HHS Public Access

Author manuscript

Psychiatry Res Neuroimaging. Author manuscript; available in PMC 2019 November 30.

Published in final edited form as:

Psychiatry Res Neuroimaging. 2018 November 30; 281: 85–91. doi:10.1016/j.pscychresns.2018.09.003.

Alexithymia and Reactive Aggression: The Role of the Amygdala

Theodora Farah[a,*,+], **Shichun Ling**[b,+], **Adrian Raine**[c], **Yaling Yang**[d], and **Robert Schug**[e]

[a]Department of Psychology, University of Pennsylvania, 425 S. University Ave, Philadelphia, PA 19104

[b]Department of Criminology, University of Pennsylvania, 3809 Walnut St., Suite 201, Philadelphia, PA 19104

[c]Departments of Criminology, Psychology, and Psychiatry, University of Pennsylvania, 3809 Walnut St., Suite 204, Philadelphia, PA 19104

[d]Department of Pediatrics, Children's Hospital Los Angeles, University of Southern California, 4650 Sunset Boulevard, Los Angeles, CA 90027

[e]School of Criminology, Criminal Justice, and Emergency Management, California State University, Long Beach, 1250 Bellflower Boulevard, Long Beach, CA 90840

Abstract

Past research suggests an association between reactive aggression and alexithymia, but neural mechanisms underlying this association remain unknown. Furthermore, the relationship between proactive aggression and alexithymia remains untested. This study aimed to: (1) test whether alexithymia is more related to reactive than proactive aggression; and (2) determine whether amygdala, insula, and/or anterior cingulate cortical (ACC) volume could be neurobiological mechanisms for this association. One hundred and fifty-six community males completed the Reactive-Proactive Aggression Questionnaire and the Toronto Alexithymia Scale. Amygdala, insula, and ACC volumes were assessed using MRI. Alexithymia was positively associated with reactive but not proactive aggression. Alexithymia was positively and bilaterally associated with amygdala and anterior cingulate volumes. Reactive aggression was positively associated with right amygdala volume. Controlling for right amygdala volume rendered the alexithymia-reactive aggression relationship non-significant. Results suggest that increased right amygdala volume is a common neurobiological denominator for both alexithymia and reactive aggression. Findings suggest that greater right hemisphere activation may reflect a vulnerability to negative affect, which in turn predisposes to experiencing negative emotions leading to increased aggression. Findings are among the first to explicate the nature of the alexithymia-aggression relationship, with potential clinical implications.

[*]Corresponding author: tfarah@sas.upenn.edu, Phone: 267-254-6336.
[+]Shared first-authorship

Keywords

emotion; proactive aggression; impulsivity; volume; structural MRI

1. Introduction

Research on aggression often distinguishes between reactive and proactive aggression (Teten et al., 2008). Reactive aggression (RA), also called “impulsive aggression”, is associated with high emotional arousal and anxiety (Bubier and Drabick, 2009; Raine et al., 2006), and usually occurs as an impulsive response to a perceived threat or provocation. Proactive aggression (PA), also called “instrumental aggression,” is generally planned in advance and motivated by the anticipation of a reward (Euler, Steinlin and Stadler, 2017). These two constructs are highly related (Raine et al., 2006), and share common correlates such as drug use and parental violence (Connor et al., 2003). However, there are also unique risk factors associated with each form of aggression. Whereas hyperactivity, low IQ, and higher attentional bias towards aggression-related words have been linked to RA (Brugman et al., 2015; Connor et al., 2003), PA appears to be associated with lower levels of cognitive and affective empathy, as well as lower attentional bias towards aggression-related words (Brugman et al., 2015; Euler, Steinlin, and Stadler, 2017). Given the conceptual differences between RA and PA, as well as their distinct correlates, findings about one form of aggression may not be generalizable to the other.

1.1. Alexithymia and aggression

One phenomenon that has been studied in relation to aggression is alexithymia. Alexithymia, a term first used by Sifneos (1973), refers to a psychological construct characterized by difficulty in understanding, identifying, and expressing one’s own emotions (Nemiah, 1977). Research has suggested that alexithymia is related to a wide range of psychiatric conditions, including depression (Honkalampi et al., 2000), anxiety (Berardis et al., 2006), psychosis (van der Velde et al., 2015), and alcohol dependence (Thorberg et al., 2009). The small body of research examining the relationship between alexithymia and aggression has found alexithymia to be associated with increased aggression (Velotti et al., 2016). However, these studies have either looked at RA exclusively or failed to distinguish between RA and PA. This leaves the relationship between PA and alexithymia unexplored.

Examining the relationship between alexithymia and each form of aggression may shed light on both the causes of aggression and the nature of alexithymia. If alexithymia is related to PA as well as RA, it might suggest that both forms of aggression stem from an emotional disturbance, despite the common conception of RA as being the “emotional” form of aggression and PA as being unrelated to emotion. On the other hand, if alexithymia is only related to RA, it would suggest that understanding and identifying one’s own emotions is important for behavioral inhibition and regulation, given that RA tends to be impulsive and driven by unregulated emotion (Vitiello and Stoff, 1997).

There is reason to believe that alexithymia may be exclusively related to RA. Past research has indicated that alexithymia is associated with impulsivity (Velotti et al., 2016), which

itself is related to RA (Connor et al., 2003; Hecht and Latzman, 2015). PA aggression, on the other hand, is generally premeditated, so the link between alexithymia and impulsivity does not support the idea of a link between alexithymia and PA. Research has also suggested that while individuals with alexithymia have less understanding of their own emotions, they experience a greater number of emotions, particularly negative ones, and experience them more intensely (Leising, Grande and Faber, 2009). The heightened experience of negative affect in alexithymia may even be due to the lack of understanding of emotional feelings. Since RA is associated with high emotional arousal, and especially with negative affect (Blair, 2001), one might expect that a condition associated with more negative emotions and greater emotional intensity would lead to more RA.

