Development of a methodology to combine fMRI and EMG to measure emotional responses in patients with anorexia nervosa

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Abstract
Objective: Individuals with eating disorders are theorized to have basic impairments in affective appraisal and social-emotional processing that contribute to pathogenesis of the disease. We aimed to determine if facial electromyography could be used to discriminate between happy and disgust emotions during simultaneous acquisition of an fMRI BOLD sequence in efforts to establish a novel tool for investigating emotion-driven hypotheses about eating pathology. In line with standards for rigor and reproducibility, we provide detailed protocols and code to support each step of this project.

Method: Sixteen adolescents with low-weight eating disorders viewed emotional faces (Happy or Disgust) and were asked to mimic their facial expression during simultaneous BOLD and EMG (Corrugator supercilii, Lavator lavi, Zygomaticus major) acquisition. Trials were repeated with the scanner off and again with scanner on (i.e., fatigue).

Results: The Levator and Zygomaticus activation patterns discriminated disgust and happy faces successfully. The pattern held between scanner on and off conditions, but muscle activation attenuated in the Fatigue condition, especially for the Zygomaticus.

Discussion: Simultaneous fMRI–EMG is a new tool capable of discriminating specific emotions based on muscle activation patterns and can be leveraged to answer emotion-driven hypotheses about clinical populations characterized by difficulty labeling or processing emotions.

KEYWORDS
adolescent, anorexia nervosa, disgust, electromyography, emotional processing, fMRI

1 INTRODUCTION

A growing research literature documents abnormalities among individuals with anorexia nervosa (AN) on a range of measures relevant to emotion (Lavender et al., 2015), with several emotion-specific models to characterize psychopathology and guide treatment resulting from studies in this area (Hildebrandt, Bacow, Markella, & Loeb, 2012; Treasure & Cardi, 2017; Wildes, Ringham, & Marcus, 2010). Impairments are noted in components of Theory of Mind, or the ability to infer others’ thoughts, beliefs, or emotions and process affective stimuli during the acute phase of illness and after weight restoration (Bora & Köse, 2016), recognizing facial expressions (Caglar-Nazali et al., 2014; Oldershaw et al., 2011), and diminished facial expressions in response to positive and negative stimuli (Davies et al., 2016; Leppanen et al., 2017). Problems with emotion processing appear to exert an important effect on the onset and persistence of AN (Treasure & Cardi, 2017; Treasure & Schmidt, 2013), and in predicting long-term response to treatment (Nielsen et al., 2015; Speranza, Loas, Wallier, & Corcos, 2007).
Some emerging evidence suggests the deficits observed in the emotional processing of individuals with AN may relate to how social cues are interpreted, as patients may have skill for evaluating social cues from the outside, while also being more likely to have a negative social evaluation, or view others as cold or rejecting when personally involved (Ambwani et al., 2015). Other models for the role of emotion suggest food avoidance originates and is maintained by disgust conditioning (Hildebrandt et al., 2015) and/or that symptoms are maintained by their ability to suppress emotional responses (Racine & Wildes, 2013). It is therefore important to understand specific differences in emotional processes among patients with AN, particularly through observable biological measures, including the study of underlying neural mechanisms that increase risk or maintain the illness.

The field of affective neuroscience continues to evolve, and novel methodologies have been developed to dissect the neurocircuitry of emotion. Basic neurobiological differences in emotional responses and the processing of emotional stimuli among clinical populations, like AN, have emerged. However, a major obstacle to methods that link specific emotional experiences to central nervous system responses has been the reliance of studies on self-reported affective responses (e.g., fear, anger, disgust, etc.) to social or emotional stimuli. The presence of alexithymia, or the inability to describe or recognize emotions, is well-documented among individuals with AN (e.g., Westwood et al., 2017). For populations with high levels of alexithymia, the utility of self-report measures of emotion appears limited due to difficulties regulating or processing emotion, and poor language skills (Larsen & Fredrickson, 1999; Mauss & Robinson, 2009). It is therefore unlikely that reliable answers will be obtained from any assessment where individuals with AN are asked to label their own emotional states. Measurement challenges for emotions extend to physiological markers like skin conductance, pupil dilation, cardiac monitoring, and startle, as there are limitations in reliability, continuity, obtrusiveness, and valence specificity (Heller et al., 2011). Investigators have therefore considered whether other measures of emotion may have utility in the context of brain imaging.

