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Original Article

The ADRA2B gene in the production of false memories for affective information in healthy female volunteers

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ABSTRACT

False memories are common memory distortions in everyday life and seem to increase with affectively connoted complex information. In line with recent studies showing a significant interaction between the noradrenergic system and emotional memory, we investigated whether healthy volunteer carriers of the deletion variant of the ADRA2B gene that codes for the α2b-adrenergic receptor are more prone to false memories than non-carriers. In this study, we collected genotype data from 212 healthy female volunteers; 91 ADRA2B carriers and 121 non-carriers. To assess gene effects on false memories for affective information, factorial mixed model analysis of variances (ANOVAs) were conducted with genotype as the between-subjects factor and type of memory error as the within-subjects factor. We found that although carriers and non-carriers made comparable numbers of false memory errors, they showed differences in the direction of valence biases, especially for inferential causal errors. Specifically, carriers produced fewer causal false memory errors for scripts with a negative outcome, whereas non-carriers showed a more general emotional effect and made fewer causal errors with both positive and negative outcomes. These findings suggest that putatively higher levels of noradrenaline in deletion carriers may enhance short-term consolidation of negative information and lead to fewer memory distortions when facing negative events.

1. Introduction

When memories deviate from what truly happened, diverse types of errors, including false memories, may arise (e.g. [1–4,14]). False memories are common in everyday life but the most remarkable aspect of these memory errors is that individuals not only claim that these memories are familiar, but they affirm to recollect contextual and temporal details associated with the encoding of the information. Most importantly, research on false memories has led to important contributions towards understanding normal memory functions (e.g. [5–9]), memory failures in specific brain diseases (e.g. [10]), and has highlighted the importance of considering diverse features that accompany an event in memory.

The main explanation put forward to account for the generation of false memories refers to the semantic elaboration hypothesis which suggests that false memories increase as the semantic elaboration of to-be-remembered information increases [11,12]. For example, developmental studies [13] found that children, who typically have reduced semantic processing and do not spontaneously form interconnected meanings unless the information being encoded is consistent with the gist of experience, were less prone to false memories. Ref. [13] summarized global age trends for data from published experiments using the DRM task. In this task, individuals who study a list of words followed by either a free recall or recognition task, generally show higher levels of false recognition for distracters that represent semantic associations of the studied lists [14]. Ref. [13] found that false memories generally increased from the age of 5 on in recall tasks and after the age of 7 for recognition tasks. Moreover, studies on text comprehension that adopt more complex stimuli (i.e., stories) emphasize that when reading stories, semantic elaboration also drives people seek to identify causal factors and to make inferences in order to link characters and events (e.g., [15] and to achieve text coherence. This search for coherence may subsequently enhance memory errors and lead to an increase in false memories. Differently, false memories may decrease if supported by abilities such as source monitoring, reductions in reliance on gist traces, and/or through effective metacognitive strategies. Indeed, studies have shown how younger and older adults are more prone to false memories as item-specific encoding decreases and gist encoding increases [16].

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False memories also seem to interact with the affective content of presented material [17]. False memories increase for mood congruent stimuli [18] but are reduced following sleep [19]. Furthermore, a recent series of research on false memories for affective content (e.g. [20–22] with complex stimuli such as scripts rather than single words, showed that false memories not only increased, but were also enhanced by the concurrent activation of self-relevant affective memories.

