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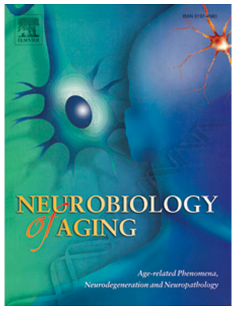

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The impact of aging on the neural networks involved in gaze and emotional processing

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Abbreviated title: Aging and gaze processing

Abstract

Normal adult aging is associated with difficulties in processing social cues to emotions such as anger, and also altered motivation to focus more on positive than negative information. Gaze direction is an important modifier of the social signals conveyed by an emotion, for example an angry face looking directly at you is considerably more threatening than an angry face looking away. In the current study we tested the hypothesis that older adults would show less neural differentiation to angry faces with direct and avert gaze compared to younger people, with the opposite prediction for happy faces. Healthy older (65-75 years; M = 69.75) and younger (17-27 years; M = 20.65) adults completed an fMRI experiment in which they were asked to identify happy and angry expressions displayed either with direct or averted gaze. While younger adults showed neural sensitivity to eye-gaze direction during recognition of angry expressions, older adults showed no effect of eye-gaze direction on neural response. In contrast, older adults showed sensitivity to eye-gaze direction during recognition of happy expressions, but younger adults did not. Additionally, brain-behavior correlations were conducted to investigate the relationships between emotion recognition and mentalizing brain network in both age groups. Younger (but not older) adults' social cognitive performance was differentially correlated with activation in two brain networks when looking at angry faces with direct compared to averted gaze. These novel findings provide evidence for age-related differences in the neural substrates underlying the capacity to integrate facial affect and eye-gaze cues. The results of this study suggest that age-related differences in integrating facial cues may be related to engagement of the mentalizing network, with potentially important implications for social cognitive functioning in late adulthood.

Introduction

People rely on eye gaze and emotional expressions to form expectations about others' mental states (Graham & Labar, 2012). For example, the personal significance of an angry expression depends on whether it is accompanied by direct or averted gaze. Aging diminishes the ability to process information from eye gaze (Slessor, Phillips, & Bull, 2008) and emotional expressions (Ruffman, Henry, Livingstone, & Phillips, 2008), as well as the integration of these cues (particularly for angry facial expressions; Slessor, Phillips, and Bull, 2010). Reduced sensitivity to expression and eye-gaze cues may be indicative of underlying structural and functional neural change in old age and may have potential consequences for social interaction in late adulthood. Emotion recognition constitutes a critical skill in effective social communication particularly for maintaining positive interaction and interpersonal relationships. Thus, any difficulties recognizing emotional expressions and facial cues have the potential to negatively impact on a person's capacity to develop and maintain strong social networks, with attendant consequences for health and wellbeing. Reduced sensitivity to emotional expressions and eye-gaze cues may be indicative of age-related changes in the underlying neural correlates involved in social cognitive processing.

There is now evidence that social cognitive processing imposes demands on a large number of different brain regions and their connectivity (see e.g. Molenberghs, Johnson, Henry, and Mattingley, 2016). However, it remains important to gain a more complete and nuanced understanding of the functional networks that subserve these processes, as well as how these networks change in the context of normal adult aging. This is because social cognitive difficulties are early and salient features of many clinical disorders, including many common neurodegenerative disorders associated with old age (Bora, Velakoulis, & Walterfang, 2016; Henry, von Hippel, Molenberghs, Lee, & Sachdev, 2016; Kemp, Despres, Sellal, & Dufour, 2012; McCade, Savage, & Naismith, 2011). A better understanding of the neural networks that subserve core aspects of change in social cognitive function in late adulthood could inform differential diagnosis and treatment of social cognitive impairment in this age group.

A number of neuroimaging studies have assessed age-related differences in processing emotional facial expressions (e.g., for a review see Ziaei and Fischer, 2016). While some studies found age-related decline in neural response to negative facial emotions, including regions of the medial temporal lobe such as the amygdala (Iidaka et al., 2002) and anterior-ventral insula cortex (Fischer et al., 2005), other studies reported that young and older adults recruited different brain regions irrespective of emotional valence (Gunning-Dixon et al., 2003). Direct comparisons between happy and angry expressions revealed two main findings (Ebner, Johnson, & Fischer, 2012). First, greater ventromedial prefrontal cortex (vmPFC) activity was seen during recognition of happy (relative to angry) faces across both age groups. Second, greater dorsomedial PFC (dmPFC) activity in response to angry (relative to happy) faces was more pronounced for older relative to younger adults. Taken together, these findings suggest that older and younger adults differ in the neural networks they recruit when processing emotional expressions, and that for older adults, more cognitive effort may be required to recognize angry (relative to happy) facial expressions. However, whether there are also age differences in the brain networks involved in processing and integrating communicative facial cues (i.e., directed and averted gaze), and in interaction with facial expressions, remains to be established. It also remains unclear whether age-related neural differences in processing facial affective cues are related to social cognitive functioning, such as theory of mind and social behavior. To our knowledge, our study is the first to examine the age-related changes in the neural networks involved in processing facial communicative cues and their implications for social cognitive performance.

Angry expressions in the context of direct gaze signal immediate threat to the observer. Neural responses to such threatening cues are automatic (Shepherd, 2010) and reflexive (Adams et al., 2012). In contrast, angry expressions accompanied by averted gaze signal that the anger is directed towards something else in the environment thus less likely to be interpreted as personal threat and may invoke higher-order social cognitive brain regions to determine the intentions of the angry individual (Pfeiffer, Vogeley, & Schilbach, 2013). However, because older adults show a lack of sensitivity to eye gaze in angry expressions (Slessor et al., 2010), they may also show more similar neural patterns when observing angry faces with direct and averted gaze. Additionally, age-related changes in integrating facial cues may reflect a lack of recruitment of mentalizing networks when processing social information. Recruitment of these networks may be most critical when understanding of the mental state of others is required, such as when processing angry faces with averted gaze.

Although happy expressions presented with direct versus averted eye-gaze orientations might convey different meanings, being targeted with happiness is less critical for survival than being targeted with anger. It therefore is possible that, at a neural level, there is less differentiation in the brain regions activated for direct versus averted gaze in happy expression relative to angry expressions, especially among younger adults. In contrast, given evidence that older adults are particularly motivated to attend to and process positive information such as happy faces (Carstensen, 2006; Mather & Carstensen, 2003) compared to their younger counterparts, older adults may show greater neural differentiation when processing happy expressions with different eye-gaze directions which has not been addressed in prior literature.

To fill this research gap, the aim of this study was to identify age differences in the neural substrates involved in processing happy and angry facial expressions with different eye-gaze cues. We predicted that in younger adults, distinct brain substrates would be activated in response to angry expressions with differing gaze cues. For angry faces with direct gaze, activity in the salience network, involved in identifying the most relevant stimuli in the environment and orienting attention towards them in order to adaptively guide behavior (Barrett & Satpute, 2013; Menon, 2015) should be more prominent. On the other hand, in averted gaze conditions, additional brain networks involved in mentalizing, including regions such as mPFC and superior temporal gyrus (STS) (Frith & Frith, 2006; Roy, Shohamy, & Wager, 2012; Van Overwalle, 2009; Van Overwalle & Baetens, 2009), should be engaged in decoding intentions. This study is the first to test this prediction and will therefore provide novel insights on how brain networks involved in processing facial features changing in the context of healthy aging. Because older adults showed less distinction between angry direct and averted eye gaze cues, we hypothesized attenuated neural differentiation between these conditions in older adults.

Consistent with socioemotional selectivity theory (SST) (Carstensen, Fung, & Charles, 2003), we expected older adults might show greater differentiation in processing facial expressions of happiness, because of their high motivation to attend to positive stimuli. However, the neural differentiation between direct and averted gaze should be smaller for happy than for angry expressions in younger adults. We expected to observe increased activity in the reward brain network, including regions such as vmPFC (Kringelbach & Rolls, 2004; O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001; Roy et al., 2012), during recognition of happy expressions.

Material & Methods

Participants

Twenty-one healthy older adults (aged 65-75 years; *M* = 69.75, *SD* = 2.97; 10 females) and 21 healthy younger adults (aged 17-27 years; *M* = 20.65, *SD* = 2.66; 10 females) participated in this study. One older and one younger adult were excluded from the analysis due to brain signal loss, leaving 20 participants in each group. Younger adults were undergraduate students at the University of Queensland who were reimbursed with either course credits or $15 AUD per hour. The older adults were community volunteers who were reimbursed with $20 AUD per hour. Older adults were recruited through advertising in public notice boards of different clubs, libraries, churches, and the University of Queensland's Aging Mind Initiative. All participants were right-handed English speakers who had normal or corrected-to-normal vision using MRI compatible glasses and no history of neurological impairment, psychiatric illnesses, head or heart surgery, or cardiovascular disease. Participants were screened for MRI compatibility as well as claustrophobia, neurological and psychiatric medication including mood disorder and epilepsy before taking part in this study. Participants took part in two separate sessions of testing, the first involving fMRI scanning and the second involving behavioral/neuropsychological assessment. The two sessions were conducted 3 to 4 days apart from each other. All participants were provided with written consent forms approved by the Human Research Ethics Committee at the University of Queensland and were debriefed upon the completion of the second session.

Task materials

Angry, happy, and neutral faces (100 for each expression) were drawn from the FACES database (Ebner, Riediger, & Lindenberger, 2010). Neutral faces were used as control to remove the effects of the visual perception component. All faces were colored, front-view, and high quality (300 Dots per Inch). The presented faces comprised two age groups (young posers: 18-31 years and old posers: 69-80 years). The gazes of the posers were photoshopped so that an equal number of direct and averted gazes were used for the scanner task. All faces were categorized into five lists, using MATLAB (The MathWorks Inc., MA), according to four selection criteria: age of the posers, gender of the posers, gaze direction, and emotional expression. The lists consisted of equal number of male and female posers (30 each), old and young posers (30 each), and emotional expressions (20 for each expression) and were presented in each fMRI run for a total of five runs. The order of the runs presented in the scanner was counterbalanced among participants. To control for effects of facial attractiveness on recognition of emotional expressions, faces in each list were also matched based on their attractiveness ratings from an independent study (M = 41.66, SD = 13.08; Ebner and Johnson, 2010). All of the stimuli were presented against a gray background using E-prime software, adjusted to be standardized in size (600 x 450 pixels) prior to presentation in the MRI scanner.