Facial electromyography (EMG) is an affective neuroscience tool available for identifying emotional appraisal of different stimuli by capturing activation of specific muscle fibers that can be used to identify positive or negative appraisal or unique emotions. This work relies heavily on the significant amount of data supporting that the core emotional states (happy/joy, anger, hunger/appetite, sadness, disgust) in humans are associated with reflexive facial signatures that occur across cultures, are present in infants, and even those who are blind (see Wolf, 2015). Research using EMG (e.g., Cacioppo et al., 2000) indicates that this method is robust, unobtrusive, objective (Cacioppo et al., 1986; Cacioppo & Tassinary, 1990), and distinguishes between several valence-specific emotions (Lang et al., 1993), which has led to interest in integrating this method with neuroimaging.

A prior report (Heller et al., 2011) presented a method for acquiring facial EMG data during blood oxygenation level dependent (BOLD) fMRI. Participants viewed negative and neutral images known to elicit negative valence and found that negative images elicited greater amygdala and corrugator supercilii responses. As facial EMG measures micro-volt (mV) level changes in muscle activity, the authors made accommodations to include 1-second “silent times” between BOLD captures to separate any effects of the fMRI magnet on EMG signaling. The authors noted that the EMG signal was “overwhelmed” by the electromagnetic noise from the fMRI, and it was not possible to detect the EMG when the magnet was operating. Although Heller and colleagues replicated prior findings for the measurement of facial EMG, suggesting the combination of EMG and fMRI was possible, the collection of data was limited by the need to stop the magnet to obtain a sufficient signal of emotion, which limits the use of this methodology. Specifically, stopping the fMRI during a task could affect participant behavior and emotional response (e.g., it is noticeable when the magnet stops due to reduced noise) and the measurement of brain activity (e.g., signal is not obtained) in times when the fMRI is off.

Other methods of simultaneous fMRI and psychophysiology model and subsequently subtract fMRI artifacts from data collected during experimental tasks in the scanner, which evolved from fMRI-electroencephalography (fMRI–EEG) methods. This technique incorporates a range of increasingly complex noise detection and filtering algorithms that perform differentially based on the specific parameters of interest and experimental design (see Grouiller et al., 2007). At least one study has applied these subtraction methods to fMRI–EMG in the context of an eye-blink startle paradigm (van Well, Visser, Scholte, & Kindt, 2012). A primary concern during simultaneous fMRI and EMG relates to gradient artifacts (GA), which are high amplitude effects that originate from switching of the magnetic field. GA effects do not overlap with the most relevant range of EMG signals, but may overlap in the frequency domain, and consequently a GA removal approach is best adapted to the specific experimental paradigm and range of electrophysiological signal of interest. In other words, the removal of unwanted effects will depend on what type of electrophysiological signal and which aspects of the signal are of primary interest (frequency, amplitude, etc.).

The purpose of the current study was therefore to develop a straightforward methodology to analyze simultaneous EMG–fMRI data efficiently during fMRI BOLD sequences to increase the likelihood of reproducibility across laboratories using this technology. Techniques from prior research (e.g., Heller et al. 2011; van Well, Visser, Scholte, & Kindt, 2012) were reviewed, and in contrast to existing methods, our analytic plan was chosen to allow for EMG measurement during an fMRI task with efficient filtering of GA. To isolate and simplify the analytic technique, data were collected during a basic assessment of facial emotions in the fMRI, with the intention to refine the GA output could be used to model the unique emotion of each stimuli. Specifically, we hypothesized differential voluntary muscle activation to happy and disgust faces (i.e., Face × Muscle type interaction), with ‘Yuck’ faces eliciting greater levator labii activation than ‘Smile’ faces and ‘Smile’ faces eliciting greater zygomaticus major activation than ‘Yuck’ faces for the same muscle.
2 | METHOD

2.1 | Participants

A total of 16 adolescent females ages 12–18 (M = 16.0; SD = 1.4) recruited from a larger ongoing study of low-weight eating disorders participated in this study; average BMI = 16.8; SD = 1.4. The sample was primarily Caucasian (94.1% non-Hispanic) and high income (82.4% earning >$100,000/year). The inclusion criteria included adolescents seeking treatment for low-weight eating disorder (anorexia nervosa, atypical anorexia nervosa), medically stable for outpatient treatment, free of psychiatric medication, or physical status that would prevent MRI. Exclusion criteria included pregnancy, a medical or physical condition/status incompatible with MRI, food allergies that would prevent participation in other aspects of the study, and any comorbid thought disorder or substance use disorder.

