AFFECTIVELY-BIASED COMPETITION FAVORING REWARDING EXPRESSIONS IS NOT MODULATED BY COMMON VARIATION IN NOREPINEPHRINE RECEPTOR FUNCTION

Kevin H. Roberts[1], Maria G. M. Manaligod[1], Colin J. D. Ross[2], Daniel J. Müller[3], Matthias J. Wieser[4], & *Rebecca M. Todd[1,5]

[1]Department of Psychology, University of British Columbia, Vancouver, BC, Canada
[2]Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC Canada
[3]Department of Psychiatry, University of Toronto and Neurogenetics Section, Centre for Addiction and Mental Health, Toronto, ON, Canada
[4]Erasmus School of Social and Behavioural Sciences, Erasmus University Rotterdam, The Netherlands
[5]Centre for Brain Health, University of British Columbia, Vancouver, BC, Canada

*Address correspondence to:
Rebecca Todd, PhD
Department of Psychology
University of British Columbia
2136 West Mall, Vancouver, BC, V6T 1Z4, Canada
Email: becket.todd@psych.ubc.ca

We would like to thank Drs. Todd Handy and Julia Kam as well as Lena Fürst for their generous contributions to this project. This research was supported by Canadian Institutes for Health Research (CIHR) Operating Grant #491746, National Engineering and Research Council (NSERC) Discovery Grant RGPIN-2014-04202, and Canadian Foundation for Innovation Leaders Opportunity Fund grant F13-03917. Individual researchers were supported by a NSERC doctoral fellowship to K. H. Roberts and CIHR New Investigator Salary awards and Michael Smith Foundation for Health Research Scholar awards to both C.J.D. Ross and R.M. Todd.

Data and analysis scripts are available here:
https://osf.io/n3g6e/?view_only=458920fd64c048028c651f78f7192f55

Abstract

It is well established that emotionally salient stimuli evoke greater visual cortex activation than neutral ones and can distract attention from competing tasks. However, less is known about the underlying neurobiological processes that give rise to such effects. As a proxy of population level *biased competition*, EEG steady-state visual evoked potentials measured at the scalp can be sensitive to competition effects from salient stimuli. In the present study, we wished to examine whether individual differences in norepinephrine activity play a role in emotionally-biased competition.

Our previous research has found robust effects of a common variation in the *ADRA2b* gene coding for alpha2 NE receptors on individual differences in emotional modulation of attention, subjective perception, and memory. In the present study of healthy young adults, our final participant sample included 87 carriers of the *ADRA2b* deletion variant and 95 non-carriers. Participants performed a change detection task in which foveal targets (gabor patches) were superimposed directly over angry, happy, and neutral faces, and indicated the number of phase changes (0-3) observed in the gabor patch. Overlapping targets and distractors were each flickered at a distinct driving frequency (15 and 20 Hz, counterbalanced within-subject) for three seconds. Relative power for faces vs. targets at the driving frequency served as an index of cortical resources allocated to each of the competing stimuli. To mitigate the danger of false positives in small sample genotyping studies, deletion carriers and non-carriers were separately randomly assigned to equal-sized discovery and replication samples and reliability of results across samples was assessed before the groups were combined for greater power.

Overall ssVEP power was higher for targets than distractors, but less so when distractor faces were happy. A difference score was calculated to index competition for each emotion condition (angry, happy neutral) as a measure of the degree to which face stimuli competed with targets. Happy faces evoked higher competition than angry or neutral faces, with strongest effects at earlier time windows, mirroring previous findings in a smaller sample with low social anxiety; however, we observed no hypothesized effects of *ADRA2b* in either sample or in the full dataset. Bayesian analyses confirmed null effects. Follow-up single-trial analysis found that increased competition from happy faces was not due to the effect of low-level visual features. Overall, our results indicate that emotionally biased competition at the neuronal population level, while reliably observed in young adults, is not influenced by individual differences in putative norepinephrine availability. They further indicate an overall pattern of affectively-biased competition for happy faces, which we interpret in relation to previously observed boundary conditions.

It is well established that emotionally relevant events are prioritized over less relevant ones, evoke higher levels of visual cortex activation, and are perceived as being relatively more vivid (Markovic, Anderson, & Todd, 2014; Pourtois, Schettino, & Vuilleumier, 2013; Todd, Talmi, Schmitz, Susskind, & Anderson, 2012). Emotionally relevant stimuli can also capture neurocognitive resources when in competition with explicit goals demanded by an experimental task [for review see (Carretie, 2014)]. Yet although biased attention to what is emotionally or motivationally relevant is ubiquitous, habitual tendencies to preferentially attend positively or negatively valenced information vary between individuals. Affective biases toward prioritizing negative or positive stimuli have been associated with personality traits such as neuroticism and extraversion respectively (Derryberry & Reed, 1994). When rigid or extreme, valenced biases are also associated with etiology and maintenance of psychopathology. For example, anxiety is associated with a bias to attend threat, and depression and addiction with reduced or enhanced attention to rewarding information, respectively (B. A. Anderson, 2016; Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van, 2007; Dalgleish et al., 2003; Peckham, McHugh, & Otto, 2010; Surguladze et al., 2004).

Research using functional magnetic resonance imaging (fMRI) has provided evidence that such biases are associated with large-scale patterns of brain activation involving amygdala and striatal systems [for review see (Todd & Manaligod, 2017)]. Less is known about underlying neuronal and neuromodulator processes. Recent research has begun to employ EEG steady-state visual evoked potentials (ssVEPs) to investigate population-level neuronal processes underlying rapid visual cortex plasticity with aversive conditioning (Kastner-Dorn, Andreatta, Pauli, & Wieser, 2018; McTeague, Gruss, & Keil, 2015; Miskovic & Keil, 2013; Wieser, Reicherts, Juravle, & von Leupoldt, 2016). As a proxy of population level *biased competition*, ssVEPs measured at the scalp can be sensitive to competition effects from salient stimuli (Wieser, McTeague, & Keil, 2012). When two spatially overlapping stimuli are driven at distinct temporal frequencies, power at the driving frequency of each can be compared to index relative allocation of attention (Kim, Grabowecky, Paller, Muthu, & Suzuki, 2007). A difference score can then be calculated as a measure of the degree to which a distractor captures resources from a task-relevant stimulus. Previous research has reported that higher levels of social anxiety are associated with biased competition for angry – relative to happy faces – when task-irrelevant emotional faces are overlaid with task-relevant gratings. For those with low social anxiety the reverse was true (Wieser et al., 2012).

The influence of emotional salience on selective attention is also modulated by the noradrenergic system, which influences gating and tuning of visual cortex neurons. Neurons in the locus coeruleus, the brainstem nucleus that primarily produces norepinephrine (NE), responds to both direct reward and punishment and very rapid learning of associations with both (Markovic et al., 2014; Sara, 2009; Sara & Bouret, 2012). A common deletion variation in the *ADRA2b* gene, which codes for inhibitory alpha2b NE receptors, is thought to be associated with higher levels of NE availability (de Quervain et al., 2007). Our own research has found that carriers of the deletion variant show enhancement of emotional modulation of cognition relative to non-carriers: Deletion carriers show attentional prioritization of negatively valenced words, enhanced neural and behavioural indices of perceptual vividness for emotionally relevant images (positive and negative), and stronger links between subjectively rated arousal

during picture viewing and subsequent emotional enhancement of memory for the pictures (Todd et al., 2015; Todd et al., 2013; Todd et al., 2014). An outstanding question concerned whether the NE system plays a key role in emotionally biased competition. As pharmacological interventions cannot precisely target specific NE receptors, genotyping for the deletion variant serves as a unique tool for examining individual differences in the NE systems mediated by alpha2b receptors. To address this question, we aimed to examine whether putative differences in NE availability indexed by *ADRA2b* are associated with biased attentional capture. The primary goal of the present study was to employ the experimental design designed by Wieser and colleagues (2012) using spatially overlapping neutral targets and emotional distractors to measure biased competition processes using ssVEPs (Wieser et al., 2012). We hypothesized that *ADRA2b* deletion carriers would show higher levels of competition associated with attentional bias for emotionally expressive faces — either for angry faces or for both angry and happy relative to neutral faces.

As previous studies had only investigated patterns of biased competition in populations either high or low in social anxiety (Wieser et al., 2012), a secondary question concerned whether we would observe overall valenced patterns of emotional modulation of attention in a relatively large sample of healthy young adults. Finally, we wished to examine whether we would replicate previously observed effects of social anxiety in a larger sample.

