

UC Berkeley

UC Berkeley Previously Published Works

Title

Diminished Visual Attention to Emotional Faces Is Associated with Poor Emotional Valence Perception in Frontotemporal Dementia

Permalink

<https://escholarship.org/uc/item/68d744qd>

Journal

Dementia and Geriatric Cognitive Disorders, 51(4)

ISSN

1420-8008

Authors

Shdo, Suzanne M
Brown, Casey L
Yuan, Joyce
[et al.](#)

Publication Date

2022

DOI

10.1159/000525958

Peer reviewed



Published in final edited form as:

Dement Geriatr Cogn Disord. 2022 ; 51(4): 331–339. doi:10.1159/000525958.

Diminished Visual Attention to Emotional Faces Is Associated with Poor Emotional Valence Perception in Frontotemporal Dementia

Suzanne M. Shdo,

Casey L. Brown,

Joyce Yuan,

Robert W. Levenson

Department of Psychology, University of California Berkeley, Berkeley, CA, USA

Abstract

Aim: The current study examined whether visual attention to emotional facial expressions is lower in individuals with frontotemporal dementia (FTD) compared to healthy controls, and whether visual attention to emotional facial expressions is associated with the ability to perceive others' emotional valence accurately.

Methods: Participants with FTD ($n = 17$) and healthy controls ($n = 23$) passively viewed pairs of emotional and neutral faces while their visual attention was measured using eye-tracking. A subsample of participants ($n = 28$) also completed an emotional valence perception task.

Results: Individuals with FTD spent less time looking at emotional faces than healthy controls. However, there was no difference in the amount of time individuals with FTD spent looking at neutral faces as compared to healthy controls. In the subsample, less time spent looking at emotional faces (but not neutral faces) was associated with a less accurate perception of others' emotional valence.

This is an Open Access article licensed under the Creative Commons Attribution-NonCommercial-4.0 International License (CC BY-NC) (<http://www.karger.com/Services/OpenAccessLicense>), applicable to the online version of the article only. Usage and distribution for commercial purposes requires written permission.

Correspondence to: Suzanne M. Shdo, shdo@berkeley.edu.

Author Contributions

Ms. Suzanne M. Shdo was the primary contributor to the coauthored research. All the authors made substantial contributions to the conception and design of the work. Dr. Joyce Yuan was involved in a significant portion of the data acquisition. Ms. Suzanne M. Shdo conducted the data analysis with guidance from Drs. Casey L. Brown and Robert W. Levenson. All the authors participated in the interpretation of data for the work. Ms. Suzanne M. Shdo drafted the manuscript with assistance from Dr. Casey L. Brown. All the authors were involved in critical revisions and made important intellectual contributions to the manuscript. All the authors approved the final version of the manuscript for publication. All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Statement of Ethics

This study protocol was reviewed and approved by the University of California Berkeley, Committee for Protection of Human Subjects (CPHS), and the Office for Protection of Human Subjects (OPHS) approval number 2010-02-861. Written informed consent was obtained from all study participants.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Conclusion: Individuals with FTD displayed diminished visual attention to emotional facial expressions compared to healthy controls. Reduced attention towards emotional faces was associated with poorer emotional valence perception. Findings point toward diminished visual attention as potentially relevant for understanding oft-observed impairments in socioemotional functioning in FTD.

Keywords

Visual attention; Emotion; Eye-tracking; Frontotemporal dementia

Introduction

Visual attention provides a valuable window into our emotional lives – the things we look at and look away from are major determinates of our feelings and behaviors [1, 2]. In neurotypical individuals, emotional facial expressions attract heightened visual attention and convey important information that helps us navigate the social world [3–5]. A smiling face may indicate an opportunity for social connection, whereas expressions of anger or fear can signal threats [6–8]. With this information in hand, sound decisions can be made about who to approach and who to avoid. Inattention to facial expressions may result in not having critical information about others' emotions, desires, and reactions, which may lead to poor behavioral choices, social errors, and damage to important social relationships.

Social and emotional deficits are common symptoms of frontotemporal dementia (FTD), a disease characterized by progressive neurodegeneration in frontal and temporal lobe circuits [9, 10]. Neurodegeneration in these circuits leads to deficits in the ability to perceive others' emotions accurately [11–15]. However, few studies have examined whether individuals with FTD have diminished visual attention towards emotional facial expressions and whether these visual attention deficits relate to deficits in emotion perception.

Behavioral variant frontotemporal dementia (bvFTD) and semantic variant primary progressive aphasia (svP-PA) are two of the major subtypes of FTD [16, 17]. Although both subtypes can lead to emotion perception deficits [18, 19], bvFTD is characterized by primary deficits in socioemotional functioning [20], whereas svPPA is characterized by primary deficits in language [17]. As svPPA progresses, expanding atrophy can result in socioemotional symptoms that are difficult to distinguish from those in bvFTD [21]. Neural regions that atrophy in these disorders, such as the amygdala [22] and ventromedial prefrontal cortex [23], are thought to play an important role in the automatic processing of emotional facial expressions and the detection of salient visual stimuli [24–28]. Thus, declines in visual attention towards emotional faces may result from damage to critical underlying circuitry in these diseases.

Existing research has not been definitive as to these issues. In one study examining visual attention to emotionally expressive faces in individuals with FTD, no significant differences were found between those with FTD and controls in the overall time spent looking at emotional faces [29]. However, participants in this study were shown one face at a time and were specifically instructed to look at each face. Thus, neither preference for emotional faces over non-emotional faces nor spontaneous attention to emotional faces was assessed.

In the current study, we take a different approach by presenting participants with pairs of faces, one neutral and one emotional, and we do not instruct participants as to where to look. This allows us to capture visual preferences for emotional versus non-emotional faces and spontaneous attention in a more naturalistic manner. Past research on neurotypical individuals suggests that preferential attention for emotional faces versus neutral faces begins in early infancy [30–32]. Research is needed to examine whether individuals with FTD display diminished visual preferences for emotional faces and whether these are linked to deficits in perceiving emotion in others.

In the current study, we examined visual attention to emotional faces in individuals with the bvFTD and svPPA subtypes of FTD and a comparison group of healthy controls. We used a task in which participants viewed neutral and emotional face-pairs without specific attentional instructions while visual attention was monitored using eye-tracking technology. A subset of participants also completed an emotion perception task in which participants tracked the changing emotional valence of a character in a film using a rating dial.

