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Psychological Science published online 20 September 2013
DOI: 10.1177/0956797613492423

Psychological Science OnlineFirst, published on September 20, 2013 as doi:10.1177/0956797613492423

Research Article

Psychological Science
XX(X) 1–10

DOI: 10.1177/0956797613492423
pss.sagepub.com

Genes for Emotion-Enhanced Remembering Are Linked to Enhanced Perceiving

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Abstract

Emotionally enhanced memory and susceptibility to intrusive memories after trauma have been linked to a deletion variant (i.e., a form of a gene in which certain amino acids are missing) of *ADRA2B*, the gene encoding subtype B of the α_2-adrenergic receptor, which influences norepinephrine activity. We examined in 207 participants whether variations in this gene are responsible for individual differences in affective influences on initial encoding that alter perceptual awareness. We examined the attentional blink, an attentional impairment during rapid serial visual presentation, for negatively arousing, positively arousing, and neutral target words. Overall, the attentional blink was reduced for emotional targets for *ADRA2B*-deletion carriers and noncarriers alike, which reveals emotional sparing (i.e., reduction of the attentional impairment for words that are emotionally significant). However, deletion carriers demonstrated a further, more pronounced emotional sparing for negative targets. This finding demonstrates a contribution of genetics to individual differences in the emotional subjectivity of perception, which in turn may be linked to biases in later memory.

Keywords

emotions, genetics, visual perception

Received 9/25/12; Revision accepted 4/29/13

Most people have experienced emotionally laden memories that flood the senses so vividly that they feel as if they are reliving them. Emotionally important events are often more vividly remembered than mundane ones (Kensinger & Corkin, 2003; Sharot, Martorella, Delgado, & Phelps, 2007), yet some people remember emotional events more vividly than other people do or are more likely than other people to suffer from intrusive memories after trauma.

Recent evidence suggests that there are important biological contributions to individual differences in the formation of emotional memory. A deletion variant is a form of a gene in which certain amino acids are missing (for more detail, see Polymorphisms in the Supplemental Material available online). The 12Glu9 deletion variant of the *ADRA2B* gene, which lacks three glutamic acids from a glutamic acid repeat element, has been linked to the emotional enhancement of memory and susceptibility to traumatic memory (de Quervain et al., 2007). However, events that are affectively salient elicit enhanced perceptual processing as well as more vivid memory. Compared with neutral stimuli, affectively salient stimuli are more likely to reach awareness when attentional resources are limited (Anderson, 2005), they evoke

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greater visual-cortex activation (Lang et al., 1998; Lim, Padmala, & Pessoa, 2009; Pessoa, Kastner, & Ungerleider, 2002), and they are perceived to be more vivid (Todd, Talmi, Schmitz, Susskind, & Anderson, 2012). We recently demonstrated that enhanced perceptual vividness for affectively salient stimuli contributes to memory vividness (Todd, Talmi, et al., 2012). Thus, a further question concerns whether *ADRA2B* is partly responsible, beyond influencing memory, for individual differences in how people perceive emotionally salient stimuli.

Deletion carriers show greater amygdala activation than noncarriers when they view negatively arousing images (Rasch et al., 2009), which supports the hypothesis that *ADRA2B* variation is linked to differences in responses to affective stimuli around the time of encoding. Nonetheless, deletion carriers fail to rate negative pictures as more intensely arousing than do noncarriers (de Quervain et al., 2007). One interpretation of this finding is that the primary influence of *ADRA2B* on memory is related not to emotional enhancement of initial perception, but rather to later influences on memory consolidation or retrieval. Yet an equivalence in arousal ratings does not preclude an influence on perception (Todd, Cunningham, Anderson, & Thompson, 2012), because explicit evaluations made seconds after viewing may not be sensitive to affective biasing of perceptual processes that occur on a subsecond scale (Todd & Anderson, 2009).

