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Impact of the Serotonin Transporter Polymorphism on Emotion Identification in Healthy Older Adults

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Abstract

Older adults exhibit reduced accuracy and efficiency for identifying facial emotion expressions yet it is unclear how genetic or cognitive variables influence these findings. This study examined the impact of serotonin transporter polymorphism 5-HTTLPR on patterns of explicit emotion identification accuracy and reaction time (RT) in healthy older adults. The impact of 5-HTTLPR on measures of processing speed, attention, and executive function as well as correlations between cognitive measures and emotion identification measures were also examined.

Methods: Forty-one individuals over the age of 50 were genotyped for bi-allelic and tri-allelic variants of 5-HTTLPR and administered an emotion recognition paradigm and tests of cognitive function.

Results: Results indicated that individuals carrying low expressing S alleles were significantly slower when identifying expressions of emotion, particularly fear and disgust. A similar pattern of results for fear and disgust was revealed for low expressing S and L_G carriers, but these findings were not held after adjustment for multiple comparisons. RTs for happy and neutral faces were correlated with performance on measures of processing speed, attention, and executive function in low expression groups, but these findings were not held after adjustment for multiple comparisons.

Conclusions: Overall, this study suggests that possession of low-expressing genetic variants of 5-HTTLPR is associated with diminished emotion identification RT performance among healthy older adults.

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Introduction

The serotonergic system plays a crucial role in the regulation of emotional processes (Canli & Lesch, 2007). The serotonin transporter regulates the reuptake of serotonin in brain regions involved in the regulation of emotional information (Hariri & Holmes, 2006). The efficiency of this reuptake is influenced by the bi-allelic 5-HTTLPR polymorphism in the promoter region of serotonin transporter gene (SLC6A4) that results in a short (S) allele and a long (L) allele variant. The S allele is associated with an approximately 50% decrease in serotonin transporter availability compared to the L allele (Lesch et al., 1996). An additional A/G single nucleotide polymorphism (SNP, rs25531) further modifies serotonin transporter expression, primarily on the L allele, such that the L_G has a similar reduction in expression to the S allele (Wendland, Martin, Kruse, Lesch, & Murphy, 2006).

Carriers of low-expressing alleles are more sensitive to manipulations of serotonin levels as indicated by studies using acute tryptophan depletion to reduce brain synthesis of serotonin (Marsh et al., 2006; Neumeister et al., 2002; Roiser et al., 2006; Walderhaug, Herman, Magnusson, Morgan, & Landrø, 2010). Presence of at least one S allele has been shown to moderate relationships between environmental stressors and depression (Caspi et al., 2003; Caspi, Hariri, Holmes, Uher, & Moffitt, 2010; Karg, Burmeister, Shedden, & Sen, 2011; Uher & McGuffin, 2010), and to modulate affective behaviors and traits that increase the risk of psychological disorders such as anxiety and depression (Munafo, Clark, Roberts, & Johnstone, 2006; Pezewas et al., 2005; Williams, Gatt, Schofield, Olivieri, Peduto & Gordon, 2009). Additionally, 5-HTTLPR has been

associated with alterations in the detection and recognition of facial expressions of emotion (Antypa, Cerit, Kruijt, Verhoeven, & Van der Does, 2011; Koizumi et al., 2013; Marsh et al., 2006).

The ability to recognize facial expressions of emotion in others is an important skill for communication and social functioning. Disruptions in the ability to recognize emotions in faces are present in many conditions, including major depression (Gur et al., 1992), schizophrenia (Williams et al., 2008), Huntington's disease (Sprengelmeyer et al., 1996), Human Immunodeficiency Virus (Lane, Moore, Batchelor, Brew, & Cysique, 2012), Alzheimer's disease (Hargrave, Maddock, & Stone, 2002; Spoletini et al., 2008), Mild Cognitive Impairment (Spoletini et al., 2008; Varjassyova et al., 2013), and fronto-temporal dementia (Keane, Calder, Hodges, & Young, 2002). Difficulties accurately recognizing facial emotions are also common in healthy older adults compared to younger adults (Calder et al., 2003; Isaacowitz et al., 2007; Lambrect, Kreifelts, & Wildgruber, 2012; Ruffman, Henry, Livingstone, & Phillips, 2008; Sullivan & Ruffman 2004; Suzuki & Akiyama, 2013; Williams, Mathersul, et al., 2009).

This age-related disruption in the ability to accurately recognize facial expressions of emotion has the potential to impact older adults' ability to effectively communicate in everyday social situations. The precise mechanisms driving emotion recognition impairments in older adults are not fully understood. Moreover, little is known about genetic contributions to emotion recognition performance. This study examined emotion identification accuracy and reaction time (RT) in older adults with and without low expressing 5-HTTLPR alleles. Cognitive measures of processing speed, attention, and

executive function were also included to examine their relationship to emotion identification performance.

Emotion Recognition in Older Adults.

Basic facial expressions of emotion are thought to be universally recognized and include expressions of fear, sadness, anger, disgust, happiness, and surprise (Ekman, 1993; Elfenbein & Ambady, 2002). The ability to recognize these expressions as well as neutral expressions can be tested as a marker of social cognitive functioning. Previous studies examining age-related differences in emotion recognition have reported that older adults are less accurate when recognizing basic facial expressions of emotion (Borod et al., 2004; Calder et al., 2003; Isaacowitz et al., 2007; Keightley, Winocur, Burianova, Hongwaanishkul, & Grady, 2006; MacPherson Phillips, & Della Sala, 2002; Malatesta et al., 1987; McDowell et al., 1994; Ruffman, et al., 2009; Sullivan & Ruffman, 2004; Suzuki, Hoshino, Shigemasu, & Kawamura, 2007). For example, Williams et al. (2009) investigated the ability to recognize emotion in facial expressions across the lifespan in 1000 individuals between the ages of 6 and 91. They demonstrated that young and middle-aged adults had better accuracy compared to children and older adults, with larger effect sizes for anger and fear expressions. However, studies have also shown preservation or improvement with age in certain emotional expressions such as surprise (Borod et al., 2004; Calder et al., 2003; MacPherson et al., 2002; Sullivan & Ruffman, 2004), disgust (Calder et al., 2003; Horning, Cornwell, & Davis, 2012; Orgeta & Phillips, 2008) and happiness (Moreno, Borod, Welkowitz, & Alpert, 2003; Orgeta & Phillips, 2008; Svärd, Wiens, & Fischer, 2012).

Studies finding age-related reductions in emotion recognition performance are not always consistent in indentifying which individual emotions are impacted by advanced age. For instance, Calder et al. (2003) revealed that older adults recognized fear and angry faces less accurately than young adults with some evidence of improvement in disgust. In contrast, Keightley, Winocur, Burianova, Hongwanishkul, and Grady, (2006) report age-related declines in the recognition of sad and fear faces, with no decline in angry, disgust, happy or surprise recognition. While results for individual emotional expressions have not been consistent across all studies, the general consensus is that accuracy for identifying negative facial expressions is particularly impacted by aging (Isaacowitz et al., 2007; Ruffman et al., 2008; Williams, Mathersul, et al., 2009). A recent meta-analysis of 28 data sets exploring the impact of age on emotion recognition across multiple modalities (including faces) suggests that recognition of anger and sadness shows age-related decline across modalities, and face recognition is most impacted for anger, sadness, and fear in older adults (Ruffman et al., 2008). They also reported that older adults had poorer identification of happy and surprised faces, but these age differences were smaller in magnitude.