In particular, crucial to understanding how emotion may affect the generation of false memories is the phenomenon that emotional stimuli are better remembered than neutral ones (the so-called emotional enhancement effect). A series of studies have shown that both valence and arousal of stimuli contributed to the emotional enhancement effect. For instance, Kensinger and Corkin (2004) proposed that the emotional enhancement effect dependent on arousal was associated with automatic encoding processes, whereas the emotional enhancement effect dependent on valence was associated with controlled encoding processes. This may explain why the effect is found in some studies but is absent in others. Others, such as Carstensen et al. (e.g., [23]) explained this emotional advantage in terms of a selectivity towards the pursuit of emotional goals linked to the awareness of the proximity of the life span. This selectivity, in turn, generates a cognitive shift towards emotion processing that boosts memory processes for affective information in general and especially for arousing self-relevant information [24]. Finally, and most relevant to our study, research in neuroscience suggests that the emotional enhancement effect may also be linked to the presence of the genetic variants [25]. In particular, neurobiological models sustain that emotion influences memory via amygdala modulation of the hippocampus and other regions of episodic memory networks and that the locus coeruleus (LC)-norepinephrine (NE) system is crucial for emotion-cognition interactions [26]. The locus coeruleus (LC) is located in the posterior area of the brainstem and receives inputs from the amygdala as well as ventral prefrontal regions and facilitates response to behavioral and biological relevant information while suppressing response to irrelevant information. Importantly, affectively arousing stimuli induce LC phasic activity and enhance encoding, irrespective of whether stimuli are positive [27,28] or negative [29]. This, in turn, further interacts with the influence of NE on longer-term memory processes and leads to enhanced memory for arousing information [30]. Indeed, whether an event is remembered or not depends on modulations in the strength of communication across synapsis and the modulation of NE release following arousing information [31].

In this regard, genetic variations linked to NE has been shown to influence LC activity and convergent evidence suggests that a gene variant, the so-called ADRA2b, is associated with higher levels of intercellular NE availability [32]. The intronless gene ADRA2B, located on the 2p13-q13 chromosome, encodes a seven-pass transmembrane protein widely distributed in the human central and peripheral nervous systems. ADRA2B protein is a subtype of alpha 2-adrenergic receptor (a2-AR) mediating biological effects of endogenous catecholamines, epinephrine and norepinephrine [33]. The presence of the ADRA2B functional polymorphism, consisting of an inframe deletion of three glutamic acids residues (301–303) in the third intracellular loop, leads to a small decrease in coupling receptor efficiency (e.g. [34]). In particular, studies show that administration of NE into the BLA both prior to and following encoding of an event in rats is associated with enhanced memory (for review see Ref. [35]). In humans, the influence of arousal on both encoding and post-encoding processes has been demonstrated by injecting epinephrine or exposing participants to emotionally arousing images prior or after encoding [36].

Again, studies on the interaction between this ADRA2B variant and emotion, with a specific focus on valence effects, show a complex picture (for a review see Ref. [37]). Some studies have found a bias for negative information (e.g. [38,39]) and an association with suicidal behavior [40] whereas others have detected a more general emotion effect since carriers were sensitive to both positive and negative stimuli (e.g. [41–43,25,37]), but all seem to indicate a relevant role of ADRA2B in affective information processing and highlight the importance of investigating genotype-differences using different behavioral paradigms and populations.

Consequently, the present study aims to investigate how affective content influences the generation of false memories as well as the role of ADRA2B in this emotion-memory interaction in healthy female volunteers. In line with recent studies showing the role of noradrenergic neurotransmission in emotion processing, especially in terms of a functional deletion variant of ADRA2B (e.g. [39,25]), we expect affective false memories to be susceptible to ADRA2B genotype differences. This may help clarify the neurobiological mechanisms underlying the generation of affective false memories.

Here, we adopted a paradigm originally proposed by Ref. [44], modified to include affective (both negative and positive) as well as neutral information, to investigate affective false memories and the effect of genotype differences in a group of female volunteers. In this paradigm, we used pictorial representations of daily routines (scripts) to investigate two diverse types of memory errors that can occur while searching for script coherence and comprehension: plausible script errors (participants say “yes” to an unseen picture representing a plausible action in the script) and inferential causal errors (participants say “yes” to an unseen picture depicting the cause of the outcome of the episode). Plausible script errors are an index that participants did process the scripts while inferential causal errors allow us to examine memory distortions determined by inferences made during script elaboration. For example, the bike script depicts the story of a girl on a bike. If participants correctly understand and encode the scripts, they may falsely recognize never seen pictures whose content is coherent with a possible cause of the outcome of the script and show a corresponding increase in the number of causal script errors. That is, they may falsely recognize a trigger picture (i.e. the girl about to cross the road) as one that had been presented and consequently produce a causal error.