The *attentional-blink* manipulation (Raymond, Shapiro, & Arnell, 1992) effectively measures biases in rapid perceptual processing and resulting awareness. The attentional blink itself is a phenomenon in which participants are typically unable to identify a target stimulus when it is presented less than approximately 500 ms after a previous target in a rapid stream of stimuli. One interpretation of this blink is that it reflects a failure of attentional filters to consolidate the second target into working memory when it appears too quickly after the first, which results in impaired perceptual awareness (Di Lollo, Kawahara, Shahab Ghorashi, & Enns, 2005). When the second target has emotional significance, there is a reduced attentional blink, or an *emotional sparing* (Anderson, 2005; Anderson & Phelps, 2001; Keil & Ihssen, 2004). This emotional sparing, or reduction of the attentional blink for emotional stimuli relative to neutral stimuli, can be seen as the relative tuning of selective attention to affective stimuli (Todd, Cunningham, et al., 2012). Although previous studies have linked genetic variations that influence dopaminergic functioning to overall attentional-blink performance (Colzato, Slagter, de Rover, & Hommel, 2011; Felten et al., 2012), tonic norepinephrine availability has been found to influence emotional sparing (De Martino, Strange, & Dolan, 2008). However, genetic markers linked to norepinephrine influences on emotional sparing have yet to be investigated. Given the role of norepinephrine in increasing sensory gain for salient stimuli (Berridge & Waterhouse, 2003; Sara, 2009), we hypothesized that if *ADRA2B* influences tonic norepinephrine levels, then the deletion variant should support trait-level differences in the influence of affective salience on perception. This would provide evidence of individual genotypic differences in how emotion shapes perception. To examine this thesis, we assessed whether carriers of the *ADRA2B* deletion variant (deletion carriers) and those who do not carry the variant (noncarriers) demonstrated different patterns of emotional sparing.

One of the features of normative and, in particular, maladaptive interactions between emotion and cognition is a prominent negativity bias (Cacioppo, Gardner, & Berntson, 1999). There is reason to believe that *ADRA2B* may be associated with this bias toward negative or threatening aspects of the world: Deletion carriers have been found to show enhanced amygdala activation relative to noncarriers when viewing negative, but not positive, scenes (Rasch et al., 2009; but see Urner et al., 2011). Thus, our goal in the present study was to investigate the influence of *ADRA2B* on affective biases that shape perceptual awareness, particularly biases for negative stimuli.

Variations in two other genes have also been associated with individual differences in affective biases (for details, see Polymorphisms in the Supplemental Material): Carrying a short allele of the serotonin-transporter-linked polymorphic region (5HTTLPR) on the serotonin transporter gene (*SLC6A4*) is associated with trait neuroticism (Canli, 2008) as well as attentional biases toward and enhanced amygdala activation for threatening stimuli (Hariri & Weinberger, 2003; Munafo, Brown, & Hariri, 2008). This gene and region will be referred to hereafter as 5HTTLPR. A valine-to-methionine mutation at Position 158 (Val158Met) in the catechol-*O*-methyltransferase (*COMT*) gene, which influences prefrontal dopamine metabolism, is also associated with increased amygdala activation (Smolka et al., 2005) and startle responses to aversive stimuli (Montag et al., 2008). Because of the high degree of reciprocal activity among the norepinephrine, dopaminergic, and serotonergic systems, we examined these polymorphisms to control for their influence on emotional sparing in the attentional blink and to probe potential Gene × Gene interactions. In addition, we measured childhood trauma as an index of life experience to examine whether biases toward seeing more threat in the world might be learned through early exposure, genetic predisposition linked to norepinephrine processing, or a combination of both.

Method

Participants

Sample size was determined by estimating that to find an effect size (η^2) of .07, which is typical for genetic influences on attention and memory performance (Rasch

et al., 2009), we would require 90 participants per genotype group for a behavioral analysis with six covariates. Based on previous findings that the *ADRA2B* deletion variant occurs in 30% of the White population (de Quervain et al., 2007), ~300 participants would be required. In this study 282 White participants were recruited from the University of Toronto. Participants either were paid $40 Canadian or were paid $10 Canadian and given credit in a first-year psychology course. Participants, who were part of a collaborative study on genetic influences on attention and memory, were between the ages of 18 and 35 years (mean age = 21.0 years) and had normal or corrected-to-normal vision. Participants who reported a history of significant head injuries, stroke, epilepsy, brain surgery, or learning disabilities were excluded. Three participants were excluded because they could not be genotyped for *ADRA2B*. Anxiety, depression, and attentional-blink performance are linked (E. Fox, Russo, & Georgiou, 2005; Koster, De Raedt, Verschuere, Tibboel, & De Jong, 2009); the presence of the 5HTTLPR short allele is associated with anxiety and depression (Canli et al., 2006; N. A. Fox et al., 2005); and the *COMT* Val158Met polymorphism and anxiety are linked (Karayiorgou et al., 1999). Therefore, a subset of participants with previous or current diagnoses or who were receiving treatment for anxiety and depression were excluded from analysis, which left a final total of 207 participants (140 women, 67 men).

