Published in final edited form as:

Biol Psychol. 2015 February ; 0: 106–114. doi:10.1016/j.biopsycho.2015.01.003.

Resting-State EEG Delta Power is Associated with Psychological Pain in Adults with a History of Depression

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Abstract

Psychological pain is a prominent symptom of clinical depression. We asked if frontal alpha asymmetry, frontal EEG power, and frontal fractal dimension asymmetry predicted psychological pain in adults with a history of depression.

Resting-state frontal EEG (F3/F4) was recorded while participants ($N=35$) sat upright with their eyes closed.

Frontal delta power predicted psychological pain while controlling for depressive symptoms, with participants who exhibited less power experiencing greater psychological pain. Frontal fractal dimension asymmetry, a nonlinear measure of complexity, also predicted psychological pain, such that greater left than right complexity was associated with greater psychological pain. Frontal alpha asymmetry did not contribute unique variance to any regression model of psychological pain.

As resting-state delta power is associated with the brain's default mode network, results suggest that the default mode network was less activated during high psychological pain. Findings are consistent with a state of arousal associated with psychological pain.

Keywords

psychological pain; mental pain; EEG; depression; nonlinear measures; default mode network

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Financial Disclosures

Nothing to declare.

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Psychological pain is a prominent symptom of clinical depression (Osmond, Mullaly, & Bisbee, 1984). Also known as mental pain, several studies have reported high levels of psychological pain in both inpatients and outpatients with depression (Li et al., 2013; Mee et al., 2011; Olié, Guillaume, Jaussent, Courtet, & Jollant, 2010; van Heeringen, Van den Abbeele, Vervaeke, Soenen, & Audenaert, 2010). Clinical depression can severely impair one's ability to satisfy important needs, which may result in feelings of deficiency in spheres such as employment, family obligations, and social interaction (American Psychiatric Association, 2010). Psychological pain is the result of negative appraisal of these inabilities and feelings of deficiency (Meerwijk & Weiss, 2011, 2014).

Despite psychological pain being common in depression and an abundance of depression-related brain imaging studies, research assessing brain activity associated with psychological pain is limited (Meerwijk, Ford, & Weiss, 2013). Research suggests that, among other brain areas, the prefrontal cortex is involved in psychological pain, but both hypofunction and hyperfunction have been reported. Van Heeringen et al. (2010), using functional magnetic resonance imaging, compared women diagnosed with depression who experienced high psychological pain versus those who experienced low psychological pain and found right sided hyperfunction in prefrontal Brodmann areas (BA) 9 and 44. Reisch et al. (2010) compared women who recalled psychological pain versus a neutral activity and reported hypofunction in left BA 6 and 46 and right BA 10, based on single photon emission computed tomography. The relationship between prefrontal brain activity and psychological pain remains mostly unexplored.

Prefrontal brain activity in depression is often assessed with electroencephalography (EEG), in particular in terms of alpha (8–13 Hz) asymmetry (Alhaj, Wisniewski, & McAllister-Williams, 2011; Henriques & Davidson, 1991; Schaffer, Davidson, & Saron, 1983), or frontal alpha asymmetry (FAA). A meta-analysis on resting-state FAA in people with depression reported small to medium effect sizes, indicating relative right activity, that is greater right than left alpha activity (Thibodeau, Jorgensen, & Kim, 2006). These results are generally assumed to reflect left frontal hypofunction, which may be related to a deficit in approach behavior or indicate negative affect (Davidson, 1998; Harmon-Jones, 2004; Watson & Tellegen, 1985). Recent studies in people who had been diagnosed with major depressive disorder were in line with relative right activity (Chang et al., 2012; Kemp et al., 2010), but null findings (Gold, Fachner, & Erkkilä, 2013; Mathersul, Williams, Hopkinson, & Kemp, 2008), and contradicting results (Gordon, Palmer, & Cooper, 2010) were also reported. Moreover, frontal alpha activity was found to be uniquely associated with specific symptoms of depression, with less bilateral alpha activity associated with greater self-reported rumination and less right frontal alpha activity associated with greater self-reported self-esteem (Putnam & McSweeney, 2008). The relationship between FAA and psychological pain has not been explored. Knowledge about the relationship between frontal brain activity and psychological pain may guide the development of interventions to alleviate psychological pain, for example through repetitive transcranial stimulation or FAA-based neurofeedback (Baehr, Rosenfeld, & Baehr, 2001; Berlim, Van den Eynde, & Jeff Daskalakis, 2013; J. Chen et al., 2013; Choi et al., 2011; Slotema, Blom, Hoek, & Sommer, 2010).

The primary aims of this exploratory study were (1) to determine whether FAA predicted psychological pain while controlling for covariates of psychological pain (e.g. depression, hopelessness, suicide ideation), and (2) to determine whether individual frontal EEG power components predicted psychological pain, in adults with a history of depression. We hypothesized that FAA would increase with increasing psychological pain. Our second aim was motivated by the fact that the few brain imaging studies that did concern psychological pain (Reisch et al., 2010; van Heeringen et al., 2010) employed techniques that reflect the complete frequency spectrum. Some of their results may be more apparent in frequency bands other than alpha. A few studies, for example, have reported on midline theta as a potential biomarker of depression (Cook, Hunter, Korb, & Leuchter, 2014; Gold et al., 2013). Others reported increased frontal gamma power in depression versus healthy controls (Strelets, Garakh, & Novototskii-Vlasov, 2007), and it was found that delta power during sleep was lower in depression versus healthy controls (Armitage, Emslie, Hoffmann, Rintelmann, & Rush, 2001). Delta power is not only observed during sleep, but also when the body is at rest and awake (Alper et al., 2006; A. C. Chen, Feng, Zhao, Yin, & Wang, 2008), and may be implicated in synchronization with autonomic functions and detection of motivationally salient stimuli (Knyazev, 2012).