Experimental design

The 50-minute scanner session consisted of two components: structural magnetic resonance imaging (sMRI), functional MRI (fMRI). Prior to the scanning, participants were provided with verbal and visual instructions about the emotion recognition task and subsequently asked to practice it until they were completely familiarized with the instructions and timing of the task. The reason for training participants prior to the fMRI task was to ensure that the behavioral performance of accurate detecting the faces for both groups was equated, so that any differences at the neural level could not simply be attributed to differences in performance. Faces used in the practice run were different to those used during the main task in the scanner.

In the scanner, participants performed two runs of the emotion recognition task (described below), followed by an sMRI acquisition, followed by another three runs of the emotion recognition task. During the emotion recognition task (Figure 1), each face was presented one at a time for 3.5 sec, followed by a fixation cross. Presentation of the fixation cross was jittered using three time intervals: 0.5 sec, 1 sec, and 1.5 sec in order to allow for an independent estimation of the blood-oxygen-level dependant (BOLD) response on a trial-by-trial basis. Furthermore, using jittered inter-trial intervals can enhance statistical power in the analyses (Huettel, Song, & McCarthy, 2014). Each of the five task runs, lasted for 4.5 minutes. Participants were required to indicate, as fast and as accurately as possible, whether each face displayed a happy, angry, or a neutral emotional expression by pressing the relevant button on an

MRI-compatible response box – using index finger for either angry or happy, the middle finger for neutral, and the ring finger for either happy or angry (counterbalanced across participants).

[Insert Figure 1 about here]

Neuropsychological measures

During the behavioral sessions, all participants were asked to complete a range of background measures assessing executive control, intelligence, emotion recognition, social functioning, personality, empathy, and theory of mind (TOM) ability. Descriptive and inferential statistics of background measures are reported in Table 1. Descriptions of the measures are as follow:

National Adult Reading Test (NART): The NART (Nelson, 1982) is a valid and reliable measure of crystalized intelligence that consists of 50 irregular words. Participants were required to read each word aloud and their responses were scored by two independent coders. Interrater reliability was reported .88 (Crawford, Parker, Stewart, Besson, & Lacey, 1989).

Trail Making Test: The Trail Making Test consists of two parts, A and B (Reitan & Wolfson, 1986). In part A, participants were instructed to connect the circled numbers in sequential orders. In part B, they were instructed to alternate between numbers and letters (e.g., 1-A-2-B). This measure provides an index of executive control. Part A predominantly measures visuoperceptual abilities, whereas part B additionally indexes working memory and mental flexibility. In order to minimize visuoperceptual demands, we used the B-A index to provide a relatively pure indicator of executive control abilities (Sanchez-Cubillo et al., 2009).

Ekman Emotion Recognition test: The faces used in this experiment were drawn from the "Facial Expressions of Emotion: Stimuli and Test" stimulus set (Young, Perrett, Calder, Sprengelmeyer, & Ekman, 2002). Sixty black and white images from six basic emotional categories: anger, sadness, surprise, happiness, disgust, and fear, were presented for 3.5 secs. Participants were asked to choose the best label that describes each face and press the respective key on the keyboard. Reaction times and responses were recorded.

Peer-Report Social Functioning Scale (PRSF)**:** This scale is a peer-report assessment of social functioning (Henry, von Hippel, & Baynes, 2009). A 10-item subscale assesses socially inappropriate behavior (α = .87; e.g., "enquires about potentially embarrassing issues in public" or "comments negatively on someone else's physical appearance"). A 17-item subscale assesses socially appropriate behavior (α = .92; e.g., "speaks positively about others" or "lets other people have their say"). A 3-item subscale assesses prejudicial and stereotyping behavior (α = .75; e.g., "ignores stereotypes when making decision about people"). Participants' peers provided their responses on a 4-point scale with labels, *never, rarely, occasionally, frequently*. Higher scores indicate a higher level of socially inappropriate behavior, socially appropriate behavior, or prejudicial behavior on the three subscales. Internal consistency reliability was reported high (α = .94) (Henry et al., 2009).

Big Five Personality Inventory (BFI)**:** A 44-item self-report personality inventory was used (John, Donahue, & Kentle, 1991). This test comprises of five subscales measuring five personality dimensions, including *Extraversion* (α = .88; *8 items;* e.g., "I am someone who is talkative"), *Agreeableness* (α = .79; *9 items;* e.g., "I am someone who is helpful and unselfish with others"), *Conscientiousness* (α = .82; 9 items; e.g., "I am someone who does a thorough job"), *Neuroticism* (α = .84; *8 items;* e.g., "I am someone who is depressed, blue"), and *Openness* (α = .81; *10 items;* e.g., "I am someone who is original, comes up with new ideas"). Participants provided their responses on a scale from 1 (*strongly disagree*) to 5 (*strongly agree*) for each item to indicate the extent to which they agreed or disagreed with each statement. The reliability of this test has been estimated to be .83 (John & Srivastava, 1999).

Empathy Quotient (EQ): A 40-item adult version of the empathy quotient developed by Baron-Cohen and Wheelwright, 2004 was used in this study. Participants responded to this questionnaire by choosing one of the 4-scale response options; *strongly agree, slightly agree, slightly disagree, and strongly disagree*. On each item, a person can obtain 2, 1, or 0, so the EQ score has a maximum score of 80 and a minimum of zero. High test–retest reliability (α = .83) was reported (Lawrence, Shaw, Baker, Baron-Cohen, & David, 2004).

Reading the Mind in the Eye Test (RMET): This is a measure of theory of mind, which broadly refers to the ability to understand the mental states of others (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001). This test consists of a series of 36 photographs of the eye region of a person's face. Participants are required to choose which word (out of four words) best describes what the person in the picture is feeling or thinking. The RMET assesses how well people can decode others' mental states, and is one of the best-validated measures of theory of mind (Henry, Phillips, Ruffman, & Bailey, 2013).

[Insert Table 1 about here]

Image acquisition and analysis

Functional images were acquired using a 3T Siemens scanner equipped with a 32-channel head coil. The acquisition of functional data was achieved by using a whole-brain $T2^*$-weighted echo-planar image (EPI) sequence (93 interleaved slices, repetition time (TR) = 3000ms, echo time (TE) = 45ms, flip angle = 90º, field of view (FOV) = 192mm, voxel size = $2mm^3$). High resolution T1-weighted images were acquired with a MPRAGE sequence (126 slice with 1mm thickness, TR = 1900ms, TE = 2.3ms, inversion time (TI) = 900ms, FOV = 230ms, voxel size = $0.9mm^3$, flip angle = 90º). The tasks were presented to participants on a computer screen through a mirror mounted on top of the head coil. Participants were using earplugs and cushions inside the head coil to dampen the noise and minimize the head movement.

For functional analysis, images were preprocessed with Statistical Parametric Mapping Software (SPM8; http://www.fil.ion.ucl.ac.uk/spm) implemented in MATLAB 2010b. Following the realignment to a mean image for head-motion correction, the images were segmented to gray matter and white matter, and then spatially normalized into a standard stereotaxic space with a voxel size of $2mm^3$ using the Montreal Neurological Institute (MNI) template, and finally spatially smoothed with a 6-mm Gaussian Kernel. Data were examined for artifacts, such as ghosting in the initial stages, and individual time series were checked for motion artifact. Trials with more than 1 mm movement were excluded from analyses.

The imaging data were analyzed using a multivariate analytical technique Partial Least Squares analysis (PLS; McIntosh, Bookstein, Haxby, and Grady, 1996; McIntosh, Chau, and Protzner, 2004; for a detailed tutorial and review of PLS, see Krishnan, Williams, McIntosh, and Abdi, 2011, as implemented in PLS software running on MATLAB 2010b. PLS decomposes all images into a set of patterns that capture the greatest amount of covariance in the data, rather than making assumptions about conditions or imposing contrasts for each pattern. PLS analysis uses singular value decomposition (SVD) of a single matrix that contains all participants' data to find a set of orthogonal latent variables (LVs), which represent linear combinations of the original variables. Therefore, PLS enables one to differentiate the degree of contribution of different brain regions associated with task demands, behavioral or anatomical covariates, or functional seed activity.

The first LV usually accounts for the largest covariance of the data, with progressively smaller amount of covariance for subsequent LVs. Each LV delineates cohesive patterns of brain activity related to experimental conditions. Additionally, brain scores are calculated as the dot product of a participant's image volume of each LV. The brain score reflects how strongly each participant contributes to the pattern expressed in each LV. Therefore, each LV consists of a singular image of voxel saliences (*i.e*., a spatiotemporal pattern of brain activity), a singular profile of task saliences (*i.e*., a set of weights that indicate how brain activity in the singular image is related to the experimental conditions, functional seeds, or behavioral/anatomical covariates), and a singular value (*i.e*., the amount of covariance accounted for by the LV). Given that the task was event-related, the analysis was conducted on the 15-sec period (5 TRs), starting at the onset of each face to account for the duration of the BOLD response. Activity at each time point in the analysis was normalized to activity in the first TR. As the activation patterns identified by PLS and corresponding brain responses is done in a single mathematical step, there is no need for multiple comparison correction (McIntosh et al., 2004).

