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Independent Component Analysis of Self-Referential Processing in Women with Posttraumatic Stress Disorder

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ABSTRACT

Posttraumatic stress disorder (PTSD) is a condition than can develop after exposure, or repeated exposure, to a traumatic event. Recent changes to the diagnostic criteria for PTSD as well as new treatment implications reflect a shift of emphasis from fear to an emphasis on the dysregulation of emotions related to self-appraisal. Emotions of self-appraisal can be measured using valenced stimuli that relate to the participants concept of self. These paradigms are referred to as self-referential processing tasks. The current study used data from functional magnetic resonance imaging (fMRI) to investigate the activation of brain areas related to the self-referential processing of women. Activation patterns in women with PTSD were compared to those of healthy control women. Both participant groups (PTSD and control) completed the Visual-Verbal Self-Other Referential Processing Task (VV-SORP-T) to locate regions of interest in self- and other-referential processing in response to valenced social emotional stimuli. Post scanning, participants provided self-reports of their affective reaction to stimuli experienced during the task. The previous studies on this data set have provided neuroimaging results of regions of interest in control participants in response to the VV-SORP-T. It was hypothesized that analyses would show between group differences in three networks: (1) default mode network, (2) salience network, (3) executive control network. Analysis was conducted using Group Independent Component Analysis of fMRI (GIFT) toolbox and available software courtesy of Medical Image Analysis Lab using the Matrix Laboratory Toolbox (MATLAB). One-way analysis of variance (ANOVA) were used to investigate between group differences in the four conditions.

BACKGROUND

- This disorder was historically considered a fear-based anxiety disorder [2]
- New theories of PTSD place more emphasis on emotions related to the appraisal of self and the experience of social emotions [3]
- Neuroimaging research has identified a number of regions of interest in the study of PTSD: the amygdala [4, 5], the ventromedial prefrontal cortex (vmPFC) [6, 7], and the anterior cingulate cortex (ACC) [8]
- Self-referential processing (SRP) concerns stimuli that are experienced as strongly related to one's own person [9]
- The VV-SORP-T is a paradigm used in fMRI research that probes specifically for the brain regions underlying how valenced words are processed in relation to the self and to others
- Previous studies [16, 17] collected the neuroimaging data that will be used in this study
- Data of the PTSD group is currently unpublished [11]
- The current study is seeking to investigate the neural correlates of social emotional processing in women with PTSD using an SRP paradigm
- fMRI data is used to explore the research question
- This study will explore regions of interest using the Group ICA toolbox
- Hypotheses:
  - Differential activation between control and PTSD groups in three core networks: (1) default mode network; (2) salience network; (3) executive control network
  - PTSD group: greater activation of salience relative to controls
  - Control: greater activation of default mode and executive control networks relative to PTSD group

