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Genetic variation in the serotonin transporter gene influences ERP old/new effects during recognition memory

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ABSTRACT

Recognition memory is defined as the ability to recognize a previously encountered stimulus and has been associated with spatially and temporally distinct event-related potentials (ERPs). Allelic variations of the serotonin transporter gene (SLC6A4) have recently been shown to impact memory performance. Common variants of the serotonin transporter-linked polymorphic region (5HTTLPR) of the SLC6A4 gene result in long (l) and short (s) allelic variants with carriers of the s allele having lowered transcriptional efficiency. Thus, the current study examines the effects polymorphisms of the SLC6A4 gene have on performance and ERP amplitudes commonly associated with recognition memory. Electroencephalogram (EEG), genetic, and behavioral data were collected from sixty participants as they performed an item and source memory recognition task. In both tasks, participants studied and encoded 200 words, which were then mixed with 200 new words during retrieval. Participants were monitored with EEG during the retrieval portion of each memory task. EEG electrodes were grouped into four ROIs, left anterior superior, right anterior superior, left posterior superior, and right posterior superior. ERP mean amplitudes during hits in the item and source memory task were compared to correctly recognizing new items (correct rejections). Results show that s-carriers have decreased mean hit amplitudes in both the right anterior superior ROI 1000–1500 ms post stimulus during the source memory task and the left anterior superior ROI 300–500 ms post stimulus during the item memory task. These results suggest that individual differences due to genetic variation of the serotonin transporter gene influences recognition memory.

1. Introduction

Episodic memory is the memory of our life events and relies on the ability to associate the contextual details of an episode together into a coherent narrative (Eichenbaum, 2000; Eichenbaum et al., 2007). Recognition memory, which is the ability to judge whether a stimulus has been experienced in the past, is an important component of episodic memory. Two tasks typically used to examine recognition memory are item and source memory tasks (for review see Eichenbaum et al., 2007). Item memory tasks require a participant to declare whether a presented item was previously encountered, which is a recognition judgment without retrieval of associated contextual details. In contrast, source memory tasks require participants to identify a contextual detail previously associated with an item and may rely more on recollection processes (Donaldson and Rugg, 1998; Yonelinas et al., 2002; Weis et al., 2004; Eichenbaum et al., 2007; Ross and Slotnick, 2008). A recent fMRI study shows that genetic variation at the 5HTTLPR promoter region of the gene coding for the serotonin transporter (SLC6A4) significantly impacts source memory monitoring and prefrontal cortical activity in older adults (Pacheco et al., 2012). Additionally, the 5HTTLPR polymorphism of the SLC6A4 gene impairs delayed recall and visual-spatial recall in older adults (O'Hara et al., 2007; Olivier et al., 2009; Marini et al., 2011). However, it is unclear when and how 5HTTLPR polymorphisms affect memory performance. Therefore, the current study uses EEG in combination with genetic data collection in young adults to determine when polymorphisms of the serotonin transporter gene might affect item and source memory.

Event-related potential (ERP) studies of source and item memory have identified distinct electrical patterns associated with

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successful recognition, dubbed old/new effects (Wilding and Rugg, 1996; Rugg et al., 1998; Donaldson and Rugg, 1998; 1999; Curran, 2000) and late posterior negativity (Johansson and Mecklinger, 2003; Herron and Wilding, 2005; Wilding et al., 2005; Leynes and Phillips, 2008; Mecklinger et al., 2007; Evans et al., 2010; Rosburg et al., 2011; Leynes and Kakadia, 2013). Old/new effects manifest as a greater ERP positivity when a participant correctly identifies the source associated with an item and when correctly identifying a previously studied item as old ("hits") compared to when a participant correctly identifies a previously un-encountered item as new ("correct rejections"). Old/new effects can be seen in medial anterior scalp locations 300–500 ms (early frontal old/new effect), left parietal scalp sites 500–800 ms (left parietal old/new effect), and right frontal scalp locations 1000–1500 ms (late frontal old/new effect) post-stimulus presentation (Wilding and Rugg, 1996; Donaldson and Rugg, 1998; 1999; Rugg et al., 1998; Senkfor and Van Petten, 1998; Curran, 2000; Curran et al., 2001; Cycowicz and Friedman, 2003; Yonelinas et al., 2005; Woodruff et al., 2006; Rugg and Curran, 2007; Vilberg and Rugg, 2007; Curran and Hancock, 2007). The early frontal old/new effect (300–500 ms or FN400) has been linked to processes related to memory, with some researchers suggesting the FN400 supports familiarity (Rugg and Curran, 2007) while others suggest the FN400 reflects implicit conceptual priming (Voss et al., 2012). The parietal old/new effect (500–800 ms) has also been linked to memory processing, specifically recollection, where contextual details associated with an event are retrieved (Wilding and Rugg, 1996; Rugg et al., 1998; Donaldson and Rugg, 1998; 1999; Curran, 2000; Curran and Hancock, 2007; Rugg and Curran, 2007; Eichenbaum et al., 2007). These results suggest the early frontal and parietal ERP components are related to memory retrieval processing.

In contrast to the early frontal and left parietal ERP old/new effects, the late frontal old/new effect and the late posterior negativity (LPN) have been linked to cognitive control (Wilding and Rugg, 1996; Donaldson and Rugg, 1998; Ranganath and Paller, 2000; Rugg and Wilding, 2000; Werkle-Bergner et al., 2005; Ally and Budson, 2007). Specifically, the late frontal old/new effect has been linked to a general monitoring and evaluation mechanism, where the products of memory retrieval may be evaluated in order to select the necessary information for the current goal (Rugg et al., 2003; Hayama et al., 2008; Hayama and Rugg, 2009). The late posterior negativity (LPN) is a larger negative deflection in the EEG signal for successfully remembered information than for correct rejections (Johansson and Mecklinger, 2003). The LPN has been seen over midline posterior electrodes during item memory tasks when there is interference due to response conflict (Johansson and Mecklinger, 2003) and during difficult source memory tasks (Johansson and Mecklinger, 2003; Herron and Wilding, 2005; Wilding et al., 2005; Leynes and Phillips, 2008; Mecklinger et al., 2007; Evans et al., 2010; Rosburg et al., 2011; Leynes and Kakadia, 2013). The LPN is hypothesized to reflect increased evaluation of information that has been bound together in memory (Johanson and Mecklinger, 2003). These findings suggest the late frontal old/new effect and the LPN index cognitive control processes during memory retrieval. The current study uses these four well-characterized ERP components (FN400, parietal old/new effect, late frontal old/new effect, and LPN) to differentiate when and how genetic variation in the serotonin transporter gene may affect recognition memory.

The 5HTTLPR polymorphism may influence item and source memory during memory retrieval processes as indexed by the early frontal and left parietal old/new effects or during cognitive control processes as indexed by the late frontal old/new effect and the late posterior negativity. The polymorphism in the 5HTTLPR promoter region of SLC6A4 results in long (l) and short (s) allelic variants (Heils et al., 1996). S-carriers (s/s homozygotes or s/l heterozygotes) have lower transcriptional efficiency and decreased serotonin transporter function (Bennett et al., 2002) and prior research has used the same l/l homozygote/s-carrier split to examine memory (O'Hara et al., 2007; Olivier et al., 2009; Marini et al., 2011; Pacheco et al., 2012). However, it is unclear how polymorphisms of the serotonin transporter gene might affect recognition memory. Therefore, we used EEG to examine differences in ERP components commonly associated with recognition memory between l/l homozygotes and s-carriers of the 5HTTLPR polymorphism of the serotonin transporter gene. Specifically, we compared mean hit and correct rejection ERP amplitudes between l/l homozygotes and s-carriers during an item and source memory task. If the 5HTTLPR polymorphism affects memory processes, there should be changes in the FN400 and/or parietal old/new effects during recognition memory. However, if the 5HTTLPR polymorphism affects cognitive control processed during recognition memory, then there should be changes in the late frontal old/new effect and/or late posterior negativity.