Materials and procedure

Experimental tasks were presented using E-prime (Version 1.2; Schneider, Eschman, & Zuccolotto, 2001). In our primary experimental manipulation, participants performed an attentional-blink task using 84 words (28 positively arousing words, 28 negatively arousing words, and 28 neutral words) selected from the Affective Norms for English Words database (Bradley & Lang, 1999) of emotionally salient words that have been normatively rated for valence and arousal. Positive and negative words were matched for arousal, and all words were balanced for length, written frequency, and neighborhood frequency (i.e., the frequency of words of the same length that could be created by changing a single letter; Coltheart, Davelaar, Jonassen, & Besner, 1977). The Childhood Trauma Questionnaire (Bernstein et al., 1994) was administered to investigate the influence of traumatic life experience, and the Big Five Inventory (Benet-Martinez & John, 1998) was administered to control for individual differences in personality. Because neuroticism has been associated with altered attentional-blink performance (Bredemeier, Berenbaum, Most, & Simons, 2011) and with the presence of the 5HTTLPR short allele (Canli, 2008), we focused on the neuroticism subscale of the Big Five Inventory. A *K*-estimate task was used as a control measure of working memory, and a word-rating task was used to assess perceived stimulus valence and arousal (see Supplemental Methods in the Supplemental Material).

Attentional-blink task. In each trial of the experimental task, words were displayed in rapid succession (Fig. 1). Two targets were presented amid a series of distractors: Target 1 was a single digit (1–9) repeated (e.g., 555555), and Target 2 was a positively arousing, negatively arousing, or neutral word. Distractor words were presented in a black typeface, whereas the targets were presented in a green typeface. Target 1 was placed randomly in Position 3, 4, 5, or 6 of the rapid-serial-visual-presentation stream. Target 2 followed Target 1 after zero (Lag 1), one (Lag 2), three (Lag 4), or six (Lag 7) intervening distractor words, which created 12 conditions (three word conditions by four lag conditions). After the presentation of words in each trial, participants were asked to type both targets using a standard computer keyboard. Participants completed a total of 168 trials (56 trials each for negative, positive, and neutral words). To calculate accuracy in each condition, we first removed all trials on which Target 1 was not correctly recalled. The proportion of remaining trials on which Target 2 was correctly recalled was the measure of accuracy.

Practice session. To minimize differences in performance caused by individual differences in perceptual processing speed, we preceded the experiment with a practice session similar to the experimental task. This session featured 30 practice trials that tested five different stimulus-onset asynchronies (100–140 ms in 10-ms increments, balanced and randomized). Practice Target 2 stimuli were neutral words that were not repeated during the subsequent task. At the end of practice, the stimulus-onset asynchrony chosen for each participant was the fastest for which he or she reported the second target with greater than 80% accuracy when the second target appeared at Lag 7.

Genotyping

Participants were genotyped for *ADRA2B* as well as 5HTTLPR and *COMT*. A saliva sample (~2 ml) was collected from each subject in an Oragene OG-500 DNA kit (DNA Genotek, Ottawa, Ontario, Canada). DNA was extracted and genotyped at the Neurogenetics Laboratory at the Centre for Addiction and Mental Health in Toronto, Canada (see Supplemental Methods in the Supplemental Material). For each gene, we calculated the Hardy-Weinberg equilibrium using an online Hardy-Weinberg chi-square calculator (Rodriguez, Gaunt, & Day, 2009).