We tested three hypotheses: (a) individuals with FTD would have less visual attention to emotional faces compared to healthy controls; (b) individuals with FTD would lack a visual preference for emotional faces over neutral faces; and (c) less visual attention to emotional faces (but not neutral faces) would be associated with less accurate perceptions of others' emotions. Finally, because there is evidence linking declines in visual attention to global cognitive impairments (e.g., orientation, visual processing, memory) in individuals with Alzheimer's disease [29, 33, 34], we included data from an assessment of global cognitive impairments in our participants. Because global cognitive impairments are less common in FTD than in Alzheimer's disease [35], we expected that less visual attention towards emotional faces in individuals with FTD would be associated with emotional perception impairments but not with global cognitive impairments.

Materials and Methods

Participants

There were forty participants in the study, including 17 individuals with FTD and 23 healthy controls. Of the 17 individuals with FTD, 10 met diagnostic criteria for bvFTD [20] and 7 met criteria for svPPA [17]. Participants with FTD were recruited through the Memory and Aging Center at the University of California, San Francisco (UCSF). At UCSF, participants received comprehensive diagnostic testing, including neuropsychological assessment, neurological examination, and structural magnetic resonance imaging. Testing was administered by a multidisciplinary team of neurologists, psychiatrists, psychologists, and nurses. Patient diagnoses were determined by a team of neurologists, after a thorough review of the above test measures. Disease severity was measured by the Clinical Dementia Rating Scale (CDR) and the CDR sum of boxes (CDR-Box) [36], and global cognitive impairment was measured by the Mini Mental State Exam (MMSE) [37]. Healthy control participants were recruited from the Bay Area community through advertisements and word of mouth. At UC Berkeley, all controls were screened by trained clinical psychology graduate students with the CDR and the MMSE. Healthy control participants were included

and determined to be free of global cognitive and neurological impairments if they scored 0 on the CDR and 30 on the MMSE.

Procedure

All participants completed an eye-tracking face-pair task (see below) at the Berkeley Psychophysiology Laboratory at the University of California, Berkeley. Twenty-eight participants also completed an emotional valence perception task [38], including all participants with FTD ($n = 17$) and a subset of controls ($n = 11$). All procedures were approved by Berkeley's Committee for the Protection of Human subjects.

Eye-Tracking Face-Pair Task—Participants were seated 24 inches away from a 21-inch color television monitor. An Applied Sciences Laboratories head-mounted monocular eye tracking system (model number H6) was used to monitor eye movements. Following calibration procedures (using nine display points), participants passively viewed six face pairs (Fig.1), while their eye movements were monitored. Each face pair consisted of an emotional face (happy, sad, or angry) paired with a neutral face. For each face pair, participants viewed a fixation screen (2 s) and then the face pair (6 s). There were 15 s between each face pair trial. All face images were selected from the Ekman and Friesen [39] Pictures of Facial Affect database, which consists of standardized black and white photographs of adults posing emotional expressions. The images measured 6.5 (w) \times 10 (h) inches and were presented side by side on the computer monitor against a neutral gray background. Within each face pair, the person posing the emotional and neutral face was the same. Across face pairs, the persons differed, such that each face pair featured a different person. All the faces included in this task were those of males. Participants viewed two happy-neutral face pairs, two sad-neutral face pairs, and two angry-neutral face pairs. The position of the emotional and neutral faces alternated between pairs, such that each emotional face was presented on the left for one trial and on the right for one trial.

Emotional Valence Perception Task—Participants were seated in front of a color monitor with a rating dial located near their dominant hand. The rating dial consists of a small box with a rotating pointer that spans a 0–180° degree arc. The arc includes a nine-point scale and is labeled at three anchor points. The far left (0°) is labeled with the words “very bad” (depicted by a schematic frowning face), the middle (90°) is labeled “neutral” (90°), and the far right (180°) is labeled “very good” (depicted by a smiling face). Participants were instructed to adjust the rating dial as often as needed so that it consistently reflected the emotional valence of a target character in a film clip. The 80-s film clip is a Disney commercial and consists of a female target character expressing a wide range of positive and negative emotions after being given a gift by her male dinner companion. The dial generated a position-dependent voltage that was sampled by a computer every 3 milliseconds and averaged each second, resulting in a second-by-second time series of participant perceptions of the character's emotional valence.

Data Reduction

Time Spent Looking at Emotional and Neutral Faces—Using Gaze Tracker software (Version 06.04.26), regions of interest were drawn around each emotional and

neutral face in the eye-tracking face-pair task. The software derives values that reflect the percent of time that participant's gaze fell within the regions of interest during the time tracked over the 6 s presentation period. For each face-pair, the gaze tracker software derived (1) the total percent of time spent looking at the emotional face and (2) the total percent of time spent looking at the neutral face. Given that each emotional face type (happy, sad, angry) paired with a neutral face was presented twice, the two values for each emotion type and its paired neutral face were averaged, resulting in 6 values (3 emotion face values and 3 neutral face values)¹ [40].

Emotional Valence Perception Accuracy—We determined each participant's accuracy in rating the valence of the target character in the film clip by comparing participants' dial ratings with those obtained from an expert panel of graduate students trained in behavioral coding [15, 41]. In line with previous research [42, 43], time-lagged cross-correlations were used to compute the association between each participant's ratings and expert ratings. To allow for processing and motor delays, the maximum correlation coefficient was selected for lags between -10 and +10 s (correlation coefficients ranged from -0.08 to 0.94). Higher values indicate more accurate emotional valence perception.

Global Cognitive Impairment—The Mini-Mental State Examination (MMSE) was used to measure global cognitive impairment. The MMSE is a 28-item measure which examines five domains of cognitive functioning, including memory, language, concentration/attention, abstraction/problem solving, and visuospatial information. The MMSE is well validated with older adults and individuals with dementia [37, 44].

Statistical Analysis

To increase power and limit type I error, we initially conducted our group-based analyses comparing all individuals with FTD to healthy controls. We then repeated these analyses, examining differences between three diagnostic groups (bvFTD vs. svPPA vs. healthy controls). Group differences in potential confounds including age, gender, and disease severity (as measured by CDR-Box) were assessed using independent sample *t*-tests. These analyses revealed group differences for age, gender, and CDR-Box in contrast to controls. Thus, we added these variables as covariates in subsequent between-group analyses.