Despite the large body of research examining emotion recognition accuracy, there has been less focus on response times to identify emotional expressions as a marker of age-related decline. Younger adults recognize happy expressions more quickly than negative emotions, with fear identification being the slowest and least accurate (Palermo & Coltheart, 2004). Similarly, De Sonneville et al. (2002) report that positive emotions are recognized more quickly than negative emotions and adults respond faster than adolescents. Sullivan and Ruffman (2004) report that older adults respond more slowly

than younger adults overall on tasks of emotion recognition. Additionally, Keightley et al. (2006) asked younger and older individuals to identify the emotional valence of faces as positive, negative, or neutral and reported that older adults were slower overall in identifying the emotional valence of faces, especially if the facial expressions were of negative valence. A recent normative study investigating facial emotion recognition throughout the lifespan indicated a U-shaped curve in performance such that younger adults are quicker to respond compared to children and older adults, and older adults have the slowest RTs, especially for identification of fear (Williams, Mathersul, et al., 2009).

The overall pattern of emotion accuracy and RT suggests that older adults recognize negative emotion expressions less accurately and more slowly than younger adults. Prior research has proposed several potential reasons for the overall patterns of age-related change in emotion recognition. One suggestion is that older adults exhibit a positivity bias evidenced by preferential attention to, and memory for positive stimuli (Mather, & Carstensen, 2003; Werheid et al., 2010). This account is consistent with a preservation of recognition for happy faces and declines in recognition of negative emotions. However, this does not account for findings that suggest age-related changes in recognition of happiness (Ruffman et al., 2008) or the preservation (and in some cases improvement) of disgust recognition (Calder et al., 2003; Suzuki, Hoshino, Shigemasu, & Kawamura, 2007).

It could also be the case that older adults show decreased accuracy and increased RT for certain types of faces because they are inherently more difficult. Emotion identification tasks increase in difficulty as the number of response choices increases (Phillips, Channon, Tunstall, Hedenstrom, & Lyons, 2008). For example, in emotion

recognition tasks where participants are forced to choose an emotional label for each stimulus, there is typically only one positive emotion, making it easier to identify among multiple negative options. While older adults would be expected to have poorer performance on more difficult items due to general cognitive decline, Ruffman et al. (2008) suggests that this account does not fully describe the patterns of change seen in emotion recognition. Specifically, results from their meta-analysis revealed that the overall pattern of age effects did not match the difficulty level of the emotions. For example, disgust was one of the most difficult facial expressions for younger adults to identify, yet older adults showed a trend for better performance on this emotion. Additionally, they found that while sad faces were the easiest of the negative emotions for younger adults to identify, older adults found these faces to be the most difficult.

Changes in specific non-emotional cognitive abilities may be related to disruptions in emotion recognition abilities in aging individuals (Horning, Cornwell, & Davis, 2012; MacPherson, et al., 2002; Orgeta & Phillips, 2008; Sullivan & Ruffman, 2004; West et al., 2012). For instance, accounting for processing speed has been shown to reduce (but not eliminate) age-related effects on overall emotion recognition tasks that examine the ability to identify an emotion at different intensities as a face morphs from a neutral expression to an emotional expression (Orgeta & Phillips, 2008; West et al., 2012). Not all studies have suggested that cognitive function is predictive of emotion recognition performance (Keightley, et al., 2006) and individual emotions may be differentially effected. For example, Suzuki and Akiyama (2013) demonstrated that age-related declines in measures of processing speed impact recognition of facial expressions of happiness, surprise, fear, and sadness, but do not predict performance for anger or

disgust. Additionally, a study investigating predictors of performance for individual emotional expressions in a facial morphing task, indicated that age was a significant contributor to fear, sad, and happy accuracy scores even after controlling for fluid intelligence, memory, and processing speed (Horning, et al., 2012). While prior studies seem to suggest that cognitive aging plays at least a minor role in emotion recognition accuracy, it remains unknown the extent to which age-related impairment on tests of emotion identification accuracy and RT for individual emotions can be explained by changes in cognition. An analysis of the core domains in emotion recognition abilities by Mathersul et al. (2009) determined that core domains of emotion processing for explicit emotion identification, including RT, were associated with cognitive abilities such as information-processing speed, impulsivity/inhibition, working memory capacity, attention, and executive function. To further elucidate the role of cognition in age-related changes in emotion processing, several tests that tap cognitive processing speed, attention, and executive function were included in this study for comparison with emotion identification accuracy and RTs.

The pattern of age-related changes in emotion recognition performance may also be partially explained by changes in the underlying neural substrates for specific emotions. A wide range of neural systems are involved in the explicit identification of emotion expressions, mainly in frontal and temporal brain systems and processing of basic emotion expressions relies on the structure and function of somewhat distinct brain regions. For example, fear is known to rely on the integrity of the amygdala and connecting brain regions (Adolphs, 2002; Calder, Lawrence, & Young, 2001; LeDoux, 2003; Phillips et al., 2004; Williams et al., 2001; Williams et al., 2005) and disgust has

been linked to the function of the basal ganglia and insula (Calder et al., 2001; Phillips et al., 2004; Sprengelmeyer et al., 1996). Anger recognition has been associated with orbitofrontal cortex and cingulate cortex (Blair, Morris, Frith, Perrett, & Dolan, 1999; Iidaka et al., 2001; Murphy, Nimmo-Smith, & Lawrence, 2003). The anterior cingulate, fusiform gyrus, and dorsomedial prefrontal cortex have been implicated in response to sadness (Murphy et al., 2003; Phan, Wager, Taylor, & Liberzon, 2002; Surguladze et al., 2003) and happiness has been linked to the putamen and ventral striatum (Phan et al., 2002). Frontal and temporal brain regions, which are important for recognition of emotions of fear, anger, and sadness, are also associated with age-related changes in structure (Allen, Bruss, Brown, & Damasio, 2005; Bartzokis et al., 2001; Grieve, et al., 2011; Pardo et al., 2001; Raz et al., 2005; Resnick, Pham, Kraut, Zonderman, & Davatzikos, 2003; Ruffman et al., 2008; Tisserand, Visser, van Boxtel, & Jolles, 2000; West et al., 2000; Zimmerman et al., 2006). While these examples are not an exhaustive account of brain systems involved in emotion recognition, these neuroanatomical findings do suggest that it is beneficial to examine specific types of basic emotions separately when investigating physiological and behavioral contributors to accuracy and RT.

5-HTTLPR and Emotion Recognition. Given the substantial variability in findings across studies of emotion recognition, it is possible that genetic factors may partially explain individual differences in findings between studies. The serotonin neurotransmitter system plays a crucial role in the regulation of emotional processes (Canli & Lesch, 2007) and this system changes with age (Fidalgo, Ivanov, & Wood, 2013). The serotonin transporter regulates the reuptake of serotonin and this critical role

in serotonin communication is also evident in brain regions involved in the regulation of emotional information (Hariri & Holmes, 2006).

Several recent behavioral studies have begun to research the impact of 5-HTLLPR on attentional biases toward, or away, from emotional compared to neutral word, picture, and face stimuli (Beevers, Gibb, McGeary, & Miller, 2007; Beevers, Wells, Ellis, & McGeary, 2009; Fox, Ridgewell, & Ashwin, 2009; Gibb et al., 2011; Osinsky et al., 2008; Pérez-Edgar et al., 2010). In general these studies demonstrate a greater attentional bias in S allele carriers toward negative stimuli (Beevers et al., 2007; Kwang, Wells, McGeary, Swann, & Beevers, 2010; Pergamin-Height et al., 2012) including faces (Pérez-Edgar et al., 2010; Thomason et al., 2010). Beevers and colleagues (2009) conducted a series of studies using emotional and neutral face stimuli which suggested that carriers of low-expressing alleles had an attentional bias toward emotional stimuli compared to neutral. They also determined that carriers of the S allele had greater difficulty disengaging their attention from sad and happy faces compared to their homozygous L allele counterparts. Similarly, the second study revealed that individuals homozygous for low expressing S and L_G alleles had more difficulty disengaging attention from facial expressions of sadness, happiness, and fear.