In line with semantic elaboration theories and neurobiological models, we expect both deletion carriers and non-carriers to make more inferential errors than plausible script errors since inferential errors derive from erroneous inferences that depend on semantic elaboration processes. Moreover, inferences made while searching for script coherence are based on past personal experience and may ultimately increase arousal levels. In addition, if ADRA2B deletion carriers have higher levels of extracellular NE, we may find different patterns of performance according to affective outcome and arousal. If ADRA2B genotype effects are characterized by a robust negativity bias [39], we expect ADRA2B carriers to make a higher number of errors when scripts contain negative outcomes compared to positive and neutral outcomes. Differently, we might find that carriers make fewer false memories with negative outcomes. Such results would indicate that ADRA2B carriers are able to regulate their memory encoding processes and can modulate their preference for negative information as found in the study by Ref. [45]. In this study, although ADRA2B carriers preferred the story read with a negative prosody, recognition was better for positive stimuli. Alternatively, if ADRA2B genotype effects are characterized by a more general emotion effect, we expect ADRA2B carriers to generate fewer false memories when the scripts contain negative and positive outcomes with respect to neutral ones. Altogether, these findings will thus help disentangling the role of emotion in the generation of false memories (i.e. whether emotion increases or decreases the number of memory errors) and indicate a specific effect of genotype differences in emotional false memories.

2. Method

2.1. Ethics statement

The study was approved by the Departmental Ethics Committee at

the University of Chieti. In accordance with the Declaration of Helsinki, all participants gave written informed consent prior to inclusion in the study.

2.2. Participants

The sample size of the present study was established following the typical effect size (η^2) of 0.07 of genetic correlates of memory studies (e.g. [38]. We required 90 participants per genotype for a behavioral study. In line with the finding that 30% of the White population show the ADRA2b deletion variant, we recruited 300 right-handed native Italian speakers from an undergraduate pool of students from the University of Chieti for credit in a second-year psychology course. Participants were all females between the ages of 19 and 25 (mean age 20.6). Participants reporting a history of significant head injuries, stroke, epilepsy and learning disabilities were excluded. Eleven participants were excluded because they could not be genotyped for ADRA2b. A further subset of participants with previous or current diagnosis or treatment for anxiety and depression, revealed by a self-report demographics questionnaire were excluded from the analysis due to potential associations between anxiety/depression and ADRA2b [46] leaving a total of 212 female participants who were recruited for a set of experimental tasks, among them, the false memory task described in the following section. We recruited only female participants because a recent study by Ref. [43] showed that the ADRA2B deletion variant may selectively predict stress effects on memory in females, potentially underlying gender-related differences and stress effects on learning. Accordingly, we expected ADRA2B polymorphisms effects in memory to be magnified by recruiting only females.

2.3. Design

Our study adopted a 2(Group: deletion carrier versus non-carrier) × 2 (Type of Error: script consistent versus inferential) × 3 (Valence: positive, negative and neutral) mixed design.

3. Materials

We used nine episodes, or scripts, in our study. Each script was composed of fifteen colored photographs depicting young actors engaged in typical everyday activities to create each episode. Episodes included waking up (i.e., typical morning routine before going to school), going shopping (i.e., young boy going grocery shopping with his mother), dating/meeting a friend (boy and girl meeting in the park), bike trip (i.e., girl going on a bike trip in a downtown area), rock climbing (i.e., boy climbing a wall), track competition (i.e., young girls getting ready for and performing a competition), coming back from a long trip (i.e., girl coming back by train from a trip, and entering her home), playing games (i.e. video games in a bar) and a party (i.e., a girl welcoming guests and blowing out candles). Twelve of the 15 pictures of each series were used for each script. The remaining three were used as plausible script errors during the recognition phase. We created two versions of each episode so that targets and plausible script errors were counterbalanced across participants. That is, photographs that were targets in one version of each script were plausible script errors in the other and vice versa. For each script, we also created a single photograph depicting a causal scene that could be inferred as the causal antecedent of the affective outcome of the episode. Causal scenes consisted of a single picture depicting a causal antecedent followed by three different affective outcomes: one positive, one negative, and one neutral.

In each series of twelve pictures, only the eleventh picture varied between different versions of the same episode. The eleventh picture communicated the affective outcome of the episode. For example, the girl and bike on the ground and the driver, out of the car, with her hands on her head (negative), the bike at the entrance with the car already out of the entrance and the girl getting off the bike (neutral), the girl getting off the bike and hugging a friend (positive). in the "bike" episode. Valence was counterbalanced across participants so that each participant saw three episodes for each of the three affective outcomes.