To test our first hypothesis that individuals with FTD would have less attention to emotional faces, we examined diagnostic group differences in the percent of time spent looking at emotional faces using a 2 × 3 repeated measures mixed model ANOVA with diagnosis as the between subjects factor (FTD vs. healthy controls) and emotion as the within subjects factor (sad, angry, happy). Age, gender, and CDR-Box were also included in the model

¹Because each emotional face type (happy, angry, and sad) was repeated twice (with the emotional face on the right for the first repetition and on the left for the second repetition), we conducted a 2 × 2 × 3 repeated measures mixed model ANOVA with diagnosis as the between subjects factor (FTD vs. healthy controls), repetition (the emotional face presented on the right or on the left) and emotion as the within subject factor (sad, angry, happy) to determine if we could collapse across repetition. We found no significant repetition by diagnosis interaction ($F(1, 39) = 0.140, p = 0.711, \eta^2 = 0.004$). Therefore, we collapsed across repetition for future analyses. We did find a significant main effect of repetition ($F(1, 39) = F = 16.47, p < 0.001, \eta^2 = 0.315$), such that all individuals regardless of diagnosis spent more time looking at the first repetition, when the emotional face was on the left (52.3%, SE = 1.4) in contrast to the second repetition when the emotional face was on the right (44.4%, SE = 1.1). This left looking bias is common in eye-tracking studies [40].

as covariates. Bonferroni corrections to control for type I error due to conducting multiple comparisons were used for all post hoc comparisons. To test our second hypothesis that individuals with FTD would lack a preference for emotional faces (relative to neutral faces), we conducted a 2×2 repeated measures mixed model ANOVA with diagnosis (FTD vs. healthy controls) as the between subjects factor and face type (emotional or neutral) as the within subjects factor.

Finally, to test our third hypothesis that less visual attention to emotional faces but not neutral faces would be associated with poorer emotional valence perception, we used correlations to examine associations between the percent time spent looking at emotional faces and neutral faces and performance on the emotional valence perception task. We also examined how visual attention is related to cognitive impairment.

Results

Table 1 displays participant demographics. Preliminary analyses revealed group differences between participants with FTD and healthy controls in age, gender, and CDR-Box scores. The FTD group was significantly younger ($M_{\text{diff}} = 4.79$, $SE = 1.59$, $p = 0.005$); had a greater male to female ratio than the control group, $\chi^2(1, N = 39) = p < 0.027$; and had greater disease severity as compared to healthy controls ($M_{\text{diff}} = 4.71$, $SE = 0.485$, $p < 0.001$). Thus, in subsequent analyses we included age, gender, and CDR-box as covariates.

Hypothesis 1: Individuals with FTD Will Spend Less Time Looking at Emotional Faces Compared to Healthy Controls

The 2 (diagnosis) \times 3 (emotional face) repeated measures ANOVA revealed a main effect for diagnosis ($F(1, 39) = 12.9$, $p < 0.001$, $\eta^2 = 0.27$), such that individuals with FTD spent less time (42.0%) looking at emotional faces compared to healthy controls (53.7%). The main effect of emotion and the diagnosis \times emotion interaction were not significant. When we repeated these analyses comparing bvFTD, svPPA, and healthy controls, results were consistent, with a main effect of diagnosis on the time spent looking at emotional faces ($F(2, 39) = 7.34$, $p = 0.002$, $\eta^2 = 0.30$). No significant main effects of emotion or diagnosis \times emotion interactions were observed in either model. Bonferroni corrected post hoc comparisons revealed that individuals with bvFTD and svPPA did not differ in time spent looking at emotional faces ($M_{\text{diff}} = 2.8$, $SE = 2.3$, $p = 0.695$) and both the bvFTD ($M_{\text{diff}} = 14.0$, $SE = 3.7$, $p = 0.002$) and the svPPA ($M_{\text{diff}} = 11.2$, $SE = 3.3$, $p = 0.005$) groups spent significantly less percent time looking at emotional faces compared to controls.

Hypothesis 2: Individuals with FTD Will Lack a Visual Preference for Emotional Faces in Contrast to Neutral Faces

Given that there were no significant differences by emotion type, we averaged across emotion types as an indication of the total time spent looking at emotional faces and the total time spent looking at neutral faces to test this hypothesis. Comparing individuals with FTD to healthy controls, we found a face type (emotion vs. neutral) by diagnosis (FTD vs. control) interaction ($F(1, 39) = 5.40$, $p = 0.026$, $\eta^2 = 0.13$). Bonferroni corrected post hoc comparisons revealed that healthy controls spent significantly more time looking at the

emotional faces compared to the neutral faces ($M_{\text{diff}} = 6.76$, $SE = 2.48$, $p = 0.01$). However, for individuals with FTD, time spent looking at emotional faces did not differ from time spent looking at neutral faces ($M_{\text{diff}} = -0.944$, $SE = 2.55$, $p = 0.714$). Although individuals with FTD looked significantly more at emotional faces compared to neutral faces ($M_{\text{diff}} = 1.92$, $SE = 3.29$, $p = 0.001$), FTDs and controls did not differ in the amount of time spent looking at neutral faces ($M_{\text{diff}} = 11.61$, $SE = 3.18$, $p = 0.549$). Similarly, when we examined the three groups separately (bvFTD, svPPA, controls), we found a marginal face by diagnosis interaction ($F(2, 39) = 3.22$, $p = 0.052$, $\eta^2 = 0.16$) with no preference for emotional faces in contrast to neutral faces observed for individuals with bvFTD ($M_{\text{diff}} = -0.961$, $SE = 3.16$, $p = 0.763$) or svPPA ($M_{\text{diff}} = 1.20$, $SE = 2.753$, $p = 0.473$). Controls demonstrated a visual preference for emotional faces as opposed to neutral faces ($M_{\text{diff}} = 11.14$, $SE = 2.04$, $p < 0.001$). Results are displayed in Figure 2.