2. Methods

2.1. Participants

Seventy-six right-handed participants volunteered for this study. Participants were recruited from the University of Colorado Boulder community and gave informed consent in accordance with the Institutional Review Board of the University of Colorado. Sixteen participants were removed from the study for various reasons. Four participants did not participate in both EEG data recording sessions (item memory and source memory) and three participants were removed for technical reasons. Nine participants were removed due to excessive noise in the EEG recordings, including excessive blinking ($n=3$), excessive channels needing interpolation ($n=2$), lack of 20 good hit and correct rejection epochs post artifact detection ($n=3$), and lack of adequate performance in either task (chance performance, $n=1$), leaving 60 participants in the study aged 18–29 (mean $\pm$ standard deviation, 20.7 ± 2.59 years old; 27 females, 33 males). Those 60 participants were split into two groups based on 5HTTLPR polymorphism with 17 participants in the l/l homozygous group and 43 participants in the s-carrier group.

2.2. Stimuli

Eight hundred and fifteen adjectives were used as stimuli. The Kucera and Francis (1967) word norms were followed for the selection of adjectives to be used in the study. The words were presented to the participants in white uppercase letters in the center of the screen on a 26 in. LCD computer screen with a black background at a visual angle of 2.3° (Fig. 1). The average written frequency (kfreq) of all the adjectives used in the study was 34.86 and the average number of letters per word was 6.93. The average kfreq across the counterbalanced lists ranged from 34.19 to 35.93 and the average number of letters across counterbalanced lists ranged from 6.87 to 7.00 and the kfreq and number of letters did not differ between lists.

2.3. Task

Participants performed both an item and source memory task in two separate sessions. During the first visit, participants performed one study/test session, where they encoded one set of words and performed one of the memory tasks (item memory or source memory). The participants returned 2–5 days later to perform the second study/test session, where the participants

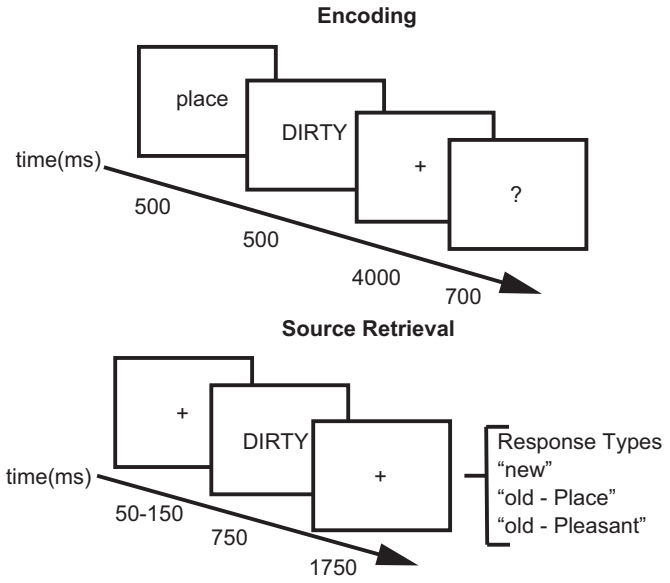

Fig. 1. Behavioral paradigm for study and test phases of experiment. During the study phase of both the item and source memory task, participants were given a place or pleasantness cue for 500 ms indicating the task to use during encoding followed by a 500 ms presentation of an adjective. Participants were given 4000 ms to perform the task and then were asked to rate how successfully they were performing the task. The bottom panel represents the retrieval phase when EEG recordings took place. A variable duration fixation cue was presented for 50–150 ms followed by an adjective for 750 ms and a fixation cross for 1750 ms. Participants could respond anytime after presentation of the adjective. Response types shown are for the source memory task. During item memory, participants were only given two choice options, "new" and "old".

encoded a new set of novel words and the memory task not performed on the first visit was administered (e.g. if the first visit was the item memory task, the second visit was the source memory task). Following the encoding period, item or source memory retrieval was tested while participants underwent EEG recording. The order of item and source memory retrieval task sessions was counterbalanced across participants. Participants underwent a short practice block before being asked to encode words in the study block. During the practice block, participants were given instructions and studied 10 words in order to familiarize them with the task. Upon completion of the practice block, the actual study phase began. Each study block (item and source memory task) consisted of 204 words, with two words at the beginning and two words at the end of the study phase acting as primacy and recency buffers. During the study blocks, participants were instructed to associate half of the words with a mental image of a location or a place corresponding to the word (Place task – e.g. for "PRETTY," the participant might imagine a field of flowers) and the other half with the pleasantness evoked by the word (Pleasant task – e.g. for "FEARFUL," the participant might imagine an unpleasant feeling) (Davachi et al., 2003; Kahn et al., 2004). Adjectives used in the place and pleasantness task were randomly intermixed during the study blocks. Participants were given the same encoding instructions for words that would subsequently be used in the item and source memory retrieval tasks. The task used during encoding served as the contextual detail to be retrieved during the source memory task. A cue indicating which of the two encoding tasks to use was presented to the participants 500 ms prior to the word presentation. A 200 ms blank screen followed the task cue instruction followed by adjective presentation for 500 ms. A fixation cross was presented for 4000 ms after adjective presentation to allow participants to perform the encoding task. Upon completion of the encoding period, a question mark popped up on the screen for 700 ms where participants were instructed to rate the degree to which they successfully encoded the adjective (Fig. 1). Participants rated their performance by pressing one of four buttons: 1, unsuccessful; 2, successful; 3, with effort; 4, with ease.

After the adjectives were encoded, participants were fitted with a 128 channel HydroCel Geodesic Sensor Net connected to an AC-coupled high-input impedance amplifier (200 MΩ, Net Amps TM, Electrical Geodesics Inc., Eugene, OR). Amplified analog voltages (0.1–100 Hz bandpass) were digitized at 250 Hz. Individual sensors were adjusted until impedances were less than 50 kΩ. Participants were given a 15-word practice test block prior to beginning the retrieval tasks. Approximately thirty minutes passed between the conclusion of the encoding phase and the beginning of the retrieval phase. Two to five days later the second encoding/retrieval session was completed. The order of retrieval sessions (item memory task and source memory task) was counterbalanced across participants.

Participants viewed 480 words during each of the item and source test conditions: 200 previously studied words, 200 new words, and 80 words serving as buffers. The adjectives were presented in blocks of 24, with two words at the beginning and end of each block serving as primacy and recency buffers. Twenty test blocks were included in the item and source memory retrieval conditions (for a total of 40 test blocks across the two testing days). For each presented adjective, there was an initial variable fixation period of 50–150 ms, followed by the test word for 750 ms and an additional fixation period of 1750 ms. Participants were permitted to respond upon word presentation. For item retrieval, participants used the index fingers of both hands and pressed one key for old (previously studied word) and another key for new. For source retrieval, participants used the index and middle finger of one hand and the index finger of another to indicate their responses. Participants pressed one key for a new word, one key for a previously studied word encoded using the place task, and another key for a previously studied word encoded with the pleasantness task (as depicted in Fig. 1). Following their response, using their index and middle finger of one hand and their index finger of their other hand, subjects responded surely, likely, or maybe depending on how confident they were of their answer. EEG data, accuracy data, and reaction time (RT) data were collected as the participants completed the task.

2.4. ERP method

EEGLAB (Delorme and Makeig, 2004) and ERPLAB (Lopez-Calderon and Luck, 2014) were used to pre-process the data. Before data pre-processing, channels with excessive noise were identified via visual inspection and interpolated using spherical spline interpolation (Srinivasan et al., 1996). No participant had more than 5 channels (4%) interpolated. Data preprocessing included filtering the data from 0.1 to 40 Hz, re-referencing to the average signal, separating the data into epochs, and artifact rejection. The data was epoched into periods 800 ms pre-stimulus presentation to 1500 ms post-stimulus presentation (−800 to 1500 ms). Epochs were sorted into bins according to their response type (hits and correct rejections). In the source memory task, hits included anytime the participant correctly remembered previously viewing the word (both source and item hits). Source hits were when participants correctly remembered the contextual detail associated with the word. Item hits were when the participant correctly indicated previously viewing the word but incorrectly identified the source. Correctly indicating that a word had never been seen before constituted a correct rejection (CR). After the data was split into epochs, artifact rejection was done. Artifact rejection was accomplished with an automated moving window search procedure where changes of 100 μV were marked for