2.2 | Procedures

To support efforts toward replicability and in keeping with evolving standards for rigor and reproducibility, appendices with step-by-step instructions and a video of the procedures involved in our study have been provided. A brief description of the other methods appears below.

2.2.1 | Maximal voluntary facial expression

While in the fMRI, participants were told they would see a picture with an individual making a specific emotional face on the screen. They were asked to mimic the face, with specific attention to activating facial muscles that would capture the emotional state of the image. Eliciting the maximum voluntary contraction of targeted muscles is a procedure that can be used to create within-subject standardization of muscle activation and to study muscle fatigue for EMG responses (Fridlund, Schwartz, & Fowler, 1984; van Boxtel, Goudsward, van der Molen, & van den Bosch, 1983). Each run (scanner on, scanner off, and fatigue) was initiated and concluded with an 8000 ms fixation. A total of 10 faces (5 happy, 5 disgust) were displayed at 4000 ms with an interstimulus interval of 8000 ms, alternating with the order counterbalanced for each condition (on, off, fatigue). Instructions stated, “You will be shown a short series of facial expressions of happiness and disgust. Please imitate the facial expressions without moving your head” on screen projected to participants in MRI. Figures were presented with E-Prime software (Psychology Software Tools, Pittsburgh, PA) which marked stimuli presentation for data acquisition through Biopac interface (see Supporting Information Material). The “On” condition included voluntary contractions during the BOLD sequence, the “Off” condition included voluntary contractions in the scanner with scanner off, and the “Fatigue” condition repeated the same block with the scanner off. The Fatigue condition provided a measure of the degree to which muscle contraction changes over repeated measurements.

2.2.2 | Electromyography

EMG data were acquired using Biopac MP-150 system equipped with EMG-100MRI module and AcqKnowledge-4 software with the sampling rate of 10 kHz. EMG-100MRI with high and low pass filters set to 10 500 Hz, respectively. A narrow band 60 Hz filter was also applied to remove components associated with the main power lines. The data acquisition was synchronized with the scanner via an external TTL trigger.

2.2.3 | Processing of raw EMG data

The processing of facial EMG data included applying a fast Fourier transformation to identify the harmonic associated with TR (10 Hz) and a band pass filter to remove high amplitude signals above 60 Hz. The filtered signals were rectified and the rectified data cut into 2 s epochs with mean amplitude calculated for each epoch within the time series (10 epochs per Condition × 3 Muscle types × 3 Conditions; n = 90 per individual). Means were transformed to within-subject standardized Z-scores (epoch mean-pooled mean/pooled SD for 4-s trial). The acknowledge files were exported to MATLAB files for preprocessing and the data were exported to R v3.4. (R Development Core Team, 2017) for statistical analysis.

2.3 | Statistical analysis

We used linear mixed models to estimate the effect of the Face stimulus (Yuck vs. Smile face), Condition (BOLD sequence ON; scanner Off, and Fatigue), Muscle (Levator, Corrugator, Zygomaticus), and trial for the 10 repeated stimuli within each block. The dependent variable was Z-score for mean activation during the first 1.5 s of each stimulus window.

2.3.1 | fMRI acquisition and analysis

Sixty-four T2*-weighted gradient-echo planar images depicting the BOLD signal (repetition time [TR] = 2000 ms, echo time = 35 ms, flip angle = 76°, field of view = 230 mm×90 × 90 matrix, in-plane resolution = 2.6 mm², slice thickness = 2.56 mm, 60 axial slices) were acquired during the emotion assessment using a 3 T Skyra MR system (Siemens, Erlangen, Germany). The data were analyzed using SPM12 software (Wellcome Trust Center for Neuroimaging, London, UK). The BOLD images were corrected for the staggered acquisition of slices, motion-corrected, co-registered to a T1-weighted anatomical image, spatially normalized to the Montreal Neurological Institute template, and smoothed with a Gaussian kernel. Subject-specific general linear models fitted beta weights to delayed boxcar functions representing face presentations, as well as motion parameters of no interest, which were all convolved with the default SPM hemodynamic response function. Linear contrasts were applied to parameter estimates for the smile and yuck faces and the resultant contrast maps were entered into group-level random-effects general linear models.