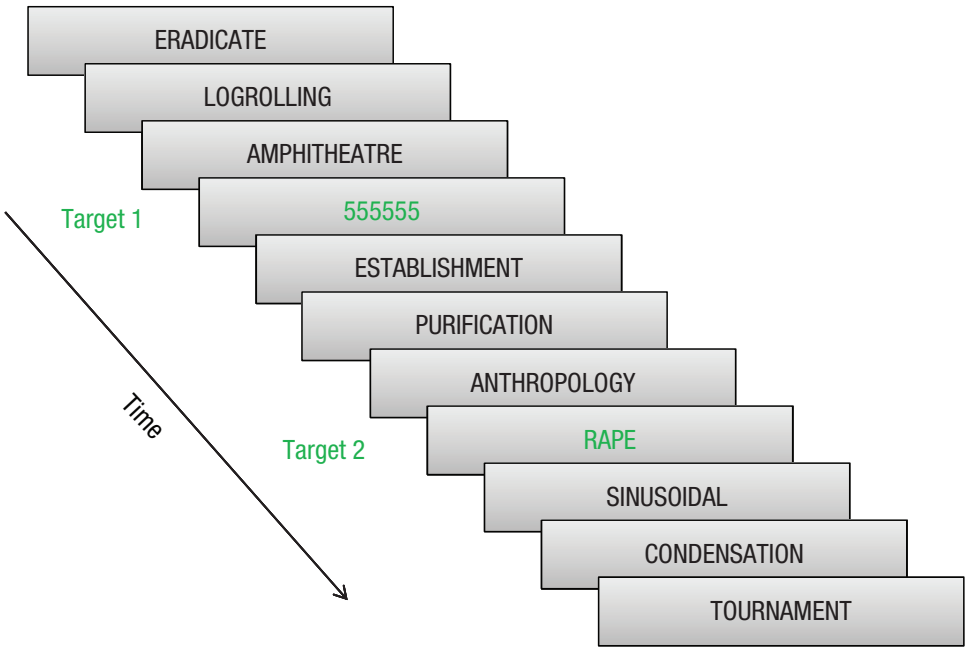

Fig. 1. Sample trial sequence in the attentional-blink task. Two targets were presented among a series of distractor words: The first target was a string of numbers, and the second was a positive, negative, or neutral word. Stimulus presentation time varied from 100 to 140 ms. Target 2 followed Target 1 after zero (Lag 1), one (Lag 2), three (Lag 4), or six (Lag 7) intervening distractor words. At the end of each trial, participants had to report both targets.

Results

All genotype frequencies fell within the Hardy-Weinberg equilibrium—*ADRA2B*: $\chi^2(1, N = 279) = 0.13$, $p > .05$; 5HTTLPR: $\chi^2(1, N = 278) = 0.29$, $p > .05$; and *COMT*: $\chi^2(1, N = 282) = 0.8$, $p > .05$. Following previous research, we treated homozygotic and heterozygotic *ADRA2B*-deletion carriers as a single group because of the low number of homozygotic carriers (de Quervain et al., 2007; Rasch et al., 2009). Likewise, homozygotic and heterozygotic carriers of the 5HTTLPR short allele (Canli & Lesch, 2007) and the *COMT* Val allele were also treated as a single group.

We examined the influence of each relevant genotype on the attentional blink by using mixed-model analyses of variance (ANOVAs). All results reported here were Greenhouse-Geisser corrected when sphericity could not be assumed, and contrasts were Bonferroni-corrected for multiple comparisons. Because of potential associations among (a) attentional-blink effects, (b) 5HTTLPR short allele and *COMT* Val158Met polymorphism, and (c) anxiety and depression (Canli et al., 2006; E. Fox et al., 2005; Karayiorgou et al., 1999; Koster et al., 2009), all analyses were run only on those participants who had no history of anxiety or depression. However, the primary results showing an influence of *ADRA2B* on the attentional blink were significant when data from the entire sample were analyzed.

Primary analyses

To assess the influence of *ADRA2B, COMT*, and 5HTTLPR genotypes on attentional-blink performance, we ran separate three-way mixed-model ANOVAs for each polymorphism; emotion category (negative, positive, neutral) and lag (1, 2, 4, 7) were included as within-subjects factors and genotype (carriers, noncarriers) was the between-subjects factor. For *ADRA2B*, participants were separated into a deletion-carrier group ($n = 113$) and a noncarrier group ($n = 94$; see Table 1). As expected, there was a main effect of lag, $F(3, 615) = 121.05$, $p < .001$, $\eta_p^2 = .71$; lower accuracy at shorter lag times was consistent with the attentional-blink phenomenon. There was also a main effect of emotion category, $F(2, 410) = 264.56$, $p < .001$, $\eta_p^2 = .50$; pairwise contrasts between emotion conditions showed greater accuracy for negative words than for neutral words ($p < .001$), greater accuracy for positive words than for neutral words ($p < .001$), and greater accuracy for negative words than for positive words ($p < .001$). These effects were qualified by an Emotion Category × Lag × Genotype interaction, $F(6, 1230) = 3.09$ $p = .005$, $\eta_p^2 = .02$. There was no Emotion Category ×

Table 1. Proportion of Correct Responses for Each Lag in the Three Emotion Conditions

	Negative words				Positive words				Neutral words			
Participant group	Lag 1	Lag 2	Lag 4	Lag 7	Lag 1	Lag 2	Lag 4	Lag 7	Lag 1	Lag 2	Lag 4	Lag 7
Overall	.52	.63	.73	.75	.48	.57	.70	.73	.41	.53	.63	.66
ADRA2B deletion												
Carriers	.55	.63	.74	.73	.48	.59	.70	.74	.41	.52	.64	.67
Noncarriers	.49	.62	.73	.76	.49	.56	.69	.71	.41	.54	.63	.66
5HTTLPR allele												
Short	.51	.61	.72	.73	.47	.56	.68	.70	.39	.51	.61	.64
Long/long	.56	.67	.77	.77	.53	.60	.75	.78	.45	.58	.68	.71
COMT polymorphism												
Val	.52	.62	.74	.75	.49	.58	.70	.73	.42	.54	.64	.66
Met/Met	.52	.64	.73	.74	.46	.56	.68	.72	.38	.51	.62	.66

Note: Only trials on which the participant correctly recalled Target 1 were included in the analysis; the proportion of remaining trials on which Target 2 was correctly recalled was the measure of accuracy.