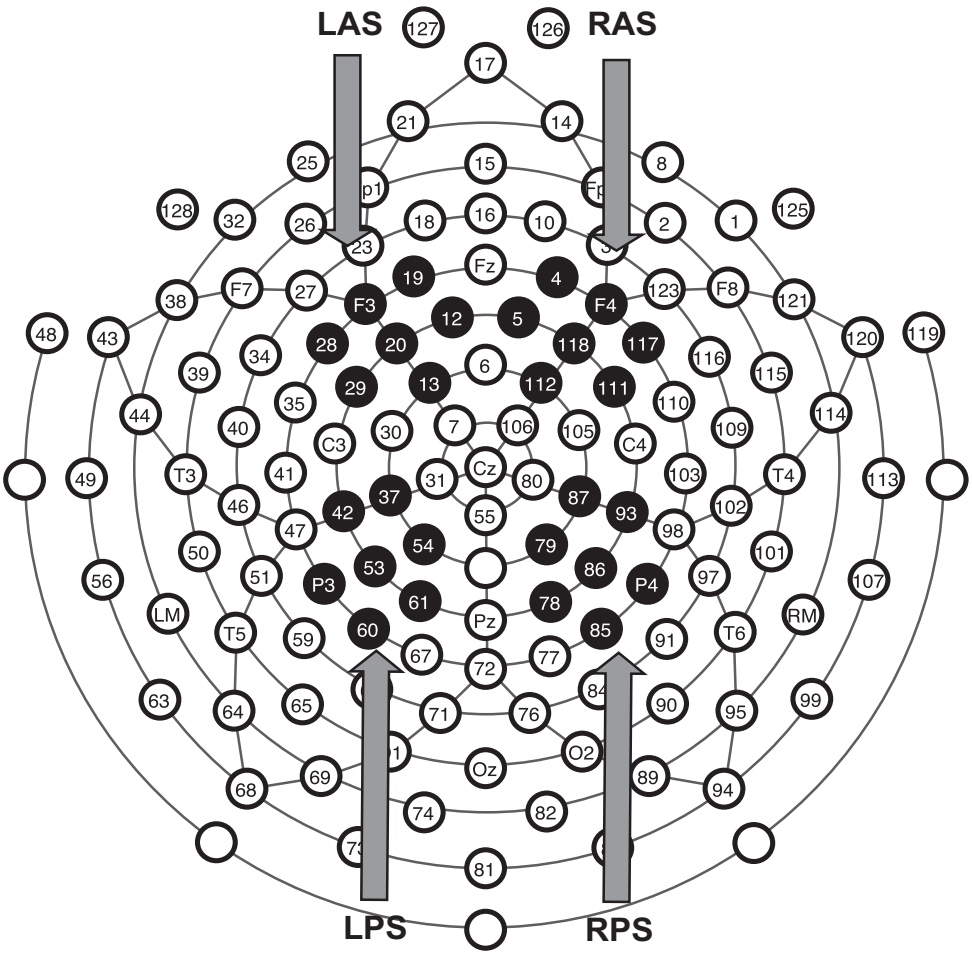

Fig. 2. Regions of interest for ERP analysis. Electrode montage representing location of all 128 electrodes. Black filled in circles represent the four different groups of 7 electrodes averaged together to form the 4 ROIs for statistical analysis. LAS=left anterior superior, RAS=right anterior superior, LPS=left posterior superior, RPS=right posterior superior.

rejection in 50 ms bins of 100 ms length. A threshold of 20 clean, artifact free epochs for each type of response was established for participant inclusion in data analyses.

2.5. ERP regions of interest

Groups of seven electrodes were averaged together to form each region of interest (ROI; Fig. 2), similar to what has been done in previous research (Curran, 2000; Ally and Budson, 2007; Nyhus and Curran, 2009). Our analysis was focused on the left anterior superior (LAS), right anterior superior (RAS), left posterior superior (LPS), and right posterior superior (RPS) ROIs. These four ROIs were selected because they consistently show old/new effects (Curran, 2000; Budson et al., 2005; Curran et al., 2006; Ally and Budson, 2007; Rugg and Curran, 2007) and incorporate electrodes demonstrating the late posterior negativity (Johansson and Mecklinger, 2003; Leynes and Phillips, 2008; Evans et al., 2010; Leynes and Kakadia, 2013). The LAS and RAS ROIs are where the FN400 (300–500 ms post-stimulus) should appear and the late (1000–1500 ms post-stimulus) frontal old/new effect should be observed in RAS. The LPS ROI is where the parietal old/new effect (500–800 ms post-stimulus) should be observed and the LPN effect (1000–1500 ms post-stimulus) should be observed in LPS and RPS.

2.6. Genotyping

Genomic DNA was isolated from saliva samples collected using a commercial product (Oragene™, DNAgenotek, Kanata, Ontario, Canada), and 5HTTLPR was genotyped as described in Haberstick et al. (2014). The genotypes were distributed according to Hardy–Weinberg Equilibrium (28% l/l, 47% s/l and 25% s/s). Participants were split into groups based on whether the variant in the 5HTTLPR region of the serotonin transporter gene (SLC6A4) was homozygous for the long allele (l/l) or contained a short allelic variant (i.e. s/s or s/l; s-carriers). Seventeen participants were l/l homozygous while 43 were carriers of the s-allele. We also examined polymorphisms of the COMT gene, which is related to production of catechol-O-methyltransferase to determine the specificity of any 5HTTLPR related effects. An A→G mutation in the COMT gene results in a valine to methionine substitution that has been associated with a four-fold reduction in enzymatic activity (Akil et al., 2003). The assay method is detailed in Haberstick and Smolen (2004). Catechol-O-methyltransferase is involved in the degradation of the catecholamines dopamine, norepinephrine, and epinephrine (Weinshilboum et al., 1999). The Val158Met polymorphism has shown an effect on prefrontal functions (Egan et al., 2001; Malholtra et al., 2002; Goldberg et al., 2003). Therefore, we conducted an analysis with COMT polymorphisms as a comparison for the 5HTTLPR results. Fifty-three of the 60 participants included in the 5HTTLPR analysis had COMT genetic data with 12 participants homozygous for met (met/met), 11 homozygous for val (val/val) and 30 heterozygotes, which were distributed in accord with Hardy–Weinberg equilibrium.

2.7. Behavioral analysis

Reaction time and accuracy during the item and source memory tasks were compared separately with 2×2 repeated measures ANOVAs. In the source memory task, source hits (correct identification of item and source) and correct rejection accuracy and reaction time were compared across genetic groups (s-car and l/l). In the item memory task, item hits and correct rejections were compared across genetic groups. Where appropriate, post-hoc tests comprised of paired samples and independent samples *t*-tests were run. Confidence ratings were used to extract ROC curves so that response sensitivity and response bias could be measured without assuming old and new strength distributions have equal variance. Response sensitivity measured using d_a and response bias c_a were compared between s-carriers and l/l homozygotes during item and source memory with independent *t*-tests. For the