Lastly, five unassociated pictures were presented at the beginning and five at the end of the encoding session to avoid primacy and recency effects. Episodes were not introduced by titles and there were no intervals between them. However, episodes differed in actors and settings to avoid confusion and allow participants to understand when a specific episode ended and a new one started. Valence and arousal levels of the pictures representing the negative, positive, and neutral outcomes were rated by 18 independent judges using the SAM (Self-Assessment Manikin) scale [47]. A series of paired-samples *t*-tests showed that the outcomes significantly differed: negative outcomes had lower valence ($M = 2.22$, $SD = 0.94$), $t(16) = 12.62$, $p < 0.001$, and positive outcomes had higher valence ($M = 7.67$, $SD = 0.79$), $t(16) = -15.04$, $p < 0.001$, than neutral outcomes ($M = 5.04$, $SD = 0.45$). Furthermore, arousal was significantly higher in both negative ($M = 7.40$, $SD = 0.88$), $t(16) = -8.74$, $p < 0.001$, and positive outcomes ($M = 6.90$, $SD = 0.93$), $t(16) = -12.92$, $p < 0.001$, than in neutral outcomes ($M = 3.89$, $SD = 1.30$). Finally, although arousal was slightly higher in the negative than in the positive outcomes, the difference did not reach significance, $t(16) = 1.64$, $p = 0.12$. Ten independent individuals were also asked to rate each picture according to typicality on a 4-point scale (1 not a typical situation at all 4 a very typical situation). Results showed that in general, episodes represented highly typical everyday activities (mean rating 3.5; range: 2.9–3.8). These individuals were then instructed to choose between two pictures the picture that seemed to best depict what had happened just before the outcome. At least 8 out of 10 individuals chose the picture that we adopted as our causal error.

We adopted a unique sequence of 90 photographs, both old and new, for recognition. Participants saw a total of 8 photographs for each episode, four old ones from the encoded script, three new ones, plausible with the script (plausible error), and one causal photograph (causal error) not seen during the encoding session but that could be inferred as a plausible causal antecedent of the episode. That is, plausible errors were photographs that depicted information that could plausibly be part of the story told by the script but could not be considered the cause of the outcome of the script. Differently, causal errors were photographs that depicted an aspect that could be inferred as causing the outcome of the script. They also saw nine old unassociated photographs and nine new unassociated photographs. Photographs were presented randomly, irrespective of episode, with the constraint that participants never saw two causal distractors in subsequent positions in the sequence and these never corresponded to the first or last position, or to the slide immediately before the photograph depicting the affective outcome (Fig. 1).

3.1. Procedure

We tested all participants individually in 2 sessions. In the first session, we collected demographic information and administered psychological general screening tests. In the second session, participants completed the false memory experimental task.

3.1.1. Encoding phase

The first 10 and last photographs of each episode were identical across all conditions and for all participants. The eleventh photograph of each episode differed according to affective valence condition. For example, in the bike episode with a negative outcome, the eleventh photograph showed the biker and bike on the ground and the driver just out of the car door. In the same episode with a neutral outcome, the biker is on the bike and the car appears to have already passed while in the episode with a positive outcome, the bike is behind the biker and the driver who are hugging. The overall duration of the encoding phase