Genotype interaction, $F(2, 410) = 0.78$, $p = .46$, because the influence of genotype on emotion category was observed only at short lag times, when attentional blink was maximal. Thus *ADRA2B*-deletion carriers showed an advantage for negative words beyond the emotional sparing typically found at the shortest lag times, precisely when the blink effect is greatest.

Participants were grouped by 5HTTLPR allele into long/long ($n = 64$) and short-allele (i.e., short/long and short/short) carriers ($n = 144$). In addition to the within-subjects main effects of lag and emotion category reported earlier, there was a main effect of genotype, $F(1, 206) = 6.18$ $p = .02$, $\eta_p^2 = .03$; homozygotic long-allele carriers showed greater overall accuracy than short-allele carriers across all lags, but there were no interactions with lag or emotion category (ps > .30). Participants were separated by *COMT* genotype into Met/Met-carrier ($n = 65$) and Val-carrier ($n = 145$) groups. Beyond the within-subjects effects of lag and emotion category reported earlier, there were no significant results, which suggests that *COMT* does not influence performance on the attentional blink (ps > .1).

Focused analyses

We further probed the effect of *ADRA2B* on emotional modulation of the attentional blink while accounting for the influence of other factors that influence performance. The blink effect is characterized by increasing accuracy as lag times increase. To index modulation of the blink, we calculated the linear slope of accuracy from Lag 1 to Lag 7 for each emotion category. To explore potential Gene × Gene interactions, we included *COMT* (Val carriers vs. Met/Met carriers) and 5HTTLPR (short-allele carriers vs. long/long carriers) genotypes in the analysis. A mixed-model analysis of covariance was performed with emotion category (positive, negative, neutral) as the within-subjects measure and genotype (*ADRA2B, COMT*, 5HTTLPR) as the between-subjects measure. Preliminary analyses showed that accuracy slope was associated with sex, working memory, and neuroticism (see Supplemental Results in the Supplemental Material), so we also included these as covariates. Childhood sexual abuse was included in the analysis to examine potential interactions between genotype and life experience.

Only *ADRA2B* genotype influenced the emotional modulation of the attentional blink. There was an *ADRA2B* × Emotion Category interaction $F(2, 350) = 5.52$, $p = .004$, $\eta_p^2 = .03$. *ADRA2B*-deletion carriers showed shallower slopes (i.e., a reduced blink) for negative words than for positive and neutral words ($p = .02$; Figs. 2a and 2b), and there were differences between the slopes for negative words and those for positive and neutral words only among *ADRA2B*-deletion carriers (ps < .05). *ADRA2B* genotype had no effect on the size of the blink for neutral targets. Thus, compared with noncarriers, *ADRA2B*-deletion carriers showed a selective enhancement effect of emotion category, particularly negative emotion, on perceptual awareness. It is noteworthy that there was no *ADRA2B* × Emotion Category × Childhood Abuse interaction, $F(2,350) = 1.13$ $p = .33$, which indicates that, at this sample size, genotype did not interact significantly with life experience in predicting emotional modulation of the attentional blink.

Results also revealed a Gene × Gene interaction between 5HTTLPR and *COMT* genotype on the overall slope for all emotion categories, $F(1, 175) = 7.43$ $p = .007$, $\eta_p^2 = .03$; the largest slope indicated the greatest blink effect for *COMT* Met/Met carriers who were also 5HTTLPR long/long carriers. However, because of the small number of participants in this group that was driving the interaction ($n = 18$), these results must be treated with caution. The interaction of 5HTTLPR, *COMT*, and