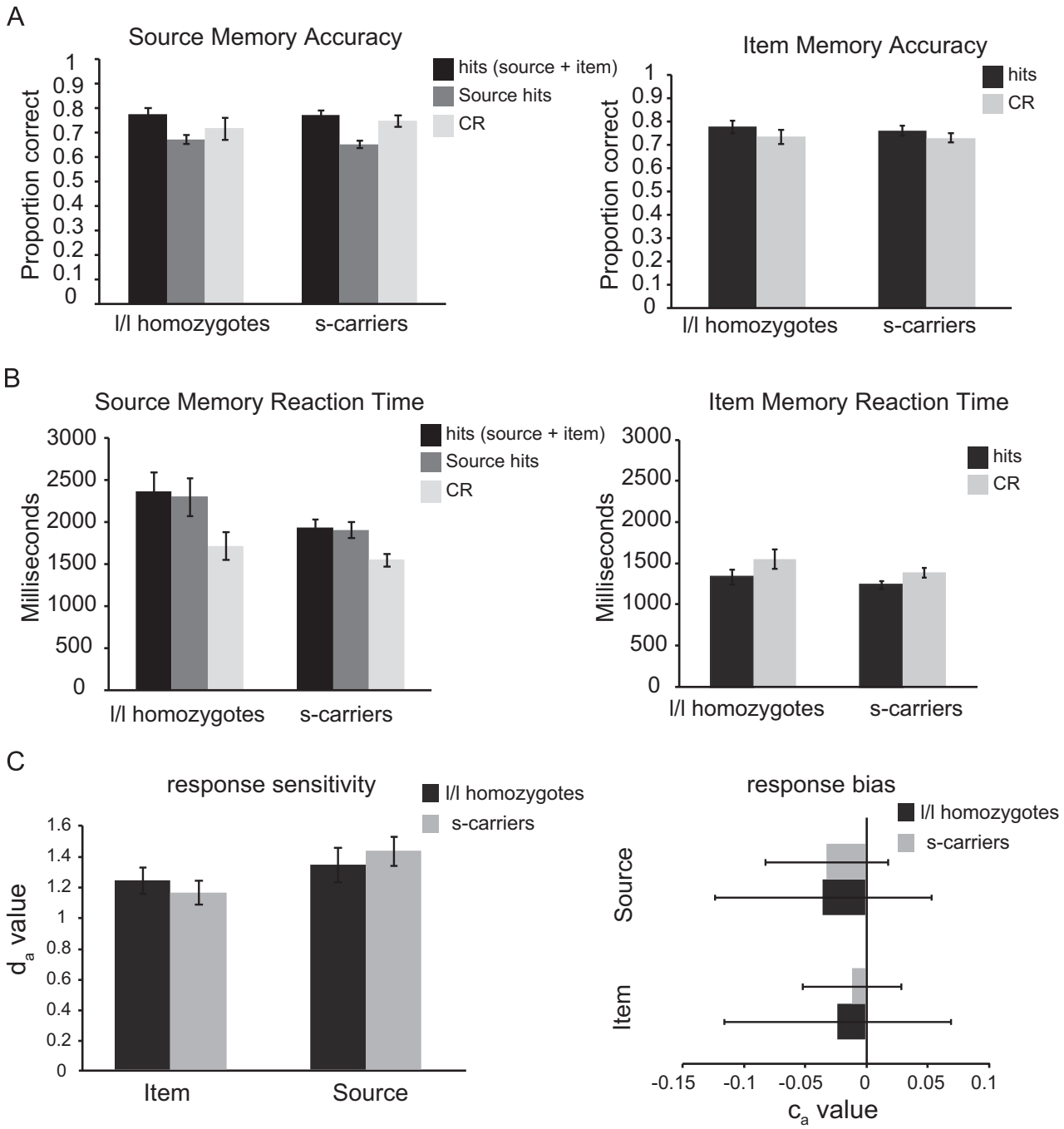

Fig. 3. Source and item memory behavioral results. (A). Source (left) and item (right) memory accuracy. The black bars illustrate the proportion of trials where the participant correctly indicated the stimulus was old with and without the correct identification of source (hits). The dark grey bars represent the proportion of trials where source information was correctly identified. The light grey bars are the proportion of trials where new items were successfully classified as new (correct rejections, CR) for l/l homozygotes and s-carriers during source memory. The proportion of source hits was significantly lower than correct rejections. The right graphs illustrate the proportion of responses where a previously presented item was successfully identified as old (hits; dark grey) and where new items were successfully classified as new (correct rejections, CR, light grey) for l/l homozygotes and s-carriers during item memory. (B). Reaction time during source memory task (left) and item memory task (right). Reaction time was significantly slower during hits and source hits than during CRs. Reaction time during item memory hits was significantly faster than during CRs. (C). Response sensitivity (left) and response bias (right) during the source memory and item memory tasks. S-carriers are represented by light grey bars and l/l homozygotes by dark grey bars. No difference was seen between genetic groups for any of the behavioral measures presented.

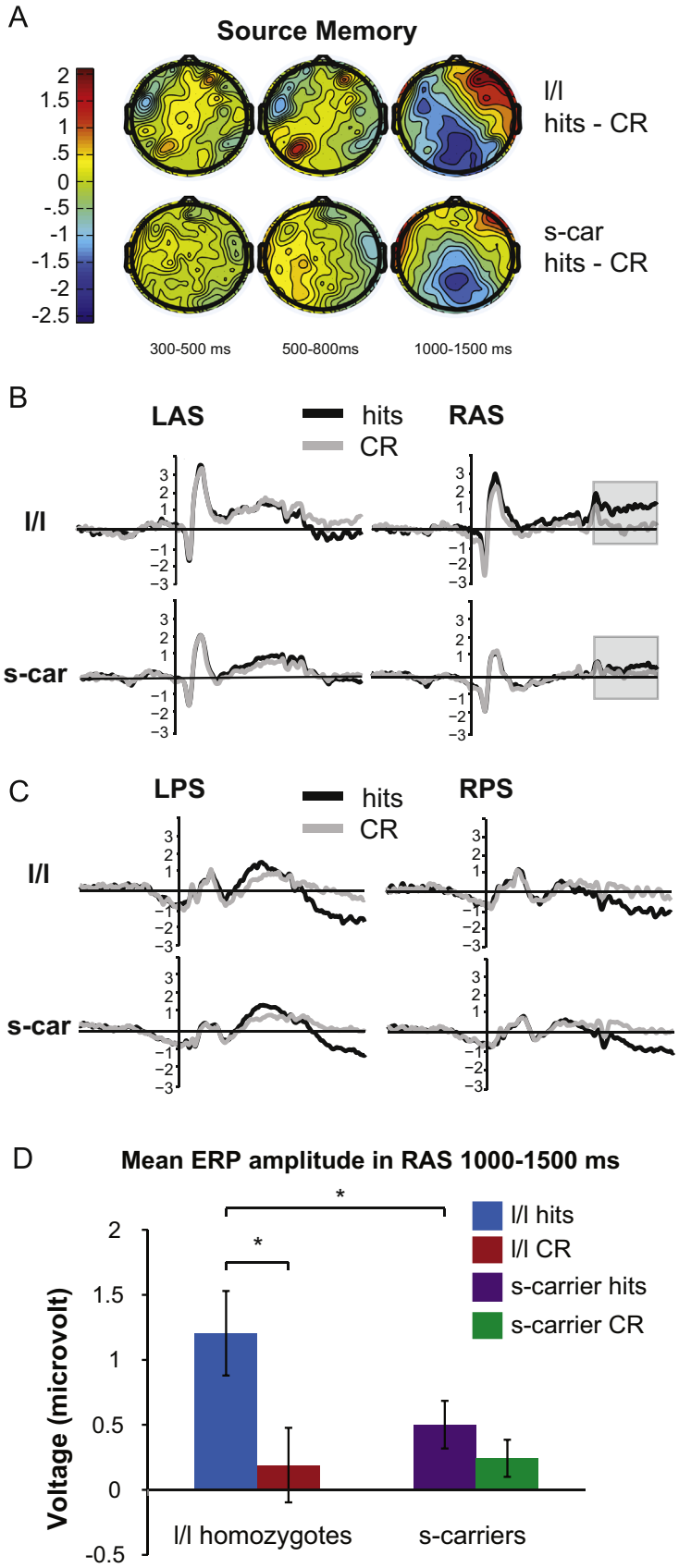

Fig. 4. Source memory task ERP results. (A). Topographical maps representing the distribution of ERP differences between hits and CRs (hits minus correct rejections) for l/l homozygotes (top) and s-carriers (s-car, bottom) across the 300–500 ms (left), 500–800 ms (middle), and 1000–1500 ms (right) time frames. (B). Averaged group ERPs in anterior ROIs. Averaged ERP waveforms from −800 to 1500 ms post-stimulus presentation (*y* axis crosses at 0 ms) in the left anterior superior (LAS, left panels) and right anterior superior (RAS, right panels) ROIs for hits in black and CRs in grey during the source memory task. L/L homozygote ERPs are represented in the top two panels and s-carriers in the bottom two panels. The grey boxes highlight the 1000–1500 ms timeframe in RAS where l/l homozygotes and s-carriers showed significant differences in the old/new effect. (C). Averaged group ERPs in posterior ROIs. Averaged ERP waveforms from −800 to 1500 ms post-stimulus presentation (*y* axis crosses at 0 ms) in the left posterior superior (LPS, left panels) ROI and right posterior superior (RPS, right panels) for hits in black and CRs in grey during the source memory task. (D). Bar graphs illustrating ERP amplitude differences in RAS 1000–1500 ms post-stimulus presentation during source memory. Average ERP amplitudes for l/l homozygotes (l/l hits, blue) and s-carriers (s-carrier hits, purple) during source memory hits. Correct rejections are represented in red for l/l homozygotes (l/l CR) and in green for s-carriers (s-carrier CR). The difference between hits and CRs in l/l homozygotes is significantly different than the difference between hits and CR in s-carriers. * represents significance at $p \leq 0.05$. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).

source memory task, d_a and c_a were calculated using all hits (all stimuli correctly identified as old).