The statistical significance of each LV was assessed using a permutation test, which determines the probability of a singular value from 500 random reordering and resampling (McIntosh et al., 1996). In addition to the permutation test, to determine the reliability of the saliences for each brain voxel, a standard error of each voxel's salience on each LV was estimated by 100 bootstrap resampling steps (Efron & Tibshirani, 1985). Peak voxels with a bootstrap ratio (BSR; *i.e*., salience/standard error) > 3.0 were considered to be reliable, as this approximates $p < 0.01$ (Sampson, Streissguth, Barr, & Bookstein, 1989). In the current study, we used task PLS and brain-behavior PLS, to examine the whole-brain activity pattern for processing each emotional category as a function of eye gaze and to assess the link between performance in the emotion recognition task and TOM ability.

The procedure of the fMRI analysis was twofold. First, our main aim was to examine the impact of age on whole-brain activity during the labeling of emotional faces presented with different eye-gaze direction. We conducted whole-brain analyses of brain activity during angry and happy conditions, which were compared between the two age groups. Neutral faces were included in the experimental design as a control condition to remove the effects of the visual perception component (for a review see Sabatinelli et al., 2011. However, the ambiguity of neutral faces may lead to uncertainty and heightened vigilance, which in turn may increase amygdala activation (Blasi et al., 2009) and may be evaluated as more negative in some situations (Lee, Kang, Park, Kim, & An, 2008). Therefore, all analyses were conducted only on happy and angry facial expressions in order to avoid activation confounds due to the presence of neutral pictures. In order to demonstrate the robustness of brain responses to happy and angry expressions, additional analyses including neutral conditions were also conducted. The results are reported in the Supplementary Material in Figure 1. Overall, the brain pattern responses to happy and angry expressions did not change as a result of including neutral expressions in the whole-brain analysis. For the whole-brain analyses, all voxel activities for both age groups were included in the analyses for the four experimental conditions; angry direct, angry averted, happy direct, and happy averted. However, for simplification and greater visual clarity, conditions are illustrated separately in Figures 3&4.

Second, given that our ability to understand and respond to emotional cues in the environment is an integral part of our social cognitive ability, we examined the relationship between the recognition of facial cues and TOM performance. To explore any age-related differences in integrating facial cues in relation to social cognitive abilities, we conducted a brain-behavior analysis, examining the relationship between the neural activation involved in gaze and emotion processes and the TOM performance, the scores obtained on the RMET. For angry expressions, we included the accuracy of behavioral performance in the scanner task and correlated them with TOM scores. Because accuracy for recognition of happy expressions was at ceiling for both age groups, TOM scores were correlated with the brain activity in the two happy experimental conditions without including the behavioral performance accuracy from the emotion recognition task. For the brain-behavior analyses, all voxel activities for both age groups, accuracy from the emotion recognition task, and behavioral scores from the TOM task were included in the analyses for the two angry conditions (see Figure 5). For simplification however, we depicted the age groups in separate figures (see Figure 6). For happy expressions, all voxel activities for both age groups as well as scores from the TOM task were included in the analyses. These results are illustrated in Figure 6.

Reaction times and accuracies during the emotion recognition task were subjected to mixed-model analyses of variance (ANOVAs) with age group as the between-subjects factor and emotional expression and eye-gaze orientation as the within-subjects factors.

Results

The descriptive and inferential statistics of all background measures were reported in Table 1. Older adults scored above the recommended cut-off of 27 on a widely-used dementia screen (M = 28.38, SD = 1.28), the Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975). Significant difference between both age groups in the TOM scores measured by RMET was also found as reported in Table 1.

Emotion identification performance

A 2 (gaze direction: direct, averted) by 2 (emotional expression: angry, happy) by 2 (age group: young, older) repeated-measures ANOVA with response accuracy as the dependent measure showed that there was a significant main effect of emotional expression, $F(1, 38) = 34.85$, $p < .01$, $\eta_p^2 = .47$. This reflected greater accuracy in recognizing happy relative to angry facial expressions in both age groups (Figure 2 & Table 1). No other main effects or interactions were significant (all *F*s <1).

A similar analysis on response times of accurate responses revealed a main effect of emotional expressions, $F(1,37) = 87.68$, $p < .01$, $\eta_p^2 = .70$, with faster responses for happy relative to angry facial expressions (Figure 2 and Table 1). None of the other main or interaction effects were significant (all *F*s <1).

[Insert Figure 2 about here]

Whole-brain analyses

The whole-brain responses for angry and happy expressions for both age groups are reported in this section. First, the findings for angry expressions and then happy expressions findings for both age groups will be presented.

Angry expressions. The results from the whole-brain analyses showed two significant and distinct LVs for recognition of angry expressions as a function of eye gaze among younger but not older adults. The first LV accounted for 33% of the covariance in the data and included brain regions such as inferior frontal gyrus (IFG), anterior cingulate cortex (ACC), inferior parietal lobule (IPL), posterior cingulate cortex (PCC), and amygdala. This pattern of brain activation in young adults was found only for angry expressions with averted gaze. In contrast, older adults recruited these regions during recognition of angry expressions with *both* direct and averted gaze (Figure 3, Panel A & Table 2). LV2, which accounted for 25% of the covariance in the data, yielded a pattern that was related to the recognition of angry expressions with direct gaze only among younger adults. This pattern included insula and medial prefrontal gyrus, the main nodes of the salience network (Menon, 2015). In older adults, there was no reliable recruitment of these regions in any of the conditions (Figure 3, Panel B & Table 2). These results indicate that social cognitive brain regions, such as mPFC, IPL, STS, amygdala (Frith & Frith, 2006; Van Overwalle, 2009), were engaged among younger adults during recognition of expressions in which the understanding of the intention of expresser was required, that is angry expressions with averted gaze. The salience network, including insula, medial prefrontal gyrus, in contrast, was activated in young participants when recognizing angry expressions with possible threatening signals to the self, i.e. direct gaze. These data further demonstrate that at the neural level, younger, but not older adults, are differentiating between angry facial expressions with direct versus averted gaze.

[Insert Figure 3 & Table 2 about here]

Happy expressions. During the recognition of happy expressions, results from the whole-brain analyses revealed two LVs. The first LV included brain regions such as ACC, PCC, precuneus, angular gyrus, middle temporal gyrus (MTG), and hippocampus – known as major nodes of the default mode network (DMN; Buckner, Andrews-Hanna, and Schacter, 2008; Raichle et al., 2001). These brain regions were engaged by older adults for happy facial expressions with direct gaze. In contrast, younger adults recruited these regions for happy expressions with both direct and averted gaze (Figure 4, Panel A & Table 3). LV2 yielded a network of brain regions including medial and middle PFC, ACC, MTG, superior temporal gyrus (STG), PCC, and precuneus. These regions were engaged by older adults for happy expression with averted gaze and by younger adults for both direct and averted gaze (Figure 4, Panel B & Table 3). Overall, the whole-brain analyses for happy expressions indicate that older, but not younger adults, recruit two orthogonal networks during recognition of happy expressions as a function of eye gaze while younger adults showed no sensitivity in their neural activity patterns to the eye-gaze orientations in happy faces.

To summarize the results so far: younger adults showed the predicted differential brain activation to angry faces with direct and averted gaze, while older adults showed no such differentiation. In contrast, older adults were sensitive to gaze direction when processing happy faces, while younger adults were not.

[Insert Figure 4 & Table 3 about here]

Brain-behavior analyses

Lack of sensitivity to eye-gaze cues during recognition of angry expressions might have consequences for social cognitive abilities. Thus, if the capacity to integrate facial cues declines in late adulthood, such age-related changes might be related to the differential engagement of mentalizing or social cognitive brain regions. Brain-behavior analyses were conducted to assess the correlation between brain activity during the angry and happy recognition conditions with TOM scores obtained on the RMET (administered outside the scanner).

Angry expressions. Accuracy scores from the angry conditions in the emotion recognition task were included in the brain-behavior analysis with the scores from the TOM task for both age groups in one single analysis. Brain-behavior analyses focused on angry expressions revealed one significant LV, which accounted for 36% of the covariance in the data and yielded two patterns of brain activity. The first of these patterns included superior, middle, and inferior PFC regions as well as insula. This network subserved recognition of angry expressions with *averted* gaze among younger adults and correlated positively with TOM scores and accuracy during the recognition of angry averted gazes. That is, those younger adults who performed better on the TOM task and the recognition of angry averted gazes engaged the frontal brain regions to a larger extent than those young adults with poorer performance (Figure 5, Panel A & Table 4). The second brain pattern mainly included posterior brain regions such as PCC, precuneus, cuneus, middle occipital gyrus, inferior temporal gyrus, MTG as well as mPFC and caudate. This network subserved the recognition of angry expressions with *direct* gaze among younger adults and was correlated positively with TOM scores and accuracy during recognition of angry faces with direct gaze. In other words, younger adults who obtained higher scores on the TOM task and were better at recognizing angry faces with direct gaze recruited a set of posterior brain regions when processing angry direct gaze faces than those younger adults with poorer performance (Figure 5, Panel A & Table 4).

In older adults group, brain-behavior analyses revealed two important findings. First, activity of the posterior brain regions (i.e., PCC, precuneus, cuneus, middle occipital gyrus, inferior temporal gyrus, MTG as well as medial PFC and caudate) was correlated with TOM scores during recognition of angry expressions, irrespective of eye-gaze directions. Moreover, these regions were only correlated with TOM scores, and not with accuracy of recognizing angry faces. In other words, there were no reliable associations between TOM scores and task performance in the scanner among older adults. Older adults who obtained higher scores on the TOM task engaged only the posterior areas while recognizing angry expressions with both direct and averted eye-gaze orientation. However, activity in these regions was not related to older adults' behavioral performance in the recognition of angry expressions in the scanner (Figure 5, Panel B & Table 4).