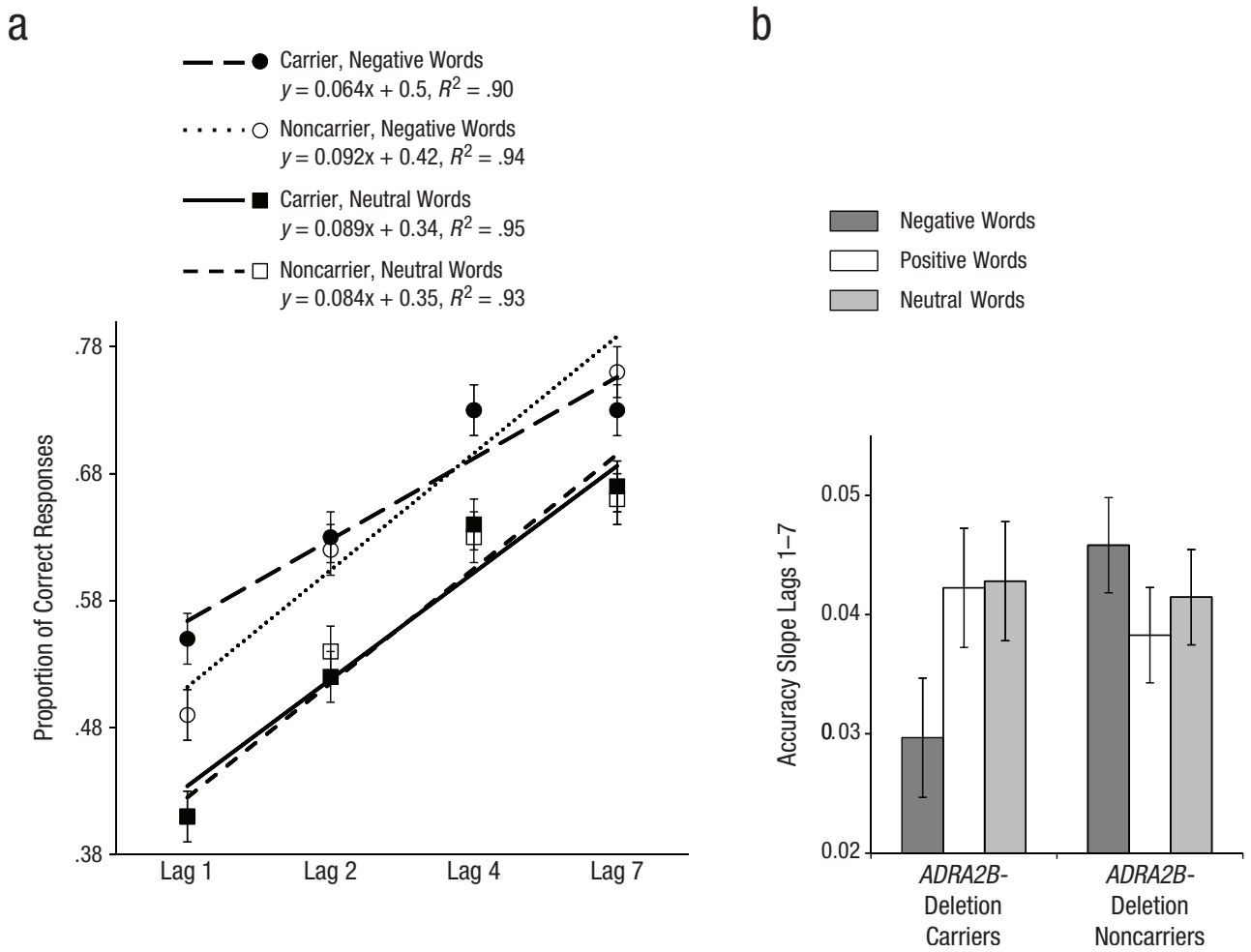

Fig. 2. Results for the *ADRA2B*-deletion carrier and noncarrier groups. The proportion of correct responses in each group is shown in (a) as a function of the lag between the two target stimuli and emotion category (negative and neutral). The symbols indicate means across subjects, and the lines show best-fitting regressions. The slope for accuracy from Lag 1 to Lag 7 is shown in (b) as a function of group and emotion category (negative, positive, and neutral). Error bars in both graphs show ±1 *SE*.

emotion category was not significant, $p > .6$. There was also an influence of sex on slope, $F(1, 175) = 4.93$ $p = .03$, $\eta_p^2 = .03$; the blink effect was larger in men than in women.