Methods

Participants. A total of 310 participants (76 males, 1 non-binary) were recruited from the University of British Columbia and received course credit or $20 for participating in the study. Participants were of European Caucasian descent, had no history of anxiety disorders, traumatic brain injury and epilepsy, and reported normal to corrected-to-normal vision. 113 were excluded due to a programming error in resulting in slow monitor refresh rates, such that no peaks were observable at the driving frequencies, 12 participants were excluded due to insufficient SNR among posterior electrodes, one participant was excluded after visual inspection of frequency amplitudes, and genotyping failed for two participants, leaving a final N of 182 (46 males, 1 non-binary, mean age = 20.75 years, SD = 2.85, 87 ADRA2b deletion carriers). All procedures were approved by the clinical research ethics review board of the University of British Columbia. Sample size was determined a priori by power analysis based on effect sizes observed for *ADRA2B* effects on emotional bias in previous studies. To mitigate against spurious false positives found in targeted polymorphisms studies with relatively small sample sizes (Grabitz et al., 2018), we adopted a split-sample approach to the data analysis: Following data collection, equal numbers of *ADRA2B* deletion carriers and noncarriers were randomly assigned to the discovery and replication samples. There were 90 participants in the discovery sample (19 male, 1 non-binary, mean age = 20.71 *SD* = 2.74, 43 deletion carriers), and 92 participants in the replication sample (26 male, mean age = 20.79, *SD* = 2.98, 44 deletion carriers). For demographic information see Table 1.

Table 1 Participant demographics

	Discovery	Replication	Full
N	90	92	183
Age	20.71 ± 2.74 years	20.79 ± 2.98 years	20.75 ± 2.85 years
Sex	70 female / 19 male / 1 non-binary	66 female / 26 male	136 females / 46 males / 1 non-binary
*ADRA*2b Genotype	43 deletion / 47 non-deletion	44 deletion / 48 non-deletion	87 deletion / 95 non-deletion
LSAS Score	30.51 ± 19.40	30.69 ± 22.16	30.62 ± 20.76

Procedure. Upon arriving in the lab, participants were asked to provide consent and respond to questions regarding vision, hours of sleep, caffeine and alcohol consumption, and history of traumatic brain injury. Additional questionnaires were also administered as part of a standard battery but were not examined for this study. EEG data was subsequently collected while participants performed a change detection task. Following EEG recording, participants performed a stimulus rating task wherein 72 facial stimuli used in the EEG task were rated on scales for valence and arousal. Finally, participants were asked to provide a (~2ml) saliva sample, collected using an Oragene OG-500 DNA kit (DNA Genotek, Ottawa, ON; http://dnagenotek.com) at the end of each testing session. Genotyping for *ADRA2b* was performed at CAMH in Toronto (1st 125 participants of the final sample) and at the BCCH (BC Children's Hospital Research Institute) in Vancouver (58 participants of the final sample).

Stimuli. Seventy-two photographs of 14 actors (12 female) posing angry, neutral, and happy facial expressions were selected from the Karolinska Directed Emotional Faces (KDEF; Lundquist, Flykt, & Ohman, 1998; http://www.facialstimuli.com). These images were converted to grayscale. A Gabor patch was overlaid on each image in a change detection task. Gabor patches were 225 x 305 pixels, with 8 cycles across the vertical dimension. Stimuli were 562 x 762 px (6.244 x 8.467 inches) images that were presented against a gray background on a 24-in monitor with a vertical refresh rate of 60 Hz using Presentation software.

Change Detection Task. Participants performed a change detection task that was adapted from Wieser, McTeague, and Keil (2012) (Figure 1). *Frequency tagging* was used to flicker overlaid stimuli at opposing frequencies, producing distinct electrocortical signatures, such that power at each driving frequency indexed allocation of cortical resources to that stimulus. In this way we could measure attentional allocation to two distinct stimuli that occupied the same regions of space. Each experimental trial consisted of a face stimulus flickered at one of two frequencies (either 15 or 20 Hz), overlaid by a semi-transparent Gabor patch that flickered at the other frequency (e.g., if the face was flickered at 15 hz, the Gabor patch was flickered at 20hz and vice versa). Both stimuli were presented foveally for 3000 ms. The driving frequencies of face vs. gabor patch were counterbalanced in blocks within subjects. Participants were asked to report the number of phase reversals (upward or downward shift of the transparent gratings 0, 1 or 2 times) via keyboard press. Thus, while the gabor patches were targets, the faces were task-irrelevant. 16 practice trials providing feedback (correct, wrong, or missed) were provided to ensure participants were performing above chance.

Stimulus rating tasks. Participants viewed the 72 face stimuli once in random order, rating each one of the Self-Assessment Manikin Scale (SAM; Bradley & Lang, 1994) for affective

valence and arousal. This self-reporting tool instructs participants to select one of five figures sitting on each of the two 9-point scales to match their experience while viewing a particular stimulus.

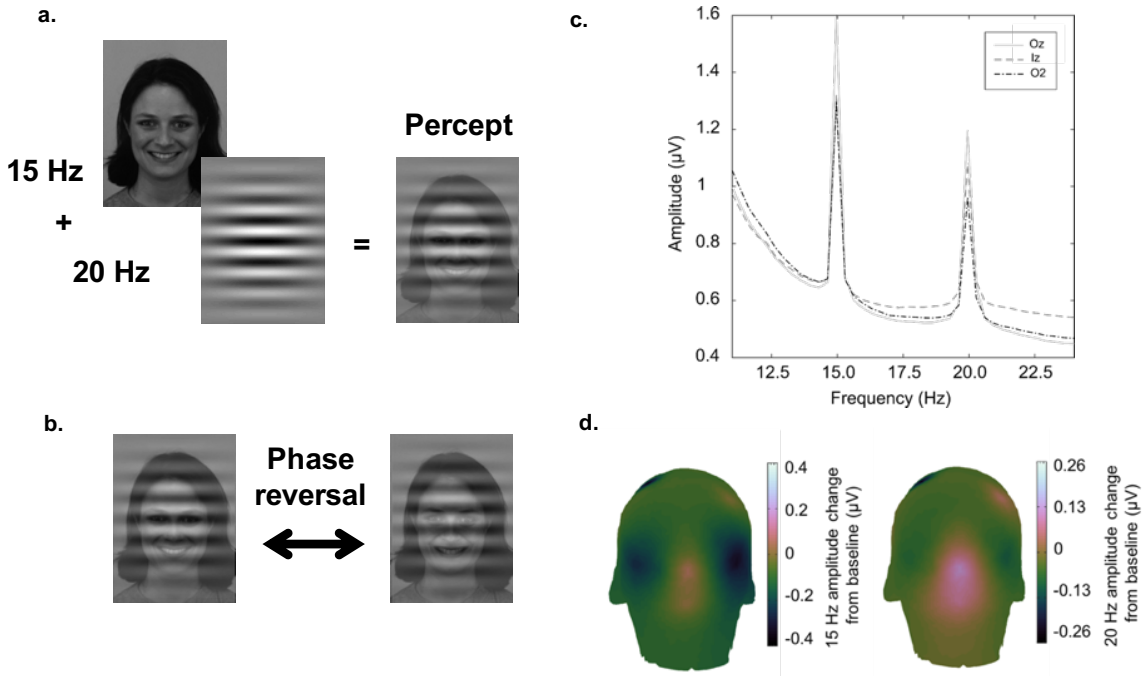


Figure 1. a. Stimuli from the change detection task. Target gabor patches and faces showing happy, angry, or neutral expressions were overlaid and flickered at 15 or 20 Hz for three seconds. The frequency of each stimulus type was counterbalanced in blocks within subject. **b.** An example of a phase reversal. For each trial participants had to report whether there were 0, 1 or 2 phase reversals. **c.** Average Fast Fourier Transforms (FFT) for 3 electrodes with the highest signal to noise ratio (SNR) at the peak frequencies. **d.** topographical plot showing 15 and 20 Hz amplitude change from baseline over early visual cortex, computed using the filter-Hilbert method.

Lower scores on the arousal scale indicate a *calm* vs an *exciting* or *agitating* feeling indicated by higher scores. On the valence scale, lower scores more negative ratings while higher scores indicate more positive ratings. Mean ratings were calculated after grouping each into the three emotions (angry, neutral, happy).

EEG Recording and Analysis. EEG was recorded from 64 active electrodes using the 10-20 Biosemi Active-Two amplifier system. Common mode sense (CMS) and driven right leg (DRL) ground electrodes were placed over medial-parietal cortex. A vertical EOG directly below the right pupil and horizontal EOGs on the left and right outer canthus were attached to record artefactual eye movements, for later correction.

EEGLAB 13.6.5b (Delorme & Makeig, 2004), ERPLAB 6.1 (Lopez-Calderon & Luck, 2014), the PREP pipeline 0.55.2 (Bigdely-Shamlo, Mullen, Kothe, Su, & Robbins, 2015) and MATLAB 2015b (The MathWorks Inc., 2015) were used for offline analysis of data. EEG was predominantly recorded at 256 Hz. EEG was inadvertently recorded at 512 Hz for 4 participants, and 2048 Hz for 2 participants; the data for these participants was downsampled to 256 Hz prior to any pre-processing. The PREP pipeline was used with default parameters to remove line noise and reference all EEG channels to a robust average reference. Bad channels were detected and were replaced with spherical spline interpolated values.