As a secondary aim, we explored the utility of an EEG asymmetry measure based on frontal fractal dimensions. Fractal dimension is a measure based on nonlinear dynamical systems theory (Shelhamer, 2007; Stam, 2006) and signifies dynamic complexity, capturing nonstationary changes in signal amplitude as well as frequency. Fractal dimension and related nonlinear measures of resting-state EEG complexity have been shown to discriminate adults with depression from healthy controls (Bachmann, Lass, Suhhova, & Hinrikus, 2013; Hosseinifard, Moradi, & Rostami, 2013). Conflicting results were reported for depressed individuals compared to healthy controls, as some found that resting-state EEG complexity was lower in adults with depression (Lee et al., 2007), some did not find a significant difference (Ahmadlou, Adeli, & Adeli, 2012), and still others reported that complexity was higher in depression (Bachmann et al., 2013). Building on the proposition that greater complexity is generally associated with a healthier, more adaptive system (Delignieres & Marmelat, 2012; Voss, Schulz, Schroeder, Baumert, & Caminal, 2009), we hypothesized that frontal fractal dimension would decrease with increasing psychological pain.

Methods and Materials

Participants

The study sample consisted of right-handed adults ($N = 35$) who had been diagnosed with a depressive disorder, but who did not necessarily experience a depressive episode at the time of participation. Their diagnosis was based on self-report, but we verified the participants' level of depression with the Beck Depression Inventory (BDI) II. Based on their BDI scores, the majority of participants experienced moderate to severe depression. We intentionally enrolled participants across various stages of recovery because this was likely to result in a sample that represented a full range of psychological pain at the time of the study. Mean time since first diagnosis was 6.8 years (SD 6.1). Participants with a history of substance

abuse or traumatic brain injury, a diagnosis of dementia or Parkinson, or women who were pregnant or had been pregnant less than 6 months prior to the study, were excluded from participation. Of 65 potential participants who passed a phone screening, 38 participants passed a face-to-face screening that included a test for right-handedness (Edinburgh Handedness Inventory laterality score > 75) and cognitive ability (Minicog). Three participants were excluded because of a positive urine drug screen that tested for common drugs of abuse on the day of data collection. Participants were recruited from a psychiatric hospital's outpatient department and psychological services centers in the San Francisco Bay Area of California, and via online advertisement on Craigslist. Participants provided written consent, and the study was approved by the Institutional Review Board at the University of California, San Francisco.

Materials

Psychological Pain was assessed with the Psychache Scale ([PS], Holden, Mehta, Cunningham, & McLeod, 2001) and the Orbach & Mikulincer Mental Pain (OMMP) questionnaire (Orbach, Mikulincer, Sirota, & Gilboa-Schechtman, 2003). The PS is a 13-item self-report instrument that results in a continuous total score (range 13 – 65), with higher scores reflecting greater psychological pain. Nine items are scored on a frequency scale ranging from never to always and four items are scored on a symmetrical scale ranging from strongly disagree to strongly agree. The instrument is well validated in diverse populations, including outpatients with depression, male prison inmates, students at risk for suicide, and homeless men (Li et al., 2013; Mills, Green, & Reddon, 2005; Patterson & Holden, 2012; Troister & Holden, 2012; Xie et al., 2013). The OMMP questionnaire is a 44-item instrument that assesses both current psychological pain (OMMP_c, at the time the questionnaire was completed) and worst-ever psychological pain (OMMP_w), resulting in a continuous total score (range 44 – 220) for each. Higher total scores reflect greater psychological pain. A 5-item response scale ranging between strongly disagree and strongly agree is used for all 44 items. The OMMP was shown to possess a high degree of validity in patients admitted for a suicide attempt, university students and the general population (Levi et al., 2008; Nahaliel et al., 2013; Orbach, Mikulincer, Gilboa-Schechtman, & Sirota, 2003; Orbach, Mikulincer, Sirota, et al., 2003; Reisch et al., 2010; Soumani et al., 2011; van Heeringen et al., 2010). In our sample, excellent internal consistency was found for the PS (Cronbach's α .92) and for the OMMP (Cronbach's α of .95 for both the OMMP_c and OMMP_w). Cronbach's α is a commonly used measure to report internal consistency as an estimate of reliability of self-report instruments (Tavakol & Dennick, 2011).

As prior research has shown that psychological pain covaries with depression, hopelessness, and suicide ideation, participants completed the BDI-II, the Beck Hopelessness Scale (BHS), and the Beck Scale for Suicide ideation (BSS) to allow for control of these variables during statistical analyses. These self-report instruments are well validated and widely used (Beck, Steer, & Brown, 1996; Meyer et al., 2010; Mystakidou et al., 2008; Nissim et al., 2010; Yin & Fan, 2000). We found excellent internal consistency by conventional standards (Cicchetti, 1994) for all three measures, with a Cronbach's α of .88, .88, and .90 for the BDI, BHS, and BSS, respectively.