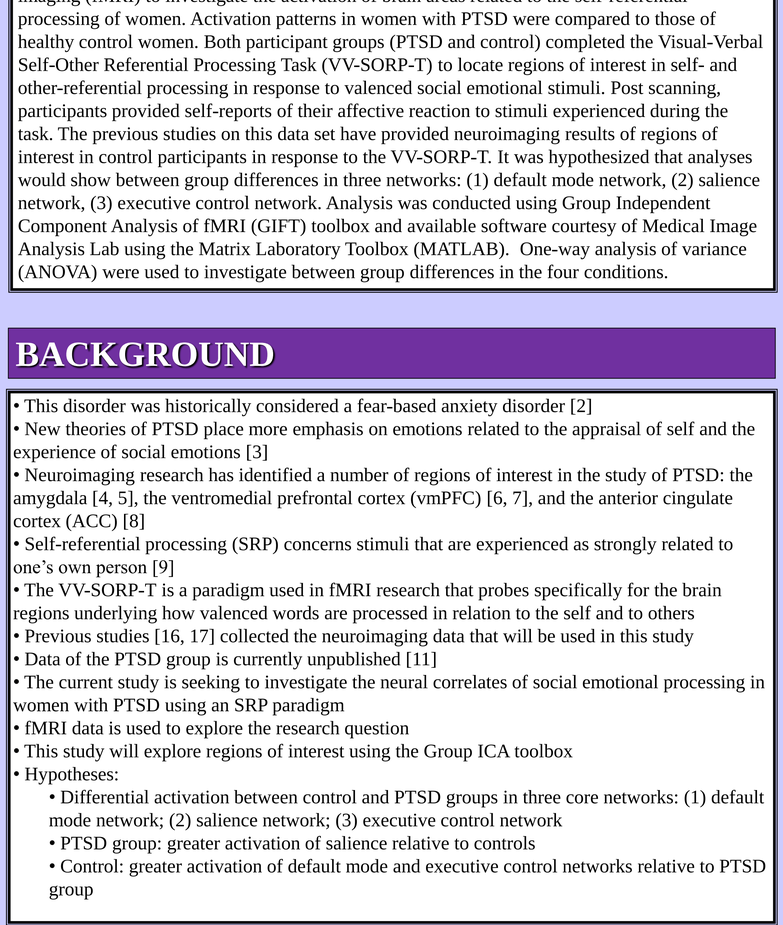

Figure 1. (a) *t*-values for significant ICs in Self-Negative Trial; (b) *t*-values for significant ICs in Self-Positive Trials, $p < .05$. Negative values reflect greater PTSD activation, $p < .05$. IC colour corresponds to spatial maps in Figure 3.

PROCEDURE

- All procedures were approved by the Health Sciences Research Ethics Board of Western University in London, Ontario, Canada
- Participants were assessed for inclusion criteria and completed a short questionnaire battery approximately two weeks before their scanning date
- On the day of scanning, participants completed a single-block (Figure 2) practice version of the VV-SORP-T paradigm in an office setting and three blocks of the paradigm while undergoing fMRI
- Before completing the VV-SORP-T, while undergoing fMRI, a resting-state functional scan of each participant's brain was also acquired
- Immediately after scanning, participants completed the affective response rating
- The experiment took approximately seventy-five minutes to complete
- Imaging was conducted at the Robarts Research Institute in London, Ontario, Canada
- Image acquisition and preprocessing has been previously published [16, 17].

ANALYSIS

- GIFT toolbox for use with MATLAB software was used to identify independent components (ICs)
- Spatial maps from Functional Imaging in Neuropsychiatric Disorders Lab (FIND Lab) [18] were used to test for correlations between significant components and networks under investigation
- One-way ANOVAs were used to determine significant differences in components between control and PTSD groups (PTSD < control)

PARTICIPANTS & MEASURES

PARTICIPANTS:

Control Group

- Twenty-four women between the ages of 18 and 52 years were included in the healthy control group
- Recruited from the general community using print and online advertisement
- Healthy control women must have scored normative levels of trait self-esteem and self-critical thinking as determined by the Rosenberg Self-Esteem Scale [12] and the Cognitive Distortion Scale [13], respectively
- Participants were excluded from the study for current or past psychiatric history using the Structured Clinical Interview for DSM-IV (SCID) [14], current substance use, head injury with loss of consciousness, left-handedness, pregnancy, metal piercings and surgical implants

Clinical Group

- Twenty women between the ages of 18 and 55 years were recruited using fliers in hospitals, London Health Sciences Centre Traumatic Stress Service and the general community using online and print advertisement
- Presence of PTSD was necessary for the clinical group and was determined by the Clinician Administered PTSD Scale (CAPS) [15]
- Participants were excluded from the study for head injury with loss of consciousness, left-handedness, current substance use, pregnancy, metal piercings and surgical implants

MEASURES:

VV-SORP-T

- Designed for use with fMRI and compares the neural correlates of valenced SRP with valenced other referential processing (ORP) using a priming methodology [16]
- Its procedure has been previously published in studies on similar populations [16, 17]
- VV-SORP-T provides 3 measurements: (1) fMRI BOLD signals, (2) participant self-reports of affective responses and (3) reaction times
- Stimulus presentations were blocked in terms of the reference (self or other) and valence (positive or negative) creating four trial types: self-negative, self-positive, other-negative and other-positive

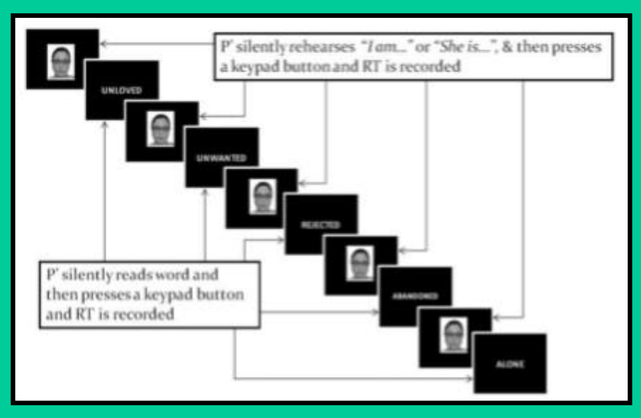

Figure 2. One block of the VV-SORP-T [16, 17]