2.8. EEG analysis

EEG data during both the item and source memory task were analyzed in the four ROIs (LAS, RAS, LPS, and RPS) at three time points post-stimulus presentation, 300–500 ms, 500–800 ms, and 1000–1500 ms. Hit and CR mean ERP amplitudes were averaged across the seven electrodes in an ROI at all three time points of interest. Using SPSS 22.0 (IBM Corp., Armonk, NY), four repeated measures ANOVAs were conducted to investigate differences between hit and CR mean amplitudes within the ROIs due to the 5HTTLPR polymorphism of the SLC6A4 gene. In the 300–500 ms time frame, a $2 \times 2 \times 2$ repeated measures ANOVA was conducted with hemisphere (LAS and RAS), condition (hit and CR) and genetic group (s-car and l/l) as factors. Two separate 2×2 repeated measures ANOVAs with condition and group as factors were run for the LPS ROI at 500–800 ms post-stimulus and in RAS 1000–1500 ms. In addition, the LPN was examined using a $2 \times 2 \times 2$ repeated measures ANOVA with hemisphere (LPS and RPS), condition (hit and CR) and genetic group as factors.

3. Results

3.1. Behavioral results

The 2 (condition) × 2 (genetic group) repeated measures ANOVA comparing source hits to CR accuracy revealed a main effect of condition ($F(1,58)=10.60$, $p<0.01$). The proportion of source hits was significantly lower than correct rejections, though there was no main effect of genetic group ($F(1,58)=0.03$, $p>0.05$) and no condition by genetic group interaction ($F(1,58)=1.43$, $p>0.05$). The 2×2 ANOVA examining reaction time in the source memory task revealed a main effect of condition ($F(1,58)=52.20$, $p<0.001$). Average reaction time during source hits was significantly slower than during correct rejections. There was also a trend towards a condition × genetic group interaction ($F(1, 58)=3.07$, $p=0.085$) though the main effect of genetic group was not significant ($F(1,58)=2.60$, $p=0.11$; and Fig. 3). A 2×2 ANOVA was run to examine whether the proportion of source misattributions (correctly saying old but indicating the wrong source) and misses (incorrectly saying new to an old stimulus) differed. There were more source misattributions (0.34 ± 0.01) than misses (0.23 ± 0.02). However, the number of source misattributions and misses did not differ based on 5HTTLPR polymorphism. We also examined whether there was a response bias in the source memory task by examining whether the proportion of false alarms attributed to the place and pleasantness task differed by 5HTTLPR group. There was a response bias in the source test as revealed by a main effect of task ($F(1,58)=11.51$, $p<0.01$), where the proportion of false alarms attributed to the pleasantness task (0.17 ± 0.015) was greater than the place task (0.11 ± 0.013). However, there was no main effect of group or a task by group interaction, indicating that the response bias in false alarms is not related to 5HTTLPR polymorphism. To ensure that there were no differences in performance between l/l homozygotes and s-carriers, we also examined whether d_a and response bias (ca) differed between groups. There were no significant differences in d_a score or response bias (ca) scores between l/l homozygotes and s-carriers during item memory or source memory (Fig. 3(C)). Responder sensitivity and response bias during source memory in Fig. 3 was calculated using all hits in the source memory task (all stimuli correctly identified as old with and without correct source retrieval).

A 2 (condition) × 2 (genetic group) repeated measures ANOVA evaluating reaction time during the item memory task revealed a main effect of condition ($F(1,58)=44.50$, $p<0.05$). Average reaction time during hits was significantly faster than correct rejections. There was no main effect of genetic group and no significant condition × genetic polymorphism interactions for reaction times in the item memory task. The ANOVA examining accuracy in the item memory task revealed no significant main effects or interaction.

3.2. Source memory ERP results

3.2.1. FN400 during source memory

The 2 (hemisphere) × 2 (condition) × 2 (genetic polymorphism) repeated measures ANOVA conducted for the LAS and RAS ROIs at 300–500 ms post-stimulus during hits (source and item) in the source memory task revealed a significant main effect of condition ($F(1,58)=8.90$, $p \leq 0.01$; Fig. 4(A and B)), where hit amplitude (0.20 ± 0.242 μV) was larger than CR amplitude (-0.01 ± 0.248 μV). Additionally, there was a significant main effect of hemisphere ($F(1,58)=8.84$, $p \leq 0.01$), with the left hemisphere showing higher mean amplitude than the right hemisphere (left$=0.38 \pm 0.25$ μV; right$=-0.20 \pm 0.27$ μV). Importantly, there was no significant main effect of group (($F1,58)=1.36$, $p>0.05$), condition by group ($F(1,58)=0.97$, $p>0.05$), hemisphere by group ($F(1,58)=0.19$, $p>0.05$), condition by hemisphere ($F(1,58)=0.40$, $p>0.05$), or condition × hemisphere × group interaction ($F(1,58)=1.89$, $p>0.05$). These results show that there was an old/new effect in the LAS ROI 300–500 ms post-stimulus presentation during source memory, which was not affected by 5HTTLPR genetic polymorphism.

3.2.2. Parietal old/new effect during source memory

The 2 (condition) × 2 (genetic group) ANOVA examining the effect of 5HTTLPR polymorphisms on ERP amplitudes in LPS 500–800 ms post-stimulus presentation revealed a main effect of condition ($F(1,58)=10.91$, $p<0.01$). The main effect of group was not significant ($F(1,58)=0.00$, $p>0.05$) and the condition × group interaction was not significant ($F(1,58)=0.06$, $p>0.05$). These results show that there was an old/new effect in LPS 500–800 ms post-stimulus presentation during source memory, which was not influenced by 5HTTLPR polymorphism (Fig. 4(A and C)).

3.2.3. LPN during source memory

The LPN during source memory was examined with a 2 (hemisphere) × 2 (condition) × 2 (group) repeated measures ANOVA conducted in the LPS and RPS ROIs 1000–1500 ms post-stimulus presentation. The ANOVA revealed a significant main effect of condition ($F(1,58)=27.13$, $p<0.001$) with hits (-0.91 ± 0.19 μV) having a significantly larger negative deflection in the EEG signal than CRs (0.10 ± 0.14 μV) confirming the presence of an LPN. However, there was no main effect of group ($F(1,58)=1.17$, $p>0.05$) and no significant group interactions (condition × group $F=0.14$; hemisphere × group $F=1.35$; condition × hemisphere × group $F=0.55$, all p's >0.05, Fig. 4(A and C)) suggesting the LPN during source memory was not influenced by 5HTTLPR polymorphism.

3.2.4. Late frontal old/new effect during source memory

The 2 (condition) × 2 (group) analysis of mean ERP amplitude in the right anterior superior frontal ROI (RAS) 1000–1500 ms post-stimulus presentation revealed a main effect of condition ($F(1,58)=18.96$, $p<0.01$) as well as a main effect of genetic group ($F(1,58)=6.68$, $p=0.01$; Fig. 4(A and B)). Critically, a significant condition by genetic group interaction was found ($F(1,58)=6.68$, $p \leq 0.05$). A paired sample t-test comparing mean ERP amplitudes during hit and CR trials within l/l homozygous participants revealed significantly higher ERP amplitude for hit trials ($t(16)=$