Electroencephalography data were recorded from 34 scalp sites using a Biosemi ActiveTwo system (www.biosemi.com) with active Ag/AgCl electrodes (input impedance 300 MOhm @ 50 Hz). The system uses an analog 1st order low-pass anti-aliasing filter (−3 dB at 3.6 kHz) and 24-bit analog-digital converter. The data were digitized at 1024 Hz and referenced offline. The common mode sense and driven right leg were placed at the C1 and C2 locations, respectively. Additional flat-type electrodes were used to record horizontal and vertical electro-oculograms from the outer canthi of the eyes, and above and below the left eye.

Procedures

Participants had been instructed to not use caffeine or nicotine within 2 hours of their appointment, and to not use alcohol within 12 hours of their appointment. Compliance with these instructions was queried before data collection. Prior to preparation for EEG recording, participants completed the BDI-II, BHS, and the BSS. After the electrodes were put in place, participants were made aware that using their facial muscles would adversely affect the EEG by having them see the effect in real-time on a computer monitor. Participants then relocated to a sound attenuated room (constant 50 dB ambient sound level, mostly from air conditioning) with a low light level where resting-state EEG measurements were conducted. The participants were sitting upright and had been instructed to keep their eyes closed, sit as still as possible, not focus on anything in particular and let their mind run free during the measurements. To let participants get used to the experimental setup, a 2-minute test session preceded the first actual recording session. Resting-state EEG was recorded during six consecutive 5-minute sessions. Short breaks of 2 – 3 minutes separated the sessions. Six sessions were used to increase reliability of the measurements, as previous research showed little improvement beyond five consecutive sessions (Allen, Coan, & Nazarian, 2004). All data were recorded between 9 am and 12 noon. The PS and OMMP were completed between the first and second recording sessions to be able to assess the effect of completing the questionnaires on measures of interest (not reported here).

Offline Processing and Initial Data Assessment

Issues regarding the processing of raw EEG data into FAA were addressed as described by Allen, Coan, and Nazarian (2004). Raw continuous EEG data were vertex (Cz) referenced and detrended using a 2nd order polynomial. A 4th order Butterworth bandpass filter was applied with cutoff frequencies at 0.25 Hz and 256 Hz. This was followed by a 2nd order Butterworth notch filter with cutoff frequencies ± 1 Hz around 60 Hz and harmonics up to 240 Hz to compensate for main power interference. We then used automated artifact detection based on an outlier approach, which is also used in the *FASTER* algorithm (Nolan, Whelan, & Reilly, 2010). Details of the artifact detection process, including removal of epochs with oculogram artifacts, are described in the appendix. A repeated measures analysis of variance indicated no significant differences in number of rejected epochs across sessions ($F = 0.667$, $p = .649$, $\epsilon = 1.0$). Across participants and sessions, 12.3% of the data were rejected. Artifact-free data were divided into nonoverlapping 2 s epochs, which were linearly detrended and windowed using a Hann window. Fast Fourier transformation (FFT) was used to determine the power spectrum within each epoch. Subsequently, power in μV^2 was determined for standard frequency bands (delta: 0.5 – 4 Hz, theta: 4 – 8 Hz, alpha: 8 –

13 Hz, beta: 13 – 30 Hz, gamma: 30 – 100 Hz). Power in each frequency band was natural log transformed to obtain more normally distributed variables. Frontal alpha asymmetry for each epoch was calculated as $(F4 - F3)/(F3 + F4)$, where F3 and F4 represent alpha power at the left (F3) and right (F4) electrodes. Finally, FAA within a measurement session was averaged over all valid epochs. Data processing was done in GNU Octave 3.2.3.

The fractal dimensions of brain activity recorded at the F3 and F4 scalp locations were derived from detrended data for each artifact-free epoch. The underlying property of the fractal dimension is called self-affinity or self-similarity, which refers to the phenomenon that the fractal dimension of a signal is the same, irrespective of the scale at which that signal is observed (Eke, Herman, Kocsis, & Kozak, 2002; Mandelbrot, 1982). The fractal dimension is a measure of signal complexity, sometimes described as roughness of the signal. We calculated the fractal dimension by means of a box-counting method, which can be visualized by assuming an arbitrary EEG signal plotted against time. For boxes that are progressively smaller in size, representing different scales to observe the signal, it is determined how many boxes are minimally needed to cover the signal. For a self-similar signal, the box size and the number of boxes that are needed will follow a power law:

$$N(\varepsilon) \propto \varepsilon^{-D}$$

where N equals the number of boxes, ε indicates box size, and D represents the box-counting, or fractal dimension (Shelhamer, 2007). The fractal dimension of a neurophysiological time series ranges between 1 and 2 (Eke et al., 2002; Stam, 2006). A sensitivity analysis of fractal algorithms (Raghavendra & Narayana Dutt, 2010) has shown that the box-counting method is more accurate than the method by Katz or Sevcik and less computationally intensive than the method by Higuchi. Frontal fractal dimension asymmetry (FFDA) was calculated analogous to FAA, using left and right fractal dimension values instead of alpha power.

We determined the intraclass correlation coefficient (ICC) for agreement between successive measurement sessions of the individual EEG power components, FAA, and FFDA. Excellent agreement was found by conventional standards (Cicchetti, 1994), with ICC values > 0.75 for all repeated measures. It was then decided to average each variable across the six measurement sessions.

When the data were assessed for distribution, it was found that the BSS, OMMP_w, and FAA were not normally distributed. Further inspection for outliers identified one participant with a OMMP_w z -score of 3.66. As the OMMP_w was normally distributed without this participant, it was decided to exclude this participant for analyses that involved OMMP_w.