[Insert Figure 5 & Table 4 about here]

Happy expressions. For the happy conditions, accuracy scores were at ceiling, thus, only the correlations between TOM scores and brain activation during the recognition of happy expressions were considered for both age groups. The corresponding analyses for happy expressions revealed one significant LV. This LV accounted for 32% of the covariance in the data and yielded a set of regions that were activated during the recognition of happy averted gaze among older adults and positively correlated with TOM scores. This network included superior, middle, and inferior PFC, ACC, STG, IPL, and precuneus regions. Older adults who obtained higher scores on the TOM task recruited these brain areas when they were recognizing happy expressions displayed with averted gaze more than with direct gaze, and more than younger adults (Figure 6 & Table 5).

[Insert Figure 6 & Table 5 about here]

Discussion

The present results provide novel insights into the neural substrates underlying age-related differences in integrating facial affect and eye gaze cues. First, the whole-brain results showed that, in contrast to younger adults, older adults' brain activity was not modulated by eye-gaze direction during the recognition of angry expressions. Second, the brain-behavior results showed that the ability to integrate angry expression and gaze cues was related to TOM ability; for younger, but not older adults. TOM ability was differentially correlated with two distinct networks of brain regions activated as a function of eye-gaze direction in the presence of an angry expression. The brain-behavior correlations indicated that older adults' lack of neural sensitivity to eye gaze with angry expressions was related to decreased recruitment of the main nodes of the mentalizing network, such as mPFC, STS, and amygdala (Frith & Frith, 2006; Molenberghs et al., 2016; Van Overwalle, 2009) in situations in which interpreting the intentions of the expresser is important; angry expressions with averted gaze.

In keeping with previous research indicating that older adults are more motivated to process positive facial expressions, older, but not younger, adults' brain activity was modulated by eye-gaze direction during the recognition of happy expressions by recruiting the major nodes of the default mode network, such as vmPFC, PCC, and precuneus (Buckner et al., 2008; Raichle et al., 2001). For happy expressions, older adults recruited the mentalizing brain regions for averted gaze conditions more than in the direct gaze condition, as well as relative to their younger counterparts. This finding is in line with the results from the whole-brain analyses, and might reflect well-documented motivational changes away from negative and towards positive information shown to occur with age (Carstensen, 2006).

Eye- gaze modulation to angry expression

Younger adults recruited areas of a more localized brain network including insula and anterior cingulate regions – major nodes of a salience network – during recognition of angry expression with direct relative to averted gaze. The engagement of the salience network is in line with the notion that angry expressions with direct gaze are considered to be more self-relevant (N'Diaye, Sander, & Vuilleumier, 2009; Sander, Grandjean, Kaiser, Wehrle, & Scherer, 2007; Sander, Grandjean, & Scherer, 2005) and important for survival. Therefore, a less distributed neural activation and fewer executive control regions should be required to recognize angry expressions with direct gaze. On the other hand, younger adults recruited a more distributed network of regions, including more fronto-parietal regions during averted gaze. Because angry expressions with averted gaze convey ambiguous signals to the observer (Adams, Gordon, Baird, Ambady, & Kleck, 2003; Adams & Kleck, 2005), it was anticipated that angry expressions with averted gaze would impose greater demands on cognitive operations such as executive control and core social cognitive brain regions to understand the mental states of the expresser. The whole-brain results therefore aligned with our predictions that two different networks of brain regions should be involved among young adults for processing angry expressions, one involved in encoding threatening signals with direct gaze and one engaged social cognitive processes when the expressions were presented with averted gaze. It has to be noted that the two LVs yield two brain patterns that are orthogonal to each other, suggesting that the two brain patterns revealed for the angry direct and averted conditions are meaningfully different from each other.

Older adults, on the other hand, recruited a distributed and large-scale pattern of brain activity, during the recognition of angry expressions irrespective of the eye gaze. This finding provides support for the age-related neural dedifferentiation hypothesis, whereby older adults show reduced distinctiveness of neural representation in domain-specific areas (Li, Lindenberger, & Sikström, 2001). Dedifferentiation has been evidenced in a variety of cognitive tasks in late adulthood, including memory processing (Carp, Gmeindl, & Reuter-Lorenz, 2010; Carp, Park, Polk, & Park, 2011; St-Laurent, Abdi, Burianová, & Grady, 2011), visual perception (Park et al., 2004), as well as cognitive load-dependent processes (Burianová et al., 2015; Grady, 2008). The pattern of dedifferentiation among older adults in the present study suggests that they might exert greater executive control than needed when processing angry expressions (Dirnberger, Lang, & Lindinger, 2010). The lack of specificity in recruiting brain networks for angry expressions with different eye gaze among older cohorts is also consistent with behavioral findings showing less distinction between interpreting angry expressions with direct and averted gaze (Slessor et al., 2010). This finding may reflect a neural inefficiency in older adults processing threatening stimuli. This pattern of response may be related to the greater cognitive control resources older adults recruit while processing angry expressions or the regulatory effort they employ during processing of these emotions (Ebner et al., 2012).

In the current study we found no age difference in behavioral performance on the emotion recognition task. However, given that the task is not demanding in general and all our older adults' participants were high functioning as indicated by their performance on the background cognitive assessments, behavioral differences were not anticipated. It is also important to note that all participants were trained and practiced the task prior to the fMRI session. The reason for training participants prior to the fMRI task was in fact to try and ensure that the performance of the groups for accurate detecting the faces was equated, so that any differences at the neural level could not simply be attributed to differences in performance. Therefore, the relatively low demands of the task, the high functioning nature of the older adult cohort, as well as the training procedure used likely all contributed to the two groups' similar behavioral performance.

Angry expressions and TOM

Younger adults who were better at recognizing angry faces with averted gaze and who also obtained higher scores on the measure of TOM obtained from RMET, showed greater recruitment of the anterior PFC regions, such as medial PFC and IFG. In revealing a correlation between activity in mPFC, TOM scores, and accuracy in emotion recognition in the present data suggests that the recognition of angry expressions with averted gaze (relative to direct gaze) may impose greater social cognitive demands relying on mPFC and IFG as key regions of the mentalizing network (Schurz, Radua, Aichhorn, Richlan, & Perner, 2014). Task-related activation differences also emerged, whereby angry expressions with averted gaze engaged anterior brain regions and angry expression with direct gaze engaged more posterior regions, supporting functional specialization of the mentalizing network (Schurz et al., 2014).

In contrast to their younger counterparts, older adults showed no reliable association between task performance and TOM scores. In addition, older adults' TOM capacity was only correlated with activity in the posterior parts of the mentalizing network, such as the parietal region, when they were making explicit judgments about emotional expression of angry faces in the scanner task. The absence of any association between anterior PFC and TOM scores in older adults is consistent with the results of Moran et al. (2012), who also found age-related decline in recruitment of dorsal mPFC during various social cognitive tasks. The age-related decline in integrating facial cues during recognition of angry expressions could potentially be associated with older adults' difficulties in reorienting social attention or higher-order mentalizing processes during averted gaze in angry faces, as this was the condition that imposed greatest demands on social cognitive ability. It is possible that the extent of age-related differences in neural regions is predictive of behavioral age differences in processing and implicitly responding to basic facial cues as well as social cognitive tasks.

Eye-gaze modulation to happy expression

For happy expressions, whole-brain analyses revealed that older adults recruited two networks of brain regions as a function of direct vs. averted gaze. This gaze-dependent differentiation was unique to older adults, as no neural modulation was found for younger adults in response to eye-gaze direction. Older adults' greater sensitivity to eye gaze when processing happy expressions coupled with older adult's *in*sensitivity to eye-gaze cues when processing angry expressions, align with findings on the positivity effect in aging (Reed & Carstensen, 2012; Reed, Chan, & Mikels, 2014), showing age-related biases in attention, memory, and decision-making towards positive emotional information (Brassen, Gamer, & Buchel, 2011; Mather & Carstensen, 2003, 2005; Ziaei, von Hippel, Henry, & Becker, 2015). Specifically, the current data showing greater sensitivity to happy expressions with different eye gaze cues may most parsimoniously be explained in terms of the well-documented motivational shifts seen in late compared to young adulthood. One of the ways in which this motivational shift is argued to manifest is via an age-related positivity effect, whereby older adults exhibit greater attention towards and memory for positive relative to negatively valenced information (Reed et al., 2014). The current study indicates that older adults' attentional bias may also be reflected at the neural level, via the recruitment of differential neural substrates toward positive expressions with different social communicative cues. As noted, this neural sensitivity was not evident for negative facial expressions. It has to be noted that depending on this region's functional network, mPFC could be involved in mentalizing, self-referential, pain, reward, or social cognitive processing (Roy et al., 2012). Although much remained to be addressed about the role of the vmPFC in each of these domains, the functional network connected to this region seems to be essential in understanding the processes that this region subserves for any particular task.

In line with the dedifferentiation hypothesis, in the present study older adults' brain activity was indistinguishable for direct and averted eye gaze. That is, older adults recruited the same, single network for both angry direct and averted gaze conditions. However, recognition of happy expressions is presumably easier for older adults and/or they are more motivated to process these expressions in general (consistent with Socioemotional Selectivity Theory). Therefore, as a result of greater availability of cognitive resources while processing happy expressions, older adults are able to differentiate between direct and averted gaze for happy expressions. Taken together, the dedifferentiation explanation for angry expressions is not in contradiction with the findings for happy expressions, as angry and happy conditions may differ in their relative cognitive demands.

Happy expressions and TOM

Additionally, the brain regions involved during recognition of happy expressions and correlated with TOM scores support the motivational shift toward positive information. Brain areas mainly included the parietal lobes, mPFC, and PCC, superior temporal gyrus - the main nodes of default mode network (Buckner et al., 2008; Raichle et al., 2001). Previous studies found increased activity of ventromedial prefrontal cortex during happy relative to angry expressions (Ebner et al., 2012). There is an overlap between the coordinates they reported with the mPFC region found in this study. Activity of this region is thought to reflect affective responses to cues which may be associated with reward (Roy et al., 2012) and lower cognitive demand. In other words, happy expressions seem to be more easily accessible and require lower cognitive demand, which consequently engage DMN more than angry expressions. Furthermore, engagement of DMN during recognition of happy expressions is consistent with TOM studies that reveal activity of DMN components. One of the subregions of this network, the mPFC, is activated when “thinking about the complex interactions among people that are conceived of as being social, interactive, and emotive like oneself” (Buckner et al., 2008, p. 24). The correlations identified between DMN activity and TOM scores during recognition of happy expressions, therefore suggest that older adults may be motivated to engage in social cognitive processing when the facial cues are of particular interest to them (i.e., depict positive affective states), and consequently they will notice the facial cues expressed with happy facial expressions more than angry expressions.

