Analysis of Galvanic Skin Response: Potential Relationships to Stimulus Responsivity and Brain Dopamine Signal

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Abstract

Fibromyalgia is a chronic pain disorder that presents itself with no apparent medical explanation for the pain. Functional alterations of neurotransmitters such as dopamine (DA) have been implicated in fibromyalgia neuropathology. It is not known how central dopamine function in pain is associated with objective peripheral measurements that are thought to be associated with the presence of pain and stress. Galvanic skin response (GSR), is a physiological measure of nervous system activation. GSR could potentially give insight to novel aspects of DA function. In this study, GSR was recorded from fibromyalgia patients (FM) and healthy controls (HC) while they underwent scanning with [^{18}F]-fallypride (FAL) Positron Emission Tomography (PET). FAL is a D_2/D_3 DA receptor antagonist that is sensitive to changes in DA levels in the brain. Given the involvement of DA in cognitive processes, FAL PET can be used to examine baseline DA activity as well as changes from baseline during cognitive load tasks. Relationships between GSR and working memory load, acute pain, and DA function were studied and compared between FM and HC.

Introduction

The prevalence of fibromyalgia has been estimated to be 1-4%.[1] It is higher in women versus men and in older versus younger adults.[1] This disorder is commonly treated with selective serotonin reuptake inhibitors and tricyclic antidepressants to some success; however, the neurological mechanisms behind fibromyalgia are not well understood.

Altered metabolism of DA and changes in DA receptor function have been reported in FM. [3, 4] DA is well known for its role in reward and was recently suggested to have pain moderating effects.[3] However, it is not currently known whether peripheral measures of physiological responsivity, such as skin conductance, are related to central DA neurotransmission.

GSR is a physiological measure of skin conductance that can be used to quantify peripheral nervous system activation. It also has the advantage of being an objective measure of physiological activation. It is simple, non-invasive, and can be acquired concurrently with other testing methods. PET is a neuroimaging technique that allows for observations *in vivo* without disturbing the system of study. Small amounts of a radioactively labeled compound can be used to measure blood flow, tissue metabolism, and receptor occupancy and density.

In this study, FAL PET was used to estimate DA function in FM concurrently with GSR recording in order to determine if skin conductance is related to DA changes in response to a working memory task. Relationships between GSR and subjective measures of pain were also examined.

Figure 1. Correlation of D_2/D_3 receptor availability in the bilateral uncus with ΔGSR during a baseline task

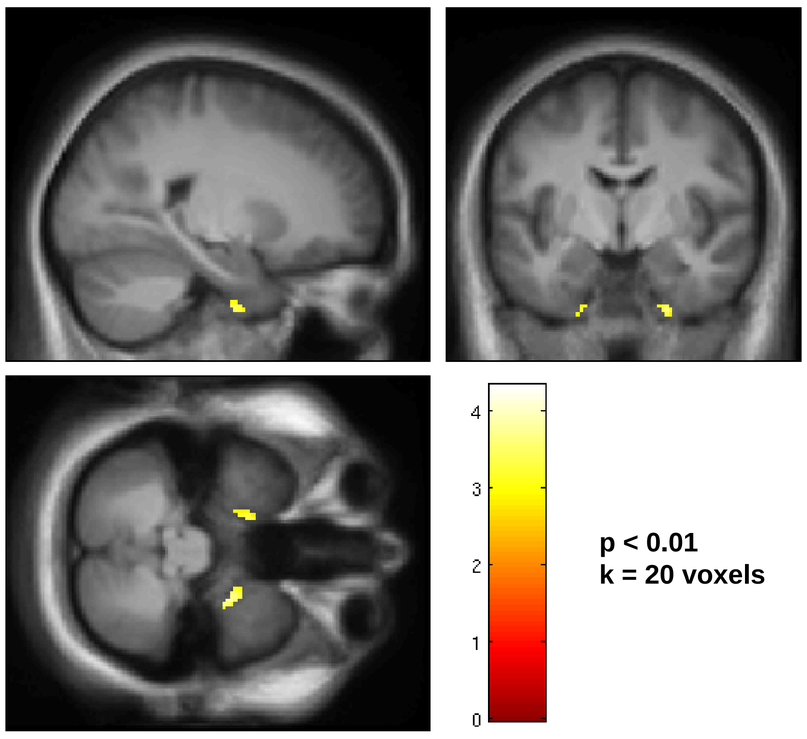
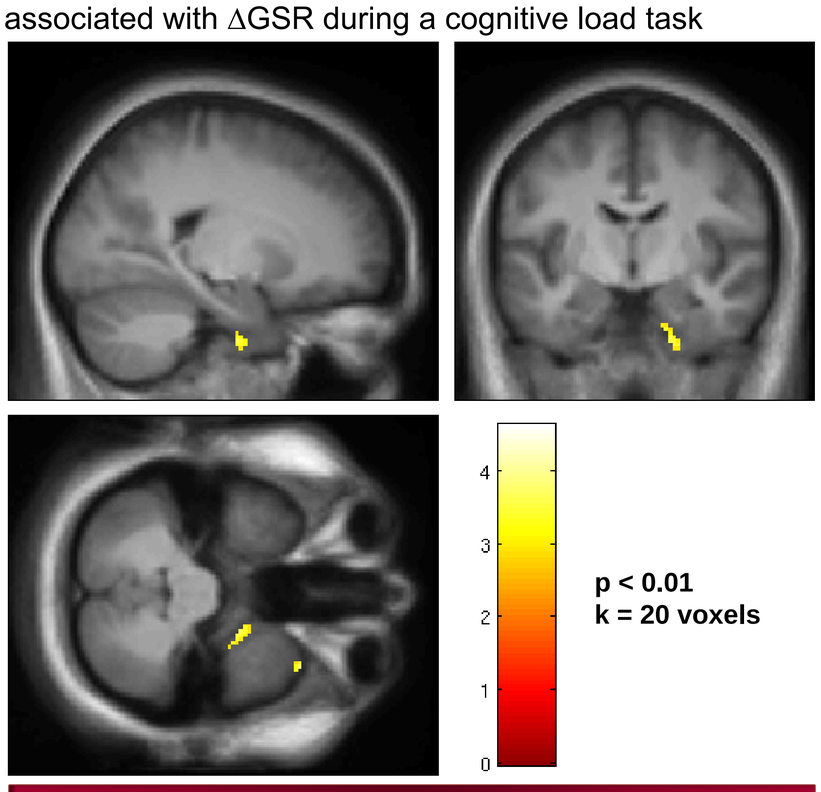