All statistical tests were computed using PASW Statistics 18.0, and statistical significance was assumed at $p < .05$. Given the cross-sectional nature of our study, we used regression analysis while controlling for the level of depression and other covariates of psychological pain. Psychological pain was regressed on FAA, FFDA, and individual EEG power components. To compensate for multiple comparisons, we tested the contribution of these

EEG predictors against a Bonferroni corrected significance level of .05 divided by the number of EEG predictors.

Results

Sample Characteristics

The average age of the participants was 35.0 years (SD 11.8), and women made up about three quarters (77.1%) of the sample. The majority of participants were single (88.6%). Almost half of the participants had been diagnosed with major depressive disorder (48.6%), and most of the remaining participants (42.9%) endorsed depression ‘not otherwise specified’. Almost half of the participants (45.7%) were using antidepressants at the time of the study. Based on their BDI score and using conventional standards (Beck et al., 1996), 80.0% of the participants experienced at least a moderate level of depression at the time of the study, and almost half of the participants (48.6%) experienced severe depression. A quarter of the participants (25.7%) indicated they had attempted suicide at least once in their lifetime.

Table 1 shows the mean scores and bivariate correlations for the psychological outcomes of interest. Medium to strong positive correlations existed between psychological pain and its covariates: depression, hopelessness, and suicide ideation. Because the study included participants who represented a range of depression levels, we compared psychological pain in our sample with scores reported for healthy adults and adults diagnosed with a depressive episode. The average level of psychological pain ($PS = 40.60$; $OMMP_c = 122.03$; $OMMP_w = 179.26$) was not significantly different from outpatients who experienced a major depressive episode, who scored 40.0 on the PS (Li et al., 2013; Xie et al., 2013), and was slightly lower than was found in patients admitted for a depressive episode, with a PS score of 46.06 and $OMMP_c$ of 135.00 (Cáceda et al., 2014; van Heeringen et al., 2010). Psychological pain was significantly higher compared to healthy adults, who scored between 13.70 and 20.60 on the PS (Cáceda et al., 2014; Xie et al., 2013). The $OMMP_c$ in our sample was also higher (not significantly) compared to healthy adults, who scored between 85.80 and 120.56 (Levi et al., 2008; Nahaliel et al., 2013).

As almost half of the participants used antidepressants at the time of the study, we used a t -test for independent samples to test for differences in EEG measures, including FAA and FFDA. None of the differences were statistically significant, but the difference in left frontal delta power showed a trend toward significance with greater power in the group that used antidepressants (16.71 vs. 16.37 $\ln[\mu V^2]$, $p = .064$).

Frontal EEG Asymmetry

Frontal α -asymmetry did not correlate significantly with any of the self-report measures, including depression (see Table 1), but a statistical trend was observed for the correlation with hopelessness ($r_s = -.32$, $p = .06$). Significant inverse correlations of medium strength were found between FFDA and both OMMP measures.

Simultaneous regressions of the three measures of psychological pain on FAA were conducted while controlling for covariates (Table 2). Suicide ideation did not contribute

significant variance to the regression model of PS or OMMP_c, and hopelessness did not contribute to the model of OMMP_w. Consequently these variables were removed from the pertinent models. While the regression models resulted in a significant overall model, FAA did not contribute significant variance to psychological pain in any model when controlling for depression and hopelessness or suicide ideation.

Similarly, we regressed psychological pain on FFDA and covariates (Table 3). Frontal fractal dimension asymmetry did not contribute significant variance to the model of PS, but a moderately strong inverse association existed between FFDA and the OMMP_c and OMMP_w scores ($\beta = -.25, p < .05, \beta = -.37, p < .05$, respectively). Moreover, FFDA contributed more unique variance to the prediction of worst-ever psychological pain than it did to the prediction of current psychological pain (R^2 13.5% vs. 5.8%). However, when tested against a Bonferroni corrected significance level of $p = .0125$ (.05 divided by the number of EEG predictors used in the study) the association between FFDA and measures of psychological pain did not reach statistical significance.

To assess whether the association between current psychological pain and fractal dimension asymmetry was unique to the frontal scalp locations, psychological pain was regressed on fractal dimension asymmetry derived from central and parietal electrode pairs (C3-C4, P3-P4). Fractal dimension asymmetry at these sites did not contribute significant variance to the model of current psychological pain.

Individual EEG components

Table 4 shows mean and standard deviation for each of the individual power components and the fractal dimension of brain activity at the F3 and F4 scalp locations. Table 5 shows that correlations between individual power components and the three measures of psychological pain were not statistically significant, except for inverse correlations of moderate strength between OMMP_w and both left and right frontal delta power ($r = -.45, p < .01, r = -.43, p < .05$, respectively). Correlations between the measures of psychological pain and left and right fractal dimension were small and nonsignificant, and strong positive correlations existed between fractal dimension and frontal gamma power.

To determine whether individual EEG power components at the F3 and F4 scalp locations predicted psychological pain, we conducted stepwise regression analyses with a backward elimination process. In order to not be overly restrictive, only predictors with a $p > .10$ were eliminated. Stepwise regression is appropriate to arrive at a more parsimonious model if there are many potential predictors and knowledge about the relationship between the predictors and the dependent variable is limited (Field, 2006; Glantz & Slinker, 2001), which is the case for psychological pain and EEG components. The initial pool of candidate predictors included the known covariates of psychological pain and the individual EEG components. Separate regressions were performed for the three measures of psychological pain and for left and right EEG components.