To select electrodes for statistical analysis, signal-to-noise ratio (SNR) was calculated for each electrode as the ratio of the stimulus driving frequencies to the average amplitude of the 20 surrounding frequency bins, excluding those bins immediately adjacent to the driving frequency as well as other frequencies at integer multiples of five to ensure that harmonic frequencies of the driving frequencies were not included in the noise estimate. This SNR calculation follows previous research [e.g., (Liu-Shuang, Norcia, & Rossion, 2014)] with the exception of the additional exclusion of harmonic frequencies. ssVEPs were calculated for each participant as the amplitude at 15 Hz and 20 Hz among the three electrodes with the highest SNR. To obtain 15 Hz and 20 Hz amplitudes for each electrode and trial, the filter-Hilbert method was used with a 12th order Butterworth filter. Obtained amplitudes were then baseline corrected by subtracting the amplitude present at 400 to 200 ms prior to trial onset. As in previous studies (Wieser & Keil, 2011), ssVEP amplitudes for the face and the Gabor patch were then extracted for the full time window (100 to 3000 ms post-stimulus) and for three time windows (100 to 700 ms; 800 to 1400 ms; 1700 to 2300 ms). For difference score analyses, each time window, a difference score was calculated ($ssVEP_{Face} - ssVEP_{Gabor\ patch}$) such that positive values indicate higher face ssVEP amplitudes than Gabor patch ssVEP amplitudes, and negative values indicate higher Gabor patch ssVEP amplitudes than face ssVEP amplitudes. For the item analysis, this difference score was extracted for each trial, and then averaged across participants to obtain an average measure of attentional allocation for each trial. For the participant-level analysis, the trial-level data was first averaged within each block, and then across blocks, so that each participant has an average ssVEP amplitude for the face, the Gabor patch, and a difference between these two amplitudes, at each specified time window.

Genotyping. Participants were genotyped for the *ADRA2b* deletion variant. Extraction and genotyping of the DNA was performed at the Neurogenetics Laboratory at the Centre for Addiction and Mental Health in Toronto, Canada for the first 125 participants and at the BC Children's Hospital Research Institute in Vancouver for the last 58 participants included in the final sample. For each variant, Hardy-Weinberg equilibrium was calculated using an online Hardy-Weinberg Chi Square calculator (Rodriguez, Gaunt, & Day, 2009).

Assays. The *ADRA2B* 9bp insertion/deletion variant was assayed using PCR followed by Sanger sequencing. A total of 50ng genomic DNA was combined with 1xAmpliTaq Gold 360 buffer, 2.0 mM Magnesium Chloride, 360GC Enhancer 4ul, 200 uM dNTPs, 0.5 uM Forward primer ACGAAGGTGAAGCGCTTCT and 0.5 uM Reverse primer GGCCAGAAGGAGGGTGTTT, AmpliTaq Gold 360 DNA Polymerse 0.625 U/reaction and total volume 25ul in a 96 well plate. Initial denaturation was at 95°C for 8 min, followed by 38 cycles at 95°C for 50 sec, 60°C for 30 sec and 72°C for 50 sec and a final extension step of 7 min at 72 °C. The PCR products were cleaned up by ExoSAP-IT Express and analyzed by Sanger sequencing (ABI 3130, Applied Biosystems).

Results

Genotyping Results

ADRA2B genotype frequencies fell within Hardy-Weinberg equilibrium (did not differ from expected frequencies), $X^2 = 0.03$, $p > .05$. Of the 183 individuals, 95 participants did not carry the *ADRA2b* deletion variant, 73 carried one copy of the allele, and 15 were homozygous for the deletion variant. We were unable to obtain reliable genotyping for *ADRA2B* for two

participants. For all analyses, based on previous research (de Quervain et al., 2007; Rasch et al., 2009a; Todd et al., 2015; Todd et al., 2013; Todd et al., 2014), homozygote and heterozygote *ADRA2b* deletion carriers were treated as a single group due to the low number of homozygotes.

Behavioral Results

Statistical Analyses. Two-way (*ADRA2b* group) x 3 (emotion) repeated measures ANOVAs were performed on arousal and valence ratings for face stimuli in the face ratings tasks and for accuracy in the change detection task. Analyses were first conducted independently in the replication and discovery samples. After results were examined in the two separate samples, data from all participants were combined for increased power and analyses were repeated in the full sample. For all ANOVAs reported contrasts were Bonferroni corrected for multiple comparisons and Greenhouse-Geisser corrections were used when sphericity was violated. We report results of analyses of the full sample below, and note any instances where results in the full sample differ from either the replication or discovery results. Results of all behavioral analyses for Replication and Discovery samples can be found in Table 2.

Arousal Ratings

There was a main effect of emotion, $F(1.74, 311.81) = 86.57$, $p < .001$, $\eta_p^2 = .33$, with higher levels of arousal for happy than neutral faces and higher levels of arousal for angry than happy and neutral faces (*p*s < .001). There was no main effect of *ADRA2b*, $F(1,179) = 0.55$, $p = .457$, $\eta_p^2 = 0.00$ and no emotion x interaction, $F(1.742, 311.81) = 0.15$, $p = .829$, $\eta_p^2 = 0.00$. Thus, confirming our emotional manipulation, participants found angry faces to be more arousing than happy faces which in turn were more arousing than neutral faces (Figure 2). There was no evidence that carrying the *ADRA2b* deletion variant influenced subjectively rated arousal of emotional faces in either sample or the full group.

Valence Ratings

There was a main effect of emotion, $F(1.33, 236.15) = 899.42$, $p < .001$, $\eta_p^2 = .83$, indicating that, as expected, angry faces were rated as negatively valenced and happy faces were rated as positively valenced (*p*'s < .001) There was no main effect of *ADRA2b*, $F(1,178) = 0.66$, $p = .416$, $\eta_p^2 = 0.00$ and no emotion x *ADRA2b* interaction, $F(1.33, 236.15) = 0.63$, $p = .471$, $\eta_p^2 = 0.00$. These findings confirm that participants subjectively rate angry, neutral and happy faces as appropriately valenced (Figure 2). There was no evidence that carrying the *ADRA2b* deletion variant influenced subjective experience of stimulus valence.

Change Detection Accuracy

Note that there were errors in recording accuracy data for four participants, who were omitted from the analysis. There was no main effect of emotion, $F(2,352) = 2.35$, $p = .097$, $\eta_p^2 = .01$, and no main effect of *ADRA2b*, $F(1,176) = .24$, $p = .622$, $\eta_p^2 = .001$ (Figure 2). There was an emotion x *ADRA2b* interaction, $F(2,352) = 3.17$, $p = .043$, $\eta_p^2 = .02$, with non-deletion carriers demonstrating greater accuracy in trials with angry face distractors than trials with happy face distractors (paired contrast *p*'s < .05). However, this interaction was non-significant in both the Discovery and Replication samples (see Table 2). Here effect sizes were consistent across samples, indicating the power of the full sample may have been required for a small effect

showing facilitation of performance in the presence of angry faces for those who did not carry the deletion variant. This effect may be so small as to be trivial, and would require further replication to merit discussion.

ssVEP Results

Omnibus ANOVA. In order to ascertain the potential presence of competition effects between targets and distractors, we first conducted an omnibus repeated measures ANOVA on ssVEP power, with *ADRA2b* (deletion carrier vs. non-carrier) as a between-subjects factor and stimulus type (target or distractor), emotion (angry, neutral, happy) and time window (early, middle, late) as within subject factors. All results of this ANOVA are reported in Table 3. There was a main effect of stimulus type, $F(1,180) = 14.34$, $p < .001$, $\eta_p^2 = 0.07$ such that there were higher amplitudes in response to the Gabor targets than to the face distractors, indicating biased competition favoring target stimuli. There was also a main effect of emotion, $F(1.47, 264.75) = 4.88$, $p = .016$, $\eta_p^2 = 0.03$; however, this effect was observed only in the Discovery sample (see Table 3) and was highly variable between cohorts, with drastically different effect sizes. Thus, the effect in the full sample clearly reflected an effect that was strongly but solely observed in the Discovery sample. This inconsistent effect of emotion was qualified by a consistently observed stimulus type x emotion interaction, indicating the presence of affectively-biased competition, $F(2,360) = 13.06$, $p < .001$, $\eta_p^2 = 0.07$. Paired contrasts revealed that whereas amplitudes were greater for targets in the presence of all distractor types (p's < .05), the differences were smaller in trials with happy face distractors. While there was no main effect of time window, there was a time window x stimulus type interaction, $F(1.21,218.69) = 14.75$, $p = .000$, $\eta_p^2 = .08$. Pairwise contrasts indicated greater power differences between targets and face distractors in window 1 and 3 than in window 2 (ps < .005). There was also a time window x stimulus type x emotion interaction, $F(3.39, 609.60) = 4.10$, $p = .005$, $\eta_p^2 = 0.02$; however, this was observed only in the Discovery sample (see Table 3). Importantly, there was no main effect of *ADRA*2b, $F(1, 180) = .88$, $p = .350$, $\eta_p^2 = 0.00$ and no hypothesized stimulus type x emotion x *ADRA*2b interaction, $F(2, 360) = 1.49$, $p = .227$, $\eta_p^2 = 0.01$.