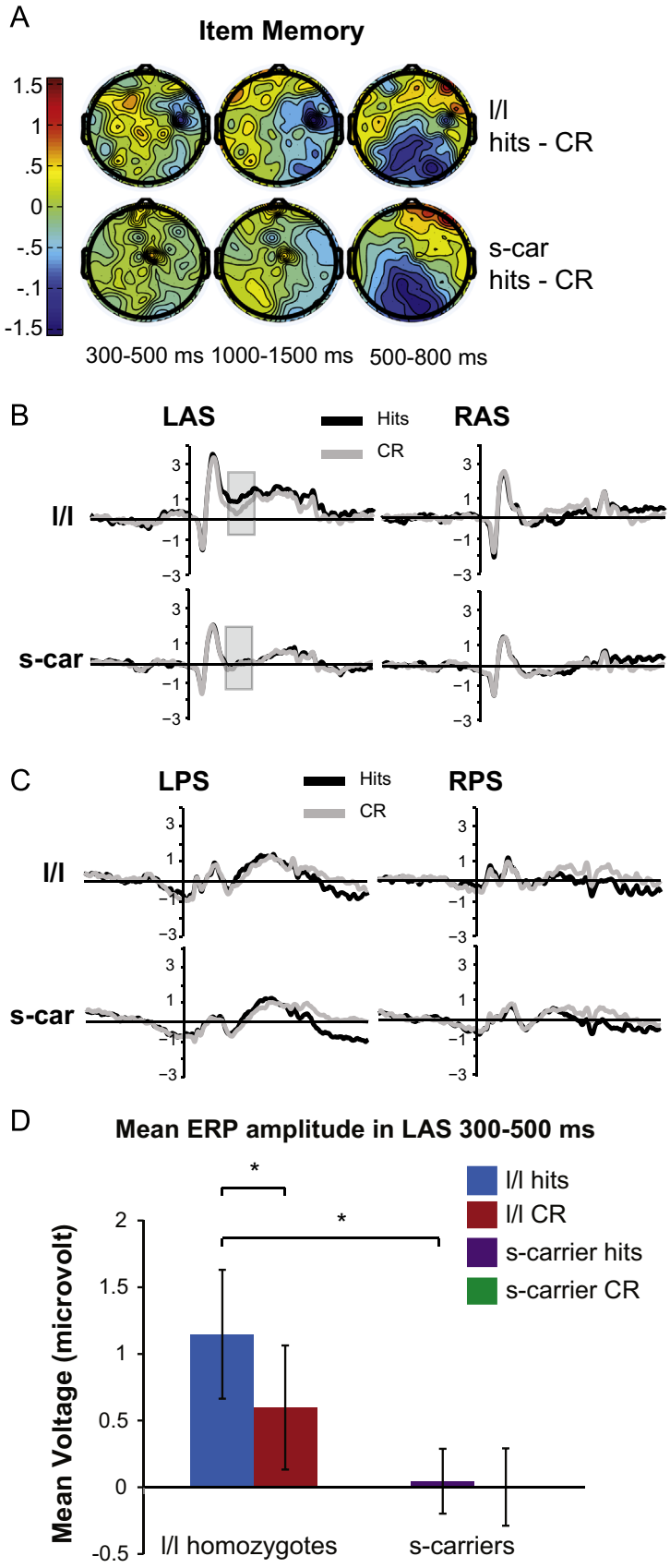

Fig. 5. Item memory task ERP results. (A). Topographical maps representing the distribution of ERP differences between hits and CRs (hits minus correct rejections) for l/l homozygotes (top) and s-carriers (s-car, bottom) across the 300–500 ms (left), 500–800 ms (middle), and 1000–1500 ms (right) time frames of interest. (B). Averaged group ERPs in anterior ROIs. Averaged ERP waveforms from −800 to 1500 ms post-stimulus presentation (*y* axis crosses at 0 ms) in the left anterior superior (LAS, left panels) and right anterior superior (RAS, right panels) ROIs for hits in black and CRs in grey during the item memory task. L/L homozygote ERPs are represented in the top two panels and s-carriers in the bottom two panels. The grey boxes highlight the 300–500 ms timeframe in LAS where l/l homozygotes and s-carriers showed significant differences in the old/new effect. (C). Averaged ERPs in posterior ROIs. Averaged ERP waveforms from −800 to 1500 ms post-stimulus presentation (*y* axis crosses at 0 ms) in the left posterior superior (LPS, left panels) ROI and right posterior superior (RPS, right panels) for hits in black and CRs in grey during the item memory task. D. Bar graphs illustrating ERP amplitude differences in LAS 300–500 ms post-stimulus presentation during item memory. Average ERP amplitudes for l/l homozygotes (l/l hits, blue) and s-carriers (s-carrier hits, purple) during item memory hits. Correct rejections are represented in red for l/l homozygotes (l/l CR) and in green for s-carriers (s-carrier CR). The difference between hits and CRs in l/l homozygotes is significant differently than the difference between hits and CR in s-carriers. * Represents significance at $p \leq 0.05$. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).

4.73, $p \leq 0.05$; hit ERP mean ± SEM = 1.20 ± 0.32 μV) compared to CR trials (0.19 ± 0.28 μV). In contrast, s-carriers did not display the old/new effect as there were no significant differences between mean ERP amplitudes during hit (0.50 ± 0.18 μV) trials compared to CR trials (0.24 ± 0.14 μV; $t(42) = 1.59$, $p \geq 0.05$; Fig. 4(D)). Independent samples *t*-tests indicated that there was no difference in CR mean amplitude between l/l homozygotes (0.19 ± 0.28 μV) and s-carriers (0.24 ± 0.14 μV; $t(58) = 0.18$, $p \geq 0.05$;) Fig. 4(D). In contrast, mean amplitudes during hits was significantly different between genetic groups ($t(58) = 1.98$, $p = 0.05$; s-carrier mean ± SEM = 0.50 ± 0.18 μV; l/l homozygous mean ± SEM = 1.20 ± 0.32 μV). Taken together, these ERP results indicate that the condition by genetic group interaction present in RAS at 1000–1500 ms post-stimulus may be driven by a decrease in mean hit amplitude in s-carriers. The decrease in mean amplitudes during hits suggests that participants possessing the s-allele of the serotonin transporter gene show a significantly attenuated late frontal old/new effect. The finding that 5HTTLPR only affected ERP amplitude during source memory 1000–1500 ms post-stimulus presentation in the RAS ROI and not in any other ROI or time point suggests the affect of the 5HTTLPR polymorphism on source memory is specific to the RAS ROI at 1000–1500 ms post-stimulus presentation.

3.3. Item memory ERP results

3.3.1. FN400 during item memory

The 2 (hemisphere) × 2 (condition) × 2 (genetic group) ANOVA examining ERP amplitude differences in the left and right anterior superior frontal ROIs (LAS and RAS) 300–500 ms post stimulus presentation during item memory revealed a significant condition × hemisphere × genetic group interaction ($F(1,58) = 8.26$, $p \leq 0.01$) as well as a condition × hemisphere interaction ($F(1,58) = 7.95$, $p \leq 0.01$) and a significant main effect of hemisphere ($F(1,58) = 14.98$, $p \leq 0.001$); Fig. 5(A and B). Collapsed across conditions and groups, LAS showed significantly higher ERP amplitudes compared to RAS (left hemisphere mean ± SEM = 0.45 ± 0.25 μV; right hemisphere = −0.23 ± 0.28 μV). Paired sample *t*-tests comparing mean ERP amplitudes during hit and CR trials revealed a significant difference in LAS of l/l homozygous participants ($t(16) = 2.62$; $p \leq 0.05$). Mean ERP amplitude for hit trials (1.14 ± 0.48 μV) was significantly higher than CR trials (0.59 ± 0.46 μV) revealing the presence of the old/new effect in l/l homozygous participants. S-carriers showed no significant difference between hit and CR amplitudes in LAS (hit trials = 0.05 ± 0.24 μV; CR trials = 0.00 ± 0.29 μV; $t(42) = 0.30$, $p \geq 0.05$; Fig. 5(D)). No significant difference between hit and CR amplitudes was seen in either group in RAS. These results suggest the s-carriers do not show the early frontal old/new effect during item memory in the LAS region of interest. Independent sample *t*-tests comparing mean hit amplitudes during item memory in the LAS ROI 300–500 ms post -stimulus presentation between l/l homozygotes and s-carriers revealed a significant difference ($t(58) = 2.25$, $p \leq 0.05$). S-carriers (0.05 ± 0.24 μV) showed decreased mean ERP amplitudes during hit trials compared to l/l homozygous participants (1.14 ± 0.48 μV). No significant difference was found in CR mean amplitude between l/l homozygotes (0.59 ± 0.46 μV) and s-carriers (0.00 ± 0.29 μV; $t(58) = 1.09$, $p \geq 0.05$, Fig. 5(D)) in the LAS ROI 300–500 ms during item memory. These ERP results indicate that the lack of an early frontal old/new effect in LAS 300–500 ms post stimulus presentation in s-carriers is related to a decrease in mean hit amplitudes during item memory.