3 | RESULTS

Figure 1 shows the results of processing data for the scanner On (with and without filtering) Condition of the levator labii in a single subject during the full 10 trial block. Visual inspection of the processed images such as Figure 1 suggested the primary EMG signal was successfully recovered. We estimated successive nested models with a random
intercept and each hypothesized source of variability in muscle activation (face, condition, muscle, and trial) and tested model fit using likelihood ratio tests. Table 1 summarizes the fit of the different models and the results of model comparisons indicating that a model with interactions between face \times muscle and muscle \times condition provided the best fit. The fit comparisons suggested that the effect of trial could be dropped from the entire model, but it was retained for theoretical relevance, as it is possible that the execution of facial expressions could show fatigue over successive trials. Table 2 summarizes the best fitting model results, which explained about 30% of the variability in muscle activation.

3.1 | Facial discrimination

A muscle type \times face interaction provided evidence of differential activation within the three muscles (corrugator, levator, and zygomaticus) for Smile and Yuck faces. Figure 2 summarizes mean differences and follow-up contrasts indicated that Levator was significantly more active in response to Yuck faces than Zygomaticus \((M_{\text{diff}} = .294, \ SE = .022, \ 95\% \ CI = .251, .337, \ t = 13.39, \ p < .0001)\) and Corrugator \((M_{\text{diff}} = .091, \ SE = .022, \ 95\% \ CI = .134, .048, \ t = 4.13, \ p < .0001)\) muscles. In contrast, Zygomaticus was significantly more active in response to Smile faces than Levator \((M_{\text{diff}} = .356, \ SE = .022, \ 95\% \ CI = .313, .399, \ t = 16.20, \ p < .0001)\) and Corrugator \(M_{\text{diff}} = .182, \ SE = .022, \ 95\% \ CI = .139, .225, \ t = 8.28, \ p < .0001)\) muscles. The Corrugator did not significantly discriminate Yuck from Smile faces \((M_{\text{diff}} = −.021, \ SE = .022, \ 95\% \ CI = −.064, .022, \ t = .97, \ p = .33)\).

3.2 | Condition

The lower order main effect of Condition was nonsignificant in the final model. However, follow-up contrasts indicated that mean activation was higher in the scanner On condition than scanner Off \((M_{\text{diff}} = .043, \ SE = .015, \ 95\% \ CI = .013, .073, \ t = .282, \ p < .001)\). As Figure 3 summarizes, this lower order effect is the result of a Condition X Muscle type interaction, which indicates that Levator was significantly more active in the Fatigue condition than the scanner Off condition \((M_{\text{diff}} = .078, \ SE = .027, \ 95\% \ CI = .230, .144, \ t = 2.87, \ p < .01)\) and Zygomaticus showed a significant decrease in activation in the Fatigue condition relative to scanner On \((M_{\text{diff}} = −.112, \ SE = .027, \ 95\% \ CI = −.165, −.593, \ t = .8.51, \ p < .0001)\) and scanner Off \((M_{\text{diff}} = −.061, \ SE = .027, \ 95\% \ CI = .165, .059, \ t = −4.16, \ p < .05)\) Condition. Consequently, there are some muscle specific differences in measurement across time with Zygomaticus showing the greatest attenuation to repeated measures.

3.3 | Trial effects

No significant linear differences were found for the repeated presentation of faces within each block. A visual inspection of the Trial \times Face and Trial \times Muscle data revealed no clear pattern to motivate nonlinear tests of the Trial sequence in the model.
1350 observations across 16 subjects. The function r2beta() yields a standardized effect size for each parameter. Total model effect size listed in intercept row above. Model includes \( \kappa = 196 \) voxels; \( x > 25 \) contiguous voxels, but differential BOLD signal changes found \( \kappa \). Model estimated using lme() function of the nlme package in R.