Hypothesis 3: Less Visual Attention to Emotional Faces Will Be Associated with Less Accurate Emotional Valence Perception

We conducted correlations among variables of interest in the subset of participants who completed the emotional valence perception task ($n = 16$). Correlations are presented in Table 2. Across all participants (individuals with FTD and healthy controls), more time spent looking at emotional faces was associated with better emotional valence perception, $r(27) = 0.450$, $p = 0.016$.

To determine whether time spent looking at emotional faces was associated with global cognitive impairment, we examined the correlation between these measures and found them to be uncorrelated $r(27) = 0.512$, $p = 0.520$. Finally, percent time spent looking at neutral faces was associated with neither emotional valence perception nor global cognitive impairment.

Discussion

Given that diminished visual attention to emotional faces may have important links to the socioemotional deficits observed in neurodegenerative diseases, the current study explored visual attention to emotional faces in individuals with FTD as well as the relationship between visual attention to emotional faces and emotional valence perception. We examined whether: (a) individuals with FTD display less visual attention to emotional faces compared to healthy controls, (b) individuals with FTD lack a visual preference for emotional faces in contrast to neutral faces, and (c) less visual attention to emotional faces is associated with worse emotion perception. To address these questions, we used an eye-tracking face-pair task in which participants passively viewed emotional and neutral face pairs, as well as an emotional valence perception task in which participants rated the changing emotions of a character in a film. We found that, compared to healthy controls, participants with FTD displayed less visual attention to emotionally expressive faces. Further, individuals with FTD lacked a visual preference for emotional faces when shown both neutral and emotional faces (healthy controls showed a preference for emotional faces). Finally, in a subset of participants, we found that less visual attention to emotionally expressive faces was associated with worse performance on the emotional valence perception task.

To our knowledge, this is the first study to demonstrate that naturalistic visual attention to emotional faces is lower in individuals with FTD compared to healthy controls. Importantly, these differences in visual attention to emotional faces remained significant when controlling for age, gender, and disease severity. Differences were observed for individuals with two subtypes of FTD (bvFTD and svPPA). Thus, the frontal and temporal lobe neurodegeneration common across FTD subtypes likely plays an important role in diminished visual attention to emotional faces. This may include regions of the salience network and circuitry in visual attention network both of which include regions that are damaged in FTD [45, 46].

Past research demonstrates that emotionally expressive faces are naturally more salient and attention-commanding to healthy individuals than neutral faces [47] due to the important social information communicated by emotional facial expressions. In line with past research, healthy controls in the current study spent significantly more time gazing at emotional faces compared to neutral faces. Our finding that individuals with FTD lack this visual preference for emotional faces suggests that emotional information portrayed in faces has decreased salience for individuals with FTD. This would be consistent with the deficits in emotion perception often observed in individuals with FTD [18, 42].

Our results also point to an important link between diminished visual attention to emotional faces and worse emotional valence perception. Similar associations have been observed in neuropsychiatric disorders such as autism spectrum disorders (ASD) and schizophrenia. For example, less visual attention to emotional faces has been associated with a range of poor socioemotional functioning, including emotion perception in these individuals [48–51]. Importantly, we found no significant associations between emotional valence perception and the time spent looking at neutral faces or global cognitive impairments, suggesting that emotion perception deficits in FTD are tied specifically to attention towards emotional faces, rather than more global cognitive or attentional deficits.

Due to the correlational nature of our analysis, we cannot make causal inferences regarding the association between visual attention to emotional faces and emotional valence perception. It is possible that lower visual attention to emotional faces impacts the ability to recognize emotional experience and it is also possible that the inability to recognize emotion results in less visual attention to human faces. Furthermore, it may be that a third factor, such as lack of motivation to understand others, impacts both visual attention to emotional faces and emotion recognition. Nonetheless, prior research suggests that training individuals to look more at emotional faces can improve their ability to perceive emotion in others [52]. Future research should explore methods to increase attention toward emotional facial expressions in the early stages of FTD, and examine whether this leads to improved emotion perception and, if so, how long it is sustained. Although neurodegenerative diseases are progressive, intervening in the early stages of the disease may have benefits for the person with the disease as well as for caregivers who suffer from more depression and other health problems when the individual they care for has emotion perception deficits [15, 53, 54].

The current study was limited by a small sample size. Future studies should aim to replicate these findings in a larger sample and utilize neuroimaging methods to pinpoint

the specific neural atrophy associated with diminished visual attention to emotional faces in FTD. Additionally, future research should examine if differences in visual preference for emotional faces in individuals with FTD are associated with diminished attention to specific facial features or atypical facial scanning patterns. This is important given that visual attention to facial features and patterns of facial scanning (e.g., the eyes-nose-mouth triangular pattern) seen in neurotypical adults [55] have been shown to be altered in individuals with neurological disorders [56]. Lastly, future studies should build upon these methods by also measuring visual attention during the emotional valence perception task. This would provide a direct measure of attentional deficits that occur during the processing of dynamic facial expressions.

Conclusion

Our study presents preliminary evidence that individuals with FTD, compared to healthy controls, display diminished visual attention to emotional facial expressions. This lack of attention towards emotional (but not neutral) facial expressions is associated with deficits in emotional valence perception. Given the aging population and the negative effects that emotion perception deficits can have on the health and well-being of individuals with neurodegenerative disease and their caregivers, future research should continue to examine naturalistic visual attention to emotional faces in FTD and work to develop and test interventions aimed at rectifying attentional deficits in the early stages of the disease.

Acknowledgements

We thank our participants and all of the past and present members of the Berkeley Psychophysiology lab for their assistance with recruitment and data collection. The authors would also like to thank Sandra Patricia S. Arriaga and Lydia R. Poon for their assistance with the preparation of tables and figures and with the organization of the references.

Funding Sources

This work was supported by the National Institute on Aging (R01AG041762 to R.W.L, P01AG019724, and K99AG073617 to C.L.B). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Data Availability Statement

The data that support the findings of this study are not publicly available because they contain information that could compromise the privacy of the study participants; however, academic, not-for-profit investigators may request data for research studies from the corresponding author, R.W.L.

References

1. Schupp HT, Stockburger J, Codispoti M, Junghöfer M, Weike AI, Hamm AO. Selective visual attention to emotion. *J Neurosci*. 2007 Jan 31 [cited 2020 Sep 11];27(5):1082–9. <https://www.jneurosci.org/content/27/5/1082>. [PubMed: 17267562]
2. Lundqvist D, Öhman A. Emotion regulates attention: the relation between facial configurations, facial emotion, and visual attention. *Vis Cogn*. 2005 Jan [cited 2020 Sep 10];12(1): 51–84. <https://www.tandfonline.com/doi/abs/10.1080/13506280444000085>.