1.2. The neural basis of alexithymia and aggression

Understanding the neural basis of the relationship between alexithymia and aggression could improve our understanding of the driving factors behind aggressive behavior, and potentially help researchers and clinicians reduce aggressive behavior in alexithymic patients. The amygdala is known to play a central role in human emotion, particularly negative emotions (Hamann et al., 2002). Indeed, prior studies have generally found smaller amygdala volume and reduced amygdala response to negative stimuli to be associated with both RA (Pardini et al., 2014) and PA (Lozier et al., 2014; Pardini et al., 2014), as well as with alexithymia (Goerlich-Dobre et al., 2015; Ihme et al., 2013). However, these findings are not entirely consistent. Higher alexithymia scores have been *positively* correlated with the strength of amygdala connectivity to other brain regions when participants process movies portraying anger (Hadjikhani et al. 2017), in line with the notion that alexithymia, or at least scores on the TAS-20, are associated with increased experiencing of negative emotions (Leising, Grande and Faber, 2009). The reason for these inconsistencies are unclear, but may be due to small sample sizes as many of these studies used fewer than 100 participants (Lozier et al., 2014; Pardini et al., 2014). They may also be due to inconsistencies in the use of the left, right, or bilateral amygdalae, or in the choice of behavioral measurements. While the direction of findings remains to be clarified, the amygdala may serve as a common factor that contributes to both alexithymia and aggression. Because the amygdala plays such a key role in emotion, it may be that amygdala abnormalities result in an increased tendency to engage in aggressive behavior, as well as difficulties in understanding one's own emotions.

While the amygdala is well-known as part of the neural circuitry for emotion and thus is a prime candidate for being a neural correlate of alexithymia and aggression, two other brain regions have been implicated in alexithymia and aggression: the insula and the anterior cingulate cortex (Dambacher et al., 2015; Goerlich-Dobre, Bruce, Martens, Aleman, & Hooker, 2014; Kano & Fukudo, 2013). Like the amygdala, the insula has been implicated in emotional processing and experiences, though prior research has suggested differential activation between these brain regions based upon the specific emotion (e.g., amygdala – fear, insula – disgust; Philips et al., 2004). The anterior cingulate cortex (ACC), on the other hand, is thought to be involved in the monitoring and regulation of subcortical structures such as the amygdala and insula as well as error monitoring and reappraisal (Bush, Luu and Posner, 2000; van Veen et al., 2001). These two regions have been thought to partly underlie alexithymia via abnormal neurotransmitter concentrations (GABA in the ACC and glutamate

in the insula) that contribute to disrupted interoceptive awareness (i.e., the perception of internal bodily sensations and changes) (Ernst et al., 2014). Moreover, both the anterior cingulate cortex and the insula have been found to be involved in reactions to provocative situations, thus impairments in these regions may contribute to aggression, particularly RA. As such, these two regions may also be a common neural mechanism that underlie both alexithymia and aggression.

1.3. The current study

The present study examines the relationships between alexithymia and both RA and PA, while considering the role of amygdala volume. It was hypothesized that alexithymia would be more related to RA and PA aggression and that amygdala volume as the primary neural candidate would account for this association. Given mixed prior findings on the amygdala and alexithymia (Hadjikhani et al. 2017) and prior findings of heightened negative affect experiences in those with alexithymia (Leising, Grande and Faber, 2009), the direction of effect regarding amygdala volume and alexithymia was left as exploratory. As secondary, exploratory analyses, the insula and ACC were also examined as other brain regions that may underlie the alexithymia – aggression relationship.

2. Methods

2.1. Participants

One hundred fifty-six male participants were recruited from temporary employment agencies, as prior research has indicated that this population yields higher rates of both antisocial/violent behavior and other forms of psychopathology (Raine et al., 2000). As such, this community sample can yield a wider range of scores on psychopathology measures and minimize skew. Exclusion criteria included lack of fluency in English, history of epilepsy or claustrophobia, neurological abnormality, use of a pacemaker, and metal implants. Ethnicity was as follows: 43.7% Black, 32.3% Caucasian, 15.8% Hispanic, 3.2% Asian, 3.8% other. Ethnicity information was not available for 1.2% of participants. Ages ranged from 21 to 66 (M = 35.34, SD = 8.82). The present data was collected as part of a larger study (Gao, Raine, and Schug, 2012). Participants gave written informed consent and all study procedures were approved by the Institutional Review Boards of the University of Southern California and the University of Pennsylvania.

2.2. Alexithymia

The Toronto Alexithymia Scale (TAS-20) was used to assess alexithymia (Bagby, Parker and Taylor, 1994). The TAS-20 is a self-report measure consisting of 20 items rated on a 5-point Likert scale to yield a total score. Previous research using the TAS-20 has found it to have high internal consistency (α = .81) (Bagby, Parker and Taylor, 1994). Though some have questioned the validity of the TAS-20 due to its strong association with other psychopathology variables, including general psychological distress (Leising, Grande and Faber, 2009), it remains the most commonly used measure of alexithymia (Bagby et al., 2006). To ensure that this was not the case, a measure of negative affect was used as a covariate in all analyses.

2.3. Reactive and proactive aggression

The Reactive-Proactive Aggression Questionnaire (RPQ) was used to assess RA or PA (Raine et al., 2006). The RPQ is a self-report measure consisting of 23 items, with 11 items measuring RA and 12 measuring PA. Items are rated on a 3-point Likert scale, and summed to yield scores for RA and PA. Previous research using the RPQ has found it to have high internal consistency, with α ranging from .89 to .91 (Raine et al., 2006).

2.4. Brain Regions of Interest

2.4.1. MRI acquisition.—MRI scanning was performed on a Siemens 3T Trio scanner. An 8-minute T1-weighted magnetization prepared rapid gradient echo (MPRAGE) structural scan was performed (256 × 256 matrix, 1 × 1 × 1 mm voxel size). The parameters were as follows: repetition time (TR) = 2000 ms, echo time (TE) = 60 ms, matrix = 64 × 64, field of view (FOV) = 192 mm, slice thickness = 3.5 mm, gap = 0 mm, 32 axial slices.

2.4.2. Image processing.—FreeSurfer (Fischl, 2012) was used to process the T1 images obtained through MRI scans and compute amygdala volume for all participants. The pre-processing steps include skull-stripping to remove non-brain tissue from images, correction of signal intensity, motion and inhomogeneity artifacts, spatial registration to Talairach space, and tissue segmentation to classify grey and white matter (Dale, Fischl and Sereno, 1999; Fischl, Sereno and Dale, 1999). Following each of these steps, images are manually inspected to ensure that non-brain material had been properly removed and grey and white matter accurately segmented. Automated segmentation of the left and right amygdala was performed, and the gray matter volumes were extracted for the study's primary hypothesis. These methods were also used to extract gray matter volume measures for the insula and anterior cingulate cortex for the study's secondary hypotheses.

