance duration of the
581 strategy-related percept ($t(9)=2.23$, $p=0.05$) in Comparison 3 as compared
582 with Comparison 2 (Figure 3B). The other two comparisons were not
583 significant (strategy-related percept: $t(9)=0.95$, $p=0.37$; mixed percept:
584 $t(9)=1.1$, $p=0.30$).

585

586 **Functional Changes during Neurofeedback Training**

587 To test if neurofeedback training resulted in progressive learning, we
588 examined whether participants demonstrated increased control of the
589 differential feedback signal over the three training days (Figure 2B). A
590 repeated-measures ANOVA with a factor of training day (3 levels; Days 1-3)
591 demonstrated a significant effect ($F(2,16)= 3.74, p= 0.047$). Post-hoc t-tests
592 demonstrated a significant increase in the differential signal from Day 2
593 onwards, suggesting a learning effect (Day 1: $t(9)=0.88, p= 0.40$; Day 2:
594 $t(9)=3.27, p=0.001$; Day 3: $t(8)=2.75, p=0.02$).

595

596 **Functional Changes during Transfer**

597 Following neurofeedback training and prior to BR, voluntary control of brain
598 activation in the absence of neurofeedback was confirmed in a 'transfer
599 session'. Differential BOLD activation (strategy-related ROI minus strategy-
600 unrelated ROI) pooled across the two transfer sessions, revealed a significant
601 effect ($t(9)=2.38, p= 0.04$).

602

603 **Functional Changes during Binocular Rivalry**

604 We examined task-related BOLD signals in the trained ROIs (FFA and PPA)
605 comparing pre-training BR with post-training BR. We observed significant
606 reductions in BOLD signals in both the strategy-related ROI ($t(9)= 3.43, p=$
607 0.007) and strategy-unrelated ROI ($t(9)= 2.26, p=0.04$), when comparing pre-
608 training BR with post-training BR.

609

610 Comparing pre-training BR versus post-training BR with concurrent trained
611 upregulation, there was a significant reduction in the activation level of the

612 strategy-unrelated ROI ($t(9) = 2.48$, $p = 0.03$). No significant change was noted
613 for the strategy-related ROI ($t(9) = 1.41$, $p = 0.19$). We performed one-tailed t-
614 tests as we had an *a priori* hypothesis that following neurofeedback training,
615 participants should be able to increase the difference in BOLD activation
616 between the two trained ROIs (Figure 4).

617

618 There were no significant changes for pre-training BR versus post-training BR
619 with concurrent non-trained mental imagery (strategy related ROI: $t(9) = 0.82$,
620 $p = 0.44$; strategy unrelated ROI: $t(9) = 0.83$, $p = 0.43$).

621

622 **Mental Imagery Control Experiment**

623

624 There was no evidence of significant changes in the cumulative dominance
625 durations of any of the three percepts (strategy-related percept $t(9) = 0.74$, $p =$
626 0.48 ; strategy-unrelated percept, $t(9) = 1.00$, $p = 0.34$; mixed percept, $t(9) =$
627 2.00 , $p = 0.07$).

628

629 ***Between Group Comparisons with 'Mental Imagery' Control Group***

630 We performed an ANOVA with a within-subjects factor of percepts (*strategy-*
631 *related percept, strategy-unrelated percept, mixed percept*) and a between-
632 subjects factor of group (Group 1: neurofeedback, Group 2: mental imagery).

633 There was a main effect of percept ($F(2,36) = 4.64$, $p = 0.02$). There was no
634 interaction ($F(2,36) = 2.65$, $p = 0.08$) between these two factors.

635

636 We performed a second ANOVA with a within-subjects factor of percepts
637 (*strategy-related percept, strategy-unrelated percept, mixed percept*) and a
638 between-subjects factor of group (Group 1: neurofeedback with concurrent-
639 upregulation, Group 2: mental imagery). There was a main effect of percept
640 ($F(2,36)=6.68, p=0.003$), and an interaction between percept and group
641 ($F(2,36)= 5.29, p= 0.01$). Follow-up two-sample t-tests looking at changes in
642 durations of the similar percepts showed a significant difference for the
643 strategy-unrelated percept ($t(9)= 2.35, p= 0.04$), but not for strategy-related
644 percept ($t(9)= 1.04, p= 0.32$) or the mixed percept, ($t(9)= 2.00, p= 0.08$).

645

646 We performed a further ANOVA with a within-subjects factor of percepts
647 (*strategy-related percept, strategy-unrelated percept, mixed percept*) and a
648 between-subjects factor of group (Group 1: neurofeedback with concurrent
649 non-trained mental imagery, Group 2: mental imagery). There was a main
650 effect of percept ($F(2,36)= 6.70, p= 0.003$), and an interaction between
651 percept and group ($F(2,36)= 3.63, p= 0.04$). Follow-up two-sample t-tests
652 looking at changes in durations of the similar percepts showed a significant
653 difference for the mixed percept ($t(9)= 2.79, p= 0.02$), but not for strategy-
654 related percept ($t(9)= 1.00, p= 0.86$) or the strategy-unrelated percept, ($t(9)=$
655 $0.29, p= 1.14$).

656

657

658

659 **Results - Structural**

660

661 The results of the longitudinal non-rigid registration were used to determine
662 volume changes in the ROIs by calculating the divergence of the velocity
663 fields. One-sampled t-tests of these values were used to calculate if any
664 significant structural changes had taken place as a result of neurofeedback
665 training. They were not significant for both ROIs i.e. FFA ($t(9) = 0.36, p > 0.05$),
666 and PPA ($t(9) = 0.46, p > 0.05$),

667

668 **Results – Canonical Variate analysis**

669

670 Plots for comparisons of combined measures in: (1) behaviour (dominance
671 durations for the three perceptual reports) and functional (BOLD changes
672 across training in FFA, PPA); and (2) behaviour and structural measures
673 (measure of the volume changes in FFA and PPA following training) are
674 presented in Figure S4, together with Bartlett's approximate chi-squared
675 statistic for Wilks' Lambda and its p-value, for each comparison.

676

677 The participant neurofeedback training measures (i.e. differential BOLD brain
678 activation) had a trend to being correlated with changes in BR behavioural
679 dynamics as recorded during BR with concurrent trained upregulation of brain
680 activation (compared with pre-training BR) (chi-squared value = 12.35, $p =$
681 0.05). Comparison of changes in the neurofeedback training measures with
682 behavioural changes during 'simple BR' before and after training was non-
683 significant (chi-square value = 11.43, $p = 0.07$). Significant correlations were

684 noted between structural changes in both ROIs and the change in BR
685 dynamics produced during concurrent trained upregulation of brain activation
686 (chi-squared value = 19.64, $p= 0.03$). Comparison of structural measures with
687 behavioural measures during 'simple BR' before and after training was non-
688 significant (chi-square value = 13.77, $p= 0.09$).

689

690 Of note, the mapping weights obtained for the behavioural measures and the
691 training-related BOLD measures were independent of the mapping weights
692 obtained for the behavioural measures and the structural measures. This is
693 because these multivariate mapping values were specific to the measures
694 used in the comparisons. Finally, the interpretation of the mapping weights in
695 relation to having a positive or negative value did not indicate a positive or
696 negative change in the values (e.g. an increase or decrease in structural
697 measures). Rather they represent a positive (or negative) contribution to the
698 mapping between the multivariate predictor variable and the outcome
699 variables.

700

701 **Discussion**

702
703

704 Participants learned to differentially regulate the amplitude of BOLD activation
705 in two higher-order visual brain regions, FFA and PPA. This was achieved in
706 realtime, through volitional control using neurofeedback training with rt-fMRI.
707 The use of a '*differential*' training signal was implemented by showing the
708 participants a 'thermometer bar' whose size represented the difference in the
709 mean BOLD signal between the two selected brain regions. By doing this, one
710 of the brain regions acted as an internal control for the other, accounting for
711 potential confounds produced by global changes in brain activation in
712 response to effects such as arousal. Furthermore, specific behavioural effects
713 linked with the direction of change of the differential training signal were
714 obtained, providing a comparison of behavioural metrics for the training
715 effect(Thibault et al., 2018). The effect on visual perception was examined
716 with an independent BR task that employed stimuli specifically engaging
717 these stimulus-selective brain regions (face stimuli for FFA, house stimuli for
718 PPA). During BR, moment-to-moment stochastic alternations between two
719 competing visual percepts are observed, while concurrent brain activity can
720 be recorded and potentially manipulated(Blake et al., 2014; Blake and
721 Logothetis, 2002).

722

723 In this study, a change in BR perceptual dynamics was observed following
724 neurofeedback training. Perception of the stimulus linked to neurofeedback
725 training was rendered more stable e.g. strategy-related percept, with a
726 reduction in the perception of the *other* stimulus e.g. strategy-unrelated

727 percept. This behavioural change occurred when comparing pre-training BR
728 with post-training BR, and additionally when participants performed post-
729 training BR while concurrently performing learned ‘upregulation’ of brain
730 activity. We compared pre-training ‘BR’ with three post-training BR conditions:
731 ‘post-training BR’, ‘post-training BR with concurrent trained upregulation’, and
732 ‘post-training BR with concurrent non-trained mental imagery’. The first
733 comparison, examining changes during BR before and after neurofeedback
734 training, showed altered BR dynamics; specifically a reduction in the
735 cumulative dominance duration of the strategy-unrelated percept. These
736 findings are important, as they show that neurofeedback training produced a
737 behavioural effect that was: (1) counter-intuitive in that percept durations were
738 not increased in line with the verbally instructed neurofeedback training
739 strategy, which was initially expected. Rather, percept durations *not* linked to
740 the neurofeedback training strategy (e.g. strategy-unrelated percept) were
741 reduced; (2) aligned with a longstanding finding in the field, namely Levelt’s
742 second proposition (discussed below); and (3) indicative of a lack of demand
743 characteristics (see also Mental Imagery Control Experiment).