Figure 2. D_2/D_3 receptor availability in the right uncus is associated with ΔGSR during a cognitive load task



Methods

The study analyzed GSR data obtained from an NIH-funded PET study, which investigated dopaminergic activity in FM versus HC participants. GSR data was collected during algometry testing, which provided measures of pain sensitivity and tolerance, and during two FAL PET scans. FAL is a radiotracer with a half life of 109.8 min that is used as an index of dopamine D_2 receptor activity. Two PET scans (baseline and challenge) were counterbalanced and done on separate days due to the relatively long half-life of the ^{18}F isotope. Differences in DA signal between baseline and challenge scans are thought to be reflective of changes in DA levels.[4] Subjective pain ratings and rest GSR were acquired each day during the second half of scan.

Algometer readings were collected each day prior to start of scanning. PET scans consisted of 2 halves, 70 and 80 min long, respectively. During baseline scan (0-back), participants were told to press a button when a particular letter appeared on screen. During the challenge scan (2-back), participants pressed a button when a letter appeared that was same as one two letters back as shown below.

V Z M T M S W

The tasks consisted of four 5 min blocks. Every 10 min for the duration of both scan halves subjective pain ratings were collected.

GSR data was collected though high pass filter (0.5 Hz), which gave GSR recordings relative to baseline (ΔGSR) using the BIOPAC MP 150 system, connected to a computer running AcqKnowledge 3.7.3 software. Analysis of PET regions of interest for relationships between ΔGSR and binding potentials was done using SPM 8. GSR and algometry were analyzed using analysis of variance (ANOVA) with post-hoc t-tests when necessary.

Results

- Significant correlations were found between ΔGSR and FAL binding potentials in all subjects (n = 12) in the right uncus during WM task (Figure 2, $p < 0.01$) and bilaterally in the uncus during the BL task (Figure 1, $p < 0.01$). When the groups were analyzed separately, the effect was retained in FM subjects (n =7, $p < 0.01$).
- The was no effect on scan day (WM vs. BL) or group (FM vs. HC) for ΔGSR. However, ΔGSR was moderately correlated with pain sensitivity measures (maximum tolerance and average unbearable) $R = 0.709$, $p < 0.05$ (Figure 3) and $R = 0.697$, $p < 0.05$ (Figure 4) respectively.
- Two factor univariate ANOVA showed no significant effects of ΔGSR between tasks ($F(1, 10) = 0.124$, $p > 0.1$) or an interaction of group*task ($F(1, 10) = 0.279$, $p > 0.1$). A significant positive correlation was found between the BL ΔGSR and WM ΔGSR ($R = 0.827$, $p < 0.01$).
- There were no significant differences between ΔGSR during either of the *n*-back tasks and ΔGSR during subjective pain ratings.