Table 6 shows the final models for each of the stepwise regression analyses. For psychological pain as assessed on the PS, none of the power components at the F3 or F4 locations contributed significant variance to the model. In fact, only depression remained in

the model, showing a strong positive association between PS and depression. For current psychological pain as assessed on the OMMP, only F4 delta power contributed unique variance to the model, while controlling for depression and hopelessness. A moderately strong inverse association existed between OMMP_c and F4 delta power ($\beta = -.27, p < .05$). F4 delta power contributed a similar amount of variance to the model of OMMP_c as did hopelessness (R^2 7.0% vs. 6.3%). When tested against a Bonferroni corrected significance level of $p = .0125$, the association between F4 delta power and current psychological pain did not reach statistical significance. For worst-ever psychological pain, both F3 delta power and F4 delta power contributed unique variance, while controlling for covariates. In fact, delta power contributed more unique variance to the model of OMMP_w than the covariates (R^2 21.0% vs. 14.3% for F3 delta; R^2 19.2% vs. 16.4% for F4 delta). A moderate to strong inverse association existed between each of the delta power components and OMMP_w ($\beta = -.46, p < .01, \beta = -.44, p < .01$, for F3 and F4, respectively). These associations remained significant when tested against a Bonferroni corrected significance level of $p = .0125$. Because our preliminary analyses indicated a statistical trend toward differences in left frontal delta power based on antidepressant use, we added antidepressant status to the regression model and tested the interaction term for significance. Antidepressant status added unique variance to the model of OMMP_w (R^2 8.3%, $\beta = .30, p < .05$), but it did not differentially affect the relationship between F3 delta power and OMMP_w (interaction $\beta = -.05, p = .83$). Thus, we did not include antidepressant status in our final model.

To assess whether associations between psychological pain and delta power were unique to the frontal scalp locations, current psychological pain was regressed on individual power components at central and parietal electrode pairs (C3-C4, P3-P4). Of the individual power components, again only delta power contributed unique variance above and beyond covariates to the final models of psychological pain based on stepwise regression. The final models for central electrodes were significant ($F = 13.43, p < .0005$ and $F = 12.24, p < .0005$) with a unique contribution to current psychological pain of C3 delta power ($\beta = -.26, p < .05$) and C4 delta power ($\beta = -.22, p < .10$). The final models for parietal electrodes were also significant ($F = 14.09, p < .0005$ and $F = 16.33, p < .0005$) with a unique contribution to current psychological pain of P3 delta power ($\beta = -.27, p < .05$), but none of the individual power components at the P4 location contributed unique variance.

Discussion

The primary aims of this study were to determine if resting-state FAA and individual EEG power components at the F3 and F4 scalp locations predicted psychological pain, while controlling for known covariates of psychological pain: depression, hopelessness, and suicide ideation. Frontal alpha-asymmetry did not predict psychological pain, but right frontal delta power predicted current psychological pain independent of depression and hopelessness, and bilateral delta power predicted worst-ever psychological pain independent of depression or suicide ideation. As a secondary aim we explored the relationship between FFDA and psychological pain and found that FFDA predicted current and worst-ever psychological pain. After adjusting for multiple comparisons, only the associations between bilateral delta power and worst-ever psychological pain reached statistical significance.

These results suggest a state and trait dependent asymmetry in brain activity, which is visible in frontal delta power and FFDA, more than in alpha power. Although the diagnosis of depression was based on participant self-report, our measures of depression and psychological pain are comparable to other studies that reported on outpatients diagnosed with a major depressive episode (Li et al., 2013; Xie et al., 2013) and comparable or slightly lower than studies that reported on inpatients with a major depressive episode (Cáceda et al., 2014; van Heeringen et al., 2010).

As noted above, the hypothesis that FAA would increase with increasing psychological pain was not supported. Frontal alpha asymmetry did not contribute unique variance in any of the regression models for current psychological pain and worst-ever psychological pain, which suggests that FAA may not be a salient predictor of psychological pain. Consistent with a meta-analysis of FAA in depression (Thibodeau et al., 2006), we found relative right activity, but less pronounced than reported for studies of people with current major depression that found an FAA ranging from $-.08$ to $-.02$ (Allen, Urry, Hitt, & Coan, 2004; Deldin & Chiu, 2005). Our sample was intentionally not homogeneous with respect to current level of depression, which could account for the finding that FAA was not quite as negative. On the other hand, previous research has shown that resting-state FAA does not significantly change with changes in severity of depression over time, indicating that resting-state FAA may be a trait variable more than an occasion-specific state variable (Allen, Urry, et al., 2004; Hagemann, Naumann, Thayer, & Bartussek, 2002).