2.5. Covariates

Whole brain volume, age, intellectual functioning, socioeconomic status, medication use, ethnicity, state and clinical anxiety, interoception, and negative affect were also assessed as potential covariates given their suggested relationships in previous studies with aggression (Bubier & Drabick, 2009; Pardini et al., 2014; Raine et al., 2006; Thijssen et al., 2015) and alexithymia (Berthoz et al., 1999; Brewer, Cook and Bird, 2016; De Berardis et al., 2008; Lane, Sechrest and Riedel, 1998; Leising, Grande and Faber, 2009: Santorelli and Ready, 2015; Shah, Hall, Catmur and Bird, 2016). Estimated IQ was based on four subscales of the WAIS-III (Wechsler, 1997; Similarities, Arithmetic, Digit Symbol, and Picture Completion). Socioeconomic status (SES) was assessed using the Hollingshead Four Factor Index of Social Status based upon participants' parental income and education level (Hollingshead, 1975). Medication use was a binary variable reflecting whether the participant was currently using any antidepressant, antipsychotic, anti-anxiety, anti-seizure, or mood stabilizing medication (0 = no, 1 = yes). The State-Trait Anxiety Inventory was used to measure state anxiety (Spielberger et al., 1983). Individual symptoms from the SCID-I Anxiety Disorders module (which included panic disorder, agoraphobia, social phobia, specific phobia, obsessive-compulsive disorder, and post traumatic stress disorder) were coded—per the user's manual—as 0 (inadequate information), 1 (absent), 2 (sub threshold) and 3

(threshold). Symptoms of anxiety disorders due to general medical conditions and substance use, and anxiety disorders not otherwise specified (NOS) were also included by default, as these diagnoses are derived from the same symptoms comprising the main anxiety disorders in this module. Symptoms were summed across all anxiety disorders into a total anxiety disorder symptoms variable which was used as a measure of clinical anxiety. Interoception was measured using a 14-item body sensations questionnaire after a social stress task (see Gao et al., 2012 for full details). Negative affect was assessed using the Positive and Negative Affect Schedule (Watson, Clark and Tellegen, 1988) following a stressful task (see Glenn et al., 2015 for full details). These covariates were included in all analyses.

2.6. Analytic plan

Analyses were conducted using SPSS version 24.0 (IBM Corp, 2016). Correlations and regression analyses were conducted to examine the relationship between alexithymia and aggression. Simple linear regressions were calculated to predict RA and PA based on alexithymia. Hierarchical regressions were used to calculate the alexithymia-aggression relationship after accounting for covariates.

3. Results

Descriptive statistics are provided in Table 1.

3.1. Alexithymia and negative affect

Some have questioned the validity of the TAS-20 because of its high associations with other psychopathology variables, particularly negative emotionality (Leising, Grande and Faber, 2009) or anxiety (Berardis et al., 2008). To ensure that TAS scores in this study were not acting as a proxy for negative emotionality or anxiety, correlation analyses were performed between TAS scores and scores of negative affect as measured by the PANAS (Watson, Clark and Tellegen, 1988) as well as DSM-IV anxiety symptoms and state anxiety as measured by the STAI (Spielberger et al., 1983).

TAS scores were not significantly correlated with PANAS negative affect change scores (r = .063, p = .484), state anxiety (r = −.029, p = .738), or clinical anxiety (r = −.015, p = .863), indicating that the TAS was not measuring negative affectivity nor state or anxiety symptoms amongst this sample. Nevertheless, taking a conservative approach, PANAS negative affect change scores, state anxiety, and clinical anxiety were included as control variables in all further analyses.

3.2. Associations between brain regions, alexithymia, and aggression

Associations between key study variables are outlined in Table 2 (for the full correlation table between all study variables, see Supplemental Materials Table S1). Alexithymia was significantly associated with RA (r = .187, p = .031) but not PA (r = .125, p = .152). For this reason, no further analyses were conducted for PA and all further analyses focused on RA.

Larger right amygdala volume was associated with increased RA (r = .252, p = .005), increased PA (r = .216, p = .016), and increased alexithymia (r = .319, p = .001). Larger left

amygdala volume was associated with increased alexithymia (r = .231, p = .014), but not RA (r = .150, p = .097) or PA (r = .155, p = .087). The left insula was associated with increased alexithymia (r = .196, p = .037), but not RA (r = .133, p = .141) or PA (r = .120, p = .187). Similarly, the right insula was associated with more alexithymia (r = .212, p = .024), but not RA (r = .170, p = .060) or PA (r = .146, p = .108) aggression. The left ACC was not associated with alexithymia (r = −.011, p = .910) or RA (r = .175, p = .052), but was associated with increased PA (r = .243, p = .007). The right ACC was not associated with alexithymia or either aggression types (ps > .087).

3.3. Alexithymia, reactive aggression and the explanatory role of the amygdala

In order to determine the impact of amygdala volume on the alexithymia-reactive aggression relationship, a hierarchical regression was run with the control variables entered in step one, left or right amygdala volume entered in step two, and alexithymia entered in step three, with RA as the dependent variable.

3.3.1. Right amygdala.—With reactive aggression as the dependent variable, covariates were entered in step one, the right amygdala was entered in step two, and alexithymia was entered in step three. At step one, no significant effect was found for the control variables, R^2 = .165, F(10, 81) = 1.597, p = .122. Adding right amygdala volume in step two led to a statistically significant F-change (p = .029; overall model: R^2 = .213, F(11, 80) = 1.974, p = .042). Introducing alexithymia in step three raised the R^2 to .237, but the F-change was not significant (p = .121; overall model: F(12, 79) = 2.048, p = .030). Thus, the relationship between alexithymia and RA was rendered non-significant after adjusting for right amygdala volume.

3.3.2. Left amygdala.—With reactive aggression as the dependent variable, covariates were entered in step one, the left amygdala was entered in step two, and alexithymia was entered in step three. At step one, no significant effect was found for the control variables, R^2 = .165, F(10, 81) = 1.597, p = .122. Adding left amygdala volume in step two did not have a significant effect, F-change p = .704; overall model: R^2 = .166, F(11, 80) = 1.450, p = .168. Introducing alexithymia in step three raised the R^2 to .220, and the F-change was significant (p = .023; overall model: F(12, 79) = 1.853, p = .054). The left amygdala therefore did not change the relationship between alexithymia and RA.