While genotype related shifts in attentional bias have important implications for emotional processing, these studies do not target the ability to explicitly label individual emotions correctly. Antypa et al. (2011) examined identification of emotional expressions of happiness, sadness, fear, and anger at different intensities and concluded that while there were no differences in accuracy, young adults with low expressing alleles identified anger and sadness at lower intensities than other genotype groups. Other

research in young adults suggests that S carriers have worse recognition accuracy for identification of happy faces, but better accuracy for faces expressing fear compared L homozygotes (Defrancesco et al., 2011). Neuroimaging studies also suggest that 5-HTTLPR is also associated with differences in neural processing of positive and negative facial expressions (Dannlowski et al., 2010; Stollstorff et al., 2013; Surguladze et al., 2008). Taken together, it is clear that 5-HTTLPR modulates processing of emotional stimuli, but is it less clear how 5-HTTLPR specifically impacts emotion recognition performance in older individuals. This study adds to the existing literature by examining the role of this genotype in explicit emotion identification accuracy and RT in older adults.

Alterations in serotonergic functioning also have important implications for non-emotional cognitive functioning. Differences between high and low expressing allele groups suggest that the low expressing S allele may be a risk factor for cognitive impairment. For example, rhesus monkeys with the SS genotype perform significantly more poorly on tests indicative of cognitive flexibility (Izquierdo, Newman, Higley, & Murray, 2007). In humans, an increased risk of MCI has been reported for S carriers (Marini et al., 2011). Additionally, a significant interaction between the S allele, cortisol secretion levels, decreased hippocampal volume, and memory impairment has been reported in healthy older adults (O'Hara et al., 2007). Taken together, these findings implicate the S allele in increased risk of cognitive dysfunction. However, recent research indicates that the low expressing S allele may actually have positive effects on cognition (Homberg & Lesch, 2011). In fact, healthy individuals carrying at least one S allele are reported to have enhanced performance on measures of executive function

(Borg & Henningsson, 2009; Enge, Fleischhaur, Lesch, & Reif, 2011), attention (Roiser, Müller, Clark, & Sahakian, 2008) and working memory (Anderson, Bell, & Awh, 2012) when compared to healthy adults homozygous for the L allele. A recently published investigation reported that while allele status did not impact performance on tests of executive function, healthy older adults with low expression did exhibit better memory performance than individuals with medium serotonin expression, suggesting a potential benefit of low expression (Salminen et al., 2014). It is currently unclear exactly how 5-HTTLPR modulates cognitive performance.

Summary

While several studies have examined relationships between 5-HTTLPR and processing of facial emotions, most of these studies include younger adults and children. The impact of this polymorphism on tasks of explicit emotion identification in a healthy older adult population remains unknown. The majority of research in older adults to date has focused specifically on emotion recognition accuracy. Relatively few studies have examined RT, which may reflect a key component of emotional processing for older adults. Additionally, cognitive functioning is known to decline with age and may be associated with changes in emotional processing. The 5-HTTLPR polymorphism contributes to individual differences in responding to emotional stimuli and performance on non-emotional cognitive tasks. The goals of this study were to examine the impact of 5-HTTLPR on emotion identification accuracy and RT in a healthy older adult sample, and to examine additional contributions of cognitive skills to emotion identification performance. The following hypotheses were tested: 1) Older adults carrying the S allele will be less accurate than older adults homozygous for the L allele when identifying

facial expressions of emotion (fear, anger, disgust, sad, happy, neutral); 2) Older adults carrying the S allele will take longer than older adults homozygous for the L allele to correctly identify facial expressions; and 3) Non-emotional cognitive performance will not account for these differences.

Design Considerations

Several important methodological issues related to the proposed research were considered. Below, several areas of potential concern and the rationale for relevant methodological design choices are discussed.

The first consideration is the grouping of participants by genotype. In this study the bi-allelic 5-HTTLPR polymorphism, which results in a short and a long variant with differing levels of serotonin transporter expression, was examined. Prior research suggests that the S allele leads to alterations in serotonin transporter expression (Lesch et al., 1996). Potentially, participants in this study could be grouped by the three genotypes separately (SS, SL, LL). However, only 8 individuals in this sample had the SS genotype. Since possession of one S allele is known to reduce serotonin transporter expression, it is common in the literature to combine the SS and SL genotypes for analyses. Further, the 5-HTTLPR polymorphism is thought to be modified by rs25531, making it functionally tri-allelic. This SNP results in the inheritance of either an A or a G nucleotide for each allele (S_AS_A, S_AS_G, S_GS_G, S_AL_A, S_AL_G, S_GL_G, S_GL_A, L_AL_A, L_AL_G, L_GL_G). The G SNP is rarely present on S alleles, so this polymorphism is thought to impact gene expression almost exclusively on the L allele with L_G showing low expression similar to that reported for the S allele (Wendland et al., 2006). Recently, this has led some researchers to group SS, SL_G, and L_GL_G carriers together as having low

serotonin transporter expression. Using this method of grouping, there are 9 individuals categorized as having low expression, 21 with medium expression (30 carriers of low expressing alleles), and 11 with high expression. Due to the prevalence in the prior literature, the decision was made to focus on the conventional bi-allelic conceptualization of genotype for primary analyses. However, the impact of rs25531 was examined in secondary analyses.

A second consideration is the potential for interactions of 5-HTTLPR with other genes relevant to emotional processing. Neurochemicals such as oxytocin, dopamine, and serotonin, and associated genes have all been implicated in emotional functioning (Skuse et al., 2013). Melchers, Montag, Markett, and Rueter (2013) recently reported that facial emotion recognition accuracy is influenced by the rs2268498 polymorphism on the OXTR-gene. This polymorphism has also been reported to interact with 5-HTTLPR, resulting in lower scores on personality dimensions of fear and sadness in individuals possessing the LL/TT variants of these genes (Montag, Fiebach, Kirsch, & Reuter, 2011). There is also evidence that 5-HTTLPR may interact with the COMT val/met polymorphism on reduced connectivity in facial emotion-processing brain circuitry (Surguladze et al., 2012). Under the current design, there is insufficient statistical power to examine interactions between multiple genes, but this signifies an important next step in this line of research. Currently, participants in this data-set are not genotyped for OXTR and COMT, but these data could be obtained from stored saliva samples for future analysis.

Another consideration is test selection. There are many types of behavioral tasks to assess emotional functioning. Prior research on the impact of the 5-HTTLPR

polymorphism has focused on biases in attention to, or away from, emotional stimuli (Beevers et al., 2009; Pérez-Edgar et al., 2010; Thomason et al., 2010). Typically, they are not being asked to explicitly identify emotions in these tasks, which is a skill known to be impacted in older adults. In studies that do examine the role of 5-HTTLPR on emotion recognition accuracy, RT is not evaluated (Antypa et al., 2011). Explicit emotion identification was chosen because it targets both of these skills, which are behaviorally relevant for older adult samples. Cognitive tasks used in this study were chosen because prior work suggests that these domains may be related to emotion identification performance.

Methods

Participants.

Data for a total of 42 individuals aged 51-85 were extracted from existing baseline data collected for the advisor's NIH-funded longitudinal aging study (R01-NS052470) investigating genetic markers of inflammation and vascular health, microstructural brain integrity, and neuropsychological performance in healthy individuals. The sample included healthy, English-speaking adults over the age of 50 who completed the IntegNeuro^{TM} battery of neuropsychological tests and provided saliva samples for genetic analysis. Exclusion criteria included self-reported history of substance abuse; psychiatric illness such as depression; head injury defined as loss of consciousness > 5 minutes; confounding neurological or medical conditions, such as multiple sclerosis, diabetes, epilepsy, blood borne illness, hand tremor, or untreated thyroid disease. Data for one subject was not available for questions regarding psychiatric illness, and this subject was not included in the final sample (n = 41).