3.3.2. Left parietal old/new effect during item memory

The 2 (condition) × 2 (genetic group) ANOVA conducted in the LPS ROI in the 500–800 ms period examining hit and CR mean amplitudes and the influence of 5HTTLPR polymorphism during item memory did not show a main effect of condition ($F(1,58) = 2.39$, $p > 0.05$), main effect of genetic group ($F(1,58) = 0.27$, $p > 0.05$), or a condition by group interaction ($F(1,58) = 0.02$, $p > 0.05$; Fig. 5(A and C)).

3.3.3. LPN during item memory

The 2 (condition) × 2 (hemisphere) × 2 (group) repeated measures ANOVA used to examine the LPN in the LPS and RPS ROIs 1000–1500 ms post-stimulus presentation during item memory did not reveal any group related effects. There was a main effect of condition ($F(1,58) = 20.68$, $p < 0.001$) with hits (−0.51 ± 0.14 μV) showing a larger negative deflection in the EEG signal than CRs (0.18 ± 0.12 μV). The main effect of condition suggests there was an LPN effect during our item memory task, though the size of the LPN was not significantly affected by 5HTTLPR polymorphism (main effect of group $F = 0.13$; condition x group $F = 0.40$; hemisphere × group $F = 0.01$; condition × hemisphere × group $F = 1.62$, all *p*'s > 0.05; Fig. 5(A and C)).

3.3.4. Late frontal effect during item memory

The 2 (condition) × 2 (genetic group) ANOVA in RAS at 1000–1500 ms during item memory revealed a significant main effect of condition ($F(1,58) = 6.43$, $p \leq 0.05$), where hit amplitudes were larger than correct rejections (Hits: 0.47 ± 0.16 μV; CR: 0.07 ± 0.14 μV; Fig. 5(A and B)). However, no main effect of group ($F(1,58) = 0.43$, $p > 0.05$) and no group by condition interaction was found ($F(1,58) = 0.03$, $p > 0.05$) suggesting the old/new effect in RAS 1000–1500 ms post-stimulus presentation is not influenced by 5HTTLPR polymorphism. In combination with the finding that 5HTTLPR polymorphism did not influence item memory ERP amplitudes in LPS 500–800 ms or 1000–1500 ms post-stimulus presentation, these results suggest the mean ERP amplitude differences between s-carriers and l/l homozygotes during item memory were specific to the left anterior superior ROI 300–500 ms post-stimulus presentation.

3.4. Direct comparison of item and source memory ERP amplitude

We ran 2 × 2 × 2 ANOVAs with task (item and source memory), condition (hits and CR), and group (s-carriers and l/l homozygotes) in the LAS ROI 300–500 ms post-stimulus and in the RAS ROI 1000–1500 ms post-stimulus. These analyses were done to determine the specificity of the 5HTTLPR group differences for item and source memory. The ANOVA in the LAS ROI 300–500 ms revealed a main effect of task ($F(1,58) = 7.57$, $p < 0.01$) with amplitudes during item memory greater than source memory. The task × condition × group interaction was only marginally significant ($F(1,58) = 3.363$, $p = 0.07$) with no other main effects or interactions reaching significance. The task × condition × group interaction suggests the difference between hit and CR amplitudes in LAS 300–500 ms post-stimulus in s-carriers and l/l homozygotes during item memory is marginally different than during source memory. The RAS ROI 1000–1500 ms post-stimulus ANOVA revealed a significant main effect of task ($F(1,58) = 4.57$, $p < 0.05$) with source memory amplitudes greater than item memory amplitudes. There was also a significant main effect of condition ($F(1,58) = 28.37$, $p < 0.001$) where hit amplitudes were larger than CR amplitudes. The condition × group ($F(1,58) = 3.27$, $p = 0.076$) and task × condition × group ($F(1,58) = 3.033$, $p = 0.087$) interactions were marginally significant. As with item memory, the interactions suggest the difference between hit and CR amplitudes between s-carriers and l/l homozygotes in RAS 1000–1500 ms post-stimulus presentation during source memory are marginally different than during item memory.

3.5. COMT analysis

After conducting the analyses using the 5HTTLPR polymorphism, we ran the same ERP analyses using genetic polymorphisms in COMT (catechol-O-methyltransferase gene) as a group variable. These post-hoc analyses were done to determine the specificity of the 5HTTLPR results. We compared those homozygous for the Met allele (Met/Met, $n=12$) to those with a Val allele (Val-carriers, Val/Val and Val/Met, $n=41$). For each of the ERP components examined (FN400, left parietal old/new effect, LPN, and late frontal old/new effect), there were no significant main effects of group, significant group interactions, or significant trends for item or source memory (all p-values > 0.1). These results suggest the significant differences seen in the 5HTTLPR genetic analyses are not related to COMT genotype.

4. Discussion

The present study investigated how genetic polymorphisms in the 5HTTLPR promoter region of the serotonin transporter gene (SCL6A4) influence recognition memory using EEG. Our results show that participants possessing an s-allele (s-carriers) in the 5HTTLPR region of the serotonin transporter gene exhibit significantly decreased mean hit amplitude in right anterior scalp locations 1000–1500 ms post stimulus during source memory as well as decreased mean hit amplitude in left anterior scalp locations 300–500 ms post stimulus during item memory. Source memory tasks ask participants to target a specific contextual detail previously associated with an object for retrieval. The targeted retrieval of a specific detail may involve cognitive control mechanisms, which are strongly linked to prefrontal cortical function (Miller and Cohen, 2001; Miller and D'Esposito, 2005; Braver et al., 2009; Barredo et al., 2013) and the late frontal old/new effect (Wilding and Rugg, 1996; Rugg and Wilding, 2000; Ally and Budson, 2007; Hayama and Rugg, 2009). In contrast, item memory tasks ask participants to remember seeing a previously viewed item and do not require contextual detail retrieval. In combination with these prior results, our results suggest that s-carriers of the serotonin transporter gene show ERP differences during item memory in memory related ERP components and in ERP components related to cognitive control during source memory.

4.1. 5HTTLPR polymorphism and source memory

Serotonin may contribute to source memory by modulating cognitive control. In source memory tasks, participants are asked to retrieve a specific contextual detail associated with a previously presented item. In order to successfully retrieve the intended target, cognitive control mechanisms may be recruited to retrieve the specific detail needed from among the many details previously associated with the item. ERP studies of recognition memory have revealed the presence of a predominantly right sided, late frontal old/new effect, which has been related to post-retrieval processing (Wilding and Rugg, 1996; Donaldson and Rugg, 1998; Ranganath and Paller, 2000; Rugg and Wilding, 2000; Werkle-Bergner et al., 2005; Ally and Budson, 2007). Post-retrieval processing involves a cognitive control mechanism where information accessed from memory is monitored and/or evaluated for use in the task at hand (Hayama et al., 2008; Hayama and Rugg, 2009). In a study in rats, increasing 5HT1A serotonin receptor or increasing 5HT2A receptor activity leads to an inability to remember the context an item previously appeared in while leaving memory for the item itself intact (Bekinschtein et al., 2013). Serotonin receptor 5-HT1A acts in an inhibitory manner and is present in pyramidal prefrontal neurons (Pazos and Palacios, 1985), with estimates at roughly 60% (Puig and Gulledge, 2011). When serotonin is acting on both receptors, the end result favors neuronal inhibition (Puig and Gulledge, 2011). Though the functional consequence of genetic variation of the 5HTTLPR promoter region of SLC6A4 is unclear, there is evidence that being an s-carrier results in increased synaptic serotonin. S-carriers exhibit both diminished serotonin transporter expression and function compared to l/l homozygotes (Heils et al., 1996; Lesch et al., 1996; Greenberg et al., 1999; Bennett et al., 2002; Caspi et al., 2003; Hu et al., 2006; Willeit and Praschak-Rieder, 2010). Decreased serotonin transporter function may result in increased synaptic serotonin. Perhaps the 5HTTLPR polymorphism results in s-carriers having more synaptic serotonin, which could activate 5HT1A receptors causing increased inhibition resulting in an inability to select which context an item was previously presented. Direct manipulation of serotonin transporter function with the selective serotonin reuptake inhibitor (SSRI) citalopram increases reaction time and the number of errors in a probabilistic learning task where executive function is critical to task performance (Chamberlain et al., 2006). Blocking serotonin transporter function in healthy young adults would result in increased synaptic serotonin levels, similar to what may be occurring in s-carriers, lending support to our hypothesis that s-carriers may have increased difficulty with cognitive control.