3. Calvo MG, Lundqvist D. Facial expressions of emotion (KDEF): identification under different display-duration conditions. *Behav Res Methods*. 2008 Feb;40(1):109–15. [PubMed: 18411533]
4. Birmingham E, Bischof WF, Kingstone A. Saliency does not account for fixations to eyes within social scenes. *Vis Res*. 2009 Dec 10; 49(24):2992–3000. [PubMed: 19782100]
5. Birmingham E, Kingstone A. Human social attention. *Prog Brain Res*. 2009;176:309–20. [PubMed: 19733765]
6. Levenson RW, Lwi SJ, Brown CL, Ford BQ, Otero MC, Verstaen A. Emotion. In: *Hand-book of psychophysiology*. 2017:444–64.
7. Ekman P, Keltner D. Universal facial expressions of emotion.pdf. In: *Nonverbal communication: where nature meets culture* [Internet]. 1997 [cited 2021 Feb 4]. p. 27–46. Available from: <https://www.paulekman.com/wp-content/uploads/2013/07/Universal-Facial-Expressions-of-Emotions1.pdf>.
8. Schmidt KL, Cohn JF. Human facial expressions as adaptations: evolutionary questions in facial expression research. *Am J Phys Anthropol*. 2001 Jan 1 [cited 2020 Sep 11]; 116(Suppl 33):3–24. <https://onlinelibrary.wiley.com/doi/full/10.1002/ajpa.20001>.
9. Rosen HJ, Perry RJ, Murphy J, Kramer JH, Mychack P, Schuff N, et al. Emotion comprehension in the temporal variant of frontotemporal dementia. *Brain*. 2002 Oct 1;125(Pt 10): 2286–95. [PubMed: 12244085]
10. Rankin KP, Kramer JH, Miller BL. Patterns of cognitive and emotional empathy in frontotemporal lobar degeneration. *Cogn Behav Neurol*. 2005;18(1):28–36. [PubMed: 15761274]
11. Otero MC, Levenson RW. Lower visual avoidance in dementia patients is associated with greater psychological distress in caregivers. *Dement Geriatr Cogn Disord*. 2017 Jun 1 [cited 2021 Feb 3];43(5–6):247–58. <https://www.karger.com/Article/FullText/468146>. [PubMed: 28395276]
12. Chen KH, Lwi SJ, Hua AY, Haase CM, Miller BL, Levenson RW. Increased subjective experience of non-target emotions in patients with frontotemporal dementia and Alzheimer’s disease. *Curr Opin Behav Sci*. 2017;15:77–84. Elsevier Ltd. [PubMed: 29457053]
13. Lavenu I, Pasquier F, Lebert F, Petit H, van der Linden M. Perception of emotion in frontotemporal dementia and Alzheimer disease. *Alzheimer Dis Assoc Disord*. 1999 [cited 2020 Sep 10];13(2):96–101. [PubMed: 10372953]
14. Kumfor F, Piguet O. Disturbance of emotion processing in frontotemporal dementia: a synthesis of cognitive and neuroimaging findings. *Neuropsychol Rev*. 2012;22(3):280–97. [PubMed: 22577002]
15. Brown CL, Lwi SJ, Goodkind MS, Rankin KP, Merrilees J, Miller BL, et al. Empathic accuracy deficits in patients with neurodegenerative disease: association with caregiver depression. *Am J Geriatr Psychiatry*. 2018 Apr 1; 26(4):484–93. [PubMed: 29289452]
16. Rascovsky K, Hodges JR, Kipps CM, Johnson JK, Seeley WW, Mendez MF, et al. Diagnostic criteria for the behavioral variant of frontotemporal dementia (bvFTD): current limitations and future directions. *Alzheimer Dis Assoc Disord*. 2007 [cited 2021 Feb 3];21(4): S14–8. <https://journals.lww.com/00002093-200710000-00011>. [PubMed: 18090417]
17. Gorno-Tempini MLL, Hillis AE, Weintraub S, Kertesz A, Mendez M, Cappa SF, et al. Classification of primary progressive aphasia and its variants. *Neurology*. 2011 Mar 15;76(11): 1006–14. [PubMed: 21325651]
18. Rosen HJ, Pace-Savitsky K, Perry RJ, Kramer JH, Miller BL, Levenson RW. Recognition of emotion in the frontal and temporal variants of frontotemporal dementia. *Dement Geriatr Cogn Disord*. 2004;17(4):277–81. [PubMed: 15178936]
19. Calabria M, Cotelli M, Adenzato M, Zanetti O, Miniussi C. Empathy and emotion recognition in semantic dementia: a case report. *Brain Cogn*. 2009 Aug 1;70(3):247–52. [PubMed: 19339096]
20. Rascovsky K, Hodges JR, Knopman D, Mendez MF, Kramer JH, Neuhaus J, et al. Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. *Brain*. 2011 Sep 1;134(Pt 9):2456–77. [PubMed: 21810890]
21. Karageorgiou E, Miller BL. Frontotemporal lobar degeneration: a clinical approach. *Semin Neurol*. 2014 Jun 25 [cited 2021 Feb 3]; 34(2):189–201. <http://www.thieme-connect.de/DOI/DOI?10.1055/s-0034-1381735>. [PubMed: 24963678]

