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A Study of brainspotting therapy in PTSD using 18FDG brain PET scan to evaluate glucose metabolism changes

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Abstract
Post Traumatic Stress Disorder (PTSD) is a psychiatric and neurological disorder characterized by repeating experiences, avoidance, and hyperarousal. Brainspotting therapy (BSP) is a new body and brain treatment that claims to be effective in treating trauma and providing access to the brain. However, limited trials using neuroimaging have been done. A single-subject pretest-posttest design was applied in this study with two subjects (n = 1 PTSD; n = 1 Healthy Control; HC). Thirty sessions with online BSP were given to the PTSD subjects. 18FDG PET measurements and clinical assessment using HAM-A, DASS, and PCL-5 were taken for both subjects before and after treatment. The SDMAC value of brain 18FDG PET derived from NeuroQTMsoftware was used quantitatively between the PTSD and HC subjects to evaluate the glucose metabolism level of the mid-frontal cortex (MFC) and medial temporal cortex(MTC), which is associated with PTSD. Measurements taken post-treatment for clinical assessment exhibited a reduction in PTSD symptoms while PET scans demonstrated varied results. The findings of this study indicate that online BSP is effective for improving PTSD symptoms and has various effects on brain glucose metabolism. The limitations and suggestions of the study are discussed for further research.

Keywords: 18FDG-PET scan, brain spotting therapy, post traumatic stress disorder

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Introduction

Post Traumatic Stress Disorder (PTSD) is a psychiatric disorder and a neurological disorder that is characterized by four major symptoms such as intrusion, avoidance, cognitive and memory impairment, and hyperarousal symptoms. Trauma also affects the brain and body (Bremner, 2006; Van Der Kolk, 2014). 70% of the population in many nations has been exposed to traumatic events (Benjet et al., 2016). Studies also showed, PTSD impacts life function, risk of harm, interpersonal relationships and the development of other psychological issues such as depression or panic attack (Shalev et al., 2017; Brockie et al., 2015). Intimate partner sexual assault (42.7%) produces the most lifetime PTSD episodes (27.8%). (Kessler et al., 2017). 51.1% of women experience intimate sexual violence (Frieden et al., 2011). Indonesia's sexual assault reports grew rapidly in 2020, reaching 6.87k (Statista, 2020). The prevalence of PTSD in the marginalised group is substantially higher, reaching up to 50% among sexual assault survivors (Creamer et al., 2001). However, Sexual assault therapy was still limited (Huda, 2021). Most victims are too embarrassed and scared to report it (Pratiwi & Niko, 2021; Noer 2021).

PTSD also affects neurological problems (Sherin & Nemeroff, 2011; Bremner, 2003). Neuroimaging studies have also shown that various regions of the brain are affected by PTSD (Bremner, 2003, Bremner, 1997). This study will examine the mid frontal cortex (MFC), and medial temporal cortex (MTC), which are related with PTSD, using 18F-fluoro-2-deoxy-D-glucose PET scans to measure glucose metabolism alterations. 18FDG PET employing resting-state paradigms is the most basic technique to evaluate baseline brain metabolism and the neurological underpinning of PTSD, according to several studies (Ramage et al., 2015; Zandieh et al., 2016). The MFC is in the frontal lobe and part of the cortical which are assumed to play a key role in emotional processing, pain perception, cognitive control, episodic memory, modulates

the stress response and understanding social interaction (Vega et al., 2016; Moreira et al., 2016; Amodio & Frith, 2006; Gehring & Fencsik, 2001; Kahnt et al., 2011; Etkin et al., 2010). Study also showed that thinking and memory stop working normally on PTSD (Bremner, 2003). Zandieh et al. (2016) found hypometabolism in the occipital, temporal, posterior cingulate cortex, parietal, and frontal lobes of torture PTSD patients.The MTC is a subcortical part of the limbic system involving the hippocampal area, fornix, amygdala, and entorhinal, perirhinal, and parahippocampal cortices, which are associated to memory, visuospatial processing, and cognitive and emotional functions (Eichenbaum et al., 2007; Squire et al., 2004; Bird & Burgess, 2008; Maguire et al., 2000; Patel & Fowler, 2019). MTC is a set of anatomically connected areas that facilitate declarative memory, learning, and reasoning (Eichenbaum et al., 2007; Squire et al., 2004; Bird & Burgess, 2008; Maguire et al., 2000). Study found MTC function is directly connected to re-experiencing and negatively related to negative emotional symptoms (Stevens et al., 2017).