### TABLE 1 Comparison of nested linear mixed models

<table>
<thead>
<tr>
<th>Model</th>
<th>( df )</th>
<th>AIC</th>
<th>BIC</th>
<th>LL</th>
<th>Test</th>
<th>Ratio</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. ( Y \sim ) intercept (subject)</td>
<td>3</td>
<td>383.82</td>
<td>399.44</td>
<td>-188.91</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. ( Y \sim ) face + (1</td>
<td>subject)</td>
<td>4</td>
<td>345.05</td>
<td>365.88</td>
<td>-168.52</td>
<td>1 vs. 2</td>
<td>40.78</td>
</tr>
<tr>
<td>3. ( Y \sim ) face + muscle + (1</td>
<td>subject)</td>
<td>6</td>
<td>341.22</td>
<td>372.47</td>
<td>-164.61</td>
<td>2 vs. 3</td>
<td>7.82</td>
</tr>
<tr>
<td>4. ( Y \sim ) face*muscle + (1</td>
<td>subject)</td>
<td>8</td>
<td>-59.64</td>
<td>-17.98</td>
<td>37.82</td>
<td>3 vs. 4</td>
<td>404.86</td>
</tr>
<tr>
<td>5. ( Y \sim ) face*muscle + trial + (1</td>
<td>subject)</td>
<td>9</td>
<td>-58.92</td>
<td>-12.05</td>
<td>38.46</td>
<td>4 vs. 5</td>
<td>1.28</td>
</tr>
<tr>
<td>6. ( Y \sim ) face*muscle + condition + trial + (1</td>
<td>subject)</td>
<td>11</td>
<td>-63.43</td>
<td>-6.14</td>
<td>42.71</td>
<td>5 vs. 6</td>
<td>8.51</td>
</tr>
<tr>
<td>7. ( Y \sim ) face<em>muscle + muscle</em>condition + trial + (1</td>
<td>subject)</td>
<td>13</td>
<td>-73.70</td>
<td>-4.418</td>
<td>51.85</td>
<td>6 vs. 7</td>
<td>18.26</td>
</tr>
</tbody>
</table>

Note. AIC = Akike Information Criterion; BIC = Bayes Information Criterion; \( df \) = degrees of freedom; LL = loglikelihood.

All interaction terms assume main effects included in the model. Test specifies the nested model comparison. Ratio is the likelihood ratio test. Random effects specified in (). All models estimated with maximum likelihood estimator using the lme() function and comparisons using anova() function in R.

### 3.4 fMRI

Separate linear models revealed similarities and differences in BOLD signal change for smile and yuck face simulation. As shown in Figure 4, smile and yuck face mimicry produced largely similar patterns of BOLD signal changes in frontoparietal regions (\( \rho < .001 \) with \( \kappa > 25 \) contiguous voxels), but differential BOLD signal changes found in ventromedial prefrontal cortex (coordinates: \( x = 2, y = 58, z = 2; \kappa = 196 \) voxels; \( t_{1,14} = 3.53, p = .002 \)) and amygdala (coordinates: \( x = 28, y = -2, z = -20; \kappa = 126 \) voxels; \( t_{1,14} = 3.86, p = .001 \)).

### 4 DISCUSSION

This study demonstrates that continuous fMRI-EMG signals can be filtered to examine activation within the primary signal domain for facial EMG (10–60 Hz) and that signals for fMRI-EMGs responses to emotional stimuli can be compared. Our study focused on discriminating smile (i.e., happy/pleasant) faces from disgust (i.e., aversive/contamination) faces using EMG signals. Facial EMG is used to quantify and identify emotions often characterizing positive and negative valence (as opposed to specific emotions). Consequently, many studies focus on the acquisition of corrugator and zygomaticus (negative vs. positive valence respectively; see Larsen & Fredrickson, 1999), in part due to increased reliability of these signals when compared with emotion specific signals (Hess et al., 2017). The results indicated that corrugator response discriminates negative facial stimuli (i.e., ‘Yuck’ face) from happy stimuli (i.e., ‘Smile’ face), an approach that could be leveraged for studying valence in addition to emotion-specific responses. With a larger sample, it is possible that statistically significant differences between fMRI-EMG and EMG signals could emerge; however, the size of the differences is expected to be small and unlikely to generate errors beyond those typically encountered with...