744

745 There was a significant reduction in the levels of activation in both ROIs,
746 comparing pre-training BR versus post-training BR. This linked neuroimaging
747 finding was unexpected, as the prediction from existing literature (Tong et al.,
748 1998) is that BOLD activation levels in extrastriate visual areas will reflect
749 dominance durations. The expected finding might have been that activation
750 levels would be lower in the strategy-unrelated ROI. Our findings instead
751 showed that both regions were affected by neurofeedback training, as we

752 expected given that participants trained on a differential signal involving both
753 ROIs. Both ROIs demonstrated a reduction in activation, which may reflect an
754 increase in neural efficiency as a result of more precise tuning of neural
755 representations(Gimenez et al., 2014; Haler et al., 1992; Heinzl et al., 2014;
756 Vartanian et al., 2013). The exact mechanisms underlying this gain are
757 unknown, particularly in the context of neurofeedback training and thus
758 warrants further study(Poldrack, 2015).

759

760 The purpose of the second comparison ('pre-training BR' versus 'post-training
761 BR with concurrent upregulation') was to examine if there was an effect of
762 concurrent trained modulation of brain activation on BR dynamics that was
763 additive or different to the effect of neurofeedback training alone. We
764 observed a change in BR dynamics that was similar and greater to that
765 observed for pre-training BR vs. post-training BR, in that there was *more of a*
766 *reduction* in the mean dominance duration of the strategy-unrelated percept.
767 This confirmed that the effect of trained upregulation was directly aligned with
768 the effect of neurofeedback training on BR dynamics. There was a decrease
769 in the level of BOLD activation in the strategy-unrelated ROI only, with no
770 significant change in the strategy-related ROI. Interestingly, these BOLD
771 activation changes were the same as those observed during neurofeedback
772 training (a reduction in activation levels of the strategy-unrelated ROI, Figure
773 2B). This provides further evidence for a similar mechanism underlying the
774 changes in BR dynamics following training and for those observed with
775 concurrent trained upregulation. The counter-intuitive effect of training and up-
776 regulation (during BR) on the brain activations in the two ROIs (i.e. opposite to

777 an *a priori* instruction and predicted direction of activation changes) is
778 intriguing and worthy of further investigation (Abel et al., 2015; Bueichekú et
779 al., 2016).

780 The third comparison ('pre-training BR' versus 'post-training BR with non-
781 trained mental imagery') served to assess the impact of using a differential
782 training signal, which was hypothesised to have an effect on both ROIs in all
783 participants. It additionally helped reveal the role of *non-trained* mental
784 imagery in the context of prior neurofeedback training. No significant change
785 in brain activation in either ROI was observed. However, BR dynamics
786 changed in a similar manner to the other two post-neurofeedback training BR
787 conditions, with a significant reduction in the duration of the percept not linked
788 to the training strategy used during training. This reduction was significant
789 when comparing changes in perceptual dynamics across conditions. These
790 behavioural findings would therefore suggest that neurofeedback training,
791 despite the lack of a statistically significant BOLD effect, produced a more
792 general effect on the neurobiology of the two trained ROIs. The exact nature
793 of this effect may be complex, given that behavioural changes observed for
794 this condition were opposite to the direction of neurofeedback training, but
795 nonetheless sufficient to produce an effect e.g. 'House' group participants
796 specifically underwent neurofeedback training with 'House-based' mental
797 imagery strategies, and yet they generated changes in BR dynamics simply
798 by using non-trained 'face' based mental imagery strategies during the
799 performance of BR. These behavioural findings are different from Rademaker
800 and Pearson's work, in which using mental imagery training *did not* produce
801 training-related changes in BR dominance duration. Five successive days of

802 mental imagery training had no effect on BR, with no benefit being conferred
803 by expending increased effort during mental imagery generation(Rademaker
804 and Pearson, 2012). On the other hand, Rademaker and Pearson’s findings
805 are in keeping with our own mental imagery control experiment, indicating the
806 relevance of neurofeedback training. We conducted a behavioural control
807 experiment in which a different group of participants performed BR before and
808 after three consecutive days of mental imagery training, which was analogous
809 to the neurofeedback training. The training was again explicitly linked to one
810 of the two stimuli used in BR (face mental imagery for a ‘Face group’, house
811 mental imagery for a ‘House group’). However there was no targeted training
812 strategy for the brain, unlike with the neurofeedback-trained groups. No
813 significant changes in dominance durations of any of the three percepts were
814 observed.

815

816 Taken together, these results indicate that short-term intensive training over 3
817 days on a neurofeedback BOLD signal produced by two brain regions,
818 engages and alters the function and biology of *both* regions. This is
819 specifically supported by the shift in perceptual dynamics during BR following
820 neurofeedback training, and the activation changes observed in both ROIs
821 (see Results: Comparison 1). It is further supported more broadly by the
822 behavioural changes observed in all of the post-neurofeedback training BR
823 conditions, which were not observed in the mental imagery control
824 experiment. Habes et al.(Habes et al., 2016) have previously confirmed that
825 although differential regulation of category-specific visual areas can be
826 achieved after a single day of training, a linked change in BR dynamics was

827 not produced. We therefore suggest that in order for mental imagery to
828 produce a change in perception, it must be linked with neurofeedback-led
829 learning, conducted over a period of days. This may be attributable to the
830 interposition of sleep with sequential daily training. Sleep has been directly
831 linked with the offline processing necessary for the consolidation of
832 neuroprosthetic learning(Gulati et al., 2014) and associated behavioural
833 output(Gulati et al., 2017).

834

835 Mental imagery may be utilised for perceptual learning of low-level visual
836 features, and to activate stimulus-selective cortical representations(O'Craven
837 and Kanwisher, 2000; Tartaglia et al., 2009). Similarly, rt-fMRI neurofeedback
838 together with implicit operant reinforcement has been used to unconsciously
839 train patterns of activation in primary visual brain regions(Amano et al., 2016;
840 Shibata et al., 2011) to produce perceptual and associative learning of low-
841 level visual features such as colour and orientation. However, to-date neither
842 approach has successfully yielded changes in higher-order visual perception.
843 In this study, we show that coupling explicitly instructed mental imagery with
844 rt-fMRI neurofeedback training of higher-order visual brain regions produces
845 an unconscious and targeted shift in the perceptual processing of visual
846 stimuli. This result is novel and significant in providing evidence for non-
847 invasively manipulating higher-order brain function, potentially at the level of
848 directly strengthening neural representations to alter higher-order
849 perception(Fahle, 2002; Watanabe et al., 2002, 2001). From a mechanistic
850 perspective, an interesting next step might be to test if unconsciously inducing
851 specific patterns of brain activations related to category-specific stimuli will

852 produce linked shifts in perception in a similar manner to that observed in this
853 study(Watanabe et al., 2017). This would provide more direct evidence of
854 modulating neural representations.

855

856 The observed behavioural findings may constitute a neural analogue of
857 Levelt's second proposition(Levelt, 1966), as applied to stimulus perception.
858 The original proposition (see Supplementary Discussion) was based on the
859 physical properties of visual stimuli. It was recently modified to indicate that
860 *'increasing the difference in stimulus strength between the two eyes will*
861 *primarily act to increase the average perceptual dominance duration of the*
862 *stronger stimulus'*(Brascamp et al., 2015). Our work may provide evidence for
863 a neural reformulation of BR. Participants were trained on a differential signal,
864 rather than specifically training to increase the level of activation in the
865 strategy-related ROI. During training, they appeared to reduce the level of
866 activation in the strategy-unrelated ROI across the three days, while
867 maintaining a fixed level of activation in the strategy-related ROI (Figure 2B).
868 This difference in activation levels as a result of training was maintained when
869 the participants undertook the transfer sessions, an assessment of
870 upregulation in the absence of neurofeedback. The difference in ROI
871 activation levels may have therefore led to a relative difference in the
872 strengths of the neural representations linked to the visual stimulus
873 categories. In keeping with this view, we observed a reduction in the mean
874 dominance duration of the strategy-unrelated percept. This resulted in greater
875 mean dominance durations of the strategy-related percept, corresponding to
876 the ROI with the strengthened neural representation. On the basis of this, we

877 propose a possible neural analogue of the Levelt's modified second
878 proposition as follows: *'increasing the difference in neural representation*
879 *strengths between the two brain regions linked to the two monocular visual*
880 *stimuli will primarily act to increase the average perceptual dominance of the*
881 *percept linked to the stronger neural representation'*. The effect of this would
882 be to produce unconscious perceptual biasing towards the strengthened
883 percept. This mechanism for perceptual 'shaping'(Lange et al., 2018) may
884 have real-world application in conditions requiring targeted enhancement of
885 perception such as in threat detection(Miranda et al., 2015), or therapeutically
886 to reduce unwanted or aberrant percepts(Taschereau-Dumouchel et al.,
887 2018).