Kim et al. (Kim et al., 2012) found that people with PTSD who experienced sexual assaulted had less glucose metabolism than controls in their left hippocampus, superior temporal gyri, and precentral gyri. A study showed PTSD glucose metabolic in the temporal cortex was reduced (Bremner, 1997). Other studies reported decreased glucose metabolic in cingulate gyri, hippocampus, and insula, and elevated in cerebellum, fusiform, temporal, and occipital cortices (Kim et al., 2012; Shin et al., 2009; Molina et al., 2010; Petrie et al., 2014). Decreased cortical activity in the temporal area appeared to be associated with decreased information integration in PTSD (Engel et al., 1997; Kim et al., 2007). Zhu et al. (2016) discovered higher glucose metabolism in the PTSD's bilateral amygdala and right posterior insular cortex, which are the regions most active when fear is induced (Whalen, 1998),. The amygdala is a structure in the medial temporal lobe that detects potential threats in the environment. Most neuroimaging studies on PTSD demonstrate hyperactivity in the limbic system, which processes emotions, and damaged medial prefrontal cortex and anterior cingulate cortex (Shin et al., 2009, Shin, 2006). Due to noninvasive neuronal imaging limitations, results are still varied (Zandieh et al., 2016, Shin et al., 2009; Molina et al., 2010; Petrie et al., 2014; Zhu et al.; 2016, Shin, 2006; Lanius et al., 2004; Chen et al., 2006; Cottraux et al., 2015; Looi et al., 2009; Yamasue et al., 2003; Rogers et al., 2009).

Brainspotting psychotherapy (BSP) is a brain body therapy which is known as a new PTSD psychotherapy approach that was developed by David Grand in 2003. BSP uses the field of vision that provides the most neurological stimulation and body action to uncover inaccessible brain trauma (Grand, 2013; Corrigan & Grand, 2013). The notion of BSP is "What you see affects how you feel" (Grand, 2011). By integrating neurobiological and relational attunement, it can access subcortical trauma and cortical visual processing (Corrigan & Grand, 2013). Dual attunement activates the mirror neuron between the cingulate and orbitofrontal cortex, producing an empathic setting and regulating the amygdala, which promotes adaptive modifications in the client and healing (MC Salvador, 2018). "Top-down" and "bottom-up" describe this well. Peripheral vision gives the most mental stimulation and physical activity, which could have helped the individual deal with unpleasant memories that were implicit or hidden (Grand, 2011, Grand, 2013).

David Grand says helping the client's brain regulate itself is part of therapy (Grand, 2013, Corrigan & Grand, 2013). Attunement develops connection and aligns the uncontrolled brain with the therapist's. Bottom-up processing helps the brain process information more efficiently by regulating emotions in the subcortical brain. Top-down processing avoids repeating events. Previous studies (Hildebrand et al., 2015) found that BSP improved PTSD symptoms and psychological disturbances in just three sessions. However, few neuroimaging studies have been done and online BSP has never been researched. The goal of this research is to evaluate online BSP's effectiveness in reducing PTSD symptoms and inducing metabolic changes in the brain using neuroimaging (18FDG PET Scan) while providing PTSD patients with the privacy, security, and accessibility of an online PTSD treatment setting. Therefore,this preliminary study will address whether an online BSP can improve PTSD symptoms in sexually abused patients and whether those changes are demonstrated in brain metabolism. It is important to note that this study was done without drugs during the COVID-19 pandemic.

Method

A single-subject control pretest-posttest design was used in this study. Data for clinical assessment and quantitative The Standard Deviation Mean Asymptomatic Control (SDMAC) was analyzed using Microsoft Excel.

Subjects

Two 21-to-24-year-old Indonesian women were recruited through ads (Table 1). One person with PTSD and one healthy control (HC). Before the study intervention, participants were told about the process and asked for informed consent. The Clinician-Administered PTSD Scale (CAPS) was used in interviews to determine the predicted criteria and the PCL-5 was used to evaluate PTSD symptom progression after BSP. Anxiety disorder and depression are common PTSD symptoms (Ramage et al., 2015). This reflects the study's subjects. Thus, clinical evaluations such as DASS and HAM-A are considered to assess psychological symptoms and help us understand PET scan results.

Table 1 <Participant Demographics>

	PTSD (n=1)	**HC (n=1)**
Gender	Female	Female
Age	21	24
Education	Bachelors	Bachelors
Occupation	Private Employee	Private Employee
Ethnicity	Javanese	Batak

The sexual assault happened a month before enrollment. She was mistreated as a child and never received treatment. She complained about her inability to function at work due to mental stress, worry, and physical problems like headaches, nausea, and insomnia. Subject's interaction with her bipolar mother led to self-harm and suicidal ideas.