One potential mechanism that may contribute to the observed age differences are the well-documented changes in neural structural integrity seen in late adulthood (For reviews see Grady, 2012; Li et al., 2001). Several studies have now shown important links between gray and white matter structural integrity and functional brain activity (Burianová et al., 2015; de Chastelaine, Wang, Minton, Muftuler, & Rugg, 2011; Legon et al., 2015; Persson et al., 2006; Zhu, Johnson, Kim, & Gold, 2015). Therefore, it is possible that structural changes underlie the age-related differences processing emotional expressions identified in the present study. Future studies are needed to test this possibility, and investigate how age-related structural changes in main nodes of emotional processing, such as the amygdala, and white matter tracks between the amygdala and PFC, such as uncinate fasciculus, are related to brain activity when processing emotional expressions.

Finally, two methodological limitations of this study need to be acknowledged. First, most of the neuroimaging literature focused on emotion processing used three emotions, angry, happy, and neutral expressions which limit inferences about potential age-related change for other emotions. Future neuroimaging studies should also include other emotional expressions such as fear and disgust to advance insight into the nature and magnitude of age-related change in the neural networks that subserve these critical social cognitive operations. Second, the perceptual properties of the happy faces, and in particular the fact that teeth were visible, could have influenced the findings of this study. This is because visible teeth have been shown to create an advantage in detecting happy faces in visual search paradigms (Horstmann & Ansorge, 2009), and may therefore have facilitated faster response times for happy expressions in both age groups. Thus, while an important consideration in this study was to use stimuli that represent natural emotional expressions as closely as possible, further investigation is now needed to examine the contribution of specific perceptual features, e.g., teeth, in integrating facial cues among both age groups.

Nevertheless, these caveats aside, the present study is the first to provide evidence that the brain networks that subserve the recognition of angry expressions are modulated by eye-gaze direction for younger but not older adults. For happy expressions, the reverse pattern of neural specificity emerged, with older (but not younger) adults showing neural sensitivity to eye gaze direction. These results are consistent with the broader gerontological literature that shows there are motivational shift toward positive emotional information in late adulthood. Moreover, the pattern of brain-behavior correlations showed that two networks of brain regions were differentially correlated with TOM abilities and the ability to recognize angry expressions as a function of eye gaze, but only among younger adults. Taken together, these findings provide novel insights into the underlying brain networks involved in processing socially communicative signals. Given that a core feature of many psychiatric, neurological, and neurodegenerative illnesses is impaired social cognitive abilities (Henry et al., 2016; Poletti, Enrici, & Adenzato, 2012; Sprong, Schothorst, Vos, Hox, & Van Engeland, 2007; Stewart, Catroppa, & Lah, 2016; Yu & Wu, 2013), in the long term, this information has the potential to be used as biomarkers for early diagnosis of many clinical disorders.

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Legends

Figure 1. Example of Experimental Design. Each trial consisted of a presentation of a face with happy, angry, or neutral expressions for 3.5 second. Equal numbers of male and female faces with direct and averted gaze were presented. Fixation crosses were jittered using 0.5 second, 1 second, and 1.5 second time intervals. In total, the task consisted of 5 runs, 4.5 minutes each. During the task, participants were required to indicate the emotional expressions of each face by using a MRI compatible response buttons. Abbreviation: ITI = Inter-Trial Interval.

Figure 2. Behavioral Results from Emotion Recognition Task. Recognition of happy expressions was faster and more accurate relative to angry expressions for both age groups. However, there were no significant differences between avert or direct gaze in accuracy rates and RTs in either of the age groups.

Figure 3. Whole-Brain Results for Angry Expressions. Patterns of whole-brain activity during the recognition of angry expressions with averted gaze among younger adults (YA) and both eye-gaze directions among older adults (OA) (A), angry expressions with direct gaze among YA, without any reliable effects among OA (B), relative to other conditions (derived from LV1 & 2). Error bars denote 95% confidence intervals for the correlations calculated from the bootstrap procedure. All reported regions have BSR ≥ 3 and cluster size ≥ 100 voxels. All of the analyses were conducted by including both age groups. In order to simplify the visuals of the findings in the figures, the results are presented separately for each age group and condition. Abbreviations: L = left hemisphere, R = right hemisphere, OA = older adults, YA = younger adults, LV = latent variable.

Figure 4. Whole-Brain Results for Happy Expressions. Pattern of whole-brain activity during the recognition of happy expressions with averted gaze among OA and both eye-gaze directions among YA (A), and happy expressions with direct gaze among OA and both eye-gaze directions among YA (B), relative to the other conditions (derived from LV1 & 2). Error bars denote 95% confidence intervals for the correlations calculated from the bootstrap procedure. All reported regions have BSR ≥ 3 and cluster size ≥ 100 voxels. All of the analyses were conducted by including both age groups. In order to simplify the visuals of the findings in the figures, the

results are presented separately for each age group and condition. Abbreviations: L = left hemisphere, R = right hemisphere, OA = older adults, YA = younger adults.

Figure 5. Brain-behavior Results for Angry Expressions and Theory of Mind Measure. (A) Left panel: a pattern of whole-brain activity during recognition of angry expressions with averted gaze (top row) and direct gaze (bottom row) that correlated with scores on theory of mind (TOM) as measured by the Reading the Mind in the Eye Test (RMET) among younger adults. Right panel: correlations between TOM scores and performance on the scanner task during recognition of angry expressions. (B) Left panel: a pattern of whole-brain activity during recognition of angry expressions that correlated with TOM scores among older adults during angry expressions with averted gaze (top row) and direct gaze (bottom row). Right panel: correlations between TOM scores and performance on the scanner task during recognition of angry expressions. The brain activity presented depicted in the Direct gaze condition for younger adults and Direct and averted gaze for older adults are identical. Error bars denote 95% confidence intervals for the correlations calculated from the bootstrap procedure. All reported regions have BSR ≥ 3 and cluster size ≥ 100 voxels. All of the analyses were conducted by including both age groups. In order to simplify the visuals of the findings in the figures, the results are presented separately for each age group and condition. Abbreviations: L = left hemisphere, R = right hemisphere.

Figure 6. Brain-behavior Results for Happy Expressions and Theory of Mind Measure. Left panel: a pattern of whole-brain activity during recognition of happy expressions with averted gaze that positively correlated with the theory of mind (TOM) scores measured by Reading the Mind in the Eye Test (RMET) among older adults. This analysis was conducted by including both age groups. Right panel: correlations between TOM scores and performance on the scanner task during recognition of happy expressions. All reported regions have BSR ≥ 3 and cluster size ≥ 100 voxels. Abbreviations: L = left hemisphere, R = right hemisphere.