888

889 Several mechanisms have been put forward to explain the neural
890 underpinnings of BR. Of note, known influences on visual perception such as
891 priming and cueing have not been shown to produce changes in BR
892 dominance durations (see also Supplementary Discussion). Neurofeedback
893 with rt-fMRI provides the most direct means of testing neuronal function
894 involved in processing visual stimuli. Using a hierarchical model of BR(Dayan,
895 1998), it may be proposed that neurofeedback training of higher order brain
896 regions strengthens neuronal representations linked to the processing of
897 specific visual stimuli, leading to unconscious perceptual biasing. Preferential
898 processing of strategy-related stimuli would result in decreased dominance
899 durations of the strategy-unrelated stimuli, as was observed here. The effect
900 of neurofeedback on BR may be further considered within a Bayesian
901 framework(Lange et al., 2018). During BR, the dominant percept at any given

902 time is maintained by the highest posterior probability, at the top of the cortical
903 hierarchy. Stimulus representations at lower levels generate error signals that
904 are compared with top-down predictions. The percept is rendered more or
905 less stable in relation to bottom-up inhibition i.e. the lower the error signal, the
906 more stable the percept(Alink et al., 2010; Hohwy et al., 2008; Summerfield
907 and Koechlin, 2008). In keeping with this, BR dynamics were shifted in the
908 direction of the information represented in the trained visual brain regions.
909 Therefore, perception of the stimulus linked to training was rendered more
910 stable, with a simultaneous reduction in the stability of the perception of the
911 other stimulus, leading to a reduction in its mean dominance duration.

912 The changes in high-level visual perception following neurofeedback training
913 in this study were associated with structural changes in the trained regions
914 (see Supplementary Materials). We used a multivariate analysis technique,
915 Canonical Variate Analysis, which can accommodate multiple measures of
916 behaviour, structure, and function to help determine the overarching effect of
917 neurofeedback training. The change in BR dynamics (i.e. cumulative
918 dominance durations) was linked with measures of structural changes in FFA,
919 and PPA (Figure S3, Supplementary Materials). These preliminary findings in
920 ten participants suggest that neurofeedback training, even over a relatively
921 short period of time (3 days) can alter perception as a result of plasticity in the
922 trained brain regions(Johansen-Berg et al., 2012; Sagi et al., 2012).

923

924 In this study, we provide a direct demonstration of the rapid changes in
925 perception and neural plasticity that can be produced by neurofeedback
926 training of higher-order visual areas using rt-fMRI. Imagery-related activation

927 in higher-order visual cortex, such as the ventral visual areas, are related to
928 semantic content, and are more flexible and abstract(Orban et al., 2014) as
929 compared to early visual cortex. Therefore, the use of higher-order visual
930 areas paired with rt-fMRI neurofeedback training may provide the most potent
931 and generalizable means of enacting a change on complex perception. Neural
932 representations that give rise to prior expectations can be directly shifted in
933 the direction of neurofeedback training, even in the presence of pre-existing
934 expectations. This could lead to targeted enhancement of specific responses
935 during discrete tasks as demonstrated here using BR, or in the reduction of
936 aberrant visual perception, such as hallucinations, for therapeutic
937 effect(Lange et al., 2018).
938

939 **References**

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941

- 942 Abel, S., Weiller, C., Huber, W., Willmes, K., Specht, K., 2015. Therapy-
943 induced brain reorganization patterns in aphasia. *Brain* 138, 1097–1112.
944 doi:10.1093/brain/awv022
- 945 Alink, A., Schwiedrzik, C.M., Kohler, A., Singer, W., Muckli, L., 2010. Stimulus
946 predictability reduces responses in primary visual cortex. *J. Neurosci.* 30,
947 2960–6. doi:10.1523/JNEUROSCI.3730-10.2010
- 948 Amano, K., Shibata, K., Kawato, M., Sasaki, Y., Watanabe, T., 2016. Learning
949 to Associate Orientation with Color in Early Visual Areas by Associative
950 Decoded fMRI Neurofeedback. *Curr. Biol.* 26, 1861–1866.
951 doi:10.1016/j.cub.2016.05.014
- 952 Ashburner, J., 2007. A fast diffeomorphic image registration algorithm.
953 *Neuroimage* 38, 95–113. doi:10.1016/j.neuroimage.2007.07.007
- 954 Ashburner, J., Friston, K.J., 2005. Unified segmentation. *Neuroimage* 26,
955 839–51. doi:10.1016/j.neuroimage.2005.02.018
- 956 Ashburner, J., Ridgway, G.R., 2012. Symmetric diffeomorphic modeling of
957 longitudinal structural MRI. *Front. Neurosci.* 6, 197.
958 doi:10.3389/fnins.2012.00197
- 959 Blake, R., Brascamp, J., Heeger, D.J., Brascamp, J., 2014. Can binocular
960 rivalry reveal neural correlates of consciousness ?
- 961 Blake, R., Logothetis, N.K., 2002. Visual competition. *Nat. Rev. Neurosci.* 3,
962 13–21. doi:10.1038/nrn701
- 963 Blefari, M.L., Sulzer, J., Hepp-Reymond, M.-C., Kollias, S., Gassert, R., 2015.
964 Improvement in precision grip force control with self-modulation of

965 primary motor cortex during motor imagery. *Front. Behav. Neurosci.* 9,
966 18. doi:10.3389/fnbeh.2015.00018

967 Brascamp, J.W., Klink, P.C., Levelt, W.J.M., 2015. The ‘laws’ of binocular
968 rivalry: 50 years of Levelt’s propositions. *Vision Res.* 109, 20–37.
969 doi:10.1016/j.visres.2015.02.019

970 Bueichekú, E., Miró-Padilla, A., Palomar-García, M.-Á., Ventura-Campos, N.,
971 Parcet, M.-A., Barrós-Loscertales, A., Ávila, C., 2016. Reduced posterior
972 parietal cortex activation after training on a visual search task.
973 *Neuroimage* 135, 204–213. doi:10.1016/j.neuroimage.2016.04.059

974 Ceccarelli, A., Rocca, M.A., Pagani, E., Falini, A., Comi, G., Filippi, M., 2009.
975 Cognitive learning is associated with gray matter changes in healthy
976 human individuals: a tensor-based morphometry study. *Neuroimage* 48,
977 585–9. doi:10.1016/j.neuroimage.2009.07.009

978 Cordes, D., Haughton, V.M., Arfanakis, K., Carew, J.D., Turski, P.A., Moritz,
979 C.H., Quigley, M.A., Meyerand, M.E., 2001. Frequencies Contributing to
980 Functional Connectivity in the Cerebral Cortex in “Resting-state” Data.
981 *AJNR Am. J. Neuroradiol.* 22, 1326–1333.

982 Dayan, P., 1998. A hierarchical model of binocular rivalry. *Neural Comput.* 10,
983 1119–35.

984 deCharms, R.C., Christoff, K., Glover, G.H., Pauly, J.M., Whitfield, S.,
985 Gabrieli, J.D., 2004. Learned regulation of spatially localized brain
986 activation using real-time fMRI. *Neuroimage* 21, 436–443.
987 doi:10.1016/j.neuroimage.2003.08.041

988 Deichmann, R., Schwarzbauer, C., Turner, R., 2004. Optimisation of the 3D
989 MDEFT sequence for anatomical brain imaging: technical implications at

990 1.5 and 3 T. *Neuroimage* 21, 757–67.
991 doi:10.1016/j.neuroimage.2003.09.062

992 Eickhoff, S.B., Heim, S., Zilles, K., Amunts, K., 2006. Testing anatomically
993 specified hypotheses in functional imaging using cytoarchitectonic maps,
994 *NeuroImage*. doi:10.1016/j.neuroimage.2006.04.204

995 Eickhoff, S.B., Stephan, K.E., Mohlberg, H., Grefkes, C., Fink, G.R., Amunts,
996 K., Zilles, K., 2005. A new SPM toolbox for combining probabilistic
997 cytoarchitectonic maps and functional imaging data, *NeuroImage*.
998 doi:10.1016/j.neuroimage.2004.12.034

999 Epstein, R., Kanwisher, N., 1998. A cortical representation of the local visual
1000 environment. *Nature* 392, 598–601. doi:10.1038/33402

1001 Fahle, M., 2002. Perceptual learning: gain without pain? *Nat. Neurosci.* 5,
1002 923–924. doi:10.1038/nn1002-923

1003 Farbota, K.D.M., Sodhi, A., Bendlin, B.B., McLaren, D.G., Xu, G., Rowley, H.
1004 a, Johnson, S.C., 2012. Longitudinal volumetric changes following
1005 traumatic brain injury: a tensor-based morphometry study. *J. Int.*
1006 *Neuropsychol. Soc.* 18, 1006–18. doi:10.1017/S1355617712000835

1007 Friston, K.J., Frith, C.D., Frackowiak, R.S.J., Turner, R., 1995. Characterizing
1008 Dynamic Brain Responses with fMRI: A Multivariate Approach.
1009 *Neuroimage* 2, 166–172. doi:10.1006/nimg.1995.1019

1010 Friston, K.J., Kahan, J., Biswal, B., Razi, A., 2014. A DCM for resting state
1011 fMRI. *Neuroimage* 94, 396–407. doi:10.1016/j.neuroimage.2013.12.009

1012 Gimenez, P., Bugescu, N., Black, J.M., Hancock, R., Pugh, K., Nagamine, M.,
1013 Kutner, E., Mazaika, P., Hendren, R., McCandliss, B.D., Hoeft, F., 2014.
1014 Neuroimaging correlates of handwriting quality as children learn to read

1015 and write. *Front. Hum. Neurosci.* 8, 155. doi:10.3389/fnhum.2014.00155

1016 Goebel, R., Esposito, F., Formisano, E., 2006. Analysis of functional image
1017 analysis contest (FIAC) data with brainvoyager QX: From single-subject
1018 to cortically aligned group general linear model analysis and self-
1019 organizing group independent component analysis. *Hum. Brain Mapp.*
1020 27, 392–401. doi:10.1002/hbm.20249

1021 Gulati, T., Guo, L., Ramanathan, D.S., Bodepudi, A., Ganguly, K., 2017.
1022 Neural reactivations during sleep determine network credit assignment.
1023 *Nat. Neurosci.* 20, 1277–1284. doi:10.1038/nn.4601

1024 Gulati, T., Ramanathan, D.S., Wong, C.C., Ganguly, K., 2014. Reactivation of
1025 emergent task-related ensembles during slow-wave sleep after
1026 neuroprosthetic learning. *Nat. Neurosci.* 17, 1107–13.
1027 doi:10.1038/nn.3759

1028 Habes, I., Rushton, S., Johnston, S.J., Sokunbi, M.O., Barawi, K., Brosnan,
1029 M., Daly, T., Ihssen, N., Linden, D.E.J., 2016. fMRI neurofeedback of
1030 higher visual areas and perceptual biases. *Neuropsychologia* 85, 208–
1031 215. doi:10.1016/j.neuropsychologia.2016.03.031

1032 Haler, R.J., Siegel, B., Tang, C., Abel, L., Buchsbaum, M.S., 1992.
1033 Intelligence and Changes in Regional Cerebral Glucose Metabolic Rate
1034 Following Learning. *Intelligence* 16, 415–426.