### TABLE 2 Summary of fixed and random effects of best fitting model

<table>
<thead>
<tr>
<th></th>
<th>( \beta )</th>
<th>SE</th>
<th>( D )</th>
<th>( t ) value</th>
<th>( p ) value</th>
<th>( R^2 )</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interception</td>
<td>-0.036</td>
<td>0.026</td>
<td>1324</td>
<td>-1.443</td>
<td>.149</td>
<td>.300</td>
<td>.342–.267</td>
</tr>
<tr>
<td>Face (yuck)</td>
<td>.021</td>
<td>.022</td>
<td>1324</td>
<td>.967</td>
<td>.333</td>
<td>.001</td>
<td>.006–.000</td>
</tr>
<tr>
<td>Muscle (corrugator)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levator</td>
<td>-0.200</td>
<td>0.022</td>
<td>1324</td>
<td>-6.24</td>
<td>.533</td>
<td>.000</td>
<td>.005–.000</td>
</tr>
<tr>
<td>Zygomaticus</td>
<td>.242</td>
<td>.032</td>
<td>1324</td>
<td>7.555</td>
<td>&lt;.0001</td>
<td>.041</td>
<td>.064–.023</td>
</tr>
<tr>
<td>Condition (fatigue)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scanner off</td>
<td>-0.014</td>
<td>0.027</td>
<td>1324</td>
<td>-5.24</td>
<td>.600</td>
<td>.000</td>
<td>.005–.000</td>
</tr>
<tr>
<td>Scanner on</td>
<td>.016</td>
<td>0.027</td>
<td>1324</td>
<td>.581</td>
<td>.561</td>
<td>.000</td>
<td>.005–.000</td>
</tr>
<tr>
<td>Trial</td>
<td>.003</td>
<td>0.002</td>
<td>1324</td>
<td>1.139</td>
<td>.254</td>
<td>.001</td>
<td>.007–.000</td>
</tr>
<tr>
<td>Face (yuck)*muscle (corrugator)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yuck*levator</td>
<td>.148</td>
<td>0.031</td>
<td>1324</td>
<td>4.730</td>
<td>&lt;.0001</td>
<td>.016</td>
<td>.032–.006</td>
</tr>
<tr>
<td>Yuck*zygomaticus</td>
<td>-.053</td>
<td>0.031</td>
<td>1324</td>
<td>-16.108</td>
<td>&lt;.0001</td>
<td>.163</td>
<td>.198–.129</td>
</tr>
<tr>
<td>Muscle (corrugator)*condition (fatigue)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle (levator)*condition (off)</td>
<td>-0.064</td>
<td>0.039</td>
<td>1324</td>
<td>-1.647</td>
<td>.100</td>
<td>.002</td>
<td>.010–.000</td>
</tr>
<tr>
<td>Muscle (zygomaticus)*condition (off)</td>
<td>.075</td>
<td>0.039</td>
<td>1324</td>
<td>1.929</td>
<td>.054</td>
<td>.003</td>
<td>.011–.000</td>
</tr>
<tr>
<td>Muscle (levator)*condition (on)</td>
<td>-0.047</td>
<td>0.038</td>
<td>1324</td>
<td>-1.221</td>
<td>.222</td>
<td>.002</td>
<td>.010–.000</td>
</tr>
<tr>
<td>Muscle (zygomaticus)*condition (on)</td>
<td>.096</td>
<td>0.038</td>
<td>1324</td>
<td>2.519</td>
<td>.012</td>
<td>.005</td>
<td>.015–.000</td>
</tr>
</tbody>
</table>

Note. Model estimated using lme() function of the nlme package in R. The effect sizes were estimates using the ‘r2glmm’ package v0.1.2 using function r2beta() which yields a standardized effect size for each parameter. Total model effect size listed in intercept row above. Model includes 1350 observations across 16 subjects.
EMG signal acquisition. Nonetheless, the acquisition of facial EMG data during fMRI has lagged behind other methods of simultaneous measurement of peripheral and central psychophysiological measures because of inadequate hardware and a standard methodology for processing data. These data build on other attempts to quantify integrated EMG–fMRI signals continuously (Likowski et al., 2012).

One of the significant design questions when assessing emotion with fMRI tasks is selecting the method with the greatest likelihood of producing data that are rigorous and reproducible. Rigor, or thoroughness in experimental design, methods, analysis or presentation of data, and reporting of outcomes, and reproducibility, or the ability to validate findings and future research, are difficult to achieve with many existing measures of emotional states employed with fMRI. Self-report, which is commonly used in the literature, is limited by bias and inaccuracies (Kahneman & Klein, 2009), and added concerns with the subjective reporting of feelings exists for patients with AN. The use of fMRI methods have also come under criticism for their poor replicability (Bennett & Miller, 2010) and the replicability of emotional response neurocircuitry may be modest (Nord, Gray, Charpentier, Robinson, & Roiser, 2017; Sauder, Hajcak, Angstadt, & Phan, 2013). Consequently, reliable psychophysiological markers may help improve the precision of these subcortical brain circuits by leveraging their signals to regress out noise in fMRI signals or answer specific questions about emotional appraisal without complications of behavioral response or difficulty labeling emotions.