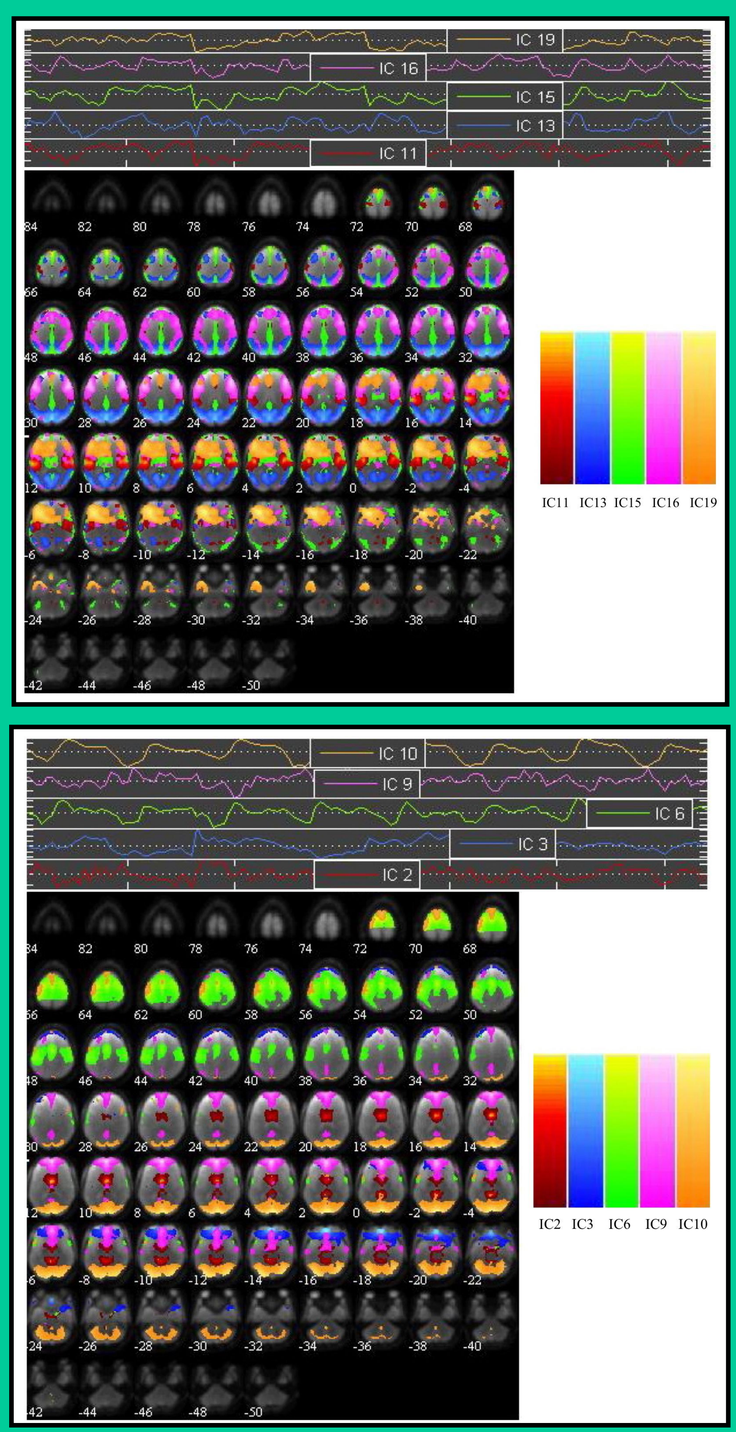

Figure 3. Ten significant ICs identified by Group Independent Component Analysis in between groups comparison.

RESULTS

- GIFT identified ten independent components as being significantly different between control and PTSD groups in response to the VV-SORP-T
- IC 9 was correlated with the dorsal default mode network ($t(1) = -2.34$, $p < .05$)
- No significant differences were found between groups for the salience network or the executive control network
- Additional components were identified that were not spatially correlated with the three network masks and are listed below by the condition in which there were found to be significant differences between groups:
  - **Self-Positive**
    - Components 10 and 15
  - **Self-Negative**
    - Components 2, 6 10 and 11
  - **Other-Positive**
    - Components 2, 3, 10, 15, 16 and 19
  - **Other Negative**
    - Components 9, 10, 13 and 15

DISCUSSION

Dorsal Default Mode Network (DMN)