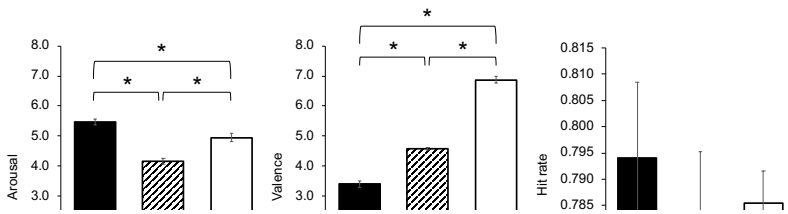


Figure 2. Arousal and valence ratings for face stimuli and accuracy for the change detection task. Angry faces were rated as more arousing than happy faces which were rated as more arousing than neutral faces. Faces were rated as appropriately valenced (lowest numbers are most negative and highest are most positive). And participants did not differ in accuracy between trials with happy, angry or neutral distractors.

In summary, in all samples there was a pattern of higher amplitudes for target stimuli, indicating competition effects indicating participants maintained greater attention to task-relevant stimuli than emotionally salient distractors. We also reliably observed an interaction between stimulus type and distractor expression, indicating that the difference in power between targets and distractors was reduced in the presence of happy faces. We further

observed that the differences in ssVEP power varied by time window. Notably, there was no evidence of any effect of *ADRA2b* genotype.

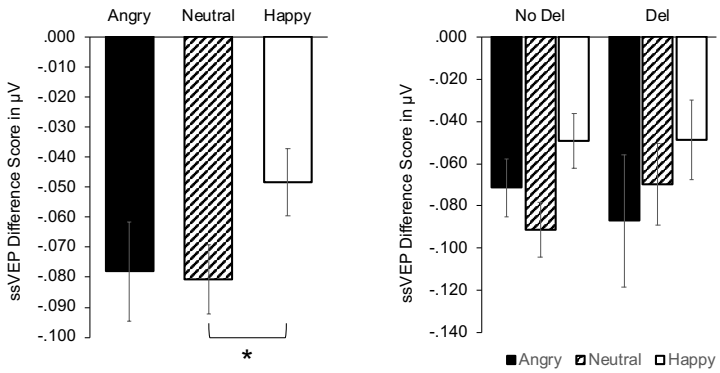
Difference Scores. To follow up on the interaction between facial expression and stimulus type, and thus better probe the characterize effects of emotion on competition for neurocognitive resources between targets and distractors, we next calculated a difference score between targets and distractors for each emotion expression in each time window. Thus, larger difference scores would indicate greater competition between targets and distractors and vice versa. Moreover, while our previous studies have found robust effects of *ADRA2b* on emotion/cognition interactions in samples of this size or smaller, suggesting our study was not underpowered to find equivalent effects, we wished to further probe the reliability of the null effects observed for *ADRA2b.* We thus next conducted a Bayesian ANOVA on the full sample using JASP (JASP Team, 2018) with default priors.

First, we conducted a mixed ANOVA with *ADRA2b* (deletion carrier vs. non-carrier) as a between subject factor and emotion (angry, neutral, happy) and time window (early, middle, late) as within subject factors. Consistent with the time window by stimulus type interaction observed in the previous analysis, there was a main effect of time window, $F(1.53,275.38) = 13.00$, $p = .000$, $\eta_p^2 = .07$ such that there were overall largest difference scores in the third time window than in either of the first 2 (ps < .001). There was also a main effect of emotion, $F(1.56, 280.02) = 4.80$, $p = .015$, $\eta_p^2 = .03$. Contrasts revealed that difference scores were smaller in trials with happy faces, indicating greater competition for neurocognitive resources from happy faces than from neutral (p < .001) or, marginally, angry ($p = .06$) faces, which in turn did not differ from each other ($p > 1$) (Figure 3). In this analysis this finding was qualified by a time window x emotion interaction, $F(3.76, 676.43) = 3.57$, $p = .008$, $\eta_p^2 = .02$, indicating that the greatest happy face bias effect was observed in time window 2 (ps < .05). Crucially, there was no main effect of *ADRA*2b, $F(1, 180) = .00$, $p = .958$, $\eta_p^2 = .00$, no emotion x *ADRA*2b interaction, $F(1.47, 264.75) = .1.16$, $p = .3$, $\eta_p^2 = .01$ (Figure 3), nor was there a time window x emotion x *ADRA*2b interaction, $F(3.76, 676.43) = .32$, $p = .853$, $\eta_p^2 = .00$.

Analysis of the effects of a Bayesian Mixed ANOVA across matched models revealed a main effect of time window ($BF_{Inclusion} = 15302.41$), a main effect of face emotion ($BF_{Inclusion} = 1064.12$) and, in this analysis, no interaction between these two factors ($BF_{Inclusion} = 0.003$). There is some evidence against the main effect of *ADRA2b* ($BF_{Inclusion} = 0.31$) and its interaction with face emotion ($BF_{Inclusion} = 0.27$) and its interaction with time window ($BF_{Inclusion} = 0.02$). There is considerable evidence against a three-way interaction among these factors ($BF_{Inclusion} = 0.002$). These results demonstrate that there is evidence against ADRA2b modulating the degree to which emotional stimuli influence biased competition.

In summary, effects that were consistent across all frequentist and Bayesian analyses of ssVEP amplitude indicated that, within each trial, competition for neurocognitive resources favouring target stimuli over face distractors increased over time. Competition was also modulated by the facial expression of the distractor, such that smiling faces captured more neurocognitive resources from targets than angry or neutral faces. Effects of time window on emotionally-biased competition were not reliable. Importantly, there was no evidence for – and some positive evidence against — our hypothesis that putative greater NE availability resulting from carrying the ADRA2b deletion variant influenced emotionally-biased competition between targets and distractors.

Figure 3. ssVEP difference scores ($ssVEP_{Face} - ssVEP_{Gabor\ patch}$) for trials with distractors for each facial emotion in the whole sample (left) and by *ADRA2b* group (del = deletion carrier, no del = non-carrier of the deletion variant). Whereas overall more cortical resources allocated to task relevant stimuli than emotion face distractors, there reduced difference scores in trials with happy faces, indicating greater competition for resources from happy faces. There was no influence of carrying the *ADRA2b* deletion variant on this pattern of results.



Effects of Social Anxiety. While reliable, the observed effects of emotional valence on difference scores were small. In order to examine whether the higher levels of competition for neurocognitive resources was modulated by social anxiety, as has been previously observed (Wieser et al., 2012), we next probed effects of emotion on the difference scores in the 25% of our sample that was highest (n = 45), and the 25% that was lowest (n =44) in social anxiety based on LSAS scores. Mean scores for social anxiety (LSAS) were (*M* = 9.68, *SD* = 7.39) in the low anxiety group and (*M* = 58.87, *SD* = 14.20) in the high anxiety group.

A 2x3x3 (LSAS group x Emotion x Time window) mixed ANOVA was performed on ssVEP difference scores described above. As previously reported, there was no main effect of emotion, $F(1.29, 112.56) = 3.26$, $p = .063$, $\eta_p^2 = .04$. There was a main effect of time window, $F(1.60, 139.57) = 5.84$, $p = .007$, $\eta_p^2 = .06$ but no time window x emotion interaction $F(4, 348) = 2.13$, $p = .076$, $\eta_p^2 = .02$. Finally, there was no main effect of LSAS, $F(1, 87) = 2.44$, $p = .122$, $\eta_p^2 = .03$ and no emotion x LSAS interaction, $F(1.29, 112.56) = 1.06$, $p = .322$, $\eta_p^2 = .01$.

To confirm the null effect of social anxiety, analysis of the effects of a Bayesian Mixed ANOVA across matched models again revealed a main effect of time window ($BF_{Inclusion} = 3.45$), a main effect of face emotion ($BF_{Inclusion} = 71.60$). There was inconclusive evidence for both a main effect of social anxiety and an interaction between social anxiety and face emotion ($BF_{Inclusion} = 0.86$; $BF_{Inclusion} = 0.418$, respectively). All remaining interactions revealed null effects (all $BF_{Inclusion} < 0.07$). Thus there was no evidence suggesting that social anxiety influenced affectively-biased competition in this sample of participants.

Trial by trial examination of low-level feature effects. An outstanding question concerned whether the effects of emotional valence on biased competition were due to the emotional content of the stimuli or capture of attention by low level features, such as contrast, that might differentiate happy faces from neutral and angry faces. To probe this question we extracted metrics of image contrast, edges, and average log luminance using the Image Processing Toolbox packaged with MATLAB 8.6.0 (The MathWorks, Natick, MA) and low and high spatial frequency content using the SHINE toolbox (Willenbockel et al., 2010) and examined correlations with ssVEP difference score values. Contrast was calculated by finding the standard deviation of the grayscale pixel values. Edges was calculated with MATLAB's edge function, using a Canny filter with a threshold of 0.5. Average log luminance was calculated as the exponential of the mean value of the logarithm of the grayscale pixel values. Spatial frequency content was calculated using the sfplot function from the SHINE toolbox, which extracts the energy at each spatial frequency in the image. From the output of this function, low frequency content was calculated as the mean energy of frequencies below the median frequency, and high frequency content was calculated as the mean energy for the remaining frequencies. A single image was removed from the analysis because it was identified visually as an outlier and had a face-Gabor ssVEP difference greater than 2.5 standard deviations from the mean. Results showed that only edges may have marginally influenced the face-Gabor ssVEP differences (r = 0.23, p = .054, 95% CI [0.00, 0.44]), while all other image properties very clearly did not correlate with this measure (p's > .418) (Figure 4).