22. Adolphs R, Baron-cohen S, Tranel D. Impaired recognition of social emotions following amygdala damage. *J Cogn Neurosci*. 2002 Nov 15;14(8):1264–74. <https://www-mit-pressjournals-org.libproxy.berkeley.edu/doi/abs/10.1162/089892902760807258> [PubMed: 12495531]
23. Winker C, Rehbein MA, Sabatinelli D, Dohn M, Maitzen J, Wolters CH, et al. Noninvasive stimulation of the ventromedial prefrontal cortex modulates emotional face processing. *Neuroimage*. 2018 Jul 15;175:388–401. [PubMed: 29605579]
24. Zhou J, Greicius MD, Gennatas ED, Growdon ME, Jang JY, Rabinovici GD, et al. Divergent network connectivity changes in behavioural variant frontotemporal dementia and Alzheimer’s disease. *Brain*. 2010 May 1;133(5): 1352–67. <https://academic.oup.com/brain/article-lookup/doi/10.1093/brain/awq075>. [PubMed: 20410145]
25. Preston TJ, Guo F, Das K, Giesbrecht B, Eckstein MP. Neural representations of contextual guidance in visual search of real-world scenes. *J Neurosci*. 2013 May 1;33(18):7846–55. [PubMed: 23637176]
26. Ranasinghe KG, Rankin KP, Pressman PS, Perry DC, Lobach IV, Seeley WW, et al. Distinct subtypes of behavioral variant frontotemporal dementia based on patterns of network degeneration. *JAMA Neurol*. 2016 Sep 1;73(9):1078–88. [PubMed: 27429218]
27. Anderson AK, Phelps EA. Lesions of the human amygdala impair enhanced perception of emotionally salient events. *Nature*. 2001 May 17;411(6835):305–9. [PubMed: 11357132]
28. Cunningham WA, Brosch T. Motivational salience: amygdala tuning from traits, needs, values, and goals. *Curr Dir Psychol Sci*. 2012 Feb 31;21(1):54–9. <http://journals.sagepub.com/doi/10.1177/0963721411430832>.
29. Hutchings R, Palermo R, Bruggemann J, Hodges JR, Piguet O, Kumfor F. Looking but not seeing: increased eye fixations in behavioural-variant frontotemporal dementia. *Cortex*. 2018 Jun 1;103:71–81. [PubMed: 29573594]
30. Bindemann M, Burton AM, Hooge ITC, Jenkins R, de Haan EHF. Faces retain attention. *Psychon Bull Rev*. 2005;12(6):1048–53. [PubMed: 16615327]
31. Bekhtereva V, Craddock M, Müller MM. Attentional bias to affective faces and complex IAPS images in early visual cortex follows emotional cue extraction. *Neuroimage*. 2015 May 5;112:254–66. [PubMed: 25818682]
32. Hoehl S, Palumbo L, Heinisch C, Striano T. Infants’ attention is biased by emotional expressions and eye gaze direction. *Neuroreport*. 2008 Mar;19(5):579–82. [PubMed: 18388742]
33. Crawford TJ, Devereaux A, Higham S, Kelly C. The disengagement of visual attention in Alzheimer’s disease: a longitudinal eye-track-ing study. *Front Aging Neurosci*. 2015 Jun 23 [cited 2021 Feb 3];7:118. <http://journal.frontiersin.org/Article/10.3389/fnagi.2015.00118/abstract>. [PubMed: 26157388]
34. Bueno APA, Sato JR, Hornberger M. Eye tracking – the overlooked method to measure cognition in neurodegeneration? *Neuropsychologia*. 2019 Oct;133:107191.
35. Park LQ, Harvey D, Johnson J, Farias ST. Deficits in everyday function differ in AD and FTD. *Alzheimer Dis Assoc Disord*. 2015 [cited 2021 May 20];29(4):301–6. [PubMed: 25590940]
36. Morris JC. Clinical dementia rating: a reliable and valid diagnostic and staging measure for dementia of the Alzheimer type. *Int Psychogeriatr*. 1997;9 Suppl 1:173–6. [PubMed: 9447441]
37. Kukull WA, Larson EB, Teri L, Bowen J, Mc-Cormick W, Pfanschmidt ML. The mini-mental state examination score and the clinical diagnosis of dementia. *J Clin Epidemiol*. 1994 Sep 1;47(9):1061–7. [PubMed: 7730909]
38. Levenson RW, Ascher E, Goodkind M, Mc-Carthy M, Sturm V, Werner K. Chapter 25 Laboratory testing of emotion and frontal cortex. *Handb Clin Neurol*. 2008;88:489–98. Elsevier [PubMed: 18631708]
39. Ekman P, Friesen WV. Pictures of facial affect. Palo Alto: Consulting Psychologists’ Press; 1976 [cited 2021 Feb 4]; Available from: <https://ci.nii.ac.jp/naid/10011335061>.
40. Butler SH, Harvey M. Perceptual biases in chimeric face processing: eye-movement patterns cannot explain it all. *Brain Res*. 2006 Dec 8;1124(1):96–9. [PubMed: 17070503]
41. Goodkind MS, Sollberger M, Gyurak A, Rosen HJ, Rankin KP, Miller B, et al. Tracking emotional valence: the role of the orbitofrontal cortex. *Hum Brain Mapp*. 2012 Apr 1; 33(4):753–62. [PubMed: 21425397]