- Involved in internally focused thought and autobiographical memory [19]
- PTSD group showed increased activation in this network relative to controls in the Other-Negative condition
- Evidence contrary to prior studies that have found patients with PTSD show reduced connectivity within DMN regions [19, 20]
- Increased role of internally focused thought for PTSD participants when presented with pictures of others associated with a negative word
  - Possible empathetic response to the pairing of a picture of another with a negative word

Cerebellum

- Represented as IC 2 and IC 10 in present study
- Areas of the cerebellum have consistently been seen to activate in studies of emotion and affect [21]
  - Role in emotion regulation [22]
- IC 2:
  - Cerebellum and thalamic regions
  - Significantly more active in control participants in the Other-Positive condition
  - Significantly more active in PTSD participants in the Self-Negative condition
    - Evidence for the role of the cerebellum in observing and reacting to other's negative emotions and the role of the cerebellum in the control of negative emotions relative to positive emotions [23]
- IC 10:
  - Activations in the IC 10 show a double dissociative pattern for reference type
  - Other-referential trials produced greater activation in the control group whereas self-referential trials produced greater activation in the PTSD group

Visual Cortex

- IC 13 represents the visual cortex in the occipital lobe and showed increased activation for control group in Other-Negative condition
- Previous studies have found subtle differences in sensory deficits in PTSD populations for both auditory [24] and visual stimuli [25]

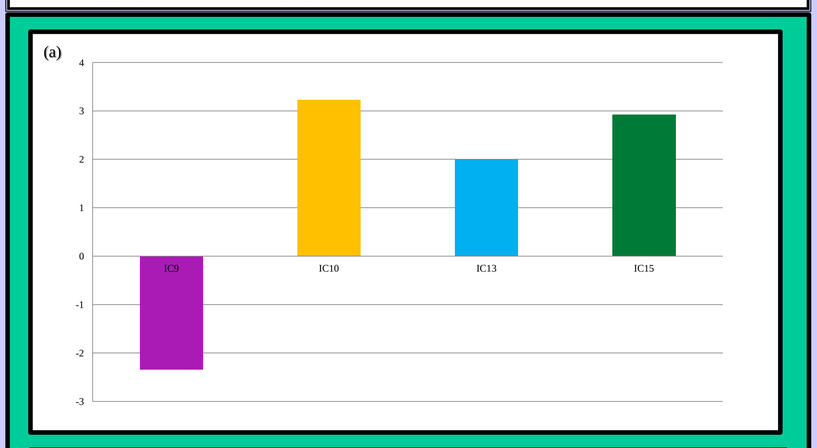

Figure 4. (a) *t*-values for significant ICs in Other-Negative Trial; (b) *t*-values for significant ICs in Other-Positive Trials, $p < .05$. Negative values reflect greater PTSD activation, $p < .05$. IC colour corresponds to spatial maps in Figure 3.