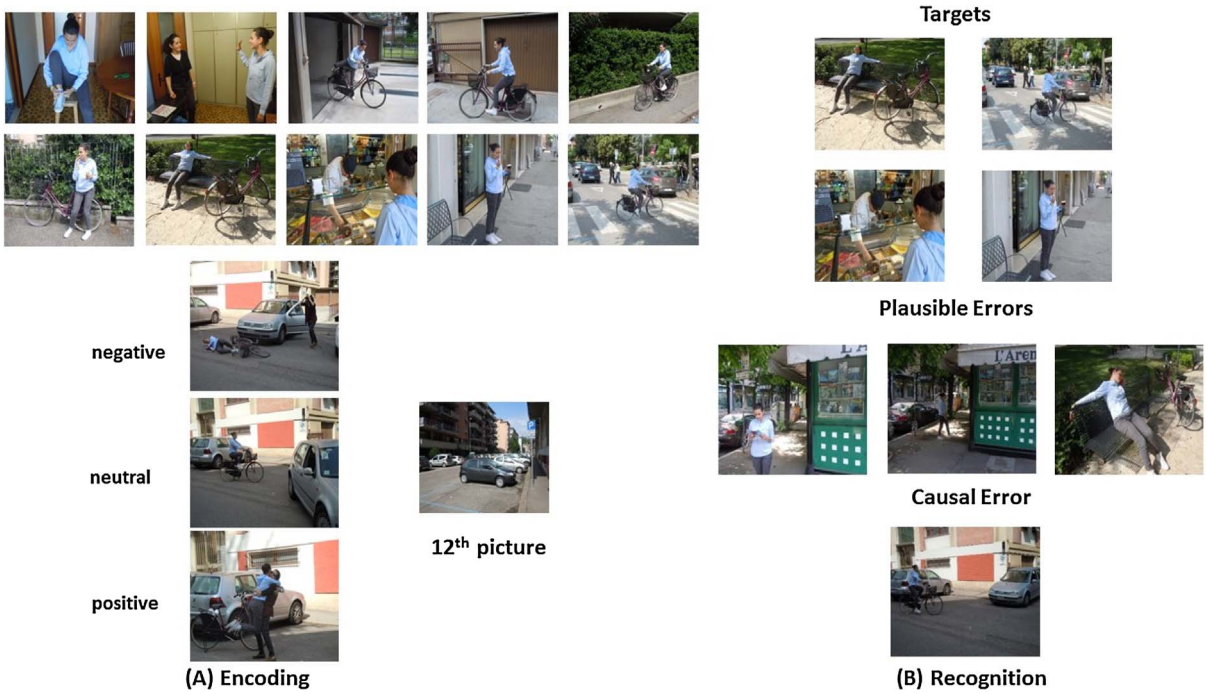

Fig. 1. The bike episode.

was 8 min and 47 s.

3.1.2. Recognition phase

Participants completed a self-paced recognition task immediately after the encoding phase. For each picture, participants were instructed to respond "yes" if they thought they had seen the image during the encoding phase, and "no" if they thought they had not.

3.2. Genetic analysis

Genomic DNA was isolated from buccal swabs using the NucleoSpin Tissue kit (Macherey-Nagel, Düren, Germany) according to manufacture instructions. PCR reaction was carried out in a final volume of 25 µl mixture using AmpliTaqGoldTMpolymerase. The forward primer, 5-AGAAGGAGGGTGTTTGTGGGG-3, and reverse primer, 5-ACCTATAGCACCCACGCCCCT-3, were employed, with an annealing temperature of 58 °C. This PCR reaction generated 200 and 209 base pair PCR products respectively for the Glu301-Glu303 deletion and wild type alleles. PCR products were resolved on a 4% Amresco (Solon, OH) Super Fine Resolution agarose gel stained with ethidium bromide. A PCR reaction which contained no DNA was performed as a negative control (see Fig. 2). In line with previous studies, (e.g. [39,25]) homozygote and heterozygote ADRA2B carriers were treated as a single group due to the small number of homozygotes.

A significance level was set at $p < 0.05$. We were primarily interested in studying the influence of ADRA2B on emotional false memory. Consequently, mixed-model analyses of variance (ANOVAs) were run on proportional scores with Valence (positive, negative and neutral) and Type of error (script consistent vs. inferential) as repeated measures factor and Group (ADRA2B carriers vs. non-carriers) as the between-subjects factor.

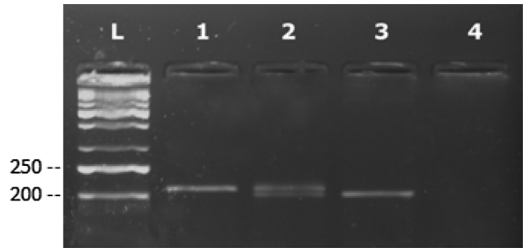

Fig. 2. PCR reaction.