Illustrations

Figure 1

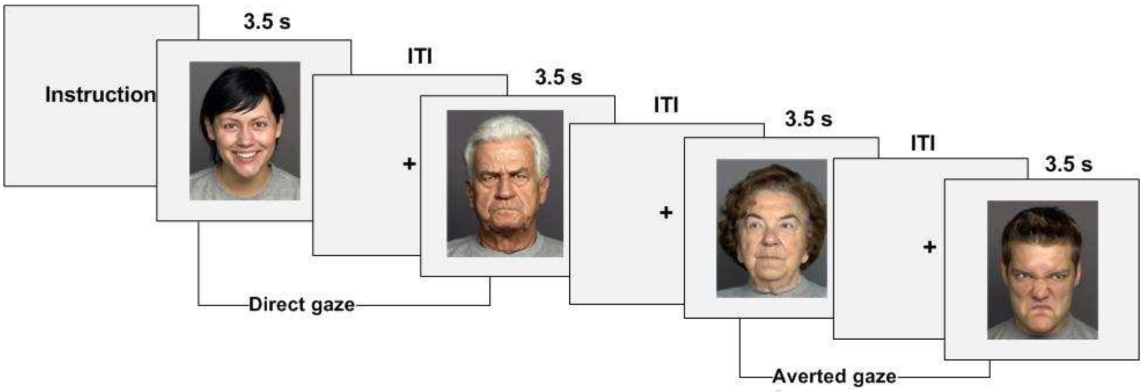


Figure 2

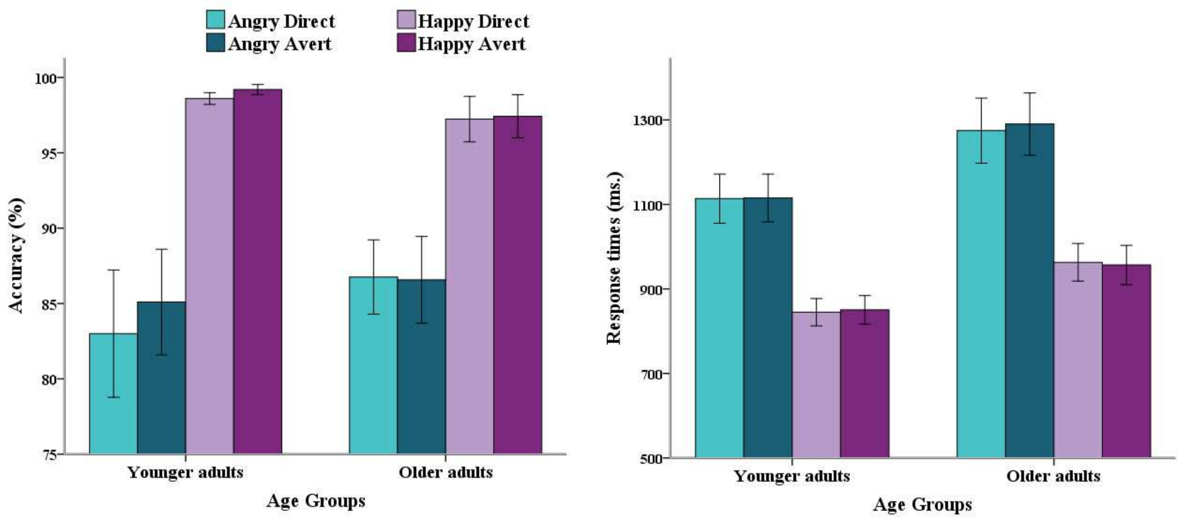


Figure 3

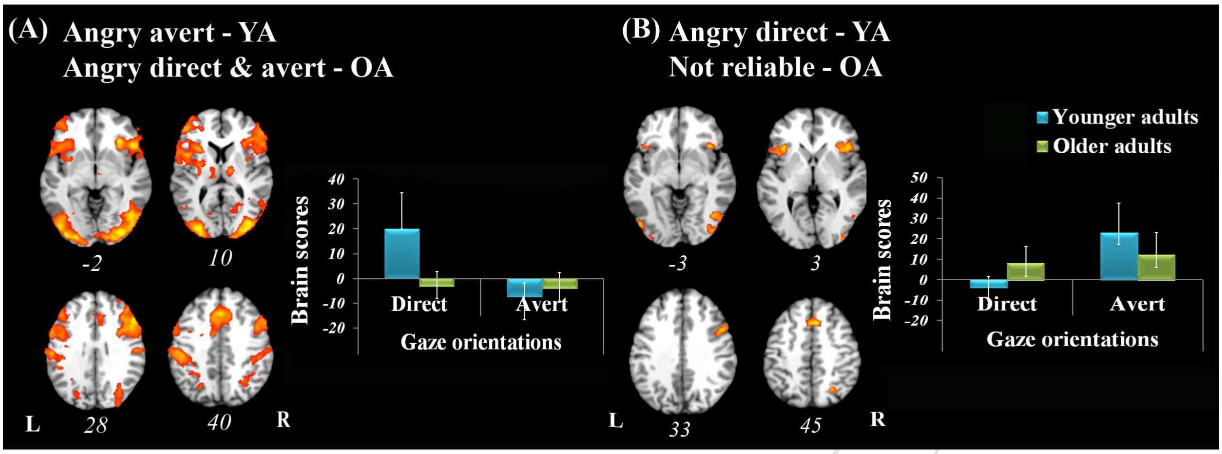


Figure 4

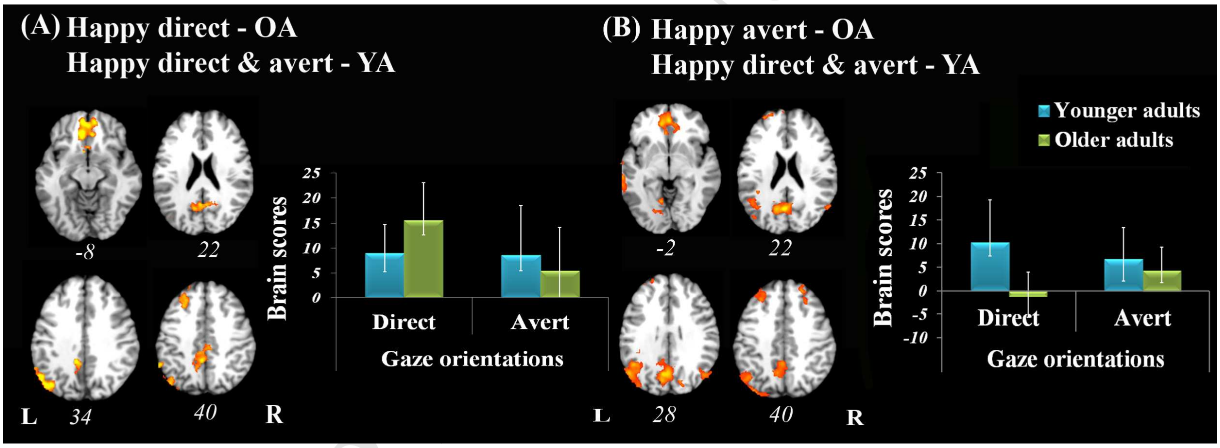


Figure 5

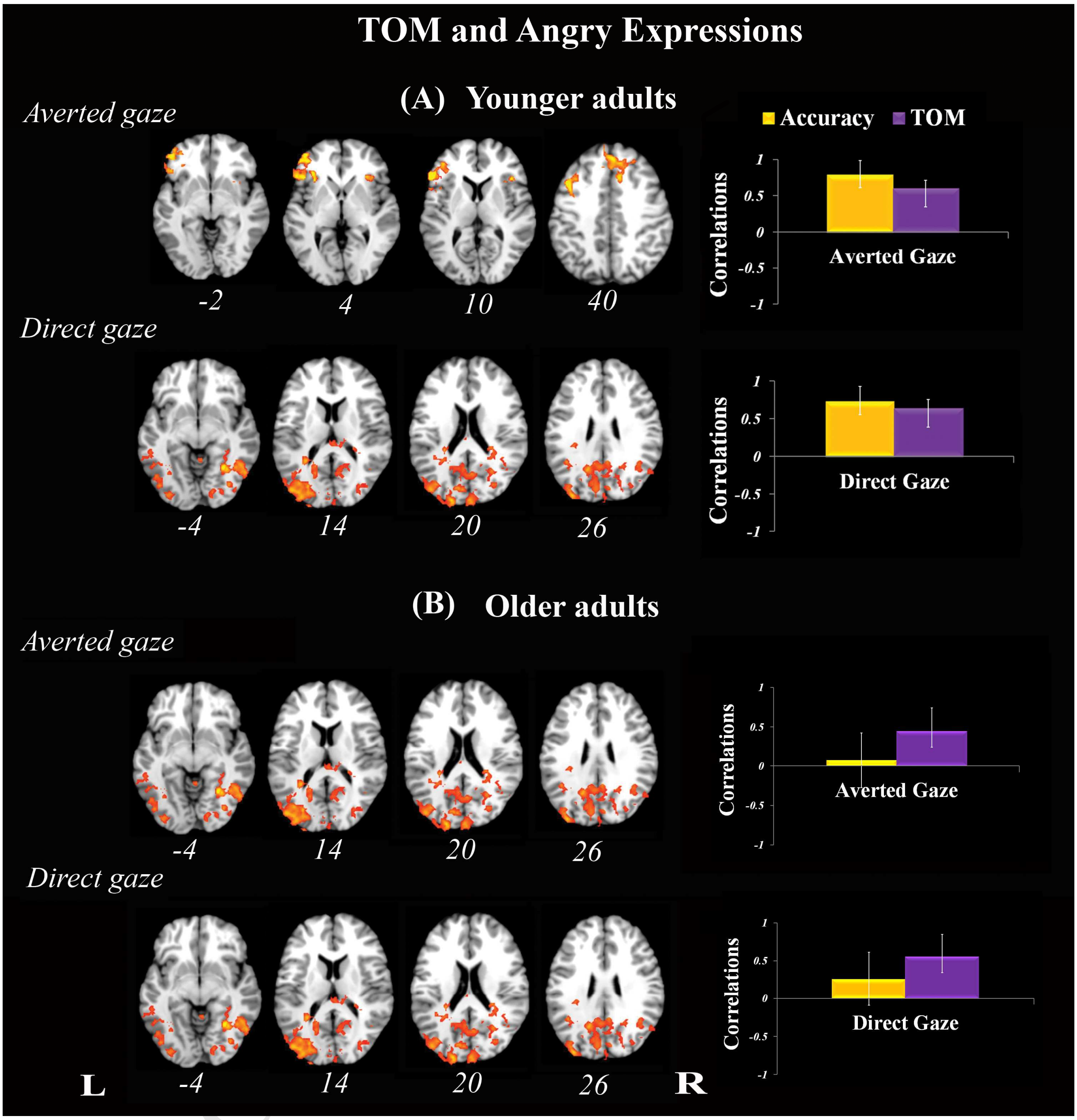
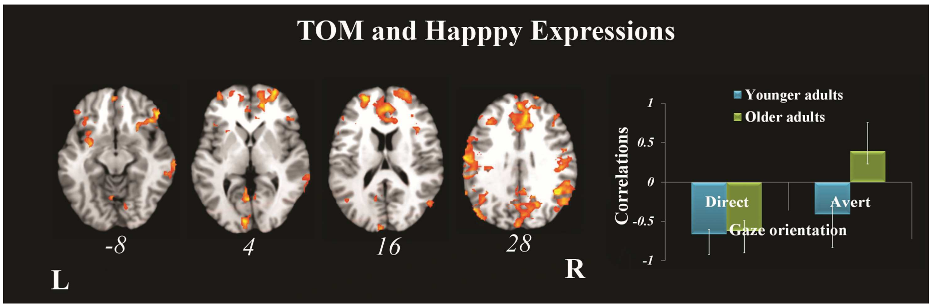

TOM and Angry Expressions
(A) Younger adults
Averted gaze
-2
4
10
40
Direct gaze
-4
14
20
26
Accuracy
TOM
Correlations
1
0.5
0
-0.5
-1
Averted Gaze
Direct Gaze
(B) Older adults
Averted gaze
Direct gaze
L
R

Figure 6


TOM and Happpy Expressions
-8
4
16
28
L
R
Younger adults
Older adults
Correlations
1
0.5
0
-0.5
-1
Direct
Avert
Gaze orientation

Tables

Table 1. Descriptive and inferential statistics for the background cognitive measures