Figure 3. Higher maximum pain tolerance values were correlated with larger changes in GSR

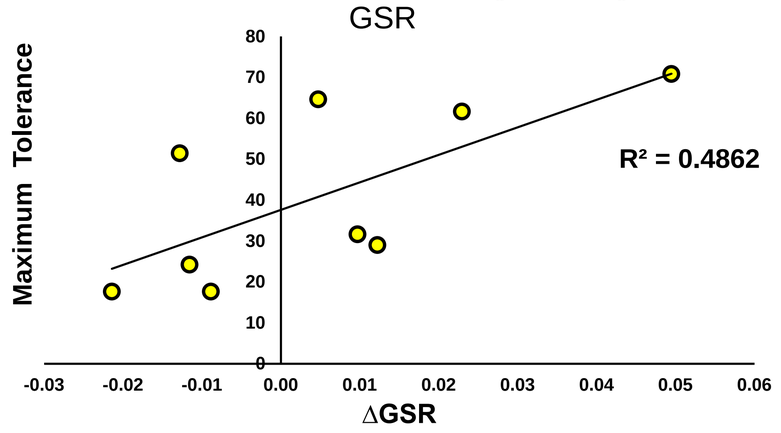
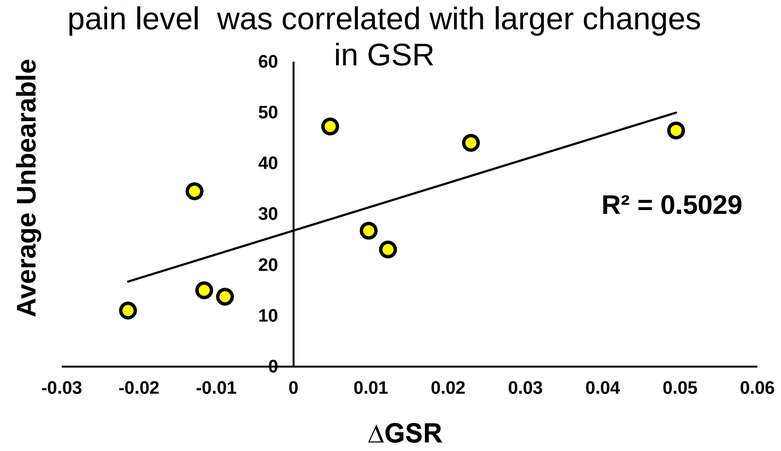


Figure 4. Ratings for average "unbearable" pain level was correlated with larger changes in GSR



References

1. Becker, S., Ceko, M., Louis-Foster, M., Elfassy, N. M., Leyton, M., Shir, Y., & Schweinhardt, P. (2013). Dopamine and Pain Sensitivity: Neither Sulpride nor Acute Phenylalanine and Tyrosine Depletion Have Effects on Thermal Pain Sensations in Healthy Volunteers. *PLOS ONE.* 8(11), e80766. doi: 10.1371/journal.pone.0080766
2. Lawrence, R. C., Felson, D. T., Helmick, C. G., Arnold, L. M., Hyon, C., Deyo, R. A., & … Wolfe, F. (2008). Estimates of the Prevalence of Arthritis and Other Rheumatic Conditions in the United States Part II. *Arthritis & Rheumatism, 58*(1), 26-35. doi: 10.1002/art.23176
3. Malt, E., Olafsson, S., Aakvaag, A., Lund, A., & Ursin, H. (2003). Altered Dopamine D2 Receptor Function in Fibromyalgia Patients: A Neuroendocrine Study with Buspirone in Women with Fibromyalgia Compared to Female Populations Based Controls. *Journal of Affective Disorders, 75*(1), 77. doi: 10.1016/S0165-0327(02)00025-3
4. Wood, P. B., Patterson, J., Sunderland, J. J., Tainter, K. H., Glabus, M. F., & Lilien, D. L. (2007). Reduced Presynaptic Dopamine Activity in Fibromyalgia Syndrome Demonstrated With Positron Emission Tomography: A Pilot Study. *The Journal of Pain, 8*(1), 51-58. doi: 10.1016/j.jpain.2006.05.014
5. Yoder, K. K., Kareken, D. A., & Morris, E. D. (2011). Assessing Dopaminergic Neurotransmission with PET: Basic Theory and Application in Alcohol Research. *Current Medical Imaging Reviews, 7*(2), 118-124. doi: 1573-4056/11