Individuals were also excluded from the sample if they scored less than 24 on the Mini Mental State Exam (MMSE). The parent study was approved by the Institutional Review Board at the University of Missouri-Saint Louis. All participants gave written informed consent to participate in the study.

Genotyping

Genomic DNA was extracted from saliva samples purified using the Oragene DNA collection kit (DNA Genotek, Ottawa, Canada) and processed using the Autopure LS nucleic acid purification system (QIAgen). Genomic DNA was amplified using the QIAGEN Multiplex PCR Kit (QIAGEN Pty Ltd., Victoria, Australia) and the following primers were used: forward, 5'-TCCTCCGGTTTGGCGCCTCTTCC-3'; reverse, 5'-TGGGGGTTGCAGGGGAGATCCTG-3'. The following PCR amplification conditions were utilized: 94^{o}C for 15 min; 38 cycles of 94^{o}C for 30s, 66^{o}C for 45s and 72^{o}C for 60s; followed by 72^{o}C for 10 min. Amplicons were digested with *Hpa*II, and fragments were separated by agarose gel electrophoresis. To enable efficient digestion of the amplicon, the forward primer introduces an additional *Hpa*II site. Fragment sizes (in bp) for each allele were: LA, 506+6; LG, 396+110+6; SA, 463+6; SG, 396+67+6 (as reported in Salminen et al., 2014). Genotype frequencies in the total sample (n=41) for the bi-allelic classification were SS=8, SL=16 and LL=17; and for the tri-allelic classification were SS=8, SLa=15, LaLa=11, LaLg=6, LgLg=0, SLg=1. Genotype frequencies did not differ from Hardy-Weinberg equilibrium for either classification (p = 0.25 and 0.31 respectively). To account for the effect of the 5-HTTLPR polymorphism, participants were grouped according to their predicted levels of 5-HTT expression with carriers of S

alleles grouped together for bi-allelic analyses and carriers of S and L_G alleles together for tri-allelic analyses.

Of the 41 participants identified in the database, 24 were classified as S carriers (8 SS and 16 SL) and 17 were classified as non-carriers (LL genotype). The tri-allelic classification including the A/G SNP (rs25531) results in a total of 30 carriers of low expressing alleles (8 SS, 1 SL_G, 15 SL_A, 6 L_AL_G) and 11 non-carriers (11 L_AL_A).

Neuropsychological tests

All cognitive tests are part of the computerized IntegNeuro™ battery designed and validated to serve as a brief, multi-domain assessment of cognitive function for use in clinical and research settings (Paul et al., 2005, Williams, Mathersul et al. 2009). Each task was presented using touchscreen hardware and software with standardized instructions, presentation, and data acquisition. The battery was administered in a sound-attenuated testing room, with participants seated in front of a touch-screen computer. Luminance was not accounted for, but the testing room was well-lit and visual distractions were minimized. A test administrator was present in the room to assist participants. Each test included a practice trial prior to the test trial and tests were completed without breaks or interruptions. The proposed study focused on measures targeting explicit emotion identification, processing speed, attention, and executive function.

Emotion Identification Test. Participants were presented with a series of 48 faces depicting six emotional expressions (eight each: neutral, happy, fearful, sad, angry, or disgust) in pseudo-random order for two seconds each. They were then asked to identify the appropriate verbal label for each emotional expression among the six options

for each face. Accuracy and RT for correct responses were recorded and were used as dependent variables. Stimuli were adapted from a standardized set of facial emotion stimuli (Gur et al. 2002), and were equated for size, luminance, and alignment.

Choice Reaction Time (CRT). The CRT is a test of simple RT that measures sensorimotor and information processing speed. Participants were asked to attend to the computer screen while resting their dominant index finger on a white circle as four green target circles light up in different positions on the screen. For each of 20 trials, participants touched the illuminated green circles as quickly as possible. Mean RT across trials was recorded and used as the dependent measure.

Attention Switching. The first part of this task (AS 1) is designed to capture attention and processing speed. Participants were presented with 25 numbers and asked to touch the numbers in ascending order (1, 2, 3 etc.). The second part of this task (AS 2) taps executive function. Participants were presented with a pattern of 13 numbers and 12 letters, and asked to touch the numbers and letters in alternating and ascending sequence (1, A, 2, B etc.). Time to completion was used as the dependent measure for both tests.

Digit Span. Participants were presented with a series of digits flashed on the computer screen, at one second intervals. In part one (digits forward; DF) the participants were asked to immediately enter the digits in the same order as presented, using a touch pad. In part two (digits backward; DB) they were required to recall the presented digits in the reverse order. In each part the number of digits in each sequence was gradually increased from 3 to 9, with two trials of the same length at each level. There was a 5 second delay between each trial. The test was completed when both trials

of a single length were failed. This test measured attention and the dependent measure for each part was the maximum number of digits recalled without error.

Verbal Interference. Participants were presented with four colored words, one at a time. Below each word, the four possible names of the colors were displayed in black. In the first part (VI 1) of the test the participant read the name of each colored word as quickly as possible and chose the appropriate color name below. In the second part of the test (VI 2), participants named the contrasting color of the ink in which the word was printed as quickly as possible and chose the appropriate color name below. Accuracy in matching the name of the color in part one was recorded to assess attention. Accuracy in matching the color of the ink in part two was recorded as an indicator of executive functioning. Reaction time for identifying words was also recorded (VI RT).

Maze Task. Each participant was presented with a grid (8x8 matrix) of circles on the computer screen. The goal of the task was to identify a hidden path through the grid, from a yellow beginning point circle at the bottom of the grid, to an end point circle at the top in blue. Each subject navigated around the grid by touching directional arrow keys. Completion of the maze required 24 consecutive correct moves. Incorrect moves were signaled on the screen with an X and the sound of a tone. A different tone was heard if they made a correct move. The test was finished when the subject completed the maze twice without error or after 7 minutes, whichever came first. Time to finish was recorded and used as a dependent measure of executive function.

Analyses

Preliminary Analyses. Statistical analyses were performed using SPSS version 20. Missing data were examined before conducting analyses. Normality, outliers,

linearity, and homogeneity were also evaluated for all variables used in the primary analyses. Descriptive statistics for the sample were conducted. Demographic factors, such as age, sex, education, and ethnicity were examined using independent samples t-tests and chi-square test of independence to determine if they were significantly different between the S carrier and non-carrier groups. Given the potential importance of gender for measures of emotion recognition, differences between males and females on dependent variables for hypotheses 1 and 2 were examined using independent samples t-tests.

Primary Analyses. Multiple analyses were conducted to investigate each hypothesis. To adjust for multiple comparisons, the false discovery rate procedure (FDR; Benjamini & Hochberg, 1995) was employed for each set of analyses.

Hypothesis 1. The first goal of the study was to investigate the relationship between the low 5-HTTLPR expression and explicit emotion identification accuracy. MANOVA was utilized to assess group differences (S carrier vs. LL) in identification accuracy for faces depicting fear, angry, sad, disgust, happy, and neutral emotions. Univariate analyses were completed to examine group differences in accuracy for individual emotions. *Secondary analyses* for this hypothesis included a MANOVA to assess this relationship using the tri-allelic classification of low expressing alleles (S/L_G carriers vs. L_AL_A).

Hypothesis 2. To examine the relationship between the S allele and explicit emotion identification RT, a MANOVA was performed with 5-HTTLPR status as the independent variable and RT for each of the six emotional expressions as dependent variables. Univariate analyses were completed to examine group differences in RT for

individual emotions. *Secondary analyses* repeated the main analyses using the tri-allelic classification of genotype (S/L_G carriers vs. L_AL_A).