3.4. The insula and anterior cingulate cortex

To test the study's secondary hypotheses, covariates were entered into step one, left/right insula or ACC were entered in step two, and alexithymia was entered in step three, with RA as the dependent variable. Including each of the brain regions in step two yielded non-significant results (ps > .31) and alexithymia was still significantly associated with RA after controlling for each of the four brain regions and covariates (ps < .043) in step three. Overall, these results suggest that the insula and anterior cingulate cortex do not explain the relationship between alexithymia and RA.

4. Discussion

This study set out to examine the relationship between alexithymia and aggression, and to examine whether amygdala volume contributed to this relationship. Alexithymia was positively correlated with RA, but not PA. Left and right amygdala volume was positively related to alexithymia. Right, but not left, amygdala volume was associated with RA and PA. Once variation in right amygdala volume was accounted for, alexithymia was no longer significantly associated with RA, implicating the right amygdala volume as a common denominator for this relationship. Accounting for variation in left amygdala volume did not change the alexithymia – RA relationship. To our knowledge, this is the first study to document an underlying amygdala abnormality to both alexithymia and RA. These findings have theoretical implications regarding the relationship between the amygdala and the ability to understand one's own emotions, as well as the tendency to engage in reactively aggressive behavior.

As secondary analyses, the insula and ACC were also examined as regions of interest that potentially explained the alexithymia – RA relationship. Left and right insula were associated with alexithymia, but not RA or PA. Left ACC was associated with PA, but not RA or alexithymia. Right ACC was not associated with RA, PA, or alexithymia. Regression results indicated that these regions did not explain the relationship between alexithymia and RA.

4.1. Alexithymia and reactive aggression

This study's findings regarding the positive association between alexithymia and RA are broadly in line with previous research, which has consistently shown that alexithymia and RA are positively associated (Kupferberg et al., 2002; Teten et al., 2008). Given that alexithymia is characterized not only by reduced understanding of emotion but also with increased experience of emotion, one would expect alexithymia to be associated with aggression that is driven by strong emotion (reactive aggression), rather than aggression that is driven by goal-directed planning (proactive aggression). Given that people with higher levels of alexithymia feel more negative emotions but are less capable of understanding their emotions (Leising, Grande, and Faber, 2009), this inability to understand one's own emotions likely affects the way in which alexithymia individuals respond to negative emotions. Because RA is often elicited by strong negative emotions (Blair, 2001), alexithymia may predispose to RA by impairing the ability to respond to and deal with negative emotions in non-aggressive ways.

While there may be theoretical reasons to explain why prior studies have not examined the relationship between alexithymia and PA, our study is the first to empirically assess the relationship between these constructs. Our results suggest that while understanding and identifying one's own emotions is important specifically for behavioral inhibition and regulation of impulsive aggression (Vitiello and Stoff, 1997), it is less important in the context of predatory aggression. We caution, however, that while 156 participants is not a small sample for a brain imaging study, future studies with larger sample sizes may yield different findings.

4.2. Amygdala volume, alexithymia, and reactive aggression

A positive association was observed between right amygdala volume and alexithymia, which could be understood in the context of the role played by the amygdala in negative emotionality. The amygdala is known to play a central role in generating emotions, including the negative emotions of anger and fear (LeDoux, 2000). Given that alexithymia is not characterized by deficits in the experience of emotion, but instead by the inability to understand and articulate one's own emotions (Goerlich-Dobre et al., 2015; Leising, Grande, and Faber, 2009), this condition may stem from an amygdala abnormality. Leising, Grande, and Faber (2009) found alexithymia to be positively associated with negative emotionality. Furthermore, a meta-analysis by Mincic (2015) found a positive relationship between amygdala volume and negative emotionality-related traits, though the effect was localized to the *left* amygdala. On the other hand, Schneider et al. (2011) found that the *right* amygdala was more activated by emotional faces than the left, but only in males. The *left* amygdala has been posited to be more involved in the cognitive and intentional control of emotion while the right amygdala plays a greater role in social and automatic emotional responses (Gläscher and Adolphs, 2003; Liu et al., 2015). Higher levels of negative emotionality-related traits predispose to experiencing negative emotions more intensely and more frequently (Mincic, 2015). If greater amygdala volume and higher levels of alexithymia are both associated with greater negative emotionality, then it might reasonably be anticipated that alexithymia would be positively associated with amygdala volume.

A positive relationship was also observed between RA and amygdala volume. Prior research on this relationship has yielded mixed results. While some have found a negative relationship between amygdala volume and function and aggression (Lozier et al., 2014; Thijssen et al., 2015), others have found this relationship to be positive (Coccaro et al., 2007; Da Cunha-Bang et al., 2017). Additionally, some studies report significant findings for the *right* amygdala in relation to antisocial or externalizing behavior (Dotterer et al., 2018; Lozier et al., 2014) while others report significant findings for the *left* amygdala (Bobes et al., 2013; Gopal et al., 2013). Greater right hemisphere activation has been posited to reflect individual differences in vulnerability to negative affect, and such predispositions to experiencing negative emotions may lead to an increased inclination for aggressive behavior (Davidson & Fox, 1989; Raine et al., 1998).

In line with prior studies, the current study implicates the role of the amygdala in alexithymia. In particular, only the *right* amygdala was found to explain the RA – alexithymia relationship. Laterality differences related to affective processes have been hypothesized (Markowitsch 1998), and prior studies have suggested amygdala laterality differences in relation to alexithymia. For example, Goerlich-Dobre et al. (2015) found a positive relationship between alexithymia and amygdala volume in a study of comparable size (125 participants) using a healthy sample with both men and women, and measuring alexithymia using the Bermond-Vorst Alexithymia Questionnaire (Vorst and Bermond, 2001). Additionally, amygdala volume was calculated using SPM8 software (Wellcome Department of Imaging Neuroscience Group, London, UK; http://www.fil.ion.ucl.ac.uk/spm) rather than FreeSurfer. On the one hand, while Goerlich-Dobre et al.'s (2015) study is not entirely comparable methodologically, these similar results lend support to the robust