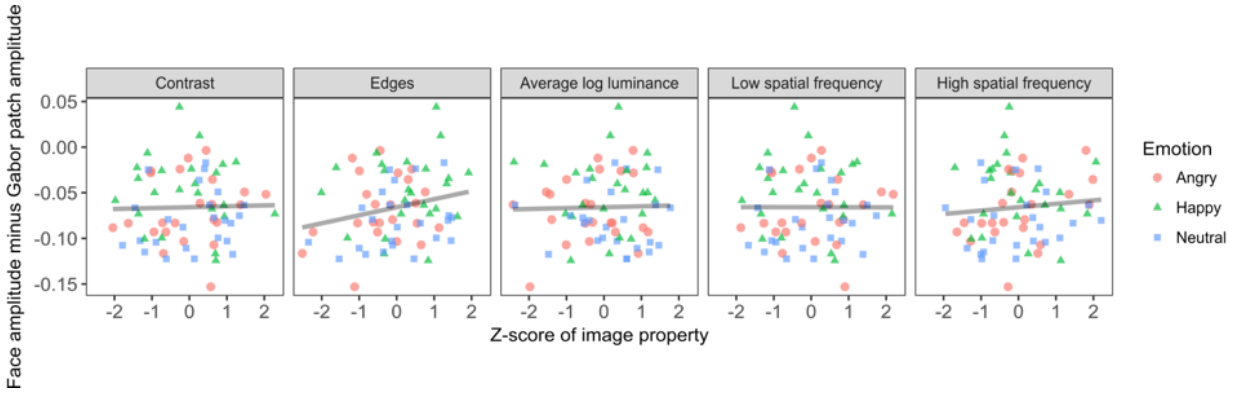


Figure 4. Correlations between metrics of low level visual features and ssVEP difference scores for trials with happy, angry and neutral faces. Only edges correlated with difference scores and differed between happy and other expressions. The happy face competition advantage remained after controlling for the effects f edges on ssVEP amplitudes.

Next, we conducted a one-way ANOVA to test whether the number of edges differed between facial emotion categories. If the ANOVA revealed that there was no difference among the face emotions on the amount of edges in the images, then our primary result demonstrating modulation of amplitude differences by face emotion should not be due to differences in the amount of edges in the image. However, the ANOVA revealed that facial emotion category had a significant impact on the number edges in an image, $F(2, 68) = 4.80$, p = .011, $\eta_p^2 = 0.12$). A follow-up regression was conducted to evaluate whether the facial emotion category influenced amplitude differences while controlling for the possible influence of edges in the images. For this regression, amplitude difference was predicted by emotion and edges,

where the emotion factor was dummy coded with neutral as the reference level. The regression revealed that when controlling for the effect of edges on amplitude difference, a robust difference remained between neutral and happy faces, $\beta = 0.79$, $t(67) = 2.90$, $p = .005$, while there was no difference between neutral and angry faces, $\beta = 0.38$, $t(67) = 1.39$, $p = .171$. Finally, when controlling for the effects of face emotion, there was no relationship between edges and amplitude difference, $\beta = 0.19$, $t(67) = 1.67$, $p = .099$. Overall, this analysis indicates that low-level features did not have an appreciable influence on ssVEP amplitude differences, and that face emotion had an influence on amplitude differences beyond that which could be attributed to edges or other low-level features.

Discussion

In the present study, we used ssVEPs to examine effects of *ADRA2B* a common genetic variation, thought to influence norepinephrine availability, on affectively-biased competition in the visual cortex. We further examined within-subject effects of emotional valence in a large sample of healthy young adults. Counter to our hypotheses, carrying a deletion variant of the *ADRA2B* gene had no influence on competition for population-level neuronal responses between task-relevant stimuli and affectively salient distractors. Thus, the evidence suggests that naturally occurring variation in NE levels putatively associated with this genetic variation neither drive nor modulate such affectively-based visual cortex competition. In the group as a whole, the presence of happy faces captured cortical resources from target stimuli, particularly at middle latencies, indicating biased competition for smiling faces at the population level of neuronal competition. Although happy faces photographs did differ from angry and neutral faces in the number of edges they contained, follow-up analyses showed that the effect of emotional expression on biased competition was not due to differences in low-level features between happy faces and other facial expressions.

Our own previous research has found robust effects for the *ADRA2B* deletion variant influencing affective biases in attention and memory. Building on findings that carrying the deletion variant influences emotional enhancement of memory (de Quervain et al., 2007), we have found that carrying this variation enhances attentional selection for emotionally relevant words, enhances the link between subjective emotional arousal in encoding and memory accuracy and confidence, and enhances the subjective perception of the relative vividness (signal to noise ratio) of emotionally salient images (Todd et al., 2015; Todd et al., 2013; Todd et al., 2014). It has also been associated with differences in responsiveness of the amygdala and VMPFC to enhanced processing of salient stimuli (Rasch et al., 2009b; Todd et al., 2015; Todd et al., 2013; Todd et al., 2014), which might be expected to drive affectively enhanced processing in the visual cortex.

The present study was motivated by the hypothesis that putatively higher levels of NE availability in deletion carriers would facilitate biased visual cortex competition favoring affectively salient stimuli, providing some mechanistic understanding of our previously-observed results. This was not the case. It is worth noting that all of our previous studies on the influence of *ADRA2b* on attention and subjective perception tapped relatively rapid processes, whereas the effects of biased competition measured here emerged more slowly. It is also notable that our previous research found that, in contrast to findings of emotionally enhanced activation in the ventromedial prefrontal cortex and the amygdala (Rasch et al., 2009b; Todd et

al., 2015), deletion carriers did not differ from non-carriers in patterns of enhanced visual cortex activation for emotionally salient stimuli. These findings are convergently consistent with the conclusion that effects of NE on emotionally-biased processing do not function via visual cortex activity.

The results of a Bayesian ANOVA further suggested our null finding was conclusive, despite the relatively small sample size for a targeted polymorphism study. Our power analysis indicated that the study was amply powered based on the weakest effect size of our previous studies examining *ADRA2B.* Thus, we conclude that commonly observed differences related to NE activity do not play a role in modulating biased competition in the visual cortex, at least not for sustained firing patterns measured here. However, it is worth noting that previous studies investigating effects of ADRA2b have used more arousing affective stimuli than emotionally expressive faces, using images and words that evoke more physiological arousal [e.g., (A. K. Anderson, Yamaguchi, Grabski, & Lacka, 2006). Thus, it is possible that a higher level of stimulus-evoked arousal may be required for differences in NE functioning to influence biased competition effects.

We did, however, find modest but reliable evidence that smiling faces capture more visual cortex resources, indexing greater attention, from task-relevant stimuli than angry or neutral faces. These findings are inconsistent with a prevalent "standard hypothesis" in affective science, which has proposed threatening stimuli such as angry faces are universally prioritized because of an evolutionary advantage for rapid threat detection (Ohman, Flykt, & Esteves, 2001; Ohman, Lundqvist, & Esteves, 2001). However, findings of attentional prioritization of threatening relative to rewarding facial expressions have been repeatedly challenged on several fronts. First, there is an extensive literature documenting systematic individual differences in the direction of biases [for review see (Todd, Cunningham, Anderson, & Thompson, 2012)]. Valence preferences can also vary with developmental stage, such that young children show far more sensitivity and prioritization of happy faces than young adults (Picardo, Baron, Anderson, & Todd, 2016; Todd, Evans, Morris, Lewis, & Taylor, 2011). Although in the present study this pattern did not reflect the individual differences in *ADRA2b* genotype and social anxiety we predicted and measured in this sample. This may be because previous studies finding social anxiety effects used participants with less extreme levels of social anxiety and less variability in the high social anxiety participants (Wieser et al., 2012). However, it is likely that given the degree of variability observed (Figure 2), and the modest effect size, this pattern is subject to individual differences linked to other traits.

Second, studies looking at overall within-subject effects of valenced stimuli on attention have yielded conflicting results. After controlling for low-level features, some researchers have observed consistent happiness superiority effects as we did (Becker, Anderson, Mortensen, Neufeld, & Neel, 2011). Such findings have been interpreted as reflecting easier visual discrimination of the unambiguous communication that is afforded by happy faces (Becker et al., 2011). Yet the happiness advantage is also subject to boundary conditions, and been linked to more subtle featural confounds (Purcell & Stewart, 2010), such as the relative orientation of face and mouth contours (Stein & Sterzer, 2012). In the case of photographic faces, prioritization of angry vs happy faces can vary depending on the stimulus set used (Savage, Becker, & Lipp, 2016; Savage, Lipp, Craig, Becker, & Horstmann, 2013). Future research will be

required to establish whether the increased biased competition from happy faces we observed generalizes to other affective stimulus sets.