REFERENCES

[1] American Psychiatric Association. (2013). *Diagnostic and statistical manual fo mental disorders (5th ed.)*. Arlington: VA: American Psychiatric Publishing.
[2] American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders*(4th ed., text rev.). Washington, DC: Author.
[3] Budden, A. (2009). The role of shame in posttraumatic stress disorder: A proposal for a socio-emotional model for DSM-V. *Social Science & Medicine, 69*, 1032 – 1039. doi:10.1016/j.socscimed.2009.07.032.
[4] Phelps, E. A., Delgado, M. R., Nearing, K. I., & LeDoux, J. E. (2004). Extinction learning in humans: Role of the amygdala and vmPFC. *Neuron, 43*, 897-905. doi:10.1016/j.neuron.2004.08.042.
[5] Rajendra, A., Gold, A. L., LaBar, K. S., Beall, S. K., Brown, V. M., Haswell, C. C., Nasset, J. D., Wagner, H. R., & McCarthy, G. (2012). Amygdala volume changes in posttraumatic stress disorder in a large case-controlled veterans group. *Journal of the American Medical Association, 69*, 1169-1178. doi: 10.1001/archgenpsychiatry.2012.50.
[6] Koenigs, M. & Grafman, J. (2009). Postraumatic stress disorder: The role of medial prefrontal cortex and amygdala. *The Neuroscientist, 15*, 540-548. doi: 10.1177/1073858409333072.
[7] Milad, M. R., Rauch, S. L., Pitman, R. K., & Quirk, G. J. (2006). Fear extinction in rats: Implications for human brain imaging and anxiety disorders. *Biological Psychology, 73*, 61-71.
[8] Dickie, E. W., Brunet, A., Akerib, V., & Armony, J. L. (2013). Anterior cingulate cortical thickness is a stable predictor of recovery from post-traumatic stress disorder. *Psychological Medicine, 43*, 645-653. doi: 10.1017/S0033291711002935.
[9] Northoff, G., Heinzel, A., de Greck, M., Bermpohl, F., Dobrowolny, D., & Panksepp, J. (2006). Self-referential processing in our brain – A meta-analysis of imaging studies on the self. *Neuroimage, 31*, 440 – 457. doi: 10.1016/j.neuroimage.2005.12.002.
[10] Northoff, G., Heinzel, A., de Greck, M., Bermpohl, F., Dobrowolny, D., & Panksepp, J. (2006). Self-referential processing in our brain – A meta-analysis of imaging studies on the self. *Neuroimage, 31*, 440 – 457. doi: 10.1016/j.neuroimage.2005.12.002.
[11] Frewen, P. A. (2014). Unpublished raw data.
[12] Rosenberg, M. (1965). *Society and the Adolescent Self-Image*. Princeton, NJ: Princeton University Press.
[13] Briere, J. (2000). *Cognitive Distortion Scales: Professional Manual*. Odessa, FL, US: Psychological Assessment Resources.
[14] First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (1995). *Structured Clinical Interview for DSM-IV.* New York: New York State. Psychiatric Institute, Biometrics Research Department.
[15] Weathers, F., Keane, T., Davidson, J. R. (2001). Clinician-administered PTSD scale: a review of the first 10 years of research. *Depression and Anxiety, 13* 132 – 156.
[16] Frewen, P. A., Lundberg, E., Brimson-Thèberge, M., Thèberge, J. (2013). Neurimaging self-esteem: a fMRI study of individual differences in women. *Social Cognitive and Affective Neuroscience, 8*, 546 – 555. doi:10.1093/scan/nss032.
[17] Frewen, P.A., Dozois, D. J. A., Neufield, R. W. J., Densmore, M., Stevens, T. K., & Lanius, R. A. (2011). Self-referential processing in women with PTSD: Affective and neural response. *Psychological Trauma: Theory, Research, Practice and Policy, 3*, 318 – 328. doi:10/1037/a0021264.
[18] Shirer W.R. , Ryali S., Rykhlevskaia, E., Menon, V, & Greicius, M. D.: Decoding subject-driven cognitive states with whole-brain connectivity patterns. *Cerebral Cortex* (In press).
[19] Sripada, R. K., King, A. P., Welsh, R. C., Garfinkel, S.N., Wang, X., Sripada, C. S. & Liberzon, I. (2012). Neural dysregulation in posttraumatic stress disorder: Evidence for disrupted equilibrium between salience and default mode brain networks. *Psychosomatic Medicine, 74*, 904 – 911.
[20] Daniels, J. K. et al. (2010). Switching between executive and default mode networks in posttraumatic stress disorder: alterations in functional connectivity. *Journal of Psychiatry and Neuroscience, 35*, 258 – 266. doi: 10.1503/jpn.080175
[21] Kober, H., Feldman Barrett, L., Joseph, J., Bliss-Moreau, E., Lindquist, K., & Wager, T. D. (2008). Functional grouping and cortical-subcortical interactions in emotion: A meta-analysis of neuroimaging studies. *Neuroimage, 42*, 998 – 1031.
[22] Schutter, D. J. L. G. & van Honk, J. (2009). The cerebellum in emotion regulation: A repetitive transcranial magnetic stimulation study. *Cerebellum, 8*, 28 – 34.
[23] Schraa-Tam, C. K. L., Rietdjik, W. J. R., Verbeke, W. J. M. I., Dietvorst, R. C., van der Berg, W. E., Bagozzi, R. P., & De Zeeuq, C. I. (2011). fMRI activities in the emotional cerebellum: A preference for negative stimuli and goal-directed behavior. *Cerebellum, 11*, 233 – 245. doi: 10.1007/s12311-011-0301-2.
[24] Clark, C. R., Galletly, C. A., Ash, D. J., Moores, K. A., Penrose, R. A., McFarlane, A. C. (2009). Evidence-based medicine evaluation of electrophysiological studies of the anxiety disorders. *Clinical EEG and Neuroscience, 40*, 84 – 112.
[25] Mueller-Pfeiffer, C., Schick, M., Schulte-Vels, T., O'Gorman, R., Michels, L., Martin-Soelch, C., Blair, J. R., Rufer, M., Schnyder, U., Zeffiro, T., & Hasler, G. (2013). Atypical visual processing in posttraumatic stress disorder. *Neuroimage: Clinical, 3I*, 531 – 538.