relationship between amygdala and alexithymia. However, Goerlich-Dobre et al.'s (2015) study found that the *left* amygdala was related to alexithymia whereas the current study found the *right* amygdala to be a key substrate. These conflicting findings need to be resolved in future studies, although the current finding broadly fit within the broader context of knowledge about emotional abnormalities and amygdala anomalies. Past research has found larger amygdala volume to be related to negative emotionality-related traits (Mincic, 2015) as well as to generalized anxiety disorder (De Bellis et al., 2000) and trait anxiety (Mikheenko et al., 2015). Similarly, numerous studies have found positive relationships between RA and trait anxiety (Storch et al., 2004; Vitaro, Brendgen, and Tremblay, 2002). Consistent with these findings, RA is frequently accompanied by anger or fear (Vitiello and Stoff, 1997) and is often elicited by a perceived threat (Blair, 2001). If higher levels of fear and anxiety are associated with higher levels of RA as well as larger amygdala volumes, then a positive relationship between RA and amygdala volume is plausible. While the current study controlled for state and clinical anxiety to isolate the effect of the amygdala on RA, future studies may investigate more complex models with anxiety as a key mechanism or predictor for the amygdala – RA relationship.

Right amygdala volume was found to account for the relationship between alexithymia and RA. There has been surprisingly little research on attempting to understand the alexithymia-reactive aggression relationship at a neural level, and the current findings contribute to filling that gap. While alexithymia involves the inability to understand emotions, it is at the same time associated with more rather than less negative emotionality (Leising, Grande, and Faber, 2009), and given the role of the amygdala in RA as well as negative affect in general, the notion of an amygdala abnormality underlying two affective psychopathologies—alexithymia and reactive aggression—is not entirely unexpected.

4.3. Limitations and future directions

This study has some limitations. The use of an all-male, all-adult sample at heightened risk for aggression calls for the findings of this study to be generalized to other populations in future studies, although there are advantages to using an at-risk population to enhance power. Studies using larger sample sizes could test replicability of the current findings, although the current sample size is not small for a brain imaging study. Future studies might also employ other methods of measuring brain segmentation, such as FSL and manual tracing. In light of studies showing that different measurement methods can lead to different results (Lyden et al., 2016; Morey et al., 2009), the use of multiple methods of measurement may be appropriate.

Doubts have also been raised about the validity of the TAS-20. Some (Leising, Grande and Faber, 2009; Marchesi et al., 2014) have questioned whether the TAS-20 is really measuring alexithymia, or whether it is actually measuring some other construct, such as negative affect. This perspective raises the possibility that the association found in the present study could reflect an association between negative affect in general and RA, rather than alexithymia in particular. Though negative affect as measured by the PANAS was not found to be correlated with alexithymia in this sample ($r = .063$, $p = .484$) and while it was controlled for in this study, future studies might benefit from the use of an additional

measure of alexithymia, such as the Bermond-Vorst Alexithymia Questionnaire (Vorst and Bermond, 2001).

Clinical methods of assessment could also help shed light on the relationships between aggression, alexithymia and the amygdala. Both the Toronto Alexithymia Scale and the Reactive-Proactive Aggression Questionnaire are self-report measures. Measuring alexithymia and RA using clinical assessments that took into account reports by others, including friends, family and medical professionals, could conceivably yield more clinically appropriate measures of these constructs.

Future studies could examine amygdala function as well as structure, a construct that was not available in the current study. Finally, an important caveat is that this study cannot firmly establish specificity of alexithymia to RA alone. PA was positively but non-significantly correlated with alexithymia. Further extension and replication of the current findings could either establish the specificity of RA to alexithymia, or alternatively challenge this position and argue that alexithymia predisposes to multiple forms of aggression.

This study aimed to examine amygdala, insula, and ACC volumes as a potential explanation of the alexithymia – aggression relationship. While confounding and mediating effects may be considered statistically similar, there are arguably important conceptual differences (MacKinnon, Krull, and Lockwood, 2000). Unlike a mediator, a confounding variable does not necessarily imply a causal relationship among variables, and at least one definition of a confound requires that the third variable *not* be an “intermediate” variable (MacKinnon et al., 2000). This study suggests that alexithymia and reactive aggression may be related through a common neurobiological mechanism, but future studies should consider examining mechanisms and models that explain how the amygdala, alexithymia, and aggression are causally related.

4.4. Clinical implications

Findings have potential clinical implications, although we caution that findings first require replication and extension. Clinicians treating patients who display RA aggression may consider assessment for alexithymia. Indeed, a program designed to increase emotional self-understanding in preschool children has been found to reduce their levels of aggressive behavior (Kam, Greenberg, and Kusché, 2004), and there is potential for the extension of this finding to adult psychopathology populations.

Similarly, understanding the experience and causes of anger is an important aspect of cognitive-behavioral therapy for anger management, which is consistently shown to be effective in reducing aggression driven by anger (Hoogsteder et al., 2015). The success of this method of anger management suggests that an improved understanding of one’s own emotions lowers one’s tendency to engage in emotionally driven aggression. A better understanding of the role of emotion and alexithymia in RA, and its neurological correlates, may aid in managing reactively aggressive behavior and reducing the damage that such aggression can cause.

4.5. Conclusions

Alexithymia is associated with RA. Larger right amygdala volume, putatively associated with emotional dysfunction, is both positively associated with both increased alexithymia and increased RA, and was found to account for the alexithymia-reactive aggression relationship. These findings suggest enlargement of the right amygdala may be a neurobiological correlate common to alexithymia and RA and may serve as an underlying mechanism contributing to the etiology of both alexithymia and RA. To our knowledge, this is the first study to document an underlying amygdala abnormality to both alexithymia and RA. Future studies are needed to further define the relationship between alexithymia, RA/PA, and amygdala abnormality. Given the importance of impulsive aggression in a wide range of psychiatric conditions (Coccaro et al., 2007), a further understanding of the neurobiological basis to the alexithymia-reactive aggression would appear warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

Bagby RM, Parker JD, Taylor GJ, 1994 The twenty-item Toronto Alexithymia Scale—I. Item selection and cross-validation of the factor structure. Journal of Psychosomatic Research 38, 23–32. [PubMed: 8126686]

Bagby RM, Taylor G, Parker JDA, Dickens SE, 2006 The development of the Toronto structured interview for Alexithymia: Item selection, factor structure, reliability, and concurrent validity. Psychotherapy and Psychosomatics 75, 25–39. [PubMed: 16361872]

Berardis DD, Campanella D, Nicola S, Gianna S, Alessandro C, Chiara C, Valchera A, Marilde C, Salerno RM, Ferro FM, 2008 The impact of alexithymia on anxiety disorders: A review of the literature. Current Psychiatry Reviews 4, 80–86.