An additional suggestion has been that, after controlling for low-level perceptual features, it is arousal rather than valence that drives attentional prioritization (Juth, Lundqvist, Karlsson, & Ohman, 2005). In the present study, the biased competition for happy faces we observed did not reflect differences in the low-level features we measured (Figure 3); however, they also did not reflect self-reported arousal, as participants rated angry faces as more arousing than happy ones (Table 2). In summary, our findings are consistent with robust evidence that in some contexts happy facial expressions, which are experienced as rewarding, are prioritized over angry ones. These findings did not reflect key low-level features nor did they reflect patterns of subjectively rated arousal. Nonetheless, such valence effects are subject to numerous boundary conditions that constrain our interpretation.

An additional advantage to employing Discovery and Replication samples is that we were able to observe the replicability of within-subject effects in independent samples that were larger than is typical of within-subject cognition-emotion studies. While some effects were observed consistently, it is notable that for the ssVEP data there was a main effect of emotion that was extremely robust in the Discovery sample, with a large effect size (n = 90, partial eta square = .14, $p < .001$), but was nonexistent in the Replication sample, with (n = 92, partial eta square = .01, $p < .54$). Such marked variability across samples is a vivid illustration of the unreliability of within-subject emotion effects, even in healthy sample sizes.

Finally, although examination of social anxiety was not the focus of this study, we failed to replicate previous findings that social anxiety modulated the biased competition effect in a larger sample (Wieser et al., 2012). Unlike the previous study, we did not screen for high and low anxiety, and our high-anxiety group had lower levels of mean anxiety than that of the previous study. Thus, it may be effects would be replicated in samples where anxiety levels are more extreme.

In sum, affective science has a history of making fairly broad claims based on assumptions of the generalizability of within-subject findings in relatively small samples. Our findings add to growing evidence indicating multiple boundary conditions for observed neurocognitive patterns of affectively-biased attention. Studies using larger sample sizes for within-subject designs, investigation of individual differences, and increased use of tools such as Bayesian analyses to probe the conclusiveness of null results – along with increased willingness to publish null results – will play an important role refining our understanding of cognition-emotion interactions.

References

Anderson, A. K., Yamaguchi, Y., Grabski, W., & Lacka, D. (2006). Emotional memories are not all created equal: evidence for selective memory enhancement. *Learn Mem, 13*(6), 711-718. doi:lm.388906 [pii]
10.1101/lm.388906

Anderson, B. A. (2016). What is abnormal about addiction-related attentional biases? *Drug and alcohol dependence, 167*, 8-14. doi:10.1016/j.drugalcdep.2016.08.002

Bar-Haim, Y., Lamy, D., Pergamin, L., Bakermans-Kranenburg, M. J., & van, I. M. H. (2007). Threat-related attentional bias in anxious and nonanxious individuals: a meta-analytic study. *Psychological Bulletin, 133*(1), 1-24. doi:10.1037/0033-2909.133.1.1

Becker, D. V., Anderson, U. S., Mortensen, C. R., Neufeld, S. L., & Neel, R. (2011). The face in the crowd effect unconfounded: happy faces, not angry faces, are more efficiently detected in single- and multiple-target visual search tasks. *J Exp Psychol Gen, 140*(4), 637-659. doi:10.1037/a0024060

Carretie, L. (2014). Exogenous (automatic) attention to emotional stimuli: a review. *Cogn Affect Behav Neurosci, 14*(4), 1228-1258. doi:10.3758/s13415-014-0270-2

Dalgleish, T., Taghavi, R., Neshat-Doost, H., Moradi, A., Canterbury, R., & Yule, W. (2003). Patterns of processing bias for emotional information across clinical disorders: a comparison of attention, memory, and prospective cognition in children and adolescents with depression, generalized anxiety, and posttraumatic stress disorder. *Journal of clinical child and adolescent psychology : the official journal for the Society of Clinical Child and Adolescent Psychology, American Psychological Association, Division 53, 32*(1), 10-21. doi:10.1207/S15374424JCCP3201_02

de Quervain, D. J., Kolassa, I. T., Ertl, V., Onyut, P. L., Neuner, F., Elbert, T., & Papassotiropoulos, A. (2007). A deletion variant of the alpha2b-adrenoceptor is related to emotional memory in Europeans and Africans. *Nat Neurosci, 10*(9), 1137-1139. doi:10.1038/nn1945

Derryberry, D., & Reed, M. A. (1994). Temperament and attention: orienting toward and away from positive and negative signals. *Journal of Personality and Social Psychology, 66*(6), 1128-1139.

Grabitz, C. R., Button, K. S., Munafo, M. R., Newbury, D. F., Pernet, C. R., Thompson, P. A., & Bishop, D. V. M. (2018). Logical and Methodological Issues Affecting Genetic Studies of Humans Reported in Top Neuroscience Journals. *J Cogn Neurosci, 30*(1), 25-41. doi:10.1162/jocn_a_01192

Juth, P., Lundqvist, D., Karlsson, A., & Ohman, A. (2005). Looking for foes and friends: perceptual and emotional factors when finding a face in the crowd. *Emotion, 5*(4), 379-395. doi:10.1037/1528-3542.5.4.379

Kastner-Dorn, A. K., Andreatta, M., Pauli, P., & Wieser, M. J. (2018). Hypervigilance during anxiety and selective attention during fear: Using steady-state visual evoked potentials (ssVEPs) to disentangle attention mechanisms during predictable and unpredictable threat. *Cortex; a journal devoted to the study of the nervous system and behavior, 106*, 120-131. doi:10.1016/j.cortex.2018.05.008

Kim, Y. J., Grabowecky, M., Paller, K. A., Muthu, K., & Suzuki, S. (2007). Attention induces synchronization-based response gain in steady-state visual evoked potentials. *Nat Neurosci, 10*(1), 117-125. doi:nn1821 [pii]
10.1038/nn1821

Liu-Shuang, J., Norcia, A. M., & Rossion, B. (2014). An objective index of individual face discrimination in the right occipito-temporal cortex by means of fast periodic oddball stimulation. *Neuropsychologia, 52*, 57-72. doi:10.1016/j.neuropsychologia.2013.10.022

Markovic, J., Anderson, A. K., & Todd, R. M. (2014). Tuning to the significant: Neural and genetic processes underlying affective enhancement of visual perception and memory. *Behavioural brain research, 259*, 229-241. doi:10.1016/j.bbr.2013.11.018

McTeague, L. M., Gruss, L. F., & Keil, A. (2015). Aversive learning shapes neuronal orientation tuning in human visual cortex. *Nat Commun, 6*, 7823. doi:10.1038/ncomms8823

Miskovic, V., & Keil, A. (2013). Visuocortical changes during delay and trace aversive conditioning: evidence from steady-state visual evoked potentials. *Emotion, 13*(3), 554-561. doi:10.1037/a0031323

Ohman, A., Flykt, A., & Esteves, F. (2001). Emotion drives attention: detecting the snake in the grass. *Journal of experimental psychology. General, 130*(3), 466-478.

Ohman, A., Lundqvist, D., & Esteves, F. (2001). The face in the crowd revisited: a threat advantage with schematic stimuli. *J Pers Soc Psychol, 80*(3), 381-396.

Peckham, A. D., McHugh, R. K., & Otto, M. W. (2010). A meta-analysis of the magnitude of biased attention in depression. *Depression and anxiety, 27*(12), 1135-1142. doi:10.1002/da.20755

Picardo, R., Baron, A. S., Anderson, A. K., & Todd, R. M. (2016). Tuning to the Positive: Age-Related Differences in Subjective Perception of Facial Emotion. *PLoS ONE, 11*(1), e0145643. doi:10.1371/journal.pone.0145643

Pourtois, G., Schettino, A., & Vuilleumier, P. (2013). Brain mechanisms for emotional influences on perception and attention: what is magic and what is not. *Biological psychology, 92*(3), 492-512. doi:10.1016/j.biopsycho.2012.02.007

Purcell, D. G., & Stewart, A. L. (2010). Still another confounded face in the crowd. *Attention, perception & psychophysics, 72*(8), 2115-2127. doi:10.3758/APP.72.8.2115

Rasch, B., Spalek, K., Buholzer, S., Luechinger, R., Boesiger, P., Papassotiropoulos, A., & de Quervain, D. J. (2009a). A genetic variation of the noradernergic system is related to differential amygdala activation during encoding of emotional memories. *Proc Natl Acad Sci U S A*.