Of the individual EEG power components at the F3 and F4 scalp locations only frontal delta power was associated with psychological pain while controlling for covariates. Delta power is typically observed during reduced alertness and sleep (Hlinka, Alexakis, Diukova, Liddle, & Auer, 2010; Knyazev, 2012), but is also observed when the body is at rest but awake (Alper et al., 2006; A. C. Chen et al., 2008). A recent simultaneous fMRI-EEG study (Neuner et al., 2014) found a strong correlation between frontal delta power and activity in the default mode network (DMN), a resting-state neural network (Broyd et al., 2009; Raichle et al., 2001). Activity in the DMN is attenuated when the brain is task oriented, and the network is more active when the brain is at rest. Attenuation may be stronger with more demanding tasks (Broyd et al., 2009). Our finding of decreasing resting-state delta power with increasing psychological pain suggests that the DMN was less activated in participants with higher psychological pain. In other words, the higher the psychological pain the less participants appeared to be at rest. Less activation of the DMN with increasing psychological pain is in line with results from research on heart rate variability, suggesting a persistent state of underlying arousal that may exist for individuals with psychological pain (Meerwijk, Chesla, & Weiss, 2014). Psychological pain at the time of the study was well below worst-ever psychological pain. We found a strong association between frontal delta power and worst-ever psychological pain, which suggests that high levels of psychological pain that the participants experienced well before study participation may have lasting effects. These effects were noticeable in both left and right frontal delta power, and could reflect plastic changes as a result of enduring interference with normal DMN activity (Baliki, Geha, Apkarian, & Chialvo, 2008). Given the nature of psychological pain, these changes in neural activity are likely associated with cognitive and emotional processes. As psychological pain is essentially an unpleasant feeling that results from negative appraisal,

we speculate that individuals with high psychological pain may be less adept at reappraising or reframing their pain and tend to ruminate more about the causes and consequences of their psychological pain. This is supported by research that found an association between the DMN and ruminating about physical pain (Kucyi et al., 2014). Rumination has also been associated with increased autonomic arousal (Ottaviani & Shapiro, 2011; Ray, Wilhelm, & Gross, 2008). Adaptive emotion regulation, like perspective taking and reappraisal of psychological pain, might alleviate the pain and potentially restore normal DMN activity (Aldao, Nolen-Hoeksema, & Schweizer, 2010; Webb, Miles, & Sheeran, 2012). It is important to note that some recall bias may have existed for participants in their estimates of worst-ever psychological pain. As a result, our interpretation is speculative until supported by further research.”

Frontal delta power can be a remnant of blinking or eye movements (Hagemann & Naumann, 2001). It is argued that this was unlikely in this study. First, participants were instructed to keep their eyes closed. Although this does not preclude eye movements entirely, it does make blinking unlikely. Second, the artifact rejection process would reject most epochs with blinks and eye movements because the mean and range of the potential within the epoch would be considered outliers, compared to other epochs. Third, current psychological pain did not only vary with frontal delta power, but also with left central delta power and left parietal delta power. Delta power at these scalp locations is less sensitive to ocular artifacts.

Contrary to FAA, it was found that FFDA predicted current and worst-ever psychological pain, while controlling for depression and hopelessness. The direction of the association indicated greater left (F3) than right (F4) complexity with increasing psychological pain. Research has indicated that greater signal complexity, that is a greater fractal dimension, is associated with a healthier, more adaptive system (Delignieres & Marmelat, 2012; Voss et al., 2009). This suggests that right frontal brain activity might be more adversely affected by current psychological pain, and is supported by our previously noted finding that right and not left frontal delta power predicted current psychological pain. As the presence of delta power is indicative of a body at rest (Alper et al., 2006; A. C. Chen et al., 2008), our results regarding FFDA could suggest that FFDA is a marker of arousal associated with psychological pain. Recent research has identified significant self-reported arousal associated with psychological pain (Xie et al., 2013).

Our fractal dimension measure was based on broadband data, which may have included spontaneous contributions of facial muscles. Subtle changes in facial muscle activity have been shown to differentiate affective responses (Cacioppo, Petty, Losch, & Kim, 1986). As muscle activity predominantly affects higher EEG frequency bands (Muthukumaraswamy, 2013; Whitham et al., 2007), evidence for a contribution of facial activity could be seen in the strong positive correlation between fractal dimension and frontal gamma power, both left and right. Because spontaneous facial muscle activity is mostly symmetrical (Ekman, Hager, & Friesen, 1981), we expect our FFDA results to be of neural rather than muscular origin.

Bornas et al. (2012) reported that decreased frontal EEG complexity was associated with self-focused emotion regulation styles, in particular rumination and self-blaming. Although

obtained in healthy undergraduate students, their results provide additional support for the hypothesis that individuals with high psychological pain may ruminate more about the causes and consequences of their psychological pain. Based on the same study sample, Morillas-Romero et al. (2013) reported decreasing attentional control with increasing right versus left parietal fractal dimension but no association for asymmetry at the frontal location. Our results for FFDA suggested decreasing right-sided complexity with increasing psychological pain, but perhaps owing to small sample size or confounding due to muscle activity, we could not confirm the hypothesis that frontal fractal dimension itself decreased with increasing psychological pain. Bornas et al. furthermore reported that complexity decreased across the scalp. Our results in the context of psychological pain suggest the decrease in EEG complexity may be limited to frontal areas. It should be noted though that our study assessed psychological pain, whereas the study reported by Bornas et al. and Morillas-Romero et al. assessed a disposition for emotion regulation style, which is a different although likely related concept. Moreover, there were differences between our study and theirs in fractal analysis method and in range of the frequency spectrum included in the analysis. Consistency in methodologies would improve the ability to compare findings across studies of nonlinear EEG characteristics.

Psychological pain as assessed on the PS was not associated with any of the EEG variables in our study. Earlier, it was reported that the wording of PS items in combination with instructions for completion of the PS may lead to different interpretations among participants (Meerwijk et al., 2014). Lack of association between EEG variables and the PS score, in contrast to significant associations for psychological pain on the OMMP, supports the conclusion that the OMMP more accurately reflects neurophysiological changes associated with psychological pain than does the PS.