Berthoz S, Consoli S, Perez-Diaz F, Jouvent R, 1999 Alexithymia and anxiety: Compounded relationships? A psychometric study. European Psychiatry 14, 372–378. [PubMed: 10683621]

Blair RJR, 2001 Neurocognitive models of aggression, the antisocial personality disorders, and psychopathy. Journal of Neurology, Neurosurgery and Psychiatry 71, 727–731.

Bobes MA, Ostrosky F, Diaz K, Romero C, Borja K, Santos Y, Valdes-Sosa M, 2013 Linkage of functional and structural anomalies in the left amygdala of reactive-aggressive men. Social, Cognitive, and Affective Neuroscience 8, 928–936. [PubMed: 22956672]

Brewer R, Cook R, Bird G, 2016 Alexithymia: A general deficit of interoception. Royal Society Open Science 3.

Brugman S, Lobbestael J, Arntz A, Cima M, Schuhmann T, Dambacher F, Sack AT, 2015 Identifying cognitive predictors of reactive and proactive aggression. Aggressive Behavior 41, 51–64. [PubMed: 27539874]

Bubier JL, Drabick DAG, 2009 Co-occurring anxiety and disruptive behavior disorders: The roles of anxious symptoms, reactive aggression, and shared risk processes. Clinical Psychology Review 29, 658–669. [PubMed: 19729235]

Bush G, Luu P, Posner MI, 2000 Cognitive and emotional influences in the anterior cingulate cortex. Trends in Cognitive Sciences 4, 215–222. [PubMed: 10827444]

Coccaro EF, McCloskey MS, Fitzgerald DA, Phan KL, 2007 Amygdala and orbitofrontal reactivity to social threat in individuals with impulsive aggression. Biological Psychiatry 62, 168–178. [PubMed: 17210136]

Connor DF, Steingard RJ, Anderson JJ, Melloni RH, 2003 Gender differences in reactive and proactive aggression. Child Psychiatry and Human Development 33, 279–294. [PubMed: 12723901]

Da Cunha-Bang S, Fisher PM, Hjordt LV, Perfalk E, Persson Skibsted A., Bock C, … Knudsen GM, 2017 Violent offenders respond to provocations with high amygdala and striatal reactivity. Social Cognitive and Affective Neuroscience 12, 802–810. [PubMed: 28338916]

Dale AM, Fischl B, Sereno MI, 1999 Cortical surface-based analysis. I. Segmentation and surface reconstruction. NeuroImage 9, 179–194. [PubMed: 9931268]

Dambacher F, Sack AT, Lobbestael J, Arntz A, Brugman S, Schuhmann T, 2015 Out of control: Evidence for anterior insula involvement in motor impulsivity and reactive aggression. Social, Cognitive, and Affective Neuroscience 10, 508–516. [PubMed: 24837479]

Davidson RJ, Fox NA, 1989 Frontal brain asymmetry predicts infants' response to material separation. Journal of Abnormal Psychology 98, 127–131. [PubMed: 2708653]

De Bellis MD, Casey BJ, Dahl RE, Birmaher B, Williamson DE, Thomas KM, … Ryan ND, 2000 A pilot study of amygdala volumes in pediatric generalized anxiety disorder. Biological Psychiatry 48, 51–57. [PubMed: 10913507]

Dotterer HL, Hyde LW, Swartz JR, Hariri AR, Williamson DE, 2017 Amygdala reactivity predicts adolescent antisocial behavior but not callous-unemotional traits. Developmental Cognitive Neuroscience 24, 84–92. [PubMed: 28279916]

Euler F, Steinlin C, Stadler C, 2017 Distinct profiles of reactive and proactive aggression in adolescents: associations with cognitive and affective empathy. Child and Adolescent Psychiatry and Mental Health 11. doi:10.1186/s13034-016-0141-4

Fischl B, 2012 FreeSurfer. NeuroImage 62, 774–781. [PubMed: 22248573]

Fischl B, Sereno MI, Dale AM, 1999 Cortical surface-based analysis. II: Inflation, flattening, and a surface-based coordinate system. NeuroImage 9, 195–207. [PubMed: 9931269]

Gao Y, Raine A, Schug RA, 2012 Somatic aphasia: Mismatch of body sensations with autonomic stress reactivity in psychopathy. Biological psychology 90, 228–233. [PubMed: 22490763]

Gläscher J, Adolphs R, 2003 Processing of the arousal of subliminal and supraliminal emotional stimuli by the human amygdala. Journal of Neuroscience 23, 10274–10282. [PubMed: 14614086]

Glenn AL, Remmel RJ, Raine A, Schug RA, Gao Y, Granger DA, 2015 Alpha-Amylase Reactivity in Relation to Psychopathic Traits in Adults. Psychoneuroendocrinology 54, 14—23. [PubMed: 25662339]

Goerlich-Dobre KS, Bruce L, Martens S, Aleman A, Hooker CI, 2014 Distinct associations of insula and cingulate volume with the cognitive and affective dimensions of alexithymia. Neuropsychologia 53, 284–92. [PubMed: 24334109]

Goerlich-Dobre KS, Lamm C, Pripfl J, Habel U, Votinov M, 2015 The left amygdala: A shared substrate of alexithymia and empathy. NeuroImage 122, 20–32. [PubMed: 26275382]

Goerlich-Dobre KS, Votinov M, Habel U, Pripfl J, Lamm C, 2015 Neuroanatomical profiles of alexithymia dimensions and subtypes. Human Brain Mapping 36, 3805–3818. [PubMed: 26094609]

Gopal A, Clark E, Allgair A, D'Amato C, Furman M, Gansler DA, Fulwiler C, 2013 Dorsal/ventral parcellation of the amygdala: Relevance to impulsivity and aggression. Psychiatry Research 211, 24–30. [PubMed: 23352275]

Hadjikhani N, Zurcher NR, Lassalle A, Hippolyte L, Ward N, Johnels JÅ, 2017 The effect of constraining eye-contact during dynamic emotional face perception—an fMRI study. Social Cognitive and Affective Neuroscience 12, 1197–1207. [PubMed: 28402536]

Hamann SB, Ely TD, Hoffman JM, Kilts CD, 2002 Ecstasy and agony: activation of the human amygdala in positive and negative emotion. Psychological Science 13, 135–141. [PubMed: 11933997]

Hecht LK, Latzman RD, 2015 Revealing the nuanced associations between facets of trait impulsivity and reactive and proactive aggression. Personality and Individual Differences 83, 192–197.