1035 Heinzl, S., Lorenz, R.C., Brockhaus, W.-R., Wustenberg, T., Kathmann, N.,
1036 Heinz, A., Rapp, M.A., 2014. Working Memory Load-Dependent Brain
1037 Response Predicts Behavioral Training Gains in Older Adults. *J.*
1038 *Neurosci.* 34, 1224–1233. doi:10.1523/JNEUROSCI.2463-13.2014

1039 Hohwy, J., Roepstorff, A., Friston, K., 2008. Predictive coding explains

1040 binocular rivalry: an epistemological review. *Cognition* 108, 687–701.
1041 doi:10.1016/j.cognition.2008.05.010

1042 Johansen-Berg, H., Baptista, C.S., Thomas, A.G., 2012. Human structural
1043 plasticity at record speed. *Neuron* 73, 1058–60.
1044 doi:10.1016/j.neuron.2012.03.001

1045 Kanwisher, N., McDermott, J., Chun, M.M., 1997. The fusiform face area: a
1046 module in human extrastriate cortex specialized for face perception. *J.*
1047 *Neurosci.* 17, 4302–11.

1048 Koush, Y., Zvyagintsev, M., Dyck, M., Mathiak, K. a, Mathiak, K., 2012. Signal
1049 quality and Bayesian signal processing in neurofeedback based on real-
1050 time fMRI. *Neuroimage* 59, 478–89.
1051 doi:10.1016/j.neuroimage.2011.07.076

1052 Lange, F.P. De, Heilbron, M., Kok, P., 2018. How Do Expectations Shape
1053 Perception ? *Trends Cogn. Sci.* 22, 764–779.
1054 doi:10.1016/j.tics.2018.06.002

1055 Levelt, W.J.M., 1966. The alternation process in binocular rivalry. *Br. J.*
1056 *Psychol.* 57, 225–238.

1057 Li, W., He, H., Lu, J., Lv, B., Li, M., Jin, Z., 2009. <title>Detection of whole-
1058 brain abnormalities in temporal lobe epilepsy using tensor-based
1059 morphometry with DARTEL</title> 7497, 749723-749723–6.
1060 doi:10.1117/12.833128

1061 Li, X., Hartwell, K.J., Borckardt, J., Prisciandaro, J.J., Saladin, M.E., Morgan,
1062 P.S., Johnson, K.A., LeMatty, T., Brady, K.T., George, M.S., 2013.
1063 Volitional reduction of anterior cingulate cortex activity produces
1064 decreased cue craving in smoking cessation: a preliminary real-time fMRI

1065 study. *Addict. Biol.* 18, 739–748. doi:10.1111/j.1369-1600.2012.00449.x

1066 McCarthy, G., Puce, A., Gore, J.C., Allison, T., 1997. Face-Specific

1067 Processing in the Human Fusiform Gyrus. *J. Cogn. Neurosci.* 9, 605–

1068 610. doi:10.1162/jocn.1997.9.5.605

1069 Miranda, R.A., Casebeer, W.D., Hein, A.M., Judy, J.W., Krotkov, E.P., Laabs,

1070 T.L., Manzo, J.E., Pankratz, K.G., Pratt, G.A., Sanchez, J.C., Weber,

1071 D.J., Wheeler, T.L., Ling, G.S.F., 2015. DARPA-funded efforts in the

1072 development of novel brain – computer interface technologies. *J.*

1073 *Neurosci. Methods* 244, 52–67.

1074 O’Craven, K.M., Kanwisher, N., 2000. Mental imagery of faces and places

1075 activates corresponding stimulus-specific brain regions. *J. Cogn.*

1076 *Neurosci.* 12, 1013–23.

1077 Orban, G. a, Zhu, Q., Vanduffel, W., 2014. The transition in the ventral stream

1078 from feature to real-world entity representations. *Front. Psychol.* 5, 695.

1079 doi:10.3389/fpsyg.2014.00695

1080 Parker, A., Alais, D., 2007. A bias for looming stimuli to predominate in

1081 binocular rivalry. *Vision Res.* 47, 2661–74.

1082 doi:10.1016/j.visres.2007.06.019

1083 Poldrack, R.A., 2015. Is “efficiency” a useful concept in cognitive

1084 neuroscience? *Dev. Cogn. Neurosci.* 11, 12–17.

1085 doi:10.1016/j.dcn.2014.06.001

1086 Rademaker, R.L., Pearson, J., 2012. Training Visual Imagery: Improvements

1087 of Metacognition, but not Imagery Strength. *Front. Psychol.* 3, 224.

1088 doi:10.3389/fpsyg.2012.00224

1089 Sagi, Y., Tavor, I., Hofstetter, S., Tzur-Moryosef, S., Blumenfeld-Katzir, T.,

1090 Assaf, Y., 2012. Learning in the Fast Lane: New Insights into
1091 Neuroplasticity. *Neuron* 73, 1195–1203.
1092 doi:10.1016/j.neuron.2012.01.025

1093 Shibata, K., Watanabe, T., Sasaki, Y., Kawato, M., 2011. Perceptual learning
1094 incepted by decoded fMRI neurofeedback without stimulus presentation.
1095 *Science* 334, 1413–5. doi:10.1126/science.1212003

1096 Sitaram, R., Ros, T., Stoeckel, L., Haller, S., Scharnowski, F., Lewis-Peacock,
1097 J., Weiskopf, N., Blefari, M.L., Rana, M., Oblak, E., Birbaumer, N., Sulzer,
1098 J., 2016. Closed-loop brain training: the science of neurofeedback. *Nat.*
1099 *Rev. Neurosci.* doi:10.1038/nrn.2016.164

1100 Subramanian, L., Hindle, J. V, Johnston, S., Roberts, M. V, Husain, M.,
1101 Goebel, R., Linden, D., 2011. Real-time functional magnetic resonance
1102 imaging neurofeedback for treatment of Parkinson’s disease. *J. Neurosci.*
1103 31, 16309–17. doi:10.1523/JNEUROSCI.3498-11.2011

1104 Summerfield, C., Koechlin, E., 2008. A neural representation of prior
1105 information during perceptual inference. *Neuron* 59, 336–47.
1106 doi:10.1016/j.neuron.2008.05.021

1107 Tartaglia, E.M., Bamert, L., Mast, F.W., Herzog, M.H., 2009. Human
1108 perceptual learning by mental imagery. *Curr. Biol.* 19, 2081–5.
1109 doi:10.1016/j.cub.2009.10.060

1110 Taschereau-Dumouchel, V., Cortese, A., Chiba, T., Knotts, J.D., Kawato, M.,
1111 Lau, H., 2018. Towards an unconscious neural reinforcement intervention
1112 for common fears. *Proc. Natl. Acad. Sci.* 201721572.
1113 doi:10.1073/pnas.1721572115

1114 Thibault, R.T., MacPherson, A., Lifshitz, M., Roth, R.R., Raz, A., 2018.

1115 Neurofeedback with fMRI: A critical systematic review. *Neuroimage* 172,
1116 786–807. doi:10.1016/j.neuroimage.2017.12.071

1117 Tong, F., Meng, M., Blake, R., 2006. Neural bases of binocular rivalry. *Trends*
1118 *Cogn. Sci.* 10, 502–511. doi:10.1016/j.tics.2006.09.003

1119 Tong, F., Nakayama, K., Vaughan, J.T., Kanwisher, N., 1998. Binocular rivalry
1120 and visual awareness in human extrastriate cortex. *Neuron* 21, 753–9.

1121 Vartanian, O., Jobidon, M.-E., Bouak, F., Nakashima, A., Smith, I., Lam, Q.,
1122 Cheung, B., 2013. Working memory training is associated with lower
1123 prefrontal cortex activation in a divergent thinking task. *Neuroscience*
1124 236, 186–194. doi:10.1016/j.neuroscience.2012.12.060

1125 Wang, Y., Yuan, L., Shi, J., Greve, A., Ye, J., Toga, A.W., Reiss, A.L.,
1126 Thompson, P.M., 2013. Applying tensor-based morphometry to
1127 parametric surfaces can improve MRI-based disease diagnosis.
1128 *Neuroimage* 74, 209–30. doi:10.1016/j.neuroimage.2013.02.011

1129 Watanabe, T., Náñez, J.E., Koyama, S., Mukai, I., Liederman, J., Sasaki, Y.,
1130 2002. Greater plasticity in lower-level than higher-level visual motion
1131 processing in a passive perceptual learning task. *Nat. Neurosci.* 5, 1003–
1132 1009. doi:10.1038/nn915

1133 Watanabe, T., Náñez, J.E., Sasaki, Y., 2001. Perceptual learning without
1134 perception. *Nature* 413, 844–848. doi:10.1038/35101601

1135 Watanabe, T., Sasaki, Y., Shibata, K., Kawato, M., 2017. Advances in fMRI
1136 Real-Time Neurofeedback. *Trends Cogn. Sci.* 21, 997–1010.
1137 doi:10.1016/j.tics.2017.09.010

1138 Weiskopf, N., Mathiak, K., Bock, S.W., Scharnowski, F., Veit, R., Grodd, W.,
1139 Goebel, R., Birbaumer, N., 2004. Principles of a brain-computer interface

1140 (BCI) based on real-time functional magnetic resonance imaging (fMRI).
1141 IEEE Trans. Biomed. Eng. 51, 966–70. doi:10.1109/TBME.2004.827063
1142 Welch, K. a, Moorhead, T.W., McIntosh, a M., Owens, D.G.C., Johnstone,
1143 E.C., Lawrie, S.M., 2013. Tensor-based morphometry of cannabis use on
1144 brain structure in individuals at elevated genetic risk of schizophrenia.
1145 Psychol. Med. 43, 2087–96. doi:10.1017/S0033291712002668
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1148

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1168 **Author contributions**

1169 J.E, F.S, and G.R designed the experiment. J.E, J.S.W, G.R.R, F.S and G.R
1170 discussed and planned data analysis. J.E collected and analysed the data.