Measure	Younger adults		Older adults		Inferential statistics		
	M	*SD*	*M*	*SD*	*t*	*df*	*Effect size (Cohen's d)*
Age	20.65	2.66	69.75	2.97			
Education (years)	14.26	1.48	15.29	3.00	1.34	38	.43
NART FSIQ	113.84	3.76	118.33	2.93	4.23**	38	1.37
Trail Making Test							
Trail A in ms.	1789.17	667.67	2780.0	635.94	4.74**	37	1.55
Trail B in ms.	3758.26	1971.73	5830.19	2103.62	3.20**	38	1.03
B-A Index	2031.00	2126.95	3050.19	1763.61	1.63	37	.53
RMET	27.47	1.94	23.65	5.54	2.69*	35	.90
Ekman emotion recognition							
Sadness	7.78	1.81	7.71	1.48	0.14	38	.04
Disgust	7.68	1.56	7.85	1.79	0.32	38	.10
Happiness	9.60	0.58	9.85	0.35	1.14	38	.36
Surprise	9.15	1.06	8.66	1.71	1.07	38	.34
Fear	7.21	2.55	7.57	2.11	0.48	38	.15
Anger	7.36	1.64	8.00	1.54	1.25	38	.40
PRSF							
Social Inappropriateness	19.73	4.90	17.28	5.44	1.49	38	.48
Social Appropriateness	58.10	6.90	61.57	5.38	1.78	38	.57
Prejudice	6.84	1.06	6.71	0.90	0.41	38	.13
Empathy Quotient	42.16	10.35	46.57	14.04	1.12	38	.36
Big Five Inventory							
Extraversion	27.89	6.05	25.61	6.25	1.16	38	.37
Agreeableness	31.31	3.41	33.33	2.72	2.07*	38	.67

Conscientiousness	30.78	5.66	36.80	5.17	3.51**	38	1.13
Neuroticism	21.10	6.17	19.05	6.26	1.03	37	.33
Openness	33.36	6.29	36.76	6.43	1.68	38	.54

Note. * $p < .05$, ** $p < .005$. NART FSIQ = National Adult Reading Test Full-Scale Intelligence Quotient, RMET = Reading the Mind in the Eye Test, PRSF = Peer-Report Social Functioning Scale, ms. = millisecond.

Table 2. Peak coordinates for clusters from whole-brain analyses for angry facial expressions

Regions	Hem	BA	MNI coordinates XYZ	BSR
Angry averted gaze – Younger adults				
Angry direct and averted gaze – Older adults				
Middle frontal gyrus	R	9	[51 26 27]	7.77
	L	9	[-58 8 26]	5.10
Inferior frontal gyrus	R	45/47	[46 22 -1]	6.77
	L	45/47	[-44 20 -6]	5.13
	L	46/10	[-43 45 10]	5.17
Anterior cingulate cortex	R	32	[0 24 41]	6.86
Insula	L	13	[-31 17 10]	5.42
	R	13	[46 21 -1]	6.63
Postcentral gyrus	L	3	[-36 -24 55]	5.81
	R	2	[54 -14 29]	4.60
Inferior parietal lobule	L	40	[-45 -26 41]	6.03
	R	40	[47 -27 41]	4.06
Posterior cingulate cortex	R	31	[32 -68 30]	4.28
Precuneus	R	7	[36 -52 48]	5.55
	L	7	[-26 -54 50]	2.97
Fusiform gyrus	R	37	[48 -64 -9]	6.83
	L	37	[-39 -67 -9]	4.40
Cerebellum	L		[-9 -76 -22]	6.60
	R		[9 -74 -22]	5.03

Middle occipital gyrus	R	18	[32 -82 3]	7.80
	L	18	[-34 -88 3]	7.44
Occipital gyrus	R	19	[32 -77 -9]	5.72
	L	19	[-34 -75 -9]	5.73
Thalamus	R		[14 -12 9]	5.07
	L		[-9 -20 9]	3.80
Amygdala	R		[23 -7 -13]	4.97
Angry direct gaze – Younger adults				
Insula	R	13	[42 22 4]	4.51
	L	13	[-34 22 4]	4.83
Medial prefrontal gyrus	R	6	[6 20 46]	5.82
Precentral gyrus	R	9	[43 12 30]	3.94

Hem = hemisphere, BA = Brodmann Area, BR = Bootstrap Ratio, x coordinate = right/ left; y coordinate = anterior/posterior; z coordinate = superior/inferior.

Table 3. Peak coordinates for clusters from whole-brain analyses for happy expressions

Regions	Hem	BA	MNI coordinates XYZ	BSR
Happy direct gaze – Older adults				
Happy direct & averted gaze – Younger adults				
Anterior cingulate cortex	L	24	[-7 36 -8]	4.83
	L	10	[-3 63 8]	3.91
Supramarginal gyrus	L	40	[-58 -50 38]	3.83
Angular gyrus	L	39	[-44 -73 38]	3.64
Middle temporal gyrus	L	21	[-54 -8 -19]	3.63
Posterior cingulate cortex	L	31	[-2 -32 44]	4.45
	L	30	[-12 -56 20]	4.23
Precuneus	R	7	[32 -66 39]	3.89
	L	23	[-4 -58 16]	4.38
Middle occipital gyrus	R	19	[36 -87 12]	4.48
Hippocampus	R		[35 -35 -9]	3.79
Happy averted gaze – Older adults				
Happy direct & averted gaze – Younger adults				
Medial prefrontal cortex	R	9	[4 60 13]	4.42
Anterior cingulate cortex	R	24	[2 28 -14]	4.69
	R	32	[0 46 -5]	5.91
Middle frontal gyrus	L	8	[-25 35 43]	3.81
	R	8	[27 30 43]	4.11
Middle temporal gyrus	R	39	[50 -66 26]	3.88

Superior temporal gyrus	L	22/42	[-64 -31 6]	5.07
	L	39	[-47 -54 26]	4.39
Posterior cingulate cortex	L	31	[-2 -45 43]	3.84
Precuneus	L	31/23	[-2 -64 25]	5.42
Cerebellum	L		[-11 -57 -5]	4.61

Hem = hemisphere, BA = Brodmann Area, BR = Bootstrap Ratio, x coordinate = right/ left; y coordinate = anterior/posterior; z coordinate = superior/inferior.

Table 4. Peak coordinates for clusters from brain-behavior analyses for angry expressions and Reading the Mind in the Eye Test (RMET) performance

Regions	Hem	BA	MNI coordinates XYZ	BSR
Angry averted – Younger adults				
Superior frontal gyrus	R	8	[0 42 41]	3.92
	L	6	[-3 14 59]	4.41
Middle frontal gyrus	L	8/9	[-44 14 43]	5.39
Inferior frontal gyrus	L	45	[-51 27 6]	4.50
Middle frontal gyrus	L	10/46	[-40 44 4]	4.15
Insula	L	13	[-32 22 4]	4.77
Angry direct – Younger adults				
Angry direct and averted – Older adults				
Medial prefrontal gyrus		6	[3 7 61]	4.70
Inferior temporal gyrus	R	37	[50 -54 -4]	4.51
	R	19	[29 -56 -4]	5.23
Middle temporal gyrus	L	39	[-41 -79 20]	4.61
	L	22	[-49 -49 0]	5.49
Middle occipital gyrus	L	19	[-34 087 12]	5.77
Posterior cingulate cortex	L	30	[-18 -62 15]	3.87
	R	31	[0 -50 33]	5.05
Precuneus	R	7	[26 -63 33]	4.66
	L	31/7	[-12 -64 33]	3.50
Cuneus	R	7	[23 -71 38]	3.75

	L	7	[-24 -81 38]	4.34
Thalamus	R		[0 -27 15]	3.23
Caudate	R		[25 -33 15]	3.75
	L		[-26 -35 20]	4.38

Hem = hemisphere, BA = Brodmann Area, BR = Bootstrap Ratio, x coordinate = right/ left; y coordinate = anterior/posterior; z coordinate = superior/inferior.

Table 5. Peak coordinates for clusters from brain-behavior analyses for happy expressions and Reading the Mind in the Eye Test (RMET) performance

Regions	Hem	BA	MNI coordinates XYZ	BSR
Happy averted gaze – Older adults				
Superior frontal gyrus	R	10	[28 60 5]	5.11
	L	10	[-21 54 18]	7.10
Anterior cingulate cortex	L	32	[-4 41 9]	4.42
Middle frontal gyrus	R	6/8	[44 15 41]	5.32
Insula	L	13	[-56 -36 24]	4.06
Inferior frontal gyrus	L	9	[-57 12 24]	5.11
	L	45/47	[-36 27 -4]	6.55
Postcentral gyrus	L	3	[-44 -17 44]	4.74
Precentral gyrus	L	4/6	[-47 -4 49]	5.10
Cingulate gyrus	L	23	[-4 -11 33]	4.07
Superior temporal gyrus	R	39	[44 -48 27]	6.63
	L	39	[-42 -56 25]	4.63
Inferior parietal lobule	L	40	[-54 -23 31]	5.14
	R	40	[52 -48 35]	7.01
Angular gyrus	L	39	[-44 -66 33]	5.11
Precuneus	R	31	[22 -64 27]	4.62
	L	31	[-4 -60 25]	4.44
Cuneus	R	18	[0 -87 25]	4.24
Cerebellum	L		[-4 -62 -4]	4.84

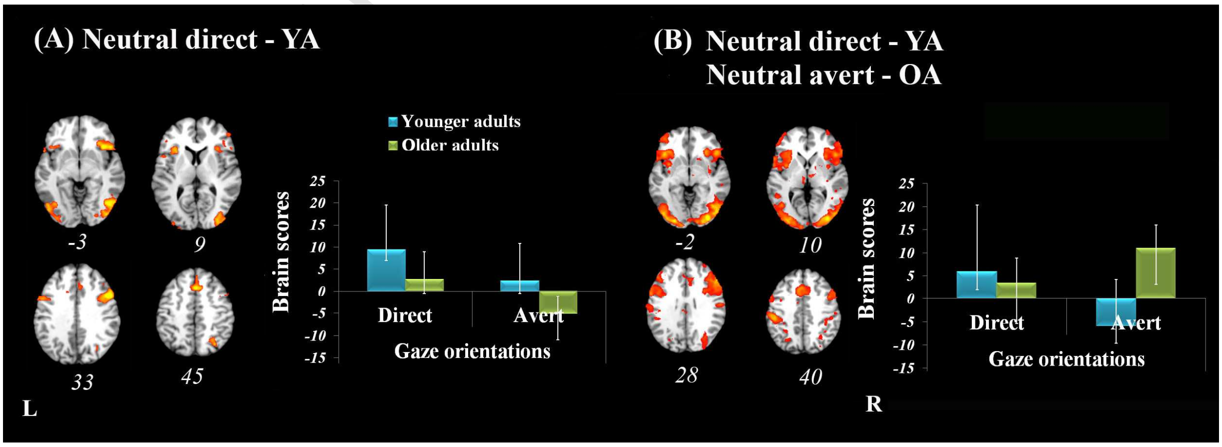
Hem = hemisphere, BA = Brodmann Area, BR = Bootstrap Ratio, x coordinate = right/ left; y coordinate = anterior/posterior; z coordinate = superior/inferior.