Rasch, B., Spalek, K., Buholzer, S., Luechinger, R., Boesiger, P., Papassotiropoulos, A., & de Quervain, D. J. (2009b). A genetic variation of the noradrenergic system is related to differential amygdala activation during encoding of emotional memories. *Proceedings of the National Academy of Sciences of the United States of America, 106*(45), 19191-19196. doi:10.1073/pnas.0907425106

Rodriguez, S., Gaunt, T. R., & Day, I. N. (2009). Hardy-Weinberg equilibrium testing of biological ascertainment for Mendelian randomization studies. *American journal of epidemiology, 169*(4), 505-514. doi:10.1093/aje/kwn359

Sara, S. J. (2009). The locus coeruleus and noradrenergic modulation of cognition. *Nature Reviews Neuroscience, 10*(3), 211-223. doi:10.1038/nrn2573

Sara, S. J., & Bouret, S. (2012). Orienting and reorienting: the locus coeruleus mediates cognition through arousal. *Neuron, 76*(1), 130-141. doi:10.1016/j.neuron.2012.09.011

Savage, R. A., Becker, S. I., & Lipp, O. V. (2016). Visual search for emotional expressions: Effect of stimulus set on anger and happiness superiority. *Cognition & emotion, 30*(4), 713-730. doi:10.1080/02699931.2015.1027663

Savage, R. A., Lipp, O. V., Craig, B. M., Becker, S. I., & Horstmann, G. (2013). In search of the emotional face: anger versus happiness superiority in visual search. *Emotion, 13*(4), 758-768. doi:10.1037/a0031970

Stein, T., & Sterzer, P. (2012). Not just another face in the crowd: detecting emotional schematic faces during continuous flash suppression. *Emotion, 12*(5), 988-996. doi:10.1037/a0026944

Surguladze, S. A., Young, A. W., Senior, C., Brebion, G., Travis, M. J., & Phillips, M. L. (2004). Recognition accuracy and response bias to happy and sad facial expressions in patients with major depression. *Neuropsychology, 18*(2), 212-218. doi:10.1037/0894-4105.18.2.212

Todd, R. M., Cunningham, W. A., Anderson, A. K., & Thompson, E. (2012). Affect-biased attention as emotion regulation. *Trends in Cognitive Sciences, 16*(7), 365-372. doi:10.1016/j.tics.2012.06.003

Todd, R. M., Ehlers, M. R., Muller, D. J., Robertson, A., Palombo, D. J., Freeman, N., . . . Anderson, A. K. (2015). Neurogenetic variations in norepinephrine availability enhance perceptual vividness. *J Neurosci, 35*(16), 6506-6516. doi:10.1523/JNEUROSCI.4489-14.2015

Todd, R. M., Evans, J. W., Morris, D., Lewis, M. D., & Taylor, M. J. (2011). The changing face of emotion: age-related patterns of amygdala activation to salient faces. *Soc Cogn Affect Neurosci, 6*(1), 12-23. doi:nsq007 [pii]
10.1093/scan/nsq007

Todd, R. M., & Manaligod, M. G. M. (2017). Implicit guidance of attention: The priority state space framework. *Cortex; a journal devoted to the study of the nervous system and behavior*. doi:10.1016/j.cortex.2017.08.001

Todd, R. M., Muller, D. J., Lee, D. H., Robertson, A., Eaton, T., Freeman, N., . . . Anderson, A. K. (2013). Genes for emotion-enhanced remembering are linked to enhanced perceiving. *Psychol Sci, 24*(11), 2244-2253. doi:10.1177/0956797613492423
0956797613492423 [pii]

Todd, R. M., Muller, D. J., Palombo, D. J., Robertson, A., Eaton, T., Freeman, N., . . . Anderson, A. K. (2014). Deletion variant in the ADRA2B gene increases coupling between emotional responses at encoding and later retrieval of emotional memories. *Neurobiol Learn Mem, 112*, 222-229. doi:10.1016/j.nlm.2013.10.008

Todd, R. M., Talmi, D., Schmitz, T. W., Susskind, J., & Anderson, A. K. (2012). Psychophysical and neural evidence for emotion-enhanced perceptual vividness. *J Neurosci, 32*(33), 11201-11212. doi:10.1523/JNEUROSCI.0155-12.2012

Wieser, M. J., & Keil, A. (2011). Temporal Trade-Off Effects in Sustained Attention: Dynamics in Visual Cortex Predict the Target Detection Performance during Distraction. *The Journal of neuroscience : the official journal of the Society for Neuroscience, 31*(21), 7784-7790. doi:10.1523/JNEUROSCI.5632-10.2011

Wieser, M. J., McTeague, L. M., & Keil, A. (2012). Competition effects of threatening faces in social anxiety. *Emotion, 12*(5), 1050-1060. doi:10.1037/a0027069

Wieser, M. J., Reicherts, P., Juravle, G., & von Leupoldt, A. (2016). Attention mechanisms during predictable and unpredictable threat - A steady-state visual evoked potential approach. *Neuroimage, 139*, 167-175. doi:10.1016/j.neuroimage.2016.06.026

Tables

Table 2. Behavioural Results. Results that are statistically significant at $p < .05$ are in bold, and those that are significant across all samples are bold and underlined.

	df	*F*	*p-value*	η_p^2
AROUSAL				
DISCOVERY SAMPLE				
Emotion	**(1.71, 150.66)**	**45.35**	**0**	**0.34**
*ADRA*2b	(1, 88)	0.29	0.593	0
*ADRA*2b * Emotion	(1.71, 150.66)	0.16	0.818	0
REPLICATION SAMPLE				
Emotion	**(1.74, 154.60)**	**43.14**	**0**	**0.33**
*ADRA*2b	(1, 89)	0.26	0.612	0.33
*ADRA*2b * Emotion	(1.74, 154.60)	0.07	0.916	0
FULL SAMPLE				
Emotion	**(1.74, 311.81)**	**86.57**	**0**	**0.33**
*ADRA*2b	(1, 179)	0.55	0.457	0
*ADRA*2b * Emotion	(1.742, 311.81)	0.15	0.829	0
VALENCE				
DISCOVERY SAMPLE				
Emotion	**(1.35, 117.38)**	**387.44**	**0**	**0.82**
*ADRA*2b	(1, 87)	0.09	0.762	0
*ADRA*2b * Emotion	(1.35, 117.38)	2.33	0.12	0.03
REPLICATION SAMPLE				
Emotion	**(1.31, 116.60)**	**554.93**	**0**	**0.86**
*ADRA*2b	(1, 89)	0.71	0.402	0.01
*ADRA*2b * Emotion	(1.31, 116.60)	0.21	0.712	0
FULL SAMPLE				
Emotion	**(1.33, 236.15)**	**899.42**	**0**	**0.83**
*ADRA*2b	(1, 178)	0.66	0.416	0
*ADRA*2b * Emotion	(1.33, 236.15)	0.63	0.471	0
ACCURACY				
DISCOVERY SAMPLE				
Emotion	(2, 176)	0.9	0.41	0.01
*ADRA*2b	(1, 88)	0.18	0.671	0
*ADRA*2b * Emotion	(2, 176)	2.77	0.065	0.03
REPLICATION SAMPLE				
Emotion	(2, 172)	2.04	0.134	0.02
*ADRA*2b	(1, 86)	0.07	0.788	0
*ADRA*2b * Emotion	(2, 172)	1.68	0.19	0.02
FULL SAMPLE				
Emotion	(2, 352)	2.35	0.097	0.01
*ADRA*2b	(1, 176)	0.24	0.622	0.001
***ADRA*2b * Emotion**	**(2, 352)**	**3.17**	**0.043**	**0.02**

LSAS				
Discovery sample				
Emotion	(2, 70)	2.32	0.106	0.06
LSAS	(1, 35)	0.52	0.474	0.02
LSAS * Emotion	(2,70)	0.01	0.988	0
REPLICATION SAMPLE				
Emotion	(1.18, 59.03)	1.72	0.195	0.03
LSAS	(1, 50)	1.81	0.184	0.04
LSAS * Emotion	(1.18, 59.03)	1.32	0.262	0.03
FULL SAMPLE				
Emotion	(1.29, 111.83)	3.04	0.074	0.03
LSAS	(1, 87)	2.44	0.122	0.03
LSAS * Emotion	(1.28, 111.83)	1.27	0.272	0.01

Table 3. ssVEP results. Results that are statistically significant are in bold, and those that are significant across all samples are bold and underlined.