Hypothesis 3. The goal of this hypothesis was to examine the impact of 5-HTTLPR on non-emotional cognitive functions and to investigate relationships between emotion identification performance and measures of processing speed, attention, and executive function. Three MANOVAs were conducted with 5-HTTLPR status as the independent variable and measures of processing speed (CRT, AS 1, VI RT), attention (DF, DB, VI 1), and executive function (AS 2, VI 2, Maze Time) as dependent variables. Bivariate correlation analyses were used to investigate the relationships between accuracy and RT for each of the emotional expressions, and individual measures of processing speed, attention, and executive function. *Secondary analyses* repeated these statistics using tri-allelic classification (S/L_G carriers vs. L_AL_A).

Results

Preliminary Analyses.

Of the 41 participants 27 were female (66%) and 14 were male (34%). The majority of participants were Caucasian (70.7%), followed by African-American (14.6%), Hispanic (12.2%), and Asian (12.4%). The average age was 62.9 (SD = 8.37) ranging from 51-85 years. The average education level was 15.59 (SD = 2.29) years. See Table 1 for descriptive statistics for each group separately. Group comparisons indicated that S allele carriers did not differ significantly from non-carriers on age (t (39) = .28, p = .78), gender (χ^2 (1, n = 41) = 1.46, p = .23), ethnicity (χ^2(1, n = 41) = 5.95, p = .11), or education (t (39) = -.42, p = .68). Comparisons of low expressing carriers and non-carriers using the tri-allelic classification revealed the same pattern of non-significant

results as reported in Table 1. No gender differences were detected on measures of emotion identification accuracy (see Table 2). A significant gender difference was identified in disgust RT (see Table 2), but no significant differences were detected for fear, anger, sad, happy, or neutral RT. Since gender did not differ between genotype groups and gender effects were not detected on most emotion identification measures, it was not included as a covariate in MANOVA analyses. A follow-up univariate analysis was included to examine the impact of genotype on disgust RT with gender as a covariate.

Emotion Recognition Accuracy

A total of 41 individuals were included in analyses for hypothesis 1. One accuracy score for neutral faces and one accuracy score for happy faces was more than three standard deviations from the mean. These scores were in the range of possible values (13% and 75% correct, respectively) and were retained for analyses. Normality statistics suggest that among the 6 emotion identification accuracy variables, all were normally distributed except for neutral and happy which showed evidence of ceiling effects.

A MANOVA was utilized to determine whether individuals carrying the S allele differed from individuals without the S allele on emotion identification accuracy. Linearity was confirmed by examining scatter plots of pairs of variables for each group. One multivariate outlier for emotion identification accuracy was revealed (Mahalanobis Distance = 27.87) which exceeded the chi-square critical value with an alpha value of p = .001. Box's Test of Equality of Covariance Matrices was used to evaluate the assumption that covariance matrices were equal, and was found to be non-significant (p = .84).

Levene's Test of equality of error variances indicated that accuracy for happy faces violated the assumption of equality of variance (F (1, 39) = 4.38, p = .04). Univariate analyses for this variable should be interpreted with caution. All other emotion identification accuracy variables satisfied the assumption of equality of variance.

There were no statistically significant differences between the S allele carriers and non-carriers on measures of emotion identification accuracy (Wilks' Lambda =.005; (F (6,34) = .88; p = .52; η_p^2 = .13). No significant differences between groups were revealed when considering accuracy in identifying each individual emotion for fear (F (1, 39) = .45, p = .16), angry (F (1, 39) = 2.06, p = .16), disgust (F (1, 39) = 1.95, p = .17), sad (F (1, 39) = .28, p = .60), happy (F (1, 39) = 1.57, p = .22) or neutral (F (1, 39) = .049, p = .825) faces. Means and standard deviations are reported in Table 3.

Secondary Analyses. It is possible that grouping by bi-allelic classification masked group differences by grouping individuals with an L_G allele with individuals homozygous for the L_A allele. In this sample, 6 cases initially classified in the higher expressing LL group were reclassified into the lower expressing group. The tri-allelic classification resulted in 30 carriers of low expressing alleles (8 SS, 1SL_G, SL_A, L_AL_G) and 11 non-carriers (L_AL_A). Hypothesis 1 analyses were repeated using this classification.

No univariate outliers were identified for any of the dependent variables. Additionally, no multivariate outliers were revealed (maximum Mahalanobis Distance = 14.74). Box's Test of equality of covariance matrices was not significant (p = .98) suggesting that the covariance matrices of the dependent variables were equal across

groups. Levene's test suggests that all emotion identification variables satisfied the assumption of equality of variance.

Differences between the low expressing allele carriers and non-carriers were not statistically significant (Wilks' Lambda = .94; F (6, 34) = .361, p = .90, η_p^2 = .06). No significant differences between groups were revealed in accuracy of identifying each individual emotion for fear (F (1, 39) = .25, p = .62), angry (F (1, 39) = .97, p = .33), disgust (F (1, 39) = .91, p = .35), sad (F (1, 39) = .12, p = .73), happy (F (1, 39) = .08, p = .78), or neutral (F (1, 39) = .43, p = .52). Means and standard deviations are reported in Table 3.

Emotion Recognition RT

RTs could not be recorded for angry faces in three individuals and for disgust faces in four individuals, therefore a smaller sample (n = 34) was used. Examination of normality statistics indicated that distributions for emotion identification RTs violated normality assumptions and warranted transformation. An inverse transformation (1/x) was chosen based on recommendations of prior literature (Ratcliff, 1993; Silverstein et al., 2010) and applied to each of these variables to reduce positive skewness and reduce the influence of outliers. A MANOVA was computed to determine whether there was a difference between S allele carriers and non-carriers on measures of RT when identifying six emotional facial expressions. The assumption of linearity was satisfied for pairs of inverse transformed correct RTs for fear, disgust, angry, sad, happy, and neutral faces. No multivariate outliers were identified which exceeded the chi-square critical value with an alpha level of p = .001 (maximum Mahalanobis distance = 15.20). Box's Test of Equality of Covariance Matrices was not significant (p = .38) indicating equal

covariance matrices across groups. Levene's test was not significant for any of the dependent variables ($p > .05$) suggesting that the equality of variance assumption was met.

S allele carriers had significantly longer RTs when correctly identifying emotional expressions (Wilks' Lambda = .61; F (6, 27) = 2.94, p = .025, ηp^2 = .40). Emotion identification RTs were significantly longer in S allele carriers compared to non-carriers when identifying expressions of fear (F (1, 32) = 10.45, p = .003, η_p^2 = .25) and disgust (F (1, 32) = 11.43, p = .002, η_p^2 = .26). These findings held with FDR adjustment for multiple comparisons. A follow-up analysis with gender as a covariate also revealed longer RTs in S allele carriers compared to non-carriers for identification of disgust (F (1, 31) = 10.87, p = .002, η_p^2 = .26). No significant differences between groups were revealed in RTs when identifying each individual emotion for angry, sad, happy, or neutral faces ($p < .05$, FDR adjusted). Raw means and standard deviations are reported in Table 4.

Secondary Analyses. To evaluate the impact of the tri-allelic classification of 5-HTTLPR genotype, analyses performed for hypothesis 2 were repeated using this grouping. No univariate outliers were identified for any of the dependent variables. Additionally, no multivariate outliers were revealed (maximum Mahalanobis Distance = 15.20). Box's Test of equality of covariance matrices was not significant (p = .21) suggesting that the covariance matrices of the dependent variables are equal across groups. Levene's test suggests that all emotion identification variables satisfied the assumption of equality of variance ($p < .05$).