Hollingshead AB, 1975 Four Factor Index of Social Status [Measurement instrument] New Haven, CT: Yale University.

Honkalampi K, Hintikka J, Tanskanen A, Lehtonen J, Viinamäki H, 2000 Depression is strongly associated with alexithymia in the general population. Journal of psychosomatic research 48, 99–104. [PubMed: 10750635]

Hoogsteder LM, Stams GJJ, Figge MA, Changoe K, van Horn JE, Hendriks J, Wissink IB, 2015 A meta-analysis of the effectiveness of individually oriented Cognitive Behavioral Treatment (CBT) for severe aggressive behavior in adolescents. The Journal of Forensic Psychiatry and Psychology 26, 22–37.

IBM Corp. Released 2016 IBM SPSS Statistics for Windows, Version 24.0 Armonk, NY: IBM Corp.

Ihme K, Dannlowski U, Lichev V, Stuhrmann A, Grotegerd D, Rosenberg N, … Suslow T, 2013 Alexithymia is related to differences in gray matter volume: a voxel-based morphometry study. Brain Research 1491, 60–67. [PubMed: 23123707]

Kam CM, Greenberg MT, Kusché CA, 2004 Sustained effects of the PATHS curriculum on the social and psychological adjustment of children in special education. Journal of Emotional and Behavioral Disorders 12, 66–78.

Kano M, Fukudo S, 2013 The alexithymia brain: The neural pathways linking alexithymia to physical disorders. BioPsychoSocial Medicine 7, 1. [PubMed: 23302233]

Kupferberg S, 2002 The relation between alexithymia and aggression in a nonclinical sample. Dissertation Abstracts International: Section B: The Sciences and Engineering 63, 3011.

Lane RD, Sechrest L, Riedel R, 1998 Sociodemographic correlates of alexithymia. Comprehensive Psychiatry 39, 377–385. [PubMed: 9829146]

LeDoux JE, 2000 Emotion circuits in the brain. Annual Review of Neuroscience 23, 155–184.

Leising D, Grande T, Faber R, 2009 The Toronto Alexithymia Scale (TAS-20): A measure of general psychological distress. Journal of Research in Personality 43, 707–710.

Liu T, Chen Y-S, Hsieh J-C, Chen L-F, 2015 Asymmetric engagement of amygdala and its gamma connectivity in early emotional face processing. PLoS One 10, e0115677 [PubMed: 25629899]

Lozier LM, Cardinale EM, Van Meter JW, Marsh AA, 2014 Mediation of the relationship between callous-unemotional traits and proactive aggression by amygdala response to fear among children with conduct problems. JAMA Psychiatry 71, 627–636. [PubMed: 24671141]

Lyden H, Gimbel SI, Del Piero L, Tsai AB, Sachs ME, Kaplan JT, Margolin G, Saxbe D, 2016 Associations between Family Adversity and Brain Volume in Adolescence: Manual vs. Automated Brain Segmentation Yields Different Results. Front. Neurosci 398.

Marchesi C, Ossola P, Tonna M, De Panfilis C, 2014 The TAS-20 more likely measures negative affects rather than alexithymia itself in patients with major depression, panic disorder, eating disorders and substance use disorders. Compr. Psychiatry 55, 972–8. [PubMed: 24439561]

MacKinnon DP, Krull JL, Lockwood CM, 2000 Equivalence of mediation, confounding and suppression effect. Prevention Science 1, 173. [PubMed: 11523746]

Marckowitsch HJ, 1998 Differential contribution of right and left amygdala to affective information processing. Behavioural Neurology 11, 233–244. [PubMed: 11568425]

Matthies S, Rusch N, Weber M, Lieb K, Philipsen A, Tuescher O, Ebert D, Hennig J, van Elst LT, 2012 Small amygdala – high aggression? The role of the amygdala in modulating aggression in healthy subjects. World Journal of Biological Psychiatry 13, 75–81. [PubMed: 22256828]

Mikheenko Y, Shiba Y, Sawiak S, Braesicke K, Cockcroft G, Clarke H, Roberts AC, 2015 Serotonergic, brain volume and attentional correlates of trait anxiety in primates. Neuropsychopharmacology 40, 1395–1404. [PubMed: 25586542]

Mincic AM, 2015 Neuroanatomical correlates of negative emotionality-related traits: A systematic review and meta-analysis. Neuropsychologia 77, 97–118. [PubMed: 26265397]

Morey RA, Petty CM, Xu Y, Hayes JP, Wagner HR, Lewis DV, et al., 2009 A comparison of automated segmentation and manual tracing for quantifying hippocampal and amygdala volumes. Neuroimage 45, 855–866. [PubMed: 19162198]

Nemiah JC, 1977 Alexithymia: Theoretical considerations. Psychotherapy and Psychosomatics 28, 199–206. [PubMed: 609679]

Pardini DA, Raine A, Erickson K, Loeber R, 2014 Lower amygdala volume in men is associated with childhood aggression, early psychopathic traits, and future violence. Biological Psychiatry 75, 73–80. [PubMed: 23647988]

Philips ML, Williams LM, Heining M, Herba CM, Russell T, Andrew C, Bullmore ET, Brammer MJ, Williams SC, Morgan M, Young AW, Gray JA, 2004 Differential neural responses to overt and

covert presentations of facial expressions of fear and disgust. Neuroimage 21, 1484–1496. [PubMed: 15050573]

Raine A, Dodge K, Loeber R, Gatzke- Kopp L, Lynam D, Reynolds C, … Liu J, 2006 The reactive–proactive aggression questionnaire: Differential correlates of reactive and proactive aggression in adolescent boys. Aggressive Behavior 32, 159–171. [PubMed: 20798781]

Raine A, Lencz T, Bihrle S, LaCasse L, Colletti P, 2000 Reduced prefrontal gray matter volume and reduced autonomic activity in antisocial personality disorder. Archives of General Psychiatry 57, 119–127. [PubMed: 10665614]