Supplementary Material

Additional Whole-brain Analyses

Additional analyses were conducted including all *three* emotions at the whole-brain level. One significant LV was found. LV1 accounted for 40% variance of the data. For older adults, LV1 reflected a brain pattern that included inferior frontal gyrus (IFG), anterior cingulate cortex (ACC), inferior parietal lobule (IPL), posterior cingulate cortex (PCC), and amygdala during recognition of neutral expressions with averted eye gaze (Supplementary Figure 1- panel B). Younger adults, however, recruited different brain regions, including insula and medial prefrontal gyrus, the main nodes of the salience network, for neutral expression with direct eye-gaze direction (Supplementary Figure 1 – panel A).

These findings are in line with previous studies suggesting that neutral emotions may be perceived as uncertain and in turn may activate the amygdala (Blasi et al., 2009) and may be evaluated as more negative (Lee et al., 2008). Future studies are now needed to clarify the factors contributing to age-related differences in perception of neutral emotions. The age of the posers used in the task provide one potential reason why brain regions known to be involved in processing angry emotions were also activated when processing neutral expression. Specifically, older posers' facial features, such as wrinkles, may have influenced the perception of the faces whereby neutral faces are more likely to be perceived as angry when expressed by older relative to younger posers.

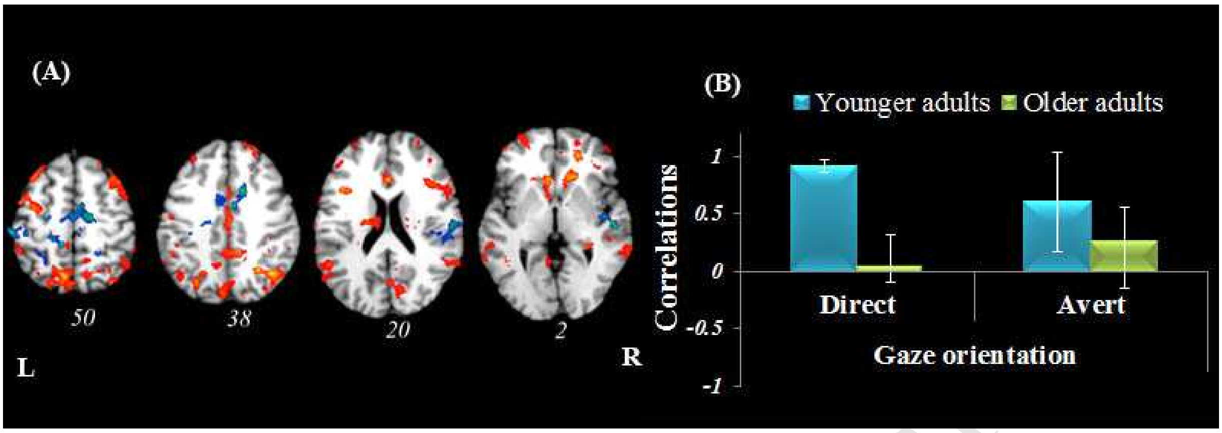


Supplementary Figure 1. Whole-Brain Results for Neutral Expressions. Pattern of whole-brain activity during the recognition of neutral expressions with direct gaze among YA (A), and neutral expressions with direct among YA and averted gaze among both OA (B), relative to the other conditions. Error bars denote 95% confidence intervals for the correlations calculated from the bootstrap procedure. All reported regions have BSR ≥ 3 and cluster size ≥ 100 voxels. All analyses were conducted by including both age groups, however, in order to simplify the visuals of the findings in the figures, we presented the results separately for each age group and condition. Abbreviations: OA = older adults, YA = younger adults, L = left hemisphere, R = right hemisphere.

Additional Brain-Behavior Analyses

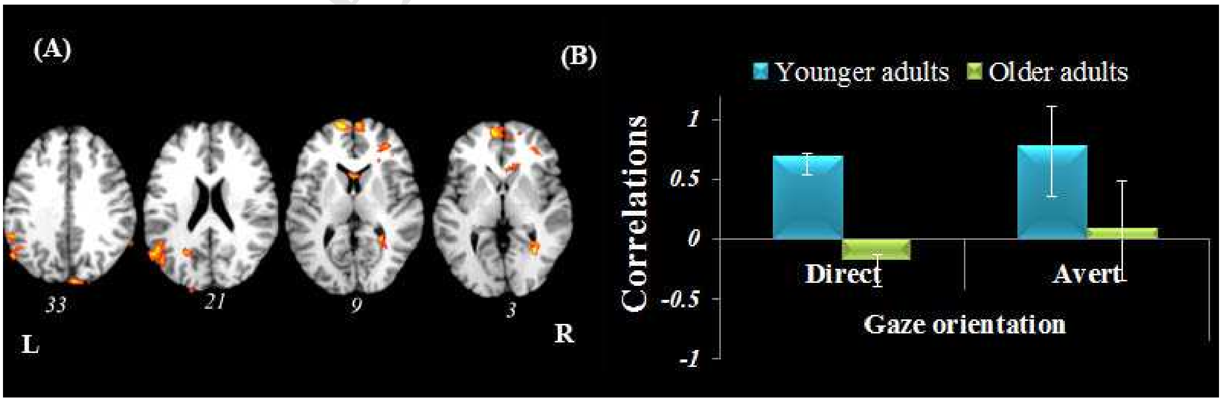
Prior to assessing brain-behavior correlations with theory of mind (TOM) scores, brain-behavior correlations were computed to investigate the brain networks that were related to performance on the emotion recognition task, as indexed by response latency and accuracy. Given that responses to happy faces were at ceiling, only behavioral performance during recognition of angry expression contributed to these analyses.

These analyses focused on angry expressions revealed one significant LV, which accounted for 46% of the covariance in the data and yielded two patterns of brain activity. The first of these patterns included right medial frontal gyrus, bilateral cingulate gyrus, superior parietal cortex, left inferior parietal lob, right insula, bilateral precuneus, and cerebellum (Blue regions in panel A, Supplementary Figure 3). This network correlated positively with RTs during the recognition of angry expression with *direct* gazes among younger adults. That is, younger adults who responded slower to angry direct gaze recruited these brain regions more. The second pattern included bilateral IFG, superior frontal gyrus, right ACC, bilateral superior temporal gyrus, left middle temporal gyrus, bilateral caudate, left thalamus, left insula, posterior cingulate gyrus, and left fusiform gyrus (yellow regions in panel A, Supplementary Figure 2). This pattern correlated with RTs for angry expressions with averted gaze among younger adults. That is, younger adults who were slower in responding to angry expressions with averted gaze engaged these brain regions to a larger extent. Neither of these patterns was reliably engaged by older adults.



Supplementary Figure 2. Brain-behavior Results for Angry Expressions and Response Times during Emotion Recognition Task. Left panel: a pattern of whole-brain activity during recognition of angry expressions that correlated with the Response latencies during the emotion recognition task which was reliable only among younger adults. Right panel: correlations between brain activities and performance during recognition of angry expressions with direct and averted gaze. Red/yellow brain pattern correspond to the averted gaze condition and blue brain pattern corresponds to the direct gaze condition. All reported regions have BSR ≥ 3 and cluster size ≥ 100 voxels. Abbreviations: L = left hemisphere, R = right hemisphere.

The analyses focused on the accuracy of angry expressions among both age groups revealed one significant LV, which accounted for 45% of the covariance of the data and yielded one pattern of brain activity. This pattern included medial frontal gyrus, middle frontal gyrus, caudate, parahippocampus, supramarginal gyrus, superior temporal gyrus and correlated with the accuracy scores during recognition of angry expressions with both *direct* and *averted* eye-gaze directions. That is, younger adults who recognized angry expressions with higher accuracy recruited these brain areas for both direct and averted gaze. Older adults did not recruit any of these brain regions reliably.



Supplementary Figure 3. Brain-behavior Results for Angry Expressions and Accuracy during Emotion Recognition Task. Left panel: a pattern of whole-brain activity during recognition of angry expressions that correlated with the accuracy in the emotion recognition task which was reliable only among younger adults. Right panel: correlations between brain activities and performance during recognition of angry expressions with direct and averted gaze. All reported regions have BSR ≥ 3 and cluster size ≥ 100 voxels. Abbreviations: L = left hemisphere, R = right hemisphere.

- Older adults demonstrate neural dedifferentiation to angry stimuli.
- Older adults do not demonstrate neural dedifferentiation to happy stimuli.
- No correlation was found between angry emotion recognition and TOM of older adults.
- Significant correlation was found between happy expressions and TOM of older adults.