The difference between low expressing allele carriers and non-carriers on emotion identification RTs examined using MANOVA was not significant under the tri-allelic grouping (Wilks' Lambda = .74, F (6, 27) = 1 .27, p = .30, η_p^2 = .22). Univariate analyses examining differences between allele groups on fear (F (1, 32) = 5.85, p = .02) and disgust (F (1, 32) = 5.83, p = .02; with gender as covariate: F (1, 31) = 5.46, p = .03, η_p^2 = .15) were significant with S/L_G allele carriers having longer RTs, but this did not survive FDR correction. Allele groups did not significantly differ on angry, sad, happy, or neutral RTs. Raw means and standard deviations are reported in Table 4.

Performances on Cognitive Tests

Two missing values were revealed for the CRT task and one for the VI 2 task. Missing values were not replaced. No significant differences were observed between S carriers and non-carriers on measures of processing speed (Wilks' Lambda =.89, F (3, 35)= , p = .24, η_p^2 = .11), attention (Wilks' Lambda =.92, F (3, 37)= 1.0, p = .39, η_p^2 = .08), or executive function (Wilks' Lambda =..87, F (4, 35)= 1.36, p = .27, η_p^2 = .13). There were also no statistically significant differences between the tri-allelic genotype groups on measures of psychomotor speed (Wilks' Lambda = .97, F (3, 35) = 32, p = .81, η_p^2 = .03), attention (Wilks' Lambda =.92, F (3, 37) = 1.11; p = .36, η_p^2 = .08), or executive function (Wilks' Lambda =.98, F (3, 36) = .24; p = .87, η_p^2 = .02). Means and standard deviations are reported in Table 5.

Since no significant differences between genotype groups were found for accuracy, these groups were combined for correlational analyses. No significant relationships were observed after correcting for multiple comparisons with FDR. Prior to

correction, a few moderate-large significant relationships were identified and are reported in Table 6.

Correlations between emotion identification RT variables and cognitive tests were conducted separately for S carrier, S/L_G carrier, LL, and L_AL_A groups. No significant correlations remained for any genotype group following FDR correction. Prior to FDR correction, several moderate-large significant correlations were observed. Happy RT and Neutral RT showed the greatest number of significant relationships prior to correction using both classifications. All correlations using the bi-allelic classification are reported in Table 7 and correlations using tri-allelic classification are reported in Table 8.

Discussion

The primary goal of this research was to determine if healthy older adults with low-expressing alleles display diminished emotion identification performance compared to those with the high-expressing alleles. The results of the present study indicate that individuals carrying at least one 5-HTTLPR S allele perform emotion identification tasks more slowly than those who do not carry the allele. Specifically, RTs for identification of fear and disgust were significantly slower in these individuals. The ability to accurately identify emotions in faces was not impacted by genotype in this sample. Classification using tri-allelic genotype groups yielded a similar pattern of results in which individuals carrying S and L_G alleles had slower RTs than L_AL_A carriers when correctly identifying fear and disgust, but this did not withstand multiple comparisons correction No significant differences were identified between allele groups on cognitive tests tapping speed of processing, attention, and executive functioning. The overall pattern of correlations suggests that RTs for correctly identified happy and neutral

expressions share a relationship with these skills, but cognitive performance did not explain differences between genotype groups revealed for fear and disgust RT.

Findings from the current study do not support a significant role of genotype in emotion recognition accuracy in older adults using either bi-allelic or tri-allelic classification. This is partially consistent with a prior study in younger adults which failed to detect significant genotype differences in accuracy for sad, angry, and neutral faces (Defrancesco et al., 2011). However, S allele carriers in the prior study were more accurate than LL carriers when identifying fearful faces and less accurate when identifying happy faces. The present results are also consistent with previous work in younger adults suggesting that S carriers and LL homozygotes do not differ in accuracy when identifying facial expressions in morphed faces (Marsh et al., 2006). While that study did not find differences in accuracy based on genotype alone, they did indicate that S carriers had impaired fear recognition in response to tryptophan depletion, suggesting that the S allele is associated with greater sensitivity to serotonin manipulation.

The mechanism by which genetic variants of 5-HTTLPR influence emotion identification is currently unclear. One explanation for the current findings is that the relationship between 5-HTTLPR status and emotion identification accuracy is moderated by additional factors that were not evaluated in the present sample. For example, 5-HTTLPR has frequently been studied in the context of psychological disorders. The serotonin neurotransmitter system is disrupted in depression and anxiety, and both of these conditions occur frequently in the older adult population (Kessler, Berglund, Demler, Jin, Merikangas, & Walters, 2005). The S allele is associated with an increased risk of depression (Karg et al., 2011) and anxiety-related personality traits (Sen,

Burmeister, and Ghosh, 2004). While the current sample did not self-report any psychiatric conditions, it is possible that undiagnosed, unreported or subclincal conditions were present. Future studies would benefit from the addition of tests that measure symptoms of anxiety and depression more explicitly. The inclusion of personality trait measures would also improve future investigations.

Interactions between genes and the environment can have substantial influence on behavioral phenotypes. Recently it has been proposed that some individuals are more susceptible to both positive and negative environmental influence based on their genetic framework (Belsky, Jonassaint, Pluess, Stanton, Brummett, and Williams, 2009, Homberg & Lesch, 2011). For example, 5-HTTLPR moderates the effects of stressful life events during early adulthood on depressive symptoms (Caspi et al., 2003). Additionally, the S allele is associated with both an increase in depressive symptoms and neuroticism for individuals experiencing negative life events, and a decrease in symptoms and less neuroticism for individuals experiencing positive life events (Pluess, Belsky, Way, and Taylor, 2010; Taylor et al., 2006). It is possible that genotype differences in emotion identification in the present study are masked or offset by an interaction with unmeasured environmental factors. Carriers of the S allele and the L_G allele are more susceptible to environmental influences, and thus additional research that examines emotion identification performance in the context of environmental stressors and positive experiences is needed.

A single genetic polymorphism is unlikely to account for more than a small proportion of the variance in complex behaviors such as emotion identification. 5-HTTLPR may also interact with other gene polymorphisms that impact emotional

processing such the Val/158/Met polymorphism of catechol-O-methyltransferase gene (COMT; Defrancesco et al., 2011, Surguladze et al., 2012) or the rs2268498 polymorphism on the OXTR gene (Melchers et al., 2013, Montag et al., 2011). The met allele is considered the susceptibility allele for COMT and previous studies have found a relationship between COMT genotype and emotion recognition abilities (Soeiro-de-Souza et al., 2012; Weiss et al., 2007). A few studies have examined both 5-HTTLPR and COMT in the same participants (Defrancesco et al., 2011; Gohier et al., 2014, Surguladze et al., 2012). While these studies have not identified an interaction between the two polymorphisms on behavioral emotion recognition tasks, Surguladze et al. (2012) suggest that an interaction between low activity alleles of COMT and 5-HTTLPR is associated with reduced connectivity in facial emotion-processing circuits for expressions of fear.

Recent research investigating the impact of intranasal oxytocin administration has revealed that oxytocin modulates facial emotion recognition performance and associated brain activity (Domes, Heinrichs, Michel, Berger, & Herpertz, 2007; Kirsch et al., 2005; Lischke et al., 2012; Schulze et al., 2011; Huffmeijer, van IJzendorn & Bakermans-Kranenburg, 2012; Shahrestani, Kemp, & Guastella, 2013). Melchers et al. (2013) report that the rs2268498 polymorphism on the OXTR gene is specifically associated with emotion recognition accuracy. Additionally, an interaction effect has been detected between 5-HTTLPR and OXTR polymorphisms on personality traits associated with negative emotionality (Montag et al., 2011). Given the importance of these genes for emotional processing, future studies should examine potential interaction effects between 5-HTTLPR and additional gene polymorphisms.