1171 J.E, Y.K, G.R.R and F.S. developed the real-time acquisition and analysis
1172 tools. J.E and E.F performed the mental imagery control experiment. A.R
1173 performed the CVA analysis. J.E and G.R wrote the paper. All authors read
1174 and commented on the manuscript.

1175

1176 **Figure legends**

1177 **Figure 1. Experiment procedure schematic.**

1178 **Stage 1 *Pre-training BR***

1179 **Stage 2 *Neurofeedback training*: 10 participants were separated into two**
1180 **groups, a ‘face’ group and a ‘house group’, and were trained to increase a**
1181 **fluctuating thermometer bar (blue bar), up to a fixed mark (orange bar). After**
1182 **the neurofeedback training sessions, the participants performed a transfer**
1183 **session with brain modulation in the absence of neurofeedback signal.**

1184 **Stage 3 *Post-training BR*: Three types of sessions: a) BR; b) BR with**
1185 **‘concurrent trained upregulation’; and c) BR with ‘concurrent non-trained**
1186 **mental imagery’.**

1187

1188 **Figure 2A. Schematic showing group ROIs (FFA and PPA statistical masks) on**
1189 **inflated canonical brains. Activation was extracted from these regions for**
1190 **production of the differential signal for neurofeedback training. The direction**
1191 **of regulation of these ROIs was specific for each group i.e. House Group, PPA**
1192 **up/ FFA down, Face Group, FFA up/ PPA down.**

1193

1194 **Figure 2B. Mean BOLD signal changes across groups, in the strategy-related**
1195 **ROI (red) and the strategy-unrelated ROI (blue), for each of the nine training**
1196 **sessions. The green line shows the difference in mean BOLD activation**
1197 **between the two brain regions and corresponds to the neurofeedback training**
1198 **signal that participants visualised in the scanner as a fluctuating bar. Error**
1199 **bars show ± 1 SEM.**

1200

1201

1202 **Figure 3A. Cumulative dominance durations across participants for pre-**
1203 **training BR, and the three post-training BR sessions: Post-training, Post-**
1204 **training BR with concurrent trained upregulation, and Post-training BR with**
1205 **concurrent non-trained mental imagery. Error bars show ± 1 SEM. The total**
1206 **duration of each BR block was 40s.**
1207

1208 **Figure 3B. Changes in cumulative dominance durations for binocular rivalry**
1209 **(BR) sessions, showing comparisons before and after neurofeedback training**
1210 **collapsed across both groups. Error bars indicate ± 1 SEM**

1211

1212 **A. Pre/post training BR comparison**

1213 **B. Pre/post-training BR with concurrent training upregulation**

1214 **C. Pre/post-training BR with concurrent non-trained mental imagery**

1215

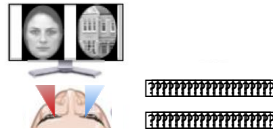
1216 *** $p < 0.05$. Double ** $p < 0.01$. Horizontal brackets indicate significant differences in**
1217 **the changes of cumulative dominance durations ($p < 0.05$) ~ over a bracket**
1218 **indicates $p = 0.07$.**

1219

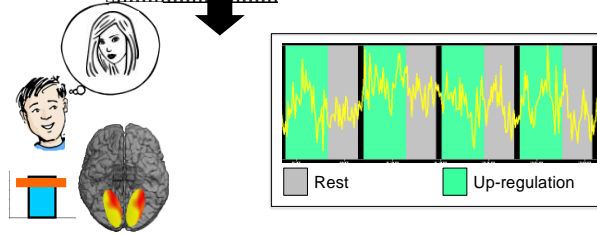
1220

1221 **Figure 4. BOLD activation changes in the trained ROIs, during binocular rivalry**
1222 **(BR) sessions, before and after neurofeedback training. There was a significant**
1223 **reduction in activation in both the strategy-related ROI and the strategy-**
1224 **unrelated ROI following training. When BR was performed with concurrent**
1225 **trained up-regulation, there was a significant further decrease in BOLD**
1226 **activation in the strategy-unrelated ROI only. Error bars indicate ± 1 SEM. (***
1227 **$p < 0.05$).**
1228

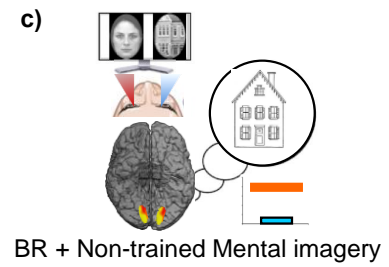
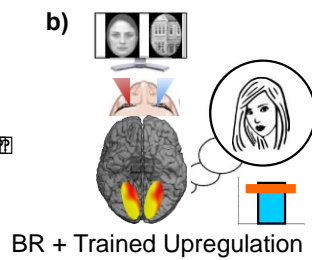
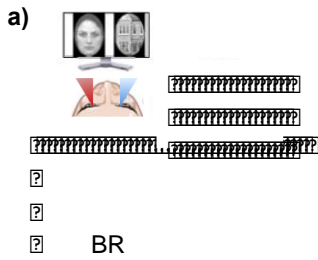
1. Pre-training BR



2. Neurofeedback training
 2 groups of 5 participants:
 -FFA minus PPA signal
 'face' strategies
 -PPA minus FFA signal
 'house' strategies



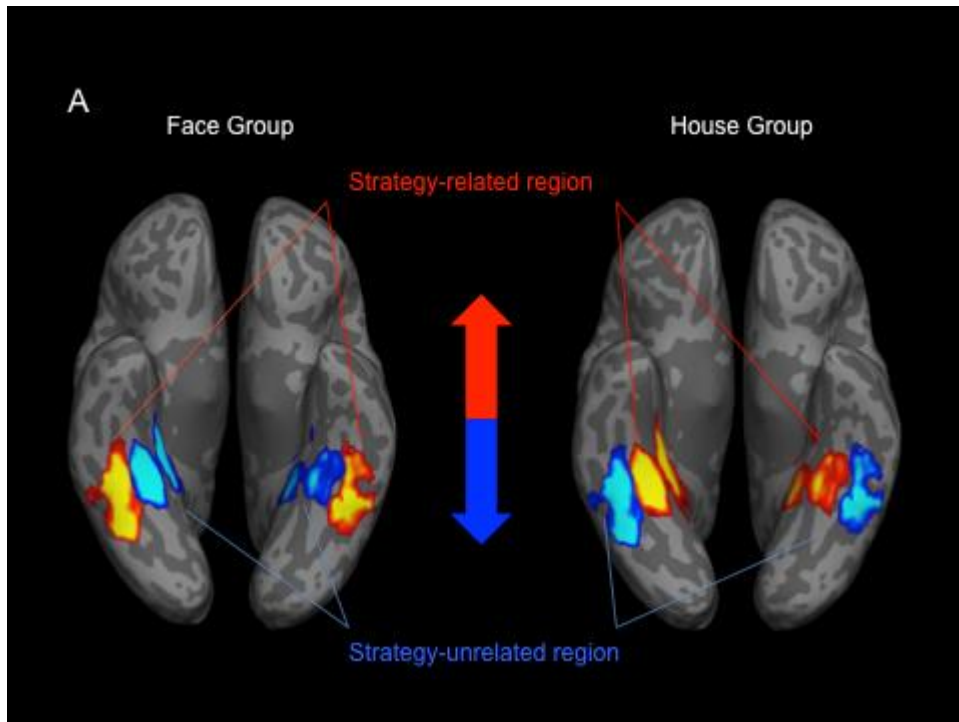
3. Post-training BR



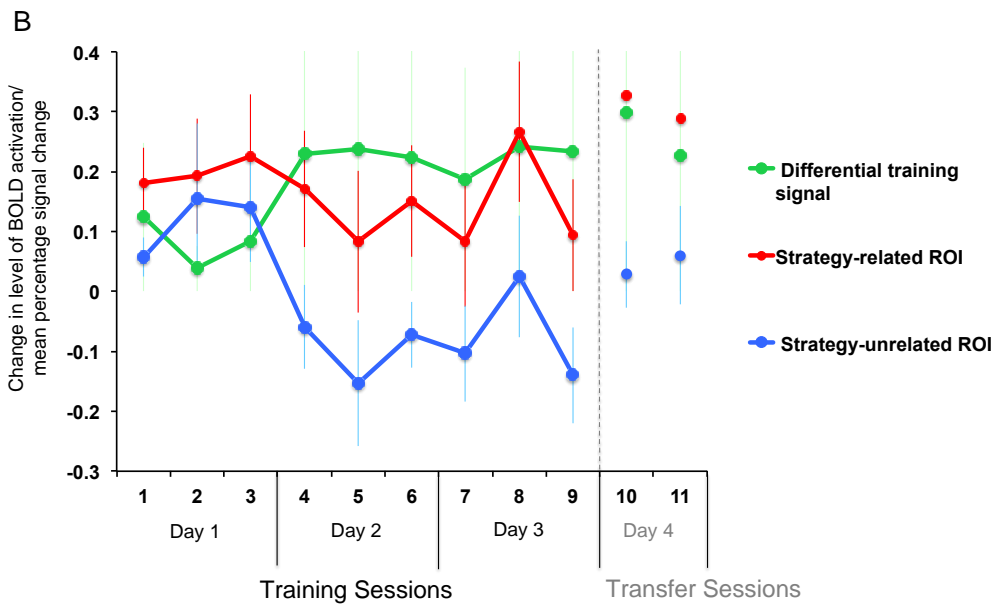
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Figure 1