42. Brown CL, Hua AY, de Coster L, Sturm VE, Kramer JH, Rosen HJ, et al. Comparing two facets of emotion perception across multiple neurodegenerative diseases. *Soc Cogn Affect Neurosci*. 2020 May 4;15(5):511–22. [PubMed: 32363385]
43. Wells JL, Brown CL, Hua AY, Soyster PD, Chen KH, Dokuru DR, et al. Neurodegenerative disease caregivers' 5-HTTLPR genotype moderates the effect of patients' empathic accuracy deficits on caregivers' well-being. *Am J Geriatr Psychiatry*. 2019 Oct 1;27(10):1046–56. [PubMed: 31133468]
44. Hensel A, Angermeyer MC, Riedel-Heller SG. Measuring cognitive change in older adults: reliable change indices for the Mini-Mental State Examination. *J Neurol Neurosurg Psychiatry*. 2007 Dec 1;78(12):1298–303. [PubMed: 17442763]
45. Seeley WW, Crawford RK, Zhou J, Miller BL, Greicius MD. Neurodegenerative diseases target large-scale human brain networks. *Neuron*. 2009 Apr 16;62(1):42–52. [PubMed: 19376066]
46. Corbetta M, Shulman GL. Control of goal-directed and stimulus-driven attention in the brain. *Nat Rev Neurosci*. 2002;3(3):201–15. <http://www.nature.com/doi/10.1038/nrn755>. [PubMed: 11994752]
47. Schindler S, Bublatzky F. Attention and emotion: an integrative review of emotional face processing as a function of attention. *Cortex*. 2020;130:362–86. [PubMed: 32745728]
48. Spezio ML, Adolphs R, Hurley RSE, Piven J. Abnormal use of facial information in high-functioning autism. *J Autism Dev Disord*. 2007 May 28;37(5):929–39. [PubMed: 17006775]
49. Pelphrey KA, Sasson NJ, Reznick JS, Paul G, Goldman BD, Piven J. Visual scanning of faces in autism. *J Autism Developmental Disord*. 2002 Aug;32(4):249–61.
50. Russell TA, Green MJ, Simpson I, Coltheart M. Remediation of facial emotion perception in schizophrenia: concomitant changes in visual attention. *Schizophr Res*. 2008 Aug 1; 103(1–3):248–56. [PubMed: 18565733]
51. Neumann D, Spezio ML, Piven J, Adolphs R. Looking you in the mouth: abnormal gaze in autism resulting from impaired top-down modulation of visual attention. *Soc Cogn Affect Neurosci*. 2006 Dec 1;1(3):194–202. [PubMed: 18985106]
52. Russo-Ponsaran NM, Evans-Smith B, Johnson J, Russo J, McKown C. Efficacy of a facial emotion training program for children and adolescents with autism spectrum disorders. *J Nonverbal Behav*. 2016 Mar 1;40(1):13–38.
53. Lwi SJ, Ford BQ, Casey JJ, Miller BL, Levenson RW, Fiske ST. Poor caregiver mental health predicts mortality of patients with neurodegenerative disease. *Proc Natl Acad Sci U S A*. 2017 Jul 11;114(28):7319–24. [PubMed: 28655841]
54. Brown CL, Wells JL, Hua AY, Chen KH, Merrilees J, Miller BL, et al. Emotion recognition and reactivity in persons with neurodegenerative disease are differentially associated with caregiver health. *Gerontologist*. 2020 Apr 7; 60(7):1233–43. [PubMed: 32293012]
55. Tatler BW, Wade NJ, Kwan H, Findlay JM, Velichkovsky BM. Yarbus, eye movements, and vision. *Iperception*. 2010 [cited 2022 Jan 20];1(1):7. Available from: /pmc/articles/PMC3563050/. [PubMed: 23396904]
56. Adolphs R, Sears L, Piven J. Abnormal processing of social information from faces in autism. *J Cogn Neurosci*. 2001 Feb 15;13(2): 232–40. [PubMed: 11244548]

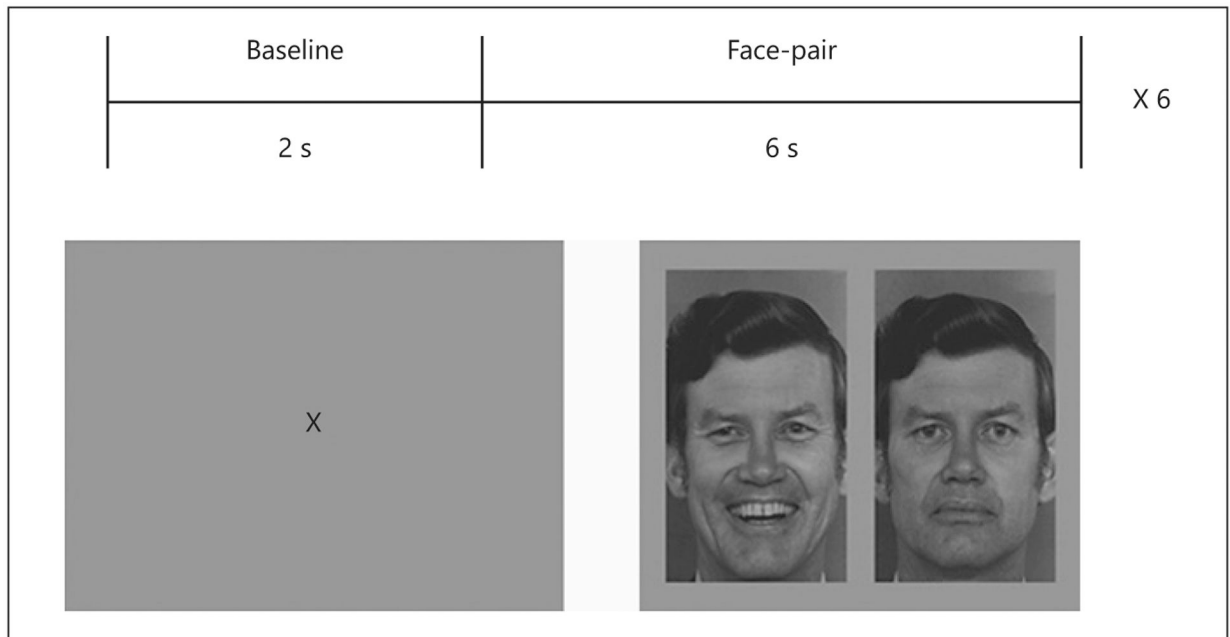


Fig. 1.

Emotional face pair task. A total of six face-pairs were presented to the participants for 6 s each. Each emotional face (happy, sad, angry) was paired with a neutral face. The location of the emotional face alternated, such that one of each emotional face appeared on the left and one appeared on the right for each of the discrete emotions. In the sample shown, the happy face appears on the left and the neutral face on the right. Each face pair was preceded by a 2 s baseline, which depicted a black fixation point and a gray background. Participants were verbally instructed to, “watch the × please.” Eye movements were tracked throughout the task.