The current data provide support for hypothesis 2 which predicted that 5-HTTLPR would impact RT for correctly identified emotional expressions in older adults. Carriers of the S allele compared to LL homozygotes had significantly longer RTs for fear and disgust with age as a covariate. Bi-allelic classification of 5-HTTLPR is commonly used in the literature, but recent studies suggest that tri-allelic grouping is more informative (Wendlend et al., 2006). To account for the influence of rs25531, the sample was reanalyzed with a tri-allelic genotype groups. The multivariate effect of genotype on RT was not significant using this classification. However, univariate analyses for both bi-allelic and tri-allelic 5-HTTLPR revealed increased RTs for identification of fear and disgust expressions. This suggests that underlying cognitive processes necessary to complete the emotion identification task are sensitive to alterations in the serotonergic system. Six individuals classified as LL genotype were identified as low expressing L_G carriers following tri-allelic grouping. Group size may have limited our ability to detect significant genotypic differences using tri-allelic groups. These results need to be replicated in larger samples.

Longer RTs could be indicative of several underlying processes. One explanation is that slower RTs are a function of general cognitive slowing that occurs with age. The present study evaluated several tasks that tap processing speed, attention, and executive function. These domains have previously been associated with emotion identification performance in older adults (Mathersul et al., 2009). None of the cognitive tests examined in this study differed significantly between carriers of low and high expressing alleles. Neutral and happy RTs in individuals with low expressing alleles showed moderate to large correlations with multiple measures of these skills. Similarly, in LL

and L_AL_A groups, RTs for happy and neutral emotions were significantly related to a measure of processing speed. Taken together, these results do not provide a clear explanation for fear and disgust RTs. Additionally, prior research examining the role of serotonergic gene polymorphisms reported no association between 5-HTTLPR and the rate of cognitive decline (Payton et al., 2005). So far the literature regarding the role of 5-HTTLPR in cognition is mixed and it is likely that interactions with other genes or environmental factors are involved in these relationships (Homberg & Lesch, 2011).

Another explanation for longer RTs for fear and disgust is that S and S/L_G carriers have biased attention for these emotions. This is consistent with prior reports of greater attentional bias in S allele carriers toward negative stimuli (Pergamin-Height et al., 2012; Beevers et al., 2007; Kwang, et al., 2010; Pérez-Edgar et al., 2010; Thomason et al., 2010). Results of one study indicate that carriers of the S allele display greater difficulty disengaging their attention from sad and happy faces compared to their homozygous L allele counterparts (Beevers et al., 2009). This study also examined attentional engagement and disengagement in both S and L_G carriers and these individuals had more difficulty disengaging attention from facial expressions of sadness, happiness, and fear. While difficulty disengaging attention from fear and disgust faces would result in longer RTs, the relationship between performance on these two types of tasks cannot be verified in the current study.

RTs for emotion identification of fear and disgust likely rely on partially distinct neural systems, and the current study would suggest that these brain regions are modulated by 5-HTTLPR. Fear processing is frequently associated with the brain integrity in the amygdala and connecting regions (Adolphs, 2002; Calder, Lawrence, &

Young, 2001; LeDoux, 2003; Phillips et al., 2004; Williams et al., 2001; Williams et al., 2005). The basal ganglia and insula have been implicated in the processing of disgust (Calder et al., 2001; Phillips et al., 2004; Sprengelmeyer et al., 1996). More research is needed to elucidate neural mechanisms associated with differences in 5-HTTLPR allele status on measures of emotional identification RT.

A few limitations are present in the current study. Individuals with low and medium serotonin transporter expression were grouped together in the present study as carriers of susceptibility alleles. The small sample size limited our ability to examine differences between low, medium, and high expression groups. Additional studies are needed to determine if low expressing alleles impact performance on emotion identification accuracy and RT in a dose dependent manner. Additionally, prior research has suggested that females are more accurate and faster than males on measures of emotion identification (Williams, Mathersul et al., 2009). The current sample was predominately female. This may have attenuated our ability to identify relevant gender effects in this study. Future work addressing the importance of gender in the relationships between 5-HTTLPR and emotion identification is needed. Nevertheless, the sample characteristics were sufficient to identify significant relationships between the serotonin transporter polymorphism and performance on the emotion tasks. The study sample comprised individuals of multiple ethnicities and was relatively small in size. Future replication studies would benefit from larger group sizes.

Conclusions

The current findings have important implications for understanding the role of serotonergic mechanisms in older adult performance on emotional processing. Carriers

of low serotonin transporter expression alleles take significantly longer to correctly identify emotional facial expressions, specifically expressions of fear and disgust. Additional work is needed to evaluate cognitive and neural correlates of longer RTs in this task. Future studies examining interactions between environmental stressors, personality traits, additional genes, and 5-HTTLPR are needed to further elucidate the role of serotonin in emotion recognition. The examination of additional tasks that tap implicit emotional processing would also be beneficial. Overall, 5-HTTLPR has been shown to contribute to individual differences in emotion recognition performance, which is known to be diminished in older adults.

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Table 1. *Sample Characteristics*

	Total Sample	S	LL	S and L_G	L_AL_A	S vs. LL	S, L_G vs. L_AL_A
	n = 41	*n* = 24	*n* = 17	*n* = 30	*n* = 11		
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Statistic	Statistic
Age	62.90 (8.37)	63.21 (8.78)	63.47 (7.99)	62.33 (8.41)	64.45 (8.45)	*t* (39) =.28	*t* (39) = -.72
Education	15.59 (2.29)	15.46 (2.65)	15.76 (1.72)	15.57 (2.54)	15.64 (1.50)	*t* (39) = -.42	*t* (39) = -.09
Gender						χ^2 = 1.46	χ^2 = .32
Male	14	10	4	11	3		
Female	27	14	13	19	8		
Ethnicity						χ^2 = 5.59	χ^2 = 1.13
Caucasian	70.7%	83.3%	52.9%	70%	72.7%		
African American	14.6%	12.5%	17.6%	16.7%	9.1%		
Hispanic	12.2%	4.2%	23.5%	10%	18.2%		
Asian	2.4%	0%	5.9%	3.3%	0%		

Table 2. *Independent Samples t-tests for Gender Differences in Emotion Identification Accuracy and RT*

	Fear % Correct	Angry % Correct	Disgust % Correct	Sad % Correct	Happy % Correct	Neutral % Correct
Gender	*t* (39) = .67	*t* (39) = -1.44	*t* (39) = -1.40	*t* (39) = -.53	*t* (39) = -1.25	*t* (39) = -.22
	Fear Correct RT	Angry Correct RT	Disgust Correct RT	Sad Correct RT	Happy Correct RT	Neutral Correct RT
Gender	*t* (39) = 1.75	*t* (36) = .63	*t* (35) = 3.21 **	*t* (39) = .93	*t* (39) = .85	*t* (39) = 1.05

N =41; RT (Reaction Time). * $p < .05$, ** $p < .01$ uncorrected

Table 3. *Comparison of Emotion Identification Accuracy across Genotype Groups*

	S carriers (n = 24)		LL (n = 17)			
	M	SD	M	SD	F	η_p^2
Accuracy					.88	.13
Fear	68.67	20.46	64.23	21.58	.45	.01
Angry	34.50	17.35	43.65	23.47	2.06	.05
Disgust	38.54	19.01	29.71	21.25	1.95	.05
Sad	64.13	26.26	68.59	27.60	.28	.01
Happy	94.83	8.14	97.82	6.56	1.57	.04
Neutral	82.54	20.10	83.94	19.55	.05	.00
	$S + L_G$ carriers (n = 30)		L_AL_A (n = 11)			
	M	SD	M	SD	F	η_p^2
Accuracy					.36	.06
Fear	65.83	20.11	69.55	23.33	.25	.01
Angry	36.40	21.35	43.45	17.15	.97	.02
Disgust	36.70	20.92	29.91	18.03	.91	.02
Sad	65.10	28.58	68.36	21.13	.12	.00
Happy	95.87	7.55	96.64	8.03	.08	.00
Neutral	81.90	20.35	86.45	18.01	.43	.01