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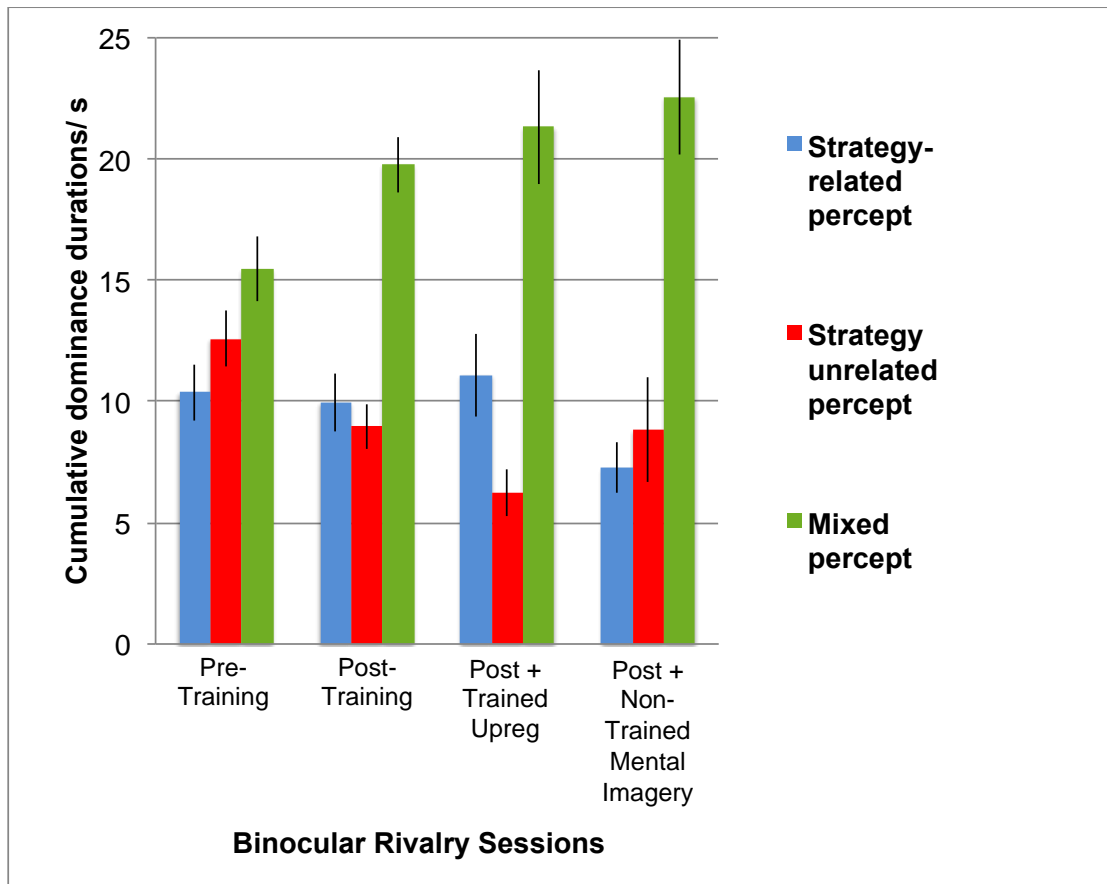


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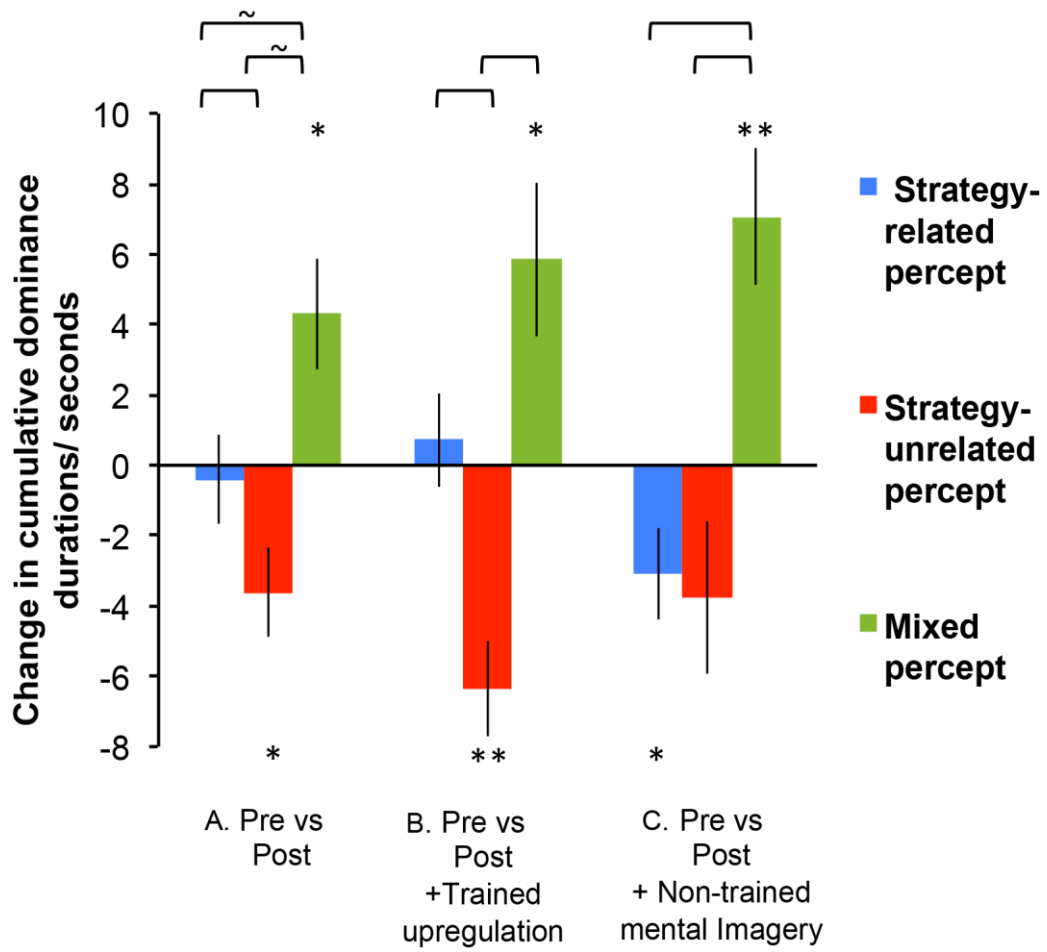
Figure 2A and B.



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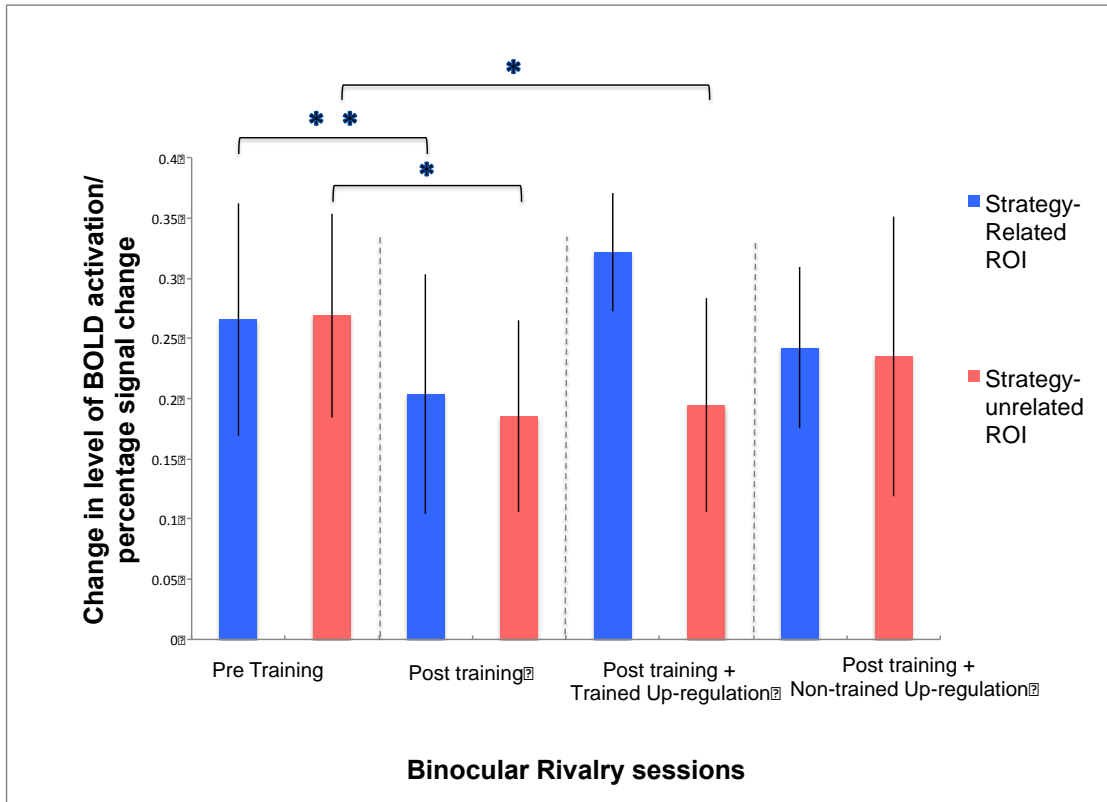
Figure 3A.