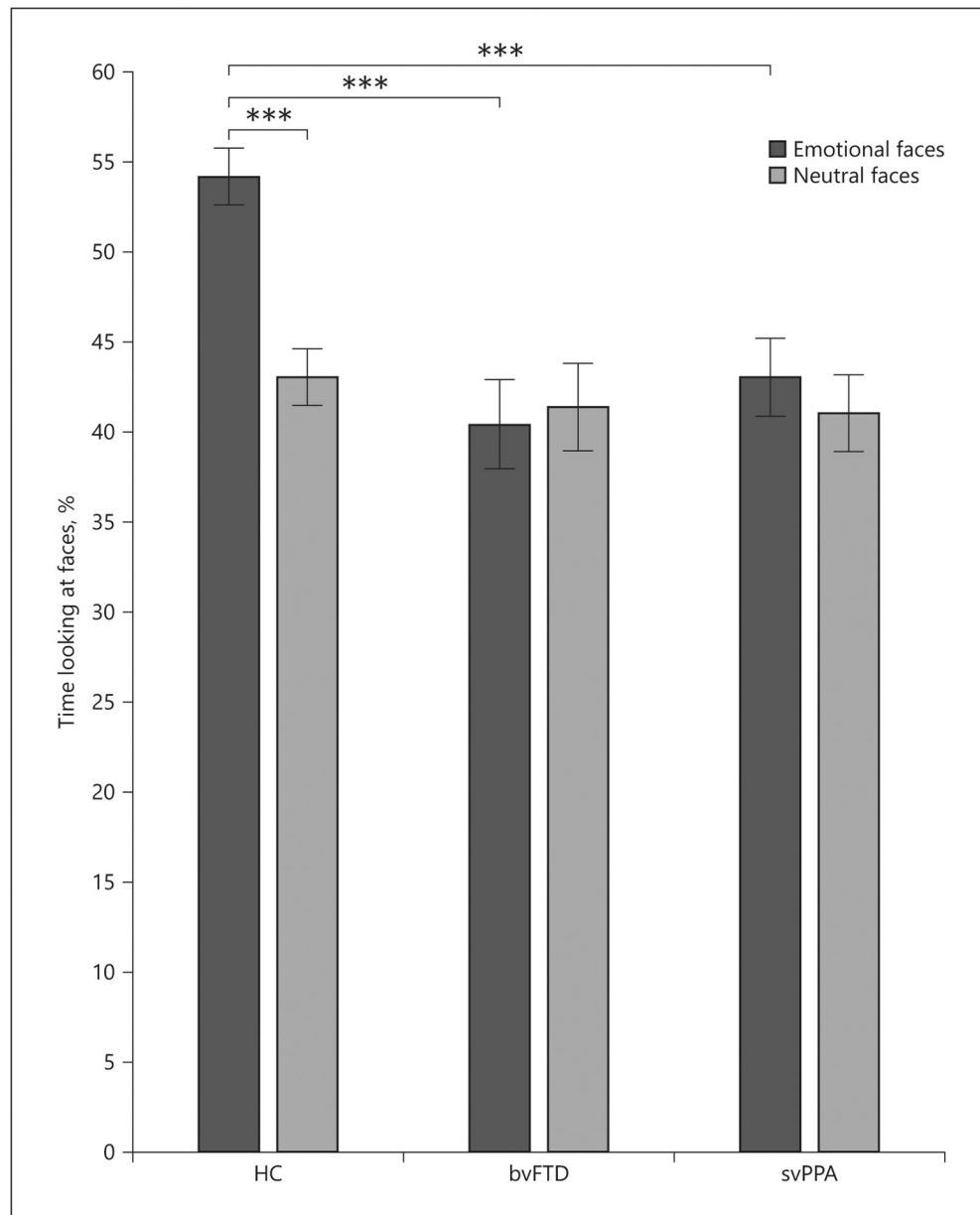


Fig. 2. Diagnostic group differences in mean time spent looking at emotional faces and neutral faces by diagnosis. *** $p < 0.001$. bvFTD = behavioral variant frontotemporal dementia, svPPA = semantic variant primary progressive aphasia, Group differences in percent time spent looking at emotional faces and neutral faces. A repeated measures mixed model ANOVA controlling for age, gender, and CDR-Box score revealed no interaction between percent time spent looking at specific emotional face type (emotional vs. neutral) and diagnosis (bvFTD, svPPA, NC), but did reveal a marginal face by diagnosis interaction ($F_{2, 39} = 3.22$, $p = 0.052$, $\eta^2 = 0.15$) such that neither individuals with bvFTD ($M_{\text{diff}} = -0.961$, $SE = 3.16$, $p = 0.763$) or individuals with svPPA ($M_{\text{diff}} = 1.20$, $SE = 2.753$, $p = 0.473$) demonstrated no preference for emotional faces in contrast to neutral faces. Healthy controls

demonstrated a visual preference for emotional faces as opposed to neutral faces ($M_{\text{diff}} = 11.14$, $SE = 2.04$, $p < 0.001$). We found diagnostic group differences in time spent looking at emotional faces such that individuals with bvFTD spent less time looking at emotional faces as compared to controls ($M_{\text{diff}} = -13.747$, $SE = 3.78$, $p < 0.001$). Similarly, individuals with svPPA spent less time looking at emotional faces as compared to controls ($M_{\text{diff}} = -11.12$, $SE = 3.30$, $p < 0.002$).

Table 1.

Participant demographic data by diagnostic group

Characteristics	HC	bvFTD	svPPA	Test statistics	Effect size (η^2)	p value
N	23	10	7			
Age	67.6 (5.0)	61.5 (5.0)*	64.7 (6.7)	F(2, 39) = 5.5	0.23	0.008
Sex (Male/Female)	9/14	9/2	5/2	$\chi^2 = (2, N=40) = 6.31$		0.04
CDR-Box (0–12)	0 (0)	5.0 (2.2)**	4.3 (2.0)**	F(2, 39) = 56.3	0.78	<0.001
MMSE (0–30)	29.5 (0.57)	26.7 (3.4)*	24.7 (5.3)**	F(2, 39) = 9.8	0.35	<0.001
Emotional valence perception, %	85.9 (2.0)	48.7 (13.2)**	47.3 (5.6)**	F(2, 26) = 8.68	0.42	<0.001

bvFTD, behavioral variant frontotemporal dementia; HC, healthy controls; svPPA, semantic variant primary progressive aphasia; MMSE, Mini-Mental State Examination (0–30); CDR, clinical dementia rating (0–3 range, with 0 indicating no impairment); CDR-Box, Clinical Dementia Rating Scale (sum of boxes). For age, CDR-Box, MMSE, and Emotion Perception, the numbers indicate means (standard error).

* Bonferroni adjusted means differed from controls at $p < 0.05$.

** Bonferroni adjusted means differed from controls at $p < 0.005$.

Table 2.

Correlation table

	Average % time looking at emotional faces	Average % time looking at neutral faces	Emotional valence perception	MMSE
Average % time looking at emotional faces	–			
Average % time looking at neutral faces	0.063	–		
Emotional valence perception	0.450 *	-0.137	–	
MMSE	0.103	0.004	0.512 **	–

MMSE, Mini-Mental State Examination

* $p > 0.05$.

** $p < 0.01$.