Table 4. *Comparison of Emotion Identification Correct Reaction Time across Genotype Groups*

	S carriers (*n* = 21)		LL (*n* = 13)			
	M[a]	SD[a]	M[a]	SD[a]	*F*	η_p^2
RT					2.94*	.40
Fear	4075.95	1433.91	2855.23	574.62	**10.45****	.25
Angry	3306.43	1295.55	2900.38	914.30	.77	.02
Disgust	4405.90	2019.75	2664.77	901.10	**11.43****	.26
Sad	3511.71	1999.30	2878.54	1227.44	.68	.02
Happy	1875.71	537.72	1659.77	695.01	3.19	.09
Neutral	2142.67	1654.96	1664.15	448.48	1.07	.03
	$S + L_G$ carriers (*n* = 24)		L_AL_A (*n* = 10)			
	M[a]	SD[a]	M[a]	SD[a]	*F*	η_p^2
RT					1.27	.22
Fear	3982.38	1394.32	2713.60	328.57	5.85*	.16
Angry	3254.50	1272.28	2903.20	870.68	.30	.01
Disgust	4146.25	2014.42	2765.60	993.65	5.83*	.15
Sad	3529.67	1965.81	2645.50	871.94	1.06	.03
Happy	1837.29	521.65	1687.20	784.28	2.15	.06
Neutral	2099.96	1558.12	1623.10	419.95	1.11	.03

a. Means and Standard Deviations reflect raw reaction time data in milliseconds.

* $p < .05$, ** $p < .01$ uncorrected; Bold indicates significance ($p < .05$) FDR adjusted.

Table 5. *Cognitive measures across Genotype Groups*

		S carriers (*n* = 24)		LL (*n* = 17)	
		M	SD	M	SD
Processing Speed	CRT[a]	734.52ms	117.11ms	739.69ms	116.31ms
	AS 1	27.82s	8.51s	24.97s	7.90s
	VI RT	1157.79ms	232.57ms	1263.71ms	296.89ms
Attention	DF	7.17	2.20	7.29	2.64
	DB	3.71	2.66	4.53	3.18
	VI 1	16.21	2.45	13.82	6.22
Executive Function	AS 2	59.46s	15.69s	53.53s	16.57s
	VI 2[b]	7.46	5.02	10.88	4.50
	Maze Time	400.46s	196.59s	422.00s	205.31s
		S + L_G carriers (*n* = 30)		L_AL_A (*n* = 11)	
		M	SD	M	SD
Processing Speed	CRT[a]	738.14ms	113.98ms	732.30ms	125.11ms
	AS 1	27.04s	7.92s	25.54s	9.52s
	VI RT	1191.33ms	271.31ms	1230.00ms	248.83ms
Attention	DF	6.93	2.24	8.00	2.61
	DB	3.77	2.60	4.82	3.57
	VI 1	15.73	3.52	13.81	6.51
Executive Function	AS 2	58.13s	15.88s	53.91s	17.17s
	VI 2[b]	8.50	5.03	9.80	5.27
	Maze Time	409.03s	199.82s	410.36s	202.50s

N = 41; a. missing 1 person in each group; b. missing 1 person in LL/L_AL_A groups.

Table 6. *Correlations between Emotion Identification Accuracy variables and Cognitive variables*

	Fear	Angry	Disgust	Sad	Happy	Neutral
CRT[a]	-.01	-.28	-.11	-.21	-.53**	-.14
AS 1	.26	-.20	-.20	.01	.02	-.09
AS 2	.10	-.22	-.14	-.05	-.24	-.21
DF	.16	.08	.26	-.02	.17	.29
DB	-.11	.09	.22	.16	-.03	.14
VI 1	.16	.06	.13	.06	-.10	.07
VI 2[b]	-.06	.27	.07	.02	.31*	.18
VI RT	-.11	.02	-.20	.01	.04	-.11
Maze Time	-.16	-.32*	-.29	-.19	.00	-.38*

$N = 41$; a. $n=39$; b. $n=40$. * Significant at $p < .05$ prior to FDR correction, ** Significant at $p < .01$ prior to FDR correction

Table 7. *Correlations between Emotion Identification RT variables and Cognitive variables for Bi-allelic Groups*

	S carriers					
	Fear	Angry	Disgust	Sad	Happy	Neutral
CRT[a]	.38	-.11	.09	.08	.60**	.57**
AS 1	.35	.47*	.32	.35	.35	.62**
AS 2	.30	.19	.25	.26	.25	.58**
DF	-.40	.14	-.36	-.39	-.44*	-.54*
DB	-.08	-.02	-.21	-.03	-.54*	-.39
VI 1	-.25	.24	-.24	-.51*	-.54*	-.50*
VI 2	-.05	-.08	.02	-.13	-.26	-.19
VI RT	.42	-.16	.35	.49*	.48*	.62*
Maze Time	.00	.11	.23	-.02	.62**	.58**
	LL (n = 13)					
	Fear	Angry	Disgust	Sad	Happy	Neutral
CRT[a]	.37	.04	.27	.27	.59*	.54
AS 1	-.19	.44	-.26	-.12	.66*	.11
AS 2	-.04	.29	.01	.30	.51	.41
DF	.05	-.20	.24	.30	-.57*	.01
DB	.45	-.38	.44	.18	.42	.16
VI 1	-.45	.05	.37	.44	.18	-.42
VI 2	-.05	-.08	.02	-.13	-.26	-.19
VI RT	.49	.32	.42	.43	.34	.76**
Maze Time	.19	.70**	.01	.25	.44	.25

*Significant at p < .05 prior to FDR correction, **Significant at p < .01 prior to FDR correction.

Table 8. *Correlations between Emotion Identification RT variables and Cognitive variables for Tri-allelic Groups*

	$S + L_G$ (n = 30)					
	Fear	Angry	Disgust	Sad	Happy	Neutral
CRT[a]	.27	-.06	.03	.15	.54**	.56**
AS 1	.39	.52**	.39	.38	.42*	.64**
AS 2	.24	.26	.22	.35	.30	.61**
DF	-.27	.15	.14	.22	-.30	-.42*
DB	-.03	-.05	-.12	-.05	-.49*	-.39
VI 1	-.19	.11	-.16	-.45*	-.50*	.50*
VI 2[b]	-.15	-.42*	-.24	-.27	-.21	-.44*
VI RT	.34	-.08	.24	.43*	.44*	.59**
Maze Time	.04	.24	.24	.06	.63**	.61**
	L_AL_A (n = 10)					
	Fear	Angry	Disgust	Sad	Happy	Neutral
CRT[a]	.42	-.10	.25	.04	.56	.52
AS 1	-.25	.32	-.38	-.50	.62	.09
AS 2	-.06	.12	-.08	-.11	.35	.22
DF	.08	-.33	.23	.33	-.73*	.01
DB	.53	-.39	.52	.47	-.41	.39
VI 1	-.42	.19	-.36	-.52	.13	-.54
VI 2[b]	-.03	.04	.15	-.05	-.21	-.13
VI RT	.48	.23	.42	.62	.30	.84**
Maze Time	.12	.61	-.12	.12	.35	-.02

*Significant at $p < .05$ prior to FDR correction, **Significant at $p < .01$ prior to FDR correction.