Binocular Rivalry Sessions Comparison

1240
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Figure 3B.



1245
 1246
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 1248

Figure 4.

1249 **Supplementary Materials List:**

- 1250 • Supplementary methods
- 1251 • Supplementary results
- 1252 • Supplementary discussion
- 1253 • Supplementary references
- 1254 • Supplementary figures S1-S4

1255

1256

1257 **Supplementary Methods**

1258

1259 **Learning Effect across Rt-fMRI Neurofeedback Training**

1260

1261 The learning effect measures the change in BOLD activation in trained brain
1262 region/s across the neurofeedback training sessions. The mean percentage
1263 signal change (PSC) for each training run and ROI was calculated and plotted
1264 (seeFigure2B in main paper, and compare with S1, S2).

1265

1266

1267

1268

1269 **Supplementary Results**

1270 **Results - Behaviour**

1271

1272 **Binocular Rivalry – Durations:**

1273 See main paper.

1274

1275 **Results – Imaging**

1276

1277 ***Strategy-related and Strategy-unrelated ROIs:***

1278 We first determined if the differential signal significantly changed over days
1279 across participants (see main paper, Result Section). We additionally
1280 examined the changes in the two ROIs used to produce the differential signal;
1281 the strategy-related ROI and the strategy-unrelated ROI (see Figure 2, main
1282 paper).

1283

1284 A one-way ANOVA (with 3 levels corresponding to the 3 training days)
1285 revealed a significant reduction in activation in the strategy-unrelated ROI
1286 over the 3 days of training ($F(2,16)= 8.71, p= 0.003$). On the other hand, a
1287 one-way ANOVA for the strategy-related ROI revealed no significant change
1288 ($F(2,16)= 0.33, p= 0.72$).

1289

1290 ***Sub-groups:***

1291 To assess whether there was any difference between the face and house
1292 group during training, an ANOVA was performed on the differential training
1293 signal across the 3 training days, with a between-subjects factor with two

1294 levels (for the two sub-groups, 'Face' and 'House'). This did not reveal a
1295 significant interaction ($F(2,14)=0.064$, $p=0.94$) between the two factors.

1296

1297 For neurofeedback training graphs for the two groups (mean percentage
1298 signal change over 9 sessions), please see Figures S2 and S3.

1299

1300

1301

1302 **Supplementary Discussion**

1303

1304 **Levelt's Second Proposition, 1966**

1305 Levelt's second proposition(Levelt, 1966), as applied to stimulus perception
1306 was based on the physical properties of visual stimuli and states: "*Variation of*
1307 *the stimulus strength in one eye will only influence the mean dominance*
1308 *duration of the contralateral eye and not the mean dominance duration of the*
1309 *ipsilateral eye*".

1310

1311 **Known Influences on Visual Perception**

1312 The role of 'priming' and 'cueing' might also be invoked as possible causes for
1313 the perceptual changes observed following neurofeedback training in this
1314 study. Prior presentation of a specific orientation grating can cause an
1315 increase in the perception of the identical grating during BR. However,
1316 dominance durations were unchanged(Denison et al., 2011). Similarly,
1317 exogenous cueing prior to BR can increase the probability of the predominant
1318 percept being linked to the cue. For example prior to BR, hearing sentences
1319 with the word 'face', results in FFA activation(Pelekanos et al., 2011).
1320 Nonetheless, no significant change in stimulus dominance between faces and
1321 houses on rivalry trials were observed when participants were cued with a
1322 word linked to one of the rivalrous stimuli. Dominance durations have also
1323 been demonstrated as being immune to the effects of volitional attention(Jung
1324 et al., 2016), and reflective of true differences in sensory processing(Dieter et
1325 al., 2016). It is therefore unlikely that the perceptual changes produced by
1326 neurofeedback training could be ascribed to participant expectation. Evidently,

1327 neither altering the level of activity in higher order brain regions involved in
1328 perception, nor applying known influences on visual perception, provide a
1329 comprehensive explanation for the lasting shifts in perceptual bistability
1330 observed following neurofeedback training in this study.

1331

1332 **Controlling the Neurofeedback Signal**

1333 With regards to the neurofeedback training signal itself (i.e. differential brain
1334 activation between two ROIs), there were five potential activation states which
1335 could increase the difference between the two brain regions (*strategy-related*
1336 *ROI minus strategy-unrelated ROI*), leading to upregulation of the training
1337 signal: These could be: (1) an increase in *strategy-related ROI*; (2) a decrease
1338 in *strategy-unrelated ROI*; (3) a combination of the two; (4) a relatively greater
1339 increase in *strategy-related ROI* as compared to *strategy-unrelated ROI*; and
1340 (5) a relatively greater decrease in the *strategy-unrelated ROI*. Based on our
1341 results (Figure 1B in main paper), the mechanism for the upregulation of the
1342 differential signal across groups during neurofeedback training appeared to be
1343 produced by maintenance of activation in the strategy-related ROI, and a
1344 reduction of activation in the strategy-unrelated ROI.

1345

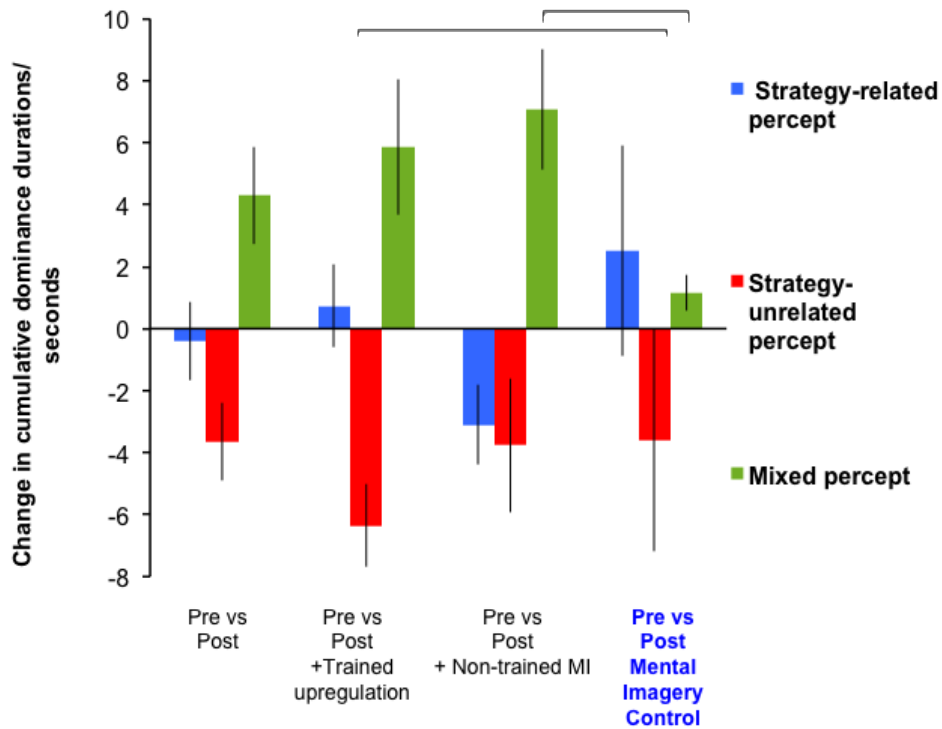
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1349

1350 **Supplementary figures**



Binocular Rivalry Sessions and Groups Comparison

1351

1352 **Figure S1. Changes in cumulative dominance durations for binocular rivalry**
 1353 **sessions, showing comparisons before and after neurofeedback training. This**
 1354 **figure is the analogous to Figure 3B in the main paper, but additionally shows**
 1355 **changes in dominance durations for the ‘Mental Imagery’ control group. Error**
 1356 **bars indicate ± 1 SEM. Horizontal brackets show significant between group**
 1357 **comparisons for percepts ($p < 0.05$).**

1358

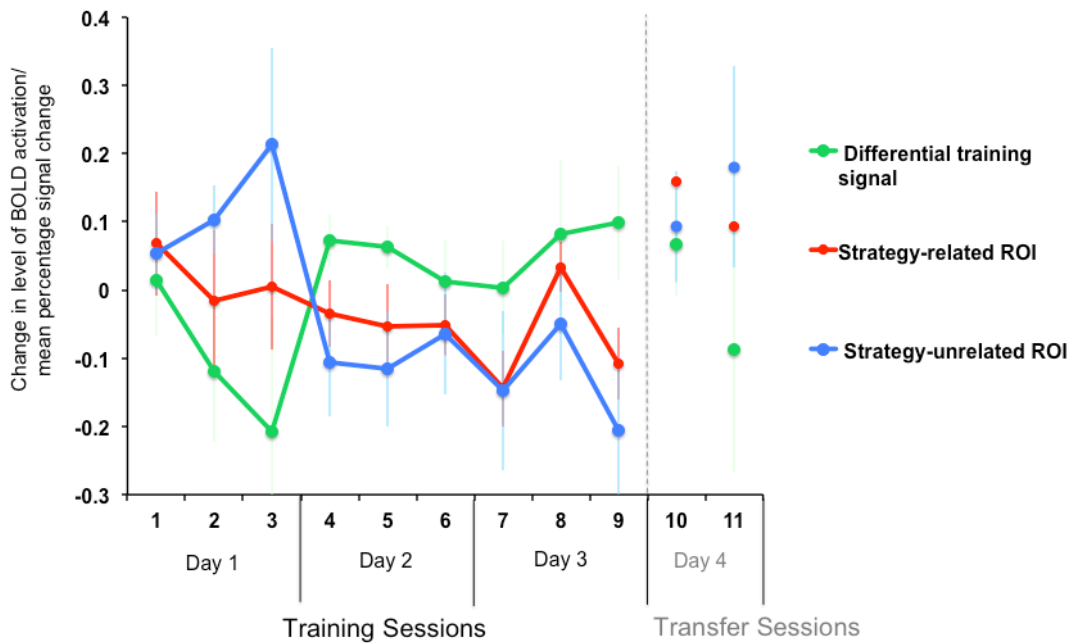
1359 **A. Pre vs. Post-training BR comparison**