A limitation of this study is the absence of a healthy control group with psychological pain. As a consequence, we cannot discard the notion that our observations may be restricted to adults with depression; however, as psychological pain does not strictly occur during depression it would be plausible to expect similar results in other populations who experience psychological pain. Other factors that limit generalizability are that the majority of participants were women and that all participants were right handed. As this study was exploratory in nature and measures of psychological pain have not before been studied in relation to EEG, the results are tentative and need verification through additional research. Future EEG studies of psychological pain should include specific measures of autonomic arousal (e.g. skin conductance, cortisol and alpha-amylase concentration), in order to verify the hypothesis that frontal delta power and FFDA are markers of arousal associated with psychological pain. Our results suggest that exploring low-frequency transcranial stimulation as a potential intervention to alleviate psychological pain may be more promising than FAA-based neurofeedback.

Acknowledgments

We thank Gwendolyn van der Linden for her assistance in data management and implementation of the fractal dimension algorithm. Source code of the box-counting algorithm is available from the first author upon request. This study was supported by research grants from the American Psychiatric Nursing Foundation and Sigma Theta Tau International Honor Society of Nursing, Alpha Eta Chapter. Esther Meerwijk received additional support

during preparation of this manuscript from the National Institute of Nursing Research Grant No. T32 NR07088. Additional support to Judith Ford during preparation of this manuscript was provided by Department of Veterans Affairs (I01CX000497) and a Research Career Scientist award. Additional support to Sandra Weiss was provided by the Robert C & Delphine Wentland Eschbach Endowment. Funding organizations were not involved in study design, data collection, analysis, or interpretation, or the decision to submit the article for publication.

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Appendix

Detection of artifacts within the EEG data was based on analysis of each participant's oculograms and the channels of interest for this study. The general approach was to detect outliers in the data with respect to: (a) an epoch's amplitude range, (b) deviation of an epoch's average from the channel's average, and (c) an epoch's variance. Statistically, outliers are defined as data with a z -score > 3.0 . A similar approach is used as part of the *FASTER* algorithm for automated artifact rejection (Nolan et al., 2010). To minimize data loss, we determined outliers for 0.5 s segments.

Oculogram Artifacts

The first step was to detect artifacts in epochs due to blinking and eye motion (e.g. saccades). Outliers in amplitude range or in deviation from the channel's average were determined in the vertical oculogram (VEO above – VEO below) and the horizontal oculogram (HEO left – HEO right). Contaminated epochs were discarded. The process was then repeated with the remaining data, until none of the epochs met the outlier criteria. During initial tests of this process where we visually inspected the results, we found that using a z -score > 5 adequately detected epochs with oculogram artifacts. Corresponding epochs across all channels were discarded if an ocular artifact was determined for that particular epoch.

Artifacts in F3 and F4

For the remaining epochs, we then determined artifacts in the F3 and F4 channels referenced to Cz. For each channel, outliers were determined based on (a) an epoch's amplitude range, (b) deviation of an epoch's average from the channel's average, and (c) an epoch's variance. Again, contaminated epochs were discarded. We found that using a z -score > 3 and repeating the process 3 times adequately detected epochs with artifacts due to, for example, shifting electrodes or subject movement. Contaminated epochs were discarded for both channels, regardless in which channel the artifact was detected.

- Lower frontal EEG delta power predicts greater psychological pain.
- Greater left than right fractal dimension predicts greater psychological pain.
- The default mode network may be less activated during high psychological pain.
- Frontal alpha asymmetry correlated with neither depression nor psychological pain.

Table 1Correlations between psychological pain, covariates, and asymmetry measures ($N = 35$)

	1	2	3 ^a	4	5	6 ^b	7 ^b	8
1. PS	-	-	-	-	-	-	-	-
2. OMMP_c	.62***	-	-	-	-	-	-	-
3. OMMP_w ^a	.19	.43*	-	-	-	-	-	-
4. BDI	.77***	.67***	.38*	-	-	-	-	-
5. BHS	.57***	.62***	.32	.64***	-	-	-	-
6. BSS ^b	.46**	.37*	.31	.59***	.61***	-	-	-
7. A _α ^b	-.05	-.15	-.16	.09	-.32	.05	-	-
8. A _{fd}	.02	-.34*	-.42*	-.19	-.05	-.16	-.15	-
<i>M</i>	40.60	122.03	179.26	27.23	11.71	4.94	-.01	.00
<i>SD</i>	10.37	27.70	21.81	10.83	5.27	6.05	.07	.01

Note. PS: psychache scale, OMMP_c: Orbach & Mikulincer current mental pain questionnaire, OMMP_w: Orbach & Mikulincer worst-ever mental pain questionnaire, BDI: Beck depression inventory, BHS: Beck hopelessness scale, BSS: Beck Scale for Suicide ideation, A_α: frontal α-asymmetry, A_{fd}: frontal fractal dimension asymmetry, *M*: mean, *SD*: standard deviation.

^a $n = 34$,

^b Spearman instead of Pearson correlations because of nonnormality.

 $p < .001$,

**
 $p < .01$,

*
 $p < .05$.