Enhanced perceptual awareness of negative events may be secondary to increased explicit evaluations of their emotional salience. In the experiments reported here, the first 130 participants rated the words used in the attentional-blink task for emotional valence and intensity (see Supplemental Methods in the Supplemental Material). There was no effect of *ADRA2B* and no *ADRA2B* × Emotion Category interaction for subjective ratings of intensity or valence (*p*s > .2) when we controlled for cognitive factors or for the other genes. By contrast, even in this smaller subset of participants, the *ADRA2B* × Emotion Category interaction with attentional-blink accuracy slope remained significant, $F(2, 74) = 4.29$, $p = .02$. These findings are consistent with previous findings of a dissociation between attentional-blink emotional sparing, on the one hand, and emotional comprehension and evaluation, on the other (Anderson & Phelps, 2001). Thus, *ADRA2B* genotype was associated with altered attentional salience and associated perceptual awareness but not with explicit evaluations of salience.

Discussion

The deletion variant of the *ADRA2B* gene has been linked to altered norepinephrine availability. Carriers of this deletion variant of the *ADRA2B* gene demonstrated a decreased attentional blink for negatively arousing events, showing greater emotional sparing relative to noncarriers. After controlling for sex, working memory, trait neuroticism, and history of childhood abuse, as well

as 5HTTLPR and *COMT* genotype, we found that *ADRA2B*-deletion carriers showed a shallower increase in the accuracy slope with increasing lag between the two target stimuli when the second target was a negative word but not when it was a neutral or positive word. This shallower slope indicates a reduced blink effect (i.e., an increased perceptual awareness of negative stimuli) in *ADRA2B*-deletion carriers under conditions of attentional challenge. These findings demonstrate that *ADRA2B* influences not only how emotions enhance later memory (de Quervain et al., 2007; Urner et al., 2011) but also how perceptions are encoded initially. Furthermore, *ADRA2B*-deletion carriers specifically show perceptual biases toward negative or threatening aspects of the world, which provides a partial genetic explanation of individual differences in how emotions shape perceptual experience.

Locus ceruleus activity that results in increased norepinephrine availability has been found to modulate attention to salient or goal-relevant stimuli (Aston-Jones & Cohen, 2005; Berridge & Waterhouse, 2003; Sara, 2009). It has also been linked to the attentional-blink phenomenon regardless of stimulus salience (Nieuwenhuis, Gilzenrat, Holmes, & Cohen, 2005). Whereas activity at norepinephrine β-adrenergic receptors has been linked to the influence of phasic norepinephrine on the attentional blink in general (Nieuwenhuis et al., 2005), emotional sparing of the blink has been linked to tonic increase in synaptic norepinephrine levels (De Martino et al., 2008). Our findings suggest that *ADRA2B* specifically influences the affective modulation of the blink, as measured by differences between *ADRA2B*-deletion carriers and noncarriers in emotional sparing for negative stimuli. The finding that carrying the *ADRA2B* deletion variant did not affect early-lag accuracy or slope across emotion categories suggests that—in contrast with the other genes we measured—it does not influence the magnitude of the overall blink. This finding is consistent with a more specific role in the emotional modulation of attention. It also provides novel evidence that links activity at α-adrenergic receptors involved in tonic inhibitory activity with enhanced perceptual encoding of affectively salient stimuli.

Although there are multiple interpretations of the attentional-blink phenomenon (e.g., Chun, 1997; Kawahara, Enns, & Di Lollo, 2006; Raymond et al., 1992), recent evidence supports the view that the blink reflects a failure of selective attention processes (Di Lollo et al., 2005; Slagter et al., 2012). In light of this model, the emotional sparing typically found (Anderson, 2005; Anderson & Phelps, 2001) may reflect norepinephrine-mediated selective attentional filters that are tuned to more affectively salient stimuli (Todd, Cunningham, et al., 2012). This interpretation is consistent with evidence that locus ceruleus-norepinephrine activity is associated with sensory tuning toward stimuli that are already salient (both appetitive and aversive) as well as rapid learning of new associations between a stimulus and its value (for a review, see Berridge & Waterhouse, 2003; Sara, 2009). Tonic activity in particular has been linked to increased excitatory activity in neurons tuned to salient stimuli, which enhances detection of salient subthreshold stimuli (Devilbiss & Waterhouse, 2011)—a potential mechanism underlying affective biases in attention.

Enhanced coactivation of the amygdala and visual cortex has been linked to emotional sparing of the attentional blink (Lim et al., 2009). Increased levels of tonic norepinephrine may also be reflected in the enhanced amygdala activation found previously for negative stimuli in *ADRA2B*-deletion carriers (Cousijn et al., 2010; Rasch et al., 2009). Our results suggest that the differential amygdala activation previously shown in *ADRA2B*-deletion carriers may be linked to enhanced processing of negative events when memories are first encoded. Although the amygdala may not necessarily be involved in very early perceptual processes (Tsuchiya, Moradi, Felsen, Yamazaki, & Adolphs, 2009), it may contribute to later perceptual processes (Todd, Talmi, et al., 2012) related to enhanced emotional memory previously found in *ADRA2B*-deletion carriers via activity in amygdalar norepinephrine α-receptors (de Quervain et al., 2007).