Raine A, Meloy JR, Bihrle S, Stoddard J, LaCasse L, Buchsbaum MS, 1998 Reduced frontal and increased subcortical brain functioning assessed using positron emission tomography in predatory and affective murderers. Behavioral Sciences and the Law 16, 319–332. [PubMed: 9768464]

Santorelli GD, Ready RE, 2015 Alexithymia and Executive Function in Younger and Older Adults. The Clinical Neuropsychologist 29, 938–955. [PubMed: 26701062]

Schneider S, Peters J, Bromberg U, Menz MM, Miedl SF, Loth E, … Büchel C, 2011 Boys do it the right way: sex-dependent amygdala lateralization during face processing in adolescents. Neuroimage 56, 1847–1853. [PubMed: 21316467]

Shah P, Hall R, Catmur C, Bird G, 2016 Alexithymia, not autism, is associated with impaired interoception. Cortex 81, 215–220. [PubMed: 27253723]

Sifneos PE, 1973 The prevalence of ‗alexithymic' characteristics in psychosomatic patients. Psychother. Psychosom 22, 255–262. [PubMed: 4770536]

Spielberger CD Gorsuch RL., Lushene R, Vagg PR, Jacobs GA1983 Manual for the State-Trait Anxiety Inventory Palo Alto, CA: Consulting Psychologists Press.

Storch EA, Bagner DM, Geffken GR, Baumeister AL, 2004 Association between overt and relational aggression and psychosocial adjustment in undergraduate college students. Violence and Victims 19, 689–700. [PubMed: 16004070]

Teten AL, Miller LA, Bailey SD, Dunn NJ, Kent TA, 2008 Empathic deficits and alexithymia in trauma- related impulsive aggression. Behavioral Sciences and the Law 26, 823–832. [PubMed: 19039794]

Thijssen S, Ringoot AP, Wildeboer A, Bakermans-Kranenburg MJ, El Marroun H, Hofman A, … White T, 2015 Brain morphology of childhood aggressive behavior: A multi-informant study in school-age children. Cognitive, Affective, and Behavioral Neuroscience 15, 564–577.

Thorberg FA, Young RM, Sullivan KA, Lyvers M, 2009 Alexithymia and alcohol use disorders: a critical review. Addictive behaviors 34, 237–245. [PubMed: 19010601]

Van der Velde J, Swart M, van Rijn S, van der Meer L, Wunderink L, Wiersma D, … Aleman A, 2015 Cognitive alexithymia is associated with the degree of risk for psychosis. PLOS ONE 10, e0124803. [PubMed: 26030357]

Van Veen V, Cohen JD, Botvinick MM, Stenger VA, Carter CS, 2001 Anterior cingulate cortex, conflict monitoring, and levels of processing. Neuroimage 14, 1302–1308. [PubMed: 11707086]

Velotti P, Garofalo C, Petrocchi C, Cavallo F, Popolo R, Dimaggio G, 2016 Alexithymia, emotion dysregulation, impulsivity and aggression: A multiple mediation model. Psychiatry research, 237 296–303. [PubMed: 26803364]

Vitaro F, Brendgen M, Tremblay RE, 2002 Reactively and proactively aggressive children: Antecedent and subsequent characteristics. Journal of Child Psychology and Psychiatry 43, 495–505. [PubMed: 12030595]

Vitiello B, Stoff DM, 1997 Subtypes of aggression and their relevance to child psychiatry. Journal of the American Academy of Child & Adolescent Psychiatry 36, 307–315. [PubMed: 9055510]

Vorst H, Bermond B, 2001 Validity and reliability of the Bermond-Vorst Alexithymia Questionnaire. Pers Individ Dif 30, 413–434.

Watson D, Clark LA, Tellegen A, 1988 Development and Validation of Brief Measures of Positive and Negative Affect: The PANAS Scales. Journal of Personality and Social Psychology 54, 1063–1070. [PubMed: 3397865]

Wechsler D, 1997 Wechsler Adult Intelligence Scale – Third Edition [Measurement instrument] San Antonio, TX: Pearson.

Highlights

- Alexithymia is associated with reactive aggression, but not proactive aggression.
- Alexithymia, reactive aggression, and amygdala volume are positively associated.
- Controlling for amygdala volume, alexithymia is unrelated to reactive aggression.
- Amygdala volume partly explains the alexithymia-reactive aggression relationship.

Table 1.

Descriptive Statistics for Study Variables (N = 156)

Variables	*n*	Min.	Max.	*M*	*SD*
Reactive Aggression	148	0	19	6.82	3.73
Proactive Aggression	148	0	18	2.05	2.83
Alexithymia	138	20	67	43.90	11.06
L. Amygdala Vol.	127	722	2237	1676.08	218.24
R. Amygdala Vol.	127	547	2634	1639.70	279.59
L. Anterior Cingulate Vol.	127	2283	6301	4250.57	785.22
R. Anterior Cingulate Vol.	127	1818	6880	4071.09	978.85
L. Insula Vol.	127	3564	8149	6202.24	774.95
R. Insula Vol.	127	3637	8259	6299.92	758.59
Socioeconomic Status	156	2	5	3.22	.77
Cognitive Intelligence	147	52	146	98.22	15.31
Age	155	51	66	35.72	8.61
Medication Use	155	0	1	.03	.18
PANAS Negative Affect Change	138	-5	44	8.21	10.48
Clinical Anxiety	149	64	155	71.51	12.17
State Anxiety	143	12	56	28.09	9.82
Body Sensations	147	14	51	22.83	7.63

Notes. N = number of participants for which data on each variable was available. Brain regions measured in mm^3.

Table 2.

Zero-Order Correlations between Key Study Variables.

	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
(1) Alexithymia	.187*	.125	.231*	.319**	−.011	.137	.196*	.212*
(2) Reactive Agg.	1	.564**	.150	.252**	.175	.155	.133	.170
(3) Proactive Agg.		1	.155	.216*	.243**	.115	.120	.146
(4) L. Amygdala			1	.795**	.427**	.364**	.612**	.613**
(5) R. Amygdala				1	.289**	.227*	.504**	.536**
(6) L. ACC					1	.400**	.562**	.563**
(7) R. ACC						1	.507**	.533**
(8) L. Insula							1	.908**
(9) R. Insula								1

*p < .05,

**p < .01.

L = left, R = right. ACC = anterior cingulate cortex. WBV = whole brain volume. Anx = Anxiety