	df	*F*	*p-value*	η_p^2
ssVEP				
DISCOVERY SAMPLE				
Time Window	(1.53, 134.22)	1.99	0.151	0.02
Stimulus type	**(1, 88)**	**7.84**	**0.006**	**0.08**
Emotion	**(2, 176)**	**13.89**	**0**	**0.14**
Stimulus type * Emotion	**(2, 176)**	**6.84**	**0.001**	**0.07**
Time Window * Stimulus Type	**(1.28, 112.50)**	**7.11**	**0.005**	**0.07**
Time Window * Emotion	**(4, 352)**	**7.2**	**0**	**0.08**
Time Window * Stimulus * Emotion	**(3.34, 293.59)**	**3.35**	**0.016**	**0.04**
*ADRA*2b	(1, 88)	0.12	0.735	0
*ADRA*2b * Time Window	(1.53, 134.22)	0.05	0.913	0
*ADRA*2b * Stimulus Type	(1, 88)	0	0.979	0
*ADRA*2b * Emotion	(2, 176)	0.85	0.427	0.01
*ADRA*2b * Stimulus Type * Time Window	(1.28, 112.50)	0.07	0.856	0
*ADRA*2b * Time Window * Emotion	(4, 352)	0.95	0.433	0.01
*ADRA*2b * Stimulus Type * Emotion	(2, 176)	2.37	0.096	0.03
*ADRA*2b * Time Window * Stimulus Type * Emotion	(3.34, 293.59)	0.8	0.507	0.01
REPLICATION SAMPLE				
Time Window	(1.28, 115.21)	1.17	0.296	0.01
Stimulus Type	**(1, 90)**	**6.5**	**0.012**	**0.07**
Emotion	(1.29,115.88)	0.47	0.541	0.01
Stimulus Type * Emotion	**(2, 180)**	**6.25**	**0.002**	**0.07**
Time Window * Stimulus Type	**(1.15, 103.56)**	**7.58**	**0.005**	**0.08**
Time Window * Emotion	(1.22, 109.84)	0.896	0.365	0.01
Time Window * Stimulus Type * Emotion	(3.25, 292.26)	1.92	0.121	0.02
*ADRA*2b	(1, 90)	2.44	0.122	0.03
*ADRA*2b * Time Window	(1.28, 115.21)	1.13	0.305	0.01
*ADRA*2b * Stimulus Type	(1, 90)	0.17	0.682	0
*ADRA*2b * Emotion	(1.29, 115.88)	0.54	0.506	0.01
*ADRA*2b * Stimulus Type * Time Window	(1.15, 103.56)	0.19	0.697	0
*ADRA*2b * Time Window * Emotion	(1.22, 109.84)	1.06	0.32	0.01
ADRA2b * Stimulus Type * Emotion	(2, 180)	0.74	0.478	0.01
*ADRA*2b * Time Window * Stimulus Type * Emotion	(3.25, 292.26)	0.26	0.869	0
FULL SAMPLE				
Time Window	(1.37, 247.14)	2.71	0.088	0.02
Stimulus Type	**(1, 180)**	**14.34**	**0**	**0.07**
Emotion	**(1.47, 264.75)**	**4.88**	**0.016**	**0.03**
Stimulus Type * Emotion Interaction	**(2, 360)**	**13.06**	**0**	**0.07**
Time Window * Stimulus Type	**(1.21, 218.69)**	**14.75**	**0**	**0.08**
Time Window * Emotion	(1.39, 251.08)	2.23	0.127	0.01
Time Window * Stimulus Type * Emotion	**(3.39, 609.60)**	**4.1**	**0.005**	**0.02**
*ADRA*2b	(1, 180)	0.88	0.35	0
*ADRA*2b * Time Window	(1.37, 247.13)	0.54	0.52	0
*ADRA*2b * Stimulus Type	(1, 180)	0.11	0.745	0
*ADRA*2b * Emotion	(1.47, 264.75)	1.16	0.303	0.01
*ADRA*2b * Stimulus Type * Time Window	(1.21, 218.69)	0.09	0.816	0
*ADRA*2b * Time Window * Emotion	(1.39, 251.08)	1.3	0.267	0.01
*ADRA*2b * Stimulus Type * Emotion	(2, 360)	1.49	0.226	0.01
*ADRA*2b * Time window * Stimulus Type * Emotion	(3.39, 609.60)	0.53	0.681	0

Supplementary Materials

Correlation (Social Anxiety (LSAS Scores) x Difference Scores)

		Angry	Neutral	Happy
LSAS Score	Pearson Correlation	-.088	-.234	-.186
	Sig. (2-tailed)	.410	.027	.082
	n	89	89	89

A Pearson product-moment correlation coefficient was calculated to examine the relationship between social anxiety (LSAS Score) and difference scores in each emotion category. There was a non-significant negative correlation between LSAS score x difference scores in the angry expression category, r = -.088, p = .410. There was a significant negative correlation between LSAS Score and difference scores in the neutral expression category, r = -.234, *p* = .027, and a non-significant negative correlation between LSAS score x difference scores in the happy emotion category, r = -.186, p = .082

Change Detection Accuracy.

In a two-way (LSAS group) x 3 (emotion) repeated measures ANOVA for accuracy in the change detection task, we found no main effect of emotion, $F(2, 166) = 1.90$, $p = .153$, $\eta_p^2 = .02$. There was no main effect of LSAS group, $F(1, 83) = 0.56$, $p = .458$, $\eta_p^2 = .01$ and no LSAS group x emotion interaction, $F(2, 166) = 0.95$, $p = .287$, $\eta_p^2 = .01$.

Difference Scores with Social Anxiety as a Covariate

We performed an ANCOVA examining difference scores while accounting for social anxiety (LSAS Score) as a covariate. There was a main effect of time window, $F(1.52, 261.27) = 13.33$, $p = .000$, a main effect of emotion, $F(1.56, 267.78) = 4.58$, $p = .011$, and an interaction between time window x emotion, $F(3.80, 654.00) = 2.39$, $p = .050$. The covariate did not interact with any of these effects ($p > .385$).

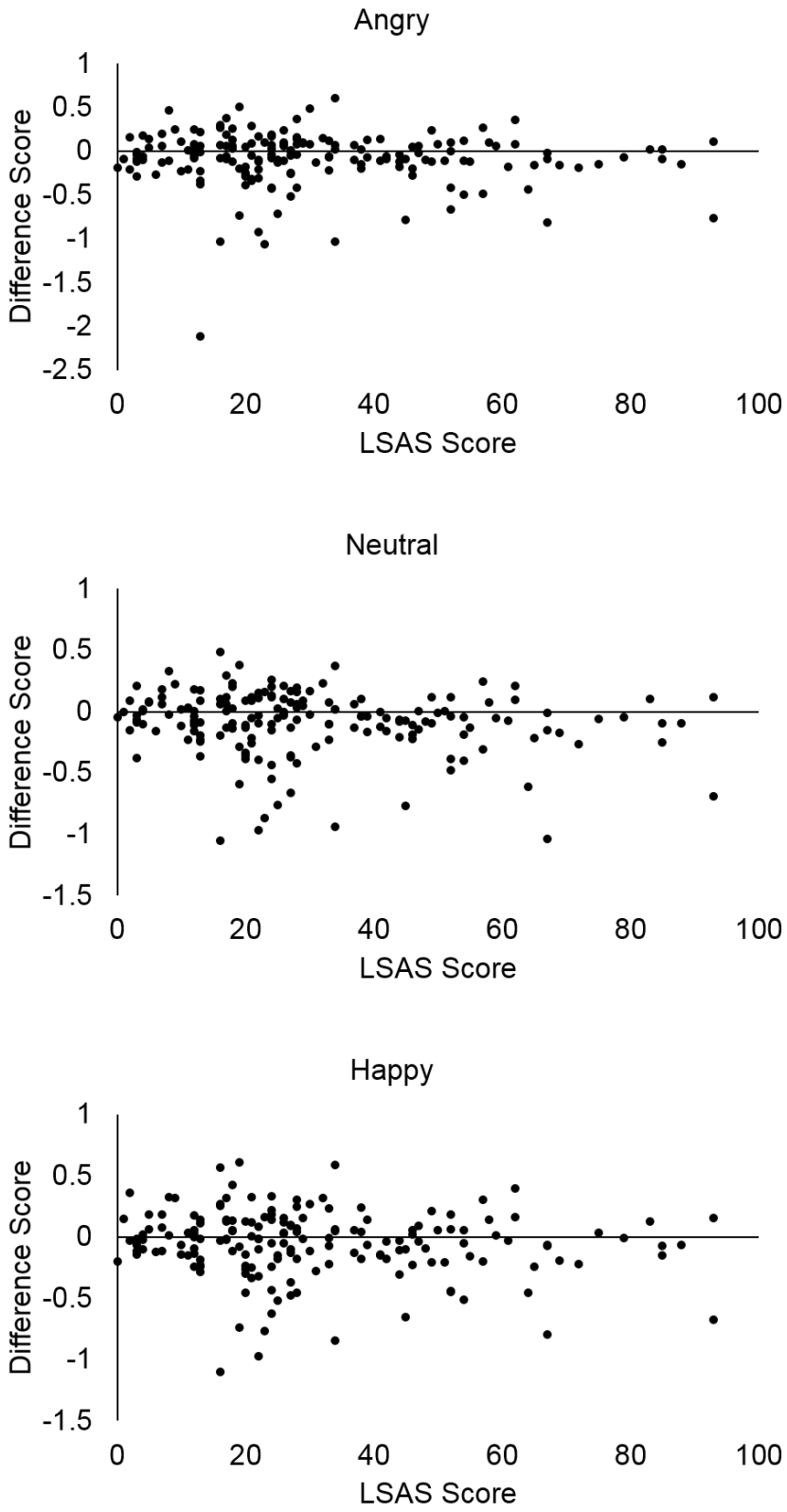


Figure S1. Plots of the relationship between LSAS score and ssVEP difference scores within each face emotion category. LSAS was not correlated with ssVEP difference scores overall, or within any emotion category.