Research on the use of facial EMG signals to capture emotional responses is evolving and diverse, but is likely to move towards greater precision and less invasive and cumbersome methods for acquisition (e.g., video capture methods) with improvements in technology. These methods are unlikely to be immediately applicable to acquisition during fMRI until better video capture is feasible during MRI, leaving room to further develop facial EMG methods for fMRI. Furthermore, with a host of machine learning algorithms evolving to increase speed and accuracy of integrated psychophysiological signals to detect and model emotion with facial EMG (e.g., Coutinho, Gentsch, van Peer, Scherer, & Schuller, 2018; Eskes et al., 2018), statistical methods are also likely to improve, which along with the results of this study, suggest that similar processes could be applied to the signal obtained from simultaneous acquisition of fMRI–EMG.

The value of fMRI–EMG methods for studying social and emotional processes in individuals with eating disorders, particularly AN, is clear. A number of fMRI studies document regional differences in activation to social–emotional stimuli that include lateral and medial prefrontal areas in acute forms of AN (McAdams & Smith, 2015), and particularly when considering BOLD responses to facial stimuli (Fonville, Giampietro, Surguladze, Williams, & Tchanturia, 2014). These differences in brain response may have implications for predicting treatment outcome (Schulte-Ruther, Mainz, Fink, Herpertz-Dahlmann, & Konrad, 2012) or identifying vulnerability in people recovered from AN (Bang, Ro, & Endestad, 2016). Despite the early stages of research in this field, these findings suggest possible anomalies in the recruitment of frontal, amygdala, and visual attentional regions in social–emotional processing in AN—a theory that could be aided by study of psychophysiological measures of emotional valence or specificity using fMRI–EMG. The results suggest these measures can be acquired simultaneously without sacrificing the quality of either signal.

Future research on fMRI–EMG methods should focus on three specific areas. First, comparing different acquisition methods to improve precision of the EMG signal and facilitate efficient data acquisition could greatly enhance the value of the method as well as its replicability across labs. Our methods are included in supplementary material (video and procedure) associated with this study as an effort to support its adoption in other labs to improve and expand upon this methodology. Secondly, the ability to use these methods to process EMG response during different types of tasks within the scanner will be an important next step in the evolution of fMRI–EMG. We did not examine the relationship between EMG signals and BOLD response; our primary question was whether we could filter the noise from fMRI to establish a valid EMG signal without interfering with the acquisition of BOLD signal changes. Its value as a time series correlate or
parametric modulator of BOLD response remains an open and important question. Lastly, the development of classification and prediction methods using machine learning algorithms has promise for better quantifying emotion in a range of fMRI tasks. The use of maximum voluntary facial expression to quantify subject-specific could help to increase precision of person-specific models of affect in relevant clinical populations. There may be other classification methods that offer value to this affective neuroscience tool.

5 | CONCLUSIONS

In summary, our analysis offers an illustration of a novel methodological tool for investigating emotion-specific hypotheses about individuals with AN. However, these data have implications for the broader use of fMRI–EMG methods in other affective neuroscience domains. The publication of analytic processing and the protocol for acquisition and preprocessing of data provides a standard method for papers using fMRI–EMG, and more generally when examining new approaches in a methodologically rigorous and reproducible way. We show evidence that specific emotional states (disgust and happy) can be discriminated via EMG. Additional commitments by researchers to offer additional materials and details in the service of rigor and reproducibility will hopefully help increase the adoption of these methods and increase rate of improvement and innovation for fMRI–EMG.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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FIGURE 4 Blood oxygen level-dependent (BOLD) signal increases for smile and yuck face simulations in adolescent females with low-weight eating disorders. Smile and yuck faces produced similar patterns of BOLD signal changes in anterior cingulate, inferior frontal, anterior insula, and parietal regions, and differential signal changes in ventromedial prefrontal cortex and amygdala. Figures are thresholded at p < .01 (corrected for multiple comparisons with a cluster threshold >25 voxels). Numbers at bottom indicate z coordinates in the Montreal Neurological Institute brain template space. L = left, R = right [Color figure can be viewed at wileyonlinelibrary.com]


**SUPPORTING INFORMATION**

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