Table 2Simultaneous multiple regressions of psychological pain on FAA, while controlling for covariates ($N = 35$)

	<i>F</i>	<i>Adj. R</i> ²	<i>b</i>	<i>SE(b)</i>	β
PS	15.71***	56.5%			
BDI			0.68	0.15	.71***
BHS			0.20	0.34	.10
FAA			-5.46	19.34	-.04
OMMP_c	11.08***	47.1%			
BDI			1.34	0.45	.52**
BHS			1.23	1.00	.24
FAA			-50.71	57.00	-.13
OMMP_w ^a	2.86	14.5%			
BDI			0.51	0.40	.24
BSS			1.03	0.68	.29
FAA			-42.22	48.45	-.14

Note. FAA: frontal alpha asymmetry, PS: psychache scale, BDI: Beck depression inventory, BHS: Beck hopelessness scale, OMMP: Orbach & Mikulincer mental pain questionnaire, _c: current pain, _w: worst-ever pain, BSS: Beck suicide ideation scale.

^a $n = 34$.

 $p < .0005$,

**
 $p < .01$,

*
 $p < .05$.

Table 3Simultaneous multiple regressions of psychological pain on FFDA, while controlling for covariates ($N = 35$)

	<i>F</i>	<i>Adj. R</i> ²	<i>b</i>	<i>SE(b)</i>	β
PS	17.27***	58.9%			
BDI			0.70	0.14	.73***
BHS			0.21	0.28	.11
FFDA			250.50	179.86	.16
OMMP_c	13.34***	52.1%			
BDI			1.01	0.40	.39*
BHS			1.86	0.81	.35*
FFDA			-1057.25	519.11	-.25*
OMMP_w ^a	5.11**	27.2%			
BDI			0.49	0.37	.23
BSS			0.86	0.63	.24
FFDA			-1323.64	534.54	-.37*

Note. FFDA: frontal fractal dimension asymmetry, PS: psychache scale, BDI: Beck depression inventory, BHS: Beck hopelessness scale, OMMP: Orbach & Mikulincer mental pain questionnaire, _c: current pain, _w: worst-ever pain, BSS: Beck suicide ideation scale.

^a
 $n = 34$.

 $p < .0005$,

**
 $p < .01$,

*
 $p < .05$.

Table 4Means and standard deviations of frontal EEG power components in $\ln(\mu V^2)$ and fractal dimension ($N = 35$)

	Left (F3)		Right (F4)	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
total power	17.38	0.49	17.39	0.46
delta	16.52	0.53	16.54	0.52
theta	15.23	0.52	15.23	0.49
alpha	15.61	0.71	15.59	0.68
beta	15.38	0.59	15.42	0.59
gamma	14.71	0.70	14.78	0.86
FD	1.57	0.01	1.57	0.01

Note. FD: fractal dimension.

Table 5Correlations between psychological pain and frontal EEG components ($N = 35$)

	1	2	3 ^a	4	5	6	7	8	9 ^b
1. PS	-	.62***	.19	.22	.16	.22	.24	.04	-.14
2. OMMP_c	.62***	-	.43*	-.21	-.14	.04	.05	-.09	-.11
3. OMMP_w ^a	.19	.43*	-	-.43*	-.23	-.15	.06	-.24	-.03
4. delta	.05	-.22	-.45**	-	.72***	.39*	.47**	.45**	-.17
5. theta	.07	-.14	-.18	.74***	-	.65***	.63***	.37*	-.28
6. alpha	.21	.08	-.12	.34*	.61***	-	.42*	.13	-.40*
7. beta	.23	.18	.13	.46**	.63***	.43*	-	.57***	.15
8. gamma	.03	.14	-.08	.35*	.26	.05	.48**	-	.66***
9. FD ^b	-.12	.12	.17	-.32†	-.45**	-.51**	-.09	.59***	-

Note. Left-sided EEG components (F3) shown below the diagonal and right-sided components (F4) shown above the diagonal. PS: psychache scale, OMMP_c: Orbach & Mikulincer current mental pain questionnaire, OMMP_w: Orbach & Mikulincer worst-ever mental pain questionnaire, FD: fractal dimension.

^a $n = 34$,

^b Spearman instead of Pearson correlations because of nonnormality.

*** $p < .001$,

** $p < .01$,

* $p < .05$,

† $p < .1$.

Table 6

Final Stepwise Regression Models Predicting Psychological Pain from Covariates and Bilateral EEG Power Components ($N = 35$)

	<i>F</i>	<i>Adj. R²</i>	<i>b</i>	<i>SE(b)</i>	β
PS ^{a,b}	47.99***	58.0%			
BDI			0.74	0.11	.77***
OMMP_c ^a	16.33***	47.4%			
BDI			1.17	0.46	.39**
BHS			1.71	0.33	.35 [†]
OMMP_c	13.96***	53.4%			
BDI			1.24	0.39	.48**
BHS			1.70	0.80	.32*
F4 delta			-14.23	6.32	-.27*
OMMP_w ^c	8.45**	31.1%			
BDI			0.82	0.31	.38*
F3 delta			-18.92	5.96	-.46**
OMMP_w ^c	8.59**	31.5%			
BSS			1.50	0.52	.42**
F4 delta			-18.33	6.02	-.44**

Note. PS: psychache scale, BDI: Beck depression inventory, BHS: Beck hopelessness scale, OMMP: Orbach & Mikulincer mental pain questionnaire, _c: current pain, _w: worst-ever pain, BSS: Beck suicide ideation scale.

^a No significant F3 contributions,

^b No significant F4 contributions,

^c $n = 34$.

 $p < .0005$,

**
 $p < .01$,

*
 $p < .05$,

[†]
 $p < .1$.