The serotonergic system has been linked to cognitive control via other genetic and pharmacological manipulation studies. In the probabilistic reversal-learning paradigm, participants must flexibly change their response after reward contingencies are switched. S-carriers are less likely to switch their response after receiving negative feedback, suggesting that s-carriers have decreased cognitive flexibility (den Ouden et al., 2013). Additionally, in a decision -making task where prefrontal cortical control is needed to overcome choice bias, s-carriers are more susceptible to bias and show decreased prefrontal cortical function measured with fMRI (Roiser et al., 2009). Finally, s-carriers have a decreased ability to monitor and update information in working memory (Weiss et al., 2014). Together, these studies suggest that genetic variation of the serotonin transporter gene is related to changes in executive function and support our hypothesis that the decreased mean ERP amplitude during hit trials in s-carriers in the right anterior superior ROI 1000–1500 ms post-stimulus presentation during source memory is related to cognitive control.

Behaviorally, s-carriers showed a slight tendency to take less time during the source memory task than l/l homozygotes. However, there were no significant accuracy differences in source memory performance between s-carriers and l/l homozygotes. Several factors may explain how s-carriers performed just as well as l/l homozygotes during source memory. The first is that the left parietal old/new effect was still present in s-carriers. The parietal old/new effect is believed to reflect recollection (Wilding and Rugg, 1996; Rugg et al., 1998; Donaldson and Rugg, 1998; 1999; Curran, 2000; Curran and Hancock, 2007; Rugg and Curran, 2007; Eichenbaum et al., 2007). As such, s-carriers may have had access to the necessary information to complete the task. Secondly, the late posterior negativity was also still present in s-carriers. The late posterior negativity is thought to reflect the continued evaluation of relevant item-context associations (Johansson and Mecklinger, 2003; Herron and Wilding, 2005; Evans et al., 2010; Rosburg et al., 2011) and is seen when source memory judgments are difficult (Leynes and Kakadia, 2013). Specifically, Leynes and Kakadia (2013) compared reality monitoring, where an external source is compared to an internally generated source, to internal source monitoring, where two internally generated sources are compared. They show that difficult internal source monitoring is related to the late posterior negativity and does not result in a frontal old/new effect (Leynes and Kakadia, 2013). In contrast, reality source monitoring revealed both the frontal old/new effect and the late

posterior negativity (Leynes and Kakadia, 2013). These results mirror our results in s-carriers and l/l homozygotes where s-carriers, who have been shown to have difficulty with cognitive control (Roiser et al. 2009; den Ouden et al., 2013), show the same pattern as the difficult internal source monitoring judgment and l/l homozygotes mirroring the easier reality monitoring results. Leynes and Kakadia (2013) interpret their results by suggesting that the reality monitoring condition only required a more general monitoring process due to the relative ease of the source judgment while the more difficult internal source judgment needed more extensive and specific monitoring. Therefore, it may be that the pattern of ERPs seen in s-carriers suggests the source task required more extensive evaluation in order to accomplish the task.

4.2. 5HTTLPR polymorphism and item memory

Polymorphisms of the serotonin transporter gene may also affect the ability to recognize a previously encountered item without retrieval of associated contextual details. S-carriers showed decreased mean hit amplitude 300–500 ms post-stimulus presentation in the left anterior superior ROI during item memory. Some ERP studies of recognition memory suggest the early frontal old/new effect is associated with familiarity (Rugg et al., 1998; Curran, 2000; Friedman and Johnson, 2000; Rugg and Curran, 2007; Curran and Hancock, 2007; Eichenbaum et al., 2007). Other studies suggest the early frontal old/new effect is related to implicit memory, specifically conceptual priming (Voss et al., 2010, 2012). Both interpretations suggest the FN400 ERP is related to some form of memory process. Our results show that the mean hit amplitude in s-carriers is the same as the mean correct rejection amplitude, effectively eliminating the early frontal old/new effect during item memory. The elimination of the early frontal old/new effect suggests that polymorphisms of the serotonin transporter gene may modulate the retrieval process during item memory.

As was the case in the source memory task, there were no behavioral differences between s-carriers and l/l homozygotes during item memory. As such, the lack of an old/new effect in the LAS ROI 300–500 ms post-stimulus presentation during item memory suggests s-carriers used other processing to successfully perform the task. We ran a post-hoc analysis using paired sample *t*-tests to directly compare mean hit amplitudes to CR amplitude in the late frontal ERP component in s-carriers and l/l homozygotes. We ran this post-hoc analysis because the late frontal old/new effect is usually only seen in item memory tasks when there is ambiguity or uncertainty involved (Rugg et al., 2000; Ullsperger et al., 2000; Henson et al., 2000; Woodruff et al., 2006) and our ANOVA suggested the late frontal effect was present during item memory. The results of the paired sample *t*-tests show that s-carriers show the late frontal old/new effect in RAS 1000–1500 ms post-stimulus whereas l/l homozygotes do not. S-carriers may not show the FN400 during the item memory task as the memory process supported by the FN400 (familiarity or conceptual priming) may not be sufficient to achieve accurate performance, suggesting s-carriers may use a different retrieval strategy than l/l homozygotes during item memory. Though speculative, it may be that during both item memory and source memory, s-carriers need more extensive evaluation of the information in order to successfully complete the tasks.

4.3. Limitations

Though our results show 5HTTLPR polymorphism dependent changes in ERP components underlying item and source memory during the test portion of the study, we cannot rule out the possibility that different strategies during encoding may have influenced the test phase results. It is possible that l/l homozygotes and s-carriers used a different strategy to encode the adjectives, which lead to the differences seen in the ERP components. Another limitation is that we only examined the 5HTTLPR polymorphism and not other genetic variations, which may have contributed to the results. Though our follow -up analyses of the COMT polymorphism suggests our results may be specific to the 5HTTLPR polymorphism, we cannot rule out the possibility that other genetic variations may have contributed to our results. There were also only 17 l/l homozygotes in the study compared to 43 s-carriers. Our interpretation of the item memory differences in s-carriers partly relies on the lack of a late frontal old/new effect in l/l homozygotes. With 17 participants, the lack of a difference may be related to power issues. However, we are confident in our findings that the left anterior superior ROI 300–500 ms post-stimulus during item memory and in the right anterior superior ROI 1000–1500 ms post-stimulus during source memory are influenced by 5HTTLPR polymorphism. Those two results rely on not finding a difference between hits and CRs in 43 participants. Finally, the direct comparisons of the differences between hit and CR amplitudes between s-carriers and l/l homozygotes in LAS 300–500 and RAS 1000–1500 ms during item and source memory were only marginally significant. One possibility is that the item memory task may include source memory for some of the items. The participants were given the same encoding instructions for the item and source memory task meaning source information was encoded during the item memory task. Though the participants were only asked to retrieve the item during the item memory task, for some items they may have accessed the source information which may explain why the differences between hit and CR amplitudes in s-carriers and l/l homozygotes during the item memory and source memory task are only marginally different.

5. Conclusion

Previous literature has elucidated various spatial and temporal factors associated with processes of recognition memory. Our study adds to our understanding of recognition memory by describing the effect genetic variation in the serotonin transporter gene (SLC6A4) has on both behavioral and electrophysiological correlates of item and source memory in young adults. Our results show that s-carriers of the 5HTTLPR promoter region of the SLC6A4 gene have decreased mean hit amplitude in right anterior scalp locations during source memory 1000–1500 ms post stimulus presentation and left anterior scalp locations during item memory 300–500 ms post stimulus presentation. These results show that the ERP correlates of item memory and source memory are different in s-carriers and l/l homozygotes with l/l homozygotes demonstrating the typical ERP patterns. The pattern of results suggests s-carriers may use more specific monitoring during both item memory and source memory in order to successfully perform the tasks at the same level as l/l homozygotes.

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