4. Results

4.1. Genotype and demographic data of participants

A group of 212 subjects were available for analysis. Homozygosity for the Glu301-Glu 303 deletion was detected in 20 participants; 71 subject were heterozygote while 121 were homozygote reference (see Fig. 1). The ADRA2B genotype frequencies were in Hardy Weinberg equilibrium (χ 2 test P value > 0.05). Participants were divided into two groups according to their ADRA2B genotype (91 carriers vs 121 non-carriers). Groups were matched in terms of age and education as well as general short-term memory (measured with the forward and backward digit spans of the Wechsler Adult Intelligence Scale-Revised (WAIS-R; [48]) and current mood (measured with the Positive and Negative Affective Scale, PANAS, [49]). Table 1 presents the demographic data of participants.

4.2. Data analysis

A preliminary analysis concerned accuracy. To this end, we carried out a first analyses on accuracy scores for the single unassociated items.

Table 1
Neuropsychological and demographic characteristics of carriers and controls.

	Carriers (91)		Controls (121)	
	M	SD	M	SD
Age	20.80	2.51	20.38	1.79
Education (in years)	15.11	1.10	15.00	0.69
Digit span forward	6.85	1.56	6.63	1.68
Digit span backward	5.34	1.94	5.82	1.64
PANAS pos	30.15	5.79	31.32	5.87
PANAS neg	21.44	6.69	21.37	6.70

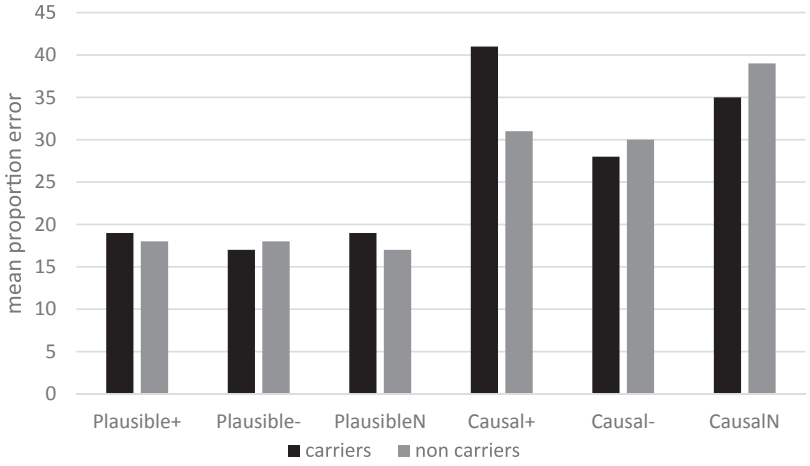

Fig. 3. Mean proportions of False Alarms for Valence, Group, and Type of Error (Plausible Script vs. Causal).

We calculated accuracy scores as HITs – FA, that is correct yes responses minus incorrect yes responses. We found no significant main effects no significant main effects nor interactions showing how the ADRA2B did not influence accurate recall.

A second analysis concerned memory errors, calculated as mean proportions (as done in previous studies, e.g. [50,51]), in reporting new pictures as old. Fig. 3 shows the mean proportions of inferential and script consistent errors.

A 2(Group: carriers vs. non-carriers) × 2 (Type of error: plausible vs. causal) × 3(Affective outcome: positive vs. negative vs. neutral) mixed analysis of variance (ANOVA), with the last two factors as within participant factors, on the proportions of false memory as the dependent measure, revealed a significant main effect of Type of Error revealing that plausible script errors were, in general, more likely to be made than causal errors, $F(1, 210) = 123{,}93$, $p < 0.01$, $\eta^2 = 0.37$. The main effect of Affective outcome was significant, $F(2, 420) = 3{,}7224$, $p < 0.05$, $\eta^2 = 02$. Post-hoc tests revealed how, in general, participants made more errors when the episode contained a positive or neutral ending compared to a negative final ($p < 0.05$). The effect was specified by a significant 3-way interaction, $F(2, 420) = 3{,}0801$, $p < 0.05$, $\eta^2 = 0.01$. Post-hoc comparisons revealed that negative inferential errors were less frequent than positive and neutral ones in deletion carriers ($p < 0.05$), while positive and negative inferential errors were less frequent than neutral ones in non-deletion carriers ($p < 0.05$).