No interactions were found between *ADRA2B* and history of childhood abuse or among *ADRA2B*, emotion category, and history of childhood abuse, which suggests that the influence of *ADRA2B* on perceptual bias is independent of early life experiences. This, in turn, suggests that there are important genetic contributions to the emotional subjectivity of perception. Specifically, genetic differences in noradrenergic expression support the trait of enhanced attentional sensitivity to the salience of negative events. However, it should be noted that the lack of interaction with childhood abuse may be due to insufficient power and the potentially low range, severity, and scope of reports of abuse among an undergraduate sample.

Epistasis, or Gene × Gene interaction, often qualifies the influence of genotype on cognitive processes (de Quervain & Papassotiropoulos, 2006). Here, although we found no interactions of the *ADRA2B* genotype with the 5HTTLPR or *COMT* genotype, there was an interaction between the 5HTTLPR and *COMT* genotypes on the overall attentional-blink effect, as measured by accuracy slopes across all emotion categories. This suggests that serotonergic and dopaminergic systems interact in overall performance regardless of stimulus salience. The relation between 5HTTLPR and accuracy is consistent with the well-documented role of serotonin in attentional processes (Canli, 2008), as well as findings that link trait

neuroticism (which is in turn associated with possession of the short allele) to an increased attentional blink (Maclean & Arnell, 2010). Moreover, the interaction is consistent with evidence that dopaminergic processes influence the attentional blink (Slagter et al., 2012). Our results suggest that the interaction of dopaminergic and serotonergic processes influences overall attentional-blink performance but not emotional modulation of the blink. However, the nature of such an interaction has yet to be elucidated. Because the sample size in our experiment was small, especially in the *COMT* Met/Met–5HTTLPR long/long group driving the interaction, these results must be treated with caution.

A number of concerns have been raised about failures to replicate as a result of low power, publication bias, and high false-discovery rates in studies of genetic behavioral influences (e.g., Duncan & Keller, 2011; Munafo et al., 2008; Plomin, Owen, & McGuffin, 1994). Most of these concerns have focused on the influence of gene-by-environment interactions on psychiatric disorders that involve complex constellations of symptoms. In contrast, our study focused on the influence of *ADRA2B*, our primary candidate gene, on a constrained cognitive process. Although such studies are not immune to replication issues, analysis of observed power for our results suggests a high degree of replicability for our primary result involving the three-way interaction of *ADRA2B*, emotion, and lag (probability that one would obtain significant results if one repeated the experiment = .92). In contrast, replicability for the 5HTTLPR × *COMT* interaction was less robust (.59), which further qualifies interpretation of these results.

In conclusion, we have demonstrated here that *ADRA2B* influences visual perceptual encoding, which suggests an important role for norepinephrine α2 receptors in affective biasing of perception. These findings suggest that, for *ADRA2B*-deletion carriers, selective attentional filters that influence initial perception are more tuned toward negative stimuli than toward positive or neutral stimuli. This bias toward negative stimuli for *ADRA2B*-deletion carriers may, in turn, be linked to carriers' increased susceptibility to intrusive traumatic memories (de Quervain et al., 2007) and may predict increased vulnerability for posttraumatic stress disorder. Future research can focus on the influence of *ADRA2B* on neural activation associated with affectively biased perceptual processes as well as its relationship to emotionally enhanced memory.

Author Contributions

R. M. Todd and A. K. Anderson developed the study concept. R. M. Todd, A. K. Anderson, D. H. Lee, D. J. Palombo, B. Levine, and T. Eaton contributed to the study design. D. J. Müller and N. Freeman contributed genotyping consultation and DNA extraction and analysis. T. Eaton and A. Robertson were responsible for data acquisition and management. R. M. Todd performed data analyses. A. K. Anderson, D. J. Palombo, B. Levine, D. J. Müller, and D. H. Lee contributed important manuscript revisions.

Acknowledgments

We thank Sajid Shaikh, David Irwin, Agnes Bacopulos, and Angela Zhang for their contributions.

Declaration of Conflicting Interests

The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

Funding

This research was supported by Canadian Institutes for Health Research (CIHR) Operating Grant 491746.

Supplemental Material

Additional supporting information may be found at http://pss.sagepub.com/content/by/supplemental-data

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