1360 **B. Pre vs. Post-training BR with concurrent training up-regulation**

1361 **C. Pre vs. Post-training BR with concurrent non-trained mental imagery**

1362 **D. Pre vs. Post training BR comparison for Mental Imagery Control group**

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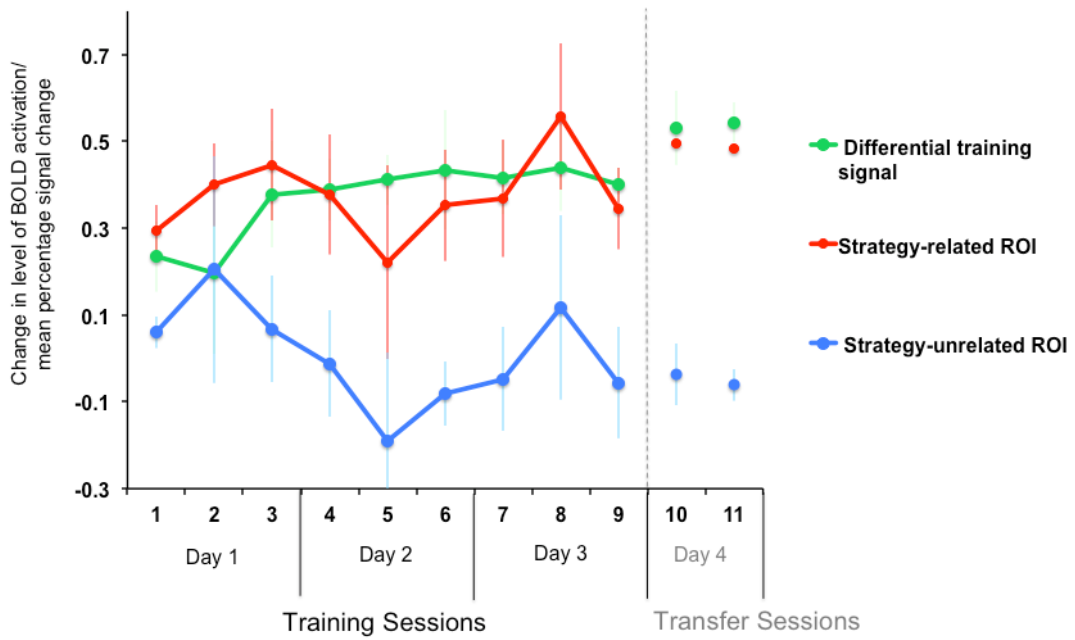
1366 **Figure S2. Mean BOLD signal changes across the House group, in the strategy-**
 1367 **related brain region (red) and the strategy-unrelated brain region (blue), for**
 1368 **each of the nine training sessions. The green line shows the difference in mean**
 1369 **BOLD activation between the two brain regions and corresponds to the**
 1370 **neurofeedback training signal. Error bars show ± 1 SEM.**

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1377 **Figure S3. Mean BOLD signal changes across the Face group, in the strategy-**
 1378 **related brain region (red) and the strategy-unrelated brain region (blue), for**
 1379 **each of the nine training sessions. The green line shows the difference in mean**
 1380 **BOLD activation between the two brain regions and corresponds to the**
 1381 **neurofeedback training signal. Error bars show ± 1 SEM.**

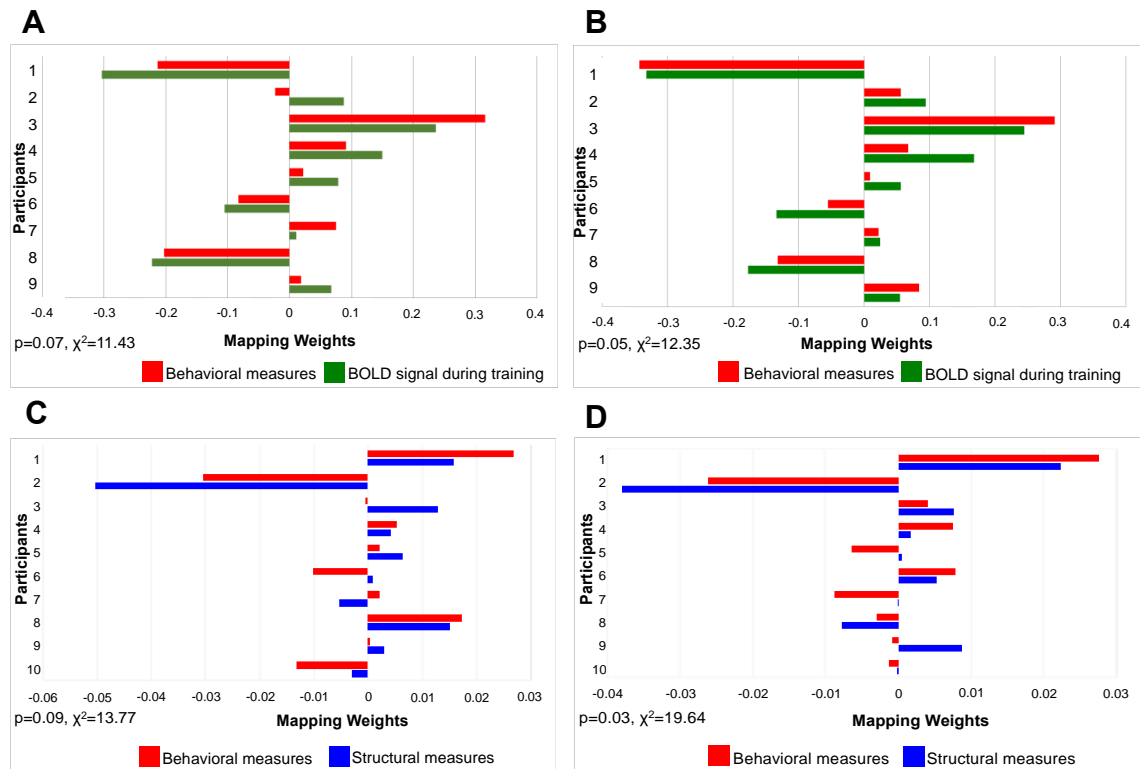
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1389 **Figure S4. Canonical variate analysis illustrating the correlation between**
 1390 **individual behaviour and physiological measures. For each participant**
 1391 **mapping weights are shown for pairs of predictor and outcome variables. This**
 1392 **approach aims to reveal relationships that may exist between multiple outcome**
 1393 **variables following neurofeedback training.**

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1395 **A,B: Comparison of BR behavioural measures (i.e. durations of mixed,**
 1396 **strategy-related and strategy-unrelated percepts), and functional BOLD signal**
 1397 **changes across training (i.e. differential signal). Nine of the ten participants**
 1398 **were included, as one of the participants did not complete all nine training**
 1399 **sessions. Participants 1-5 are Face Group, Participants 6-9 are House Group. A**
 1400 **shows a non-significant relationship ($p= 0.07$) between individual participant**
 1401 **BR measures (pre vs. post training) and functional BOLD signal changes**
 1402 **across training. B shows a non-significant relationship ($p= 0.05$) between**

1403 individual participant BR measures (pre vs. post-training with concurrent
1404 trained upregulation) and functional BOLD signal changes across training.

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1406 **C,D: Comparison of BR behaviour measures (i.e. durations of mixed, strategy-**
1407 **related and strategy-unrelated percepts), and structural measures from FFA**
1408 **and PPA (pre vs. post training). Participants 1-5 are 'Face Group', Participants**
1409 **6-10 are 'House Group'. C shows a non-significant relationship ($p= 0.09$)**
1410 **between individual participant BR measures (pre vs. post training) and**
1411 **structural measures from FFA, and PPA (pre vs. post training). D shows a**
1412 **significant relationship ($p= 0.03$) between individual participant BR measures**
1413 **(pre vs. post-training with concurrent trained upregulation) and structural**
1414 **measures from FFAand PPA (pre vs. post training).**

1415 **Supplementary References**

1416

1417 Denison, R.N., Piazza, E. a, Silver, M. a, 2011. Predictive Context Influences
1418 Perceptual Selection during Binocular Rivalry. *Front. Hum. Neurosci.* 5,
1419 166. doi:10.3389/fnhum.2011.00166

1420 Dieter, K.C., Sy, J.L., Blake, R., 2016. Individual differences in sensory eye
1421 dominance reflected in the dynamics of binocular rivalry. *Vision Res.*
1422 doi:10.1016/j.visres.2016.09.014

1423 Jung, Y., Kang, M.-S., Chong, S.C., 2016. Effect of Attention on the Initiation
1424 of Binocular Rivalry. *Perception* 45, 492–504.
1425 doi:10.1177/0301006615622324

1426 Levelt, W.J.M., 1966. The alternation process in binocular rivalry. *Br. J.*
1427 *Psychol.* 57, 225–238.

1428 Pelekanos, V., Roumani, D., Moutoussis, K., 2011. The effects of categorical
1429 and linguistic adaptation on binocular rivalry initial dominance. *Front.*
1430 *Hum. Neurosci.* 5, 187. doi:10.3389/fnhum.2011.00187

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