We also performed the same analyses using d' scores. We again found a significant 3- interaction, F(2, 420) = 3,1943, $p < 0.05$ as shown in Fig. 4a.

4.3. Response bias

Fig. 4b shows C scores for affective outcome, type of error and group. We used C as our response bias variable, computed according to Ref. [58]. Negative values of C indicate a liberal response bias (more likely to call an item "old"), and positive values of C indicate a conservative response bias (more likely to call an item "new). An ANOVA comparing deletion participants to non-deletion participants did not find an effect of group $F(1, 210) = ,01804$, $p = ,89$. The Type of error was significant $F(1, 210) = 14{,}344$, $p < 0.001$, $\eta^2 = 0.06$ because the response bias for plausible script errors was more liberal than that for causal errors. We did not find an effect of Affective outcome F(2, 420) = ,01176, p = ,99. We did not find an Affective outcome X Group interaction, $F(2, 420) = 1{,}7436$, $p = ,18$ nor a Type of error x Affective outcome interaction $F(2, 420) = ,06605$, $p = ,94$. Finally, the Type of error X Affective outcome X Group interaction was not significant, $F(2, 420) = 1{,}0144$, $p = ,36$.

5. Discussion

A recent series of neurobiological studies indicate a strong contribution of NA to emotional memories (e.g. [45]). Here, for the first time, we wanted to examine whether the ADRA2B polymorphism has a modulating effect on the production of affective false memories, in general and/or produces qualitative differences in the generation of affective false memories. We considered two types of different errors (plausible vs. inferential) and valence (positive, negative, neutral). Results can be summarized as follows. First, we observed comparable recognition performance across groups indicating that groups did not differ in terms of their general memory ability. Second, with regards to the interaction between false memory and valence, we found that false memories generally decreased with scripts that contained negative outcomes with respect to positive and neutral ones. This finding is in line with a general negativity bias in cognition of young healthy participants (e.g. [52]) which renders negative information more memorable and, consequently, less sensitive to distortions. Finally, when considering causal false memories, we found that errors decreased in ADRA2B carriers when scripts contained negative outcomes with respect to positive and neutral outcomes in line with the assumption that although carriers show an encoding preference towards negative information processing, they can later exert control over it as shown in a previous study by Ref. [45]. We did not find any ADRA2B genotype effects with plausible script errors. Regarding causal errors, carriers and non-carriers showed different patterns of performance. Carriers made fewer errors when scripts contained negative outcomes while non-carriers made fewer errors when scripts contained positive and negative outcomes.

In line with semantic elaboration hypotheses and what is known about the influence of NA on encoding and consolidation, our results suggest that putatively high-levels of NA in deletion carriers may enhance short-term consolidation of the negative information that is typically most salient to young adults [52,53]. That is, it might more selectively enhance the memory for what is already most salient or goal relevant, as predicted by Ref. [54]. Deletion carriers may preferentially focus attention on and monitor negative stimuli better in a way that leads them to later show a corresponding decrease in the number of negative false memories in line with source monitoring hypotheses that predict a decrease in false memories when judgements are supported by source monitoring abilities, reductions in reliance on gist traces, or effective metacognitive strategies (e.g. [55]). Several studies, in fact, have shown how false memories increase as item-specific encoding decreases and gist encoding increases [16]. This was not the case among ADRA2B carriers when facing negative events.

In line with recent studies that point to the involvement of NA in cognitive-affective flexibility [56,57], it seems reasonable to assume that NA may play a crucial role during affective information processing

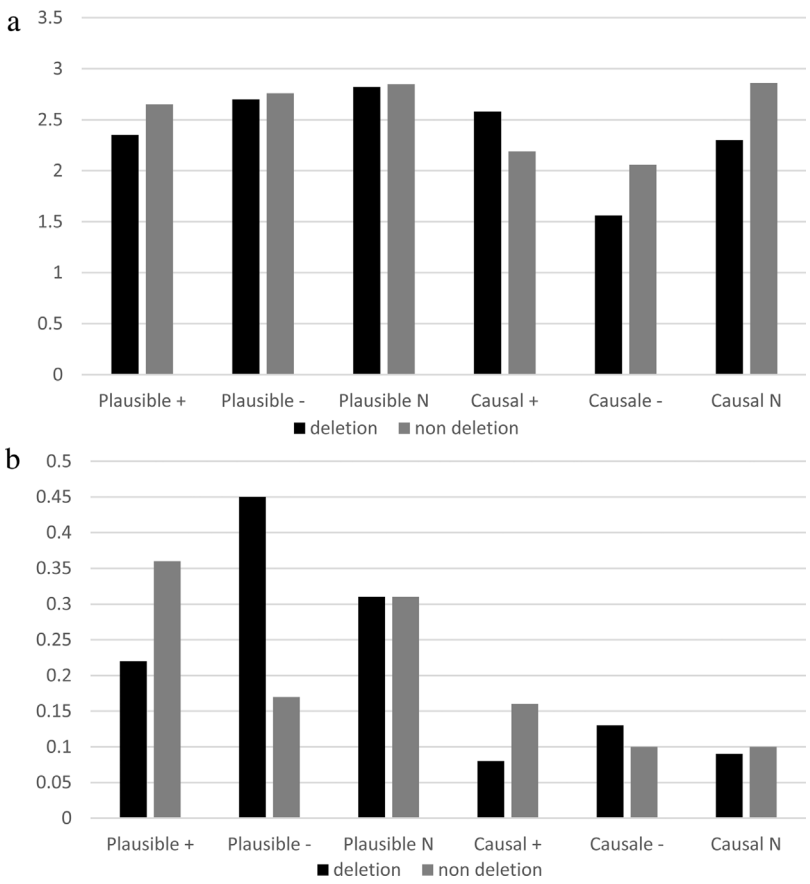

Fig. 4. (a) d' scores for affective outcome, type of error and group. (b) C scores for affective outcome, type of error and group.

in general, and in the generation of different valence biases in memory. Although this study draws mainly on NA, research has investigated effects of other neurotransmitters on emotional memory, namely, the dopamine (DA) and serotonin (5-HT) systems. A recent study with younger adults by Ref. [37], for example, showed that ADRA2B and 5HTTLPR mutually influenced each other in ventromedial prefrontal cortex regions important for evaluating the salience of stimuli. It is, therefore, reasonable to suppose that NA, DA and serotonin all contribute to shaping valence effects.

To conclude, this is one of the first studies to directly and systematically compare genetic and cognitive mechanisms involved in the production of false memories for events with affective outcomes. This convergence of behavioral and neuroscience approaches is necessary since important contributions to the explanation of emotion effects on cognition are likely to emerge from research that considers the neurobiological underpinnings of such effects and, in particular, the role that NA may play during the formation of affective memories. However, our study is not without limitations. First, as state above, future studies must also consider the role of other neurotransmitters on memory for and memory errors with affective information. Also, studies with psychiatric patient populations such as schizophrenia patients may want to examine, for instance, whether the same pattern of results emerges: that is, if patients also exhibit a higher number of inferential errors, and whether this pattern relates to individual differences in genotype. Similarly, it will be important to better investigate whether the attentional focus during 'affective' processing is predictive of their false memory pattern. For instance, one could develop a cognitive-emotional neuroimaging false memory paradigm (e.g. fMRI, ERPs) that allows to study emotion-memory interaction at both encoding vs. retrieval. We suggest that more studies of this type are needed to disentangle the role of top-down (e.g. cognitive) and bottom-up mechanisms (e.g. genetic polymorphisms) in both healthy and psychiatric populations. Lastly, although our sample size is in line with the power analysis cited by the 2009 Rasch paper on imaging genetics, there have been numerous criticisms of targeted polymorphism studies for producing non-replicable results. Accordingly, we are continuing to collect data and future studies should consider increasing the sample size even though the polymorphism is generally present in only a low proportion of the population.

Author contributions

BF and NM developed the study concept. All authors contributed to the study design. Testing and data collection were performed by BF, AD and MD. AD, MD and VG performed the data analysis and interpretation under the supervision of NM and LS. BF drafted the manuscript, and NM and LS provided critical revisions. All authors approved the final version of the manuscript for submission.

Declaration of interest

The Authors declare that there is no conflict of interest.

Role of funding source

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