The clinical evaluation results before BSP therapy showed that the PTSD subject had highly severe PTSD symptoms (PCL-5 self-reported), severe anxiety (HAM-A), and significant levels of depression, anxiety, and stress (DASS self-reported) shown in Table 2. Subjects reported a high prevalence of PTSD symptoms, possibly due to a recent sexual assault and environmental stresses such poor family relationships, employment challenges, pandemics, and a lack of social support. Clinical assessments from HAM-A and DASS support this.

Instruments

The PCL-5 is a DSM-5 PTSD Checklist (U.S. Department Of Veterans Affairs, 2013). A 20-item self-reported questionnaire was used to assess PTSD current symptoms. It is substantially linked with interview-based measures of PTSD, can successfully differentiate between both with and without a PTSD diagnosis (Blanchard et al., 1996), and appears to have good internal consistency and test-retest reliability (Wilkins et al., 2011).The total score indicates PTSD severity. The Likert scale ranges from 0 (not at all) to 4 (extremely), with a maximum score of 80.

The Hamilton Anxiety Rating Scale (HAM-A) was used to measure anxiety levels (Hamilton, 1959). A cut-off score of 10 or 11 was employed in this investigation, resulting in a sensitivity of 85.7 percent and a specificity of 63.5 percent (Kummer et al., 2010; Lovibond & Lovibond, 1995).

DASS-42 is a self-reported questionnaire with three 14-item scores (Lovibond & Lovibond, 1995). It's a well-established instrument for measuring depression, anxiety, and stress in clinical and non-clinical adult populations and potentially be used as a screening tool for depressed disorders (PTSD)(Berle et al., 2018). The Depression Scale (DASS-D) measures hopelessness, devaluation of life, and self-depreciation; the Anxiety Scale (DASS-A) measures psychological and somatic symptoms, such as autonomic arousal and situational anxiety; and the Stress Scale (DASS-S) measures difficulties relaxing and nervous arousal. The DASS asks how often symptoms happened in the preceding week and evaluates responses on a 4-point Likert scale, with 0 indicating the symptom doesn't apply and 3 indicating it occurs often. The DASS-42 has been proven to have good internal consistency (Cronbach's coefficients ranging from 0.89 to 0.96 (Brown et al., 1997), strong convergent and discriminant validity, and favorable test-retest reliability (Dahm et al., 2013). Low severity cutoffs for DASS-D, DASS-A, and DASS-S are 10, 8, and 15, respectively (Lovibond & Lovibond, 1995).

Neuroimaging

PET is a molecular imaging technology that creates three-dimensional functional maps of neural activity such as regional cerebral metabolism and blood flow. PET allows for visible signal changes (10%) in the brain and the most straightforward methods to explore baseline brain metabolism and neurological basis that use resting-state paradigms. In PET investigations, the tracer 18FDG was used to evaluate relative glucose absorption in specific brain areas as an indirect measure of neuronal activity.

Neuroimaging Procedures

The 18FDG PET scan of the brain is a non-invasive diagnostic imaging technology that can be used to assess cerebral glucose metabolism. SDMAC is an abbreviation for Standard Deviation from Patient-Mean Asymptomatic Control. It is a quantitative parameter of 18FDG PET that reflects brain glucose metabolism or the standard deviation of the difference in mean glucose metabolic activity of the brain area between asymptomatic patients and healthy people. This value reflects the level of difference in brain glucose metabolism of patients who have been standardized with the value of normal people's brain glucose metabolism. Daniel Silverman, the creator of the NeuroQ application, was the first to report this figure (Silverman et al., 2010). On a PET/CT scanner, resting brain FDG PET/CT pictures were obtained (Gemini, Philips Healthcare, USA). Before intravenously receiving FDG (dosage 0.10 mCi/kgBW (5 MBq/kg), the patient had fasted for more than 6 hours and had a blood sugar level of less than 150 mg/dL. Photos were taken after the patient had rested in the uptake room for 45 to 90 minutes. The patient was scanned at the level of the brain using a 10 mm slice thickness. The 3D-ordered-subsets expectation-maximization method was used to reconstruct images after 3 minutes of three-dimensional data gathering per bed position. X-ray CT (140 kV, 120-240 mAs) was used to correct segmented attenuation and obtain a 128 x 128 matrix image. A traditional filtered back projection approach was used to rebuild CT images.

Treatment Procedures

PTSD subjects gave informed consent before receiving 30 online BSP sessions. PTSD subjects were evaluated before and after 30 BSP sessions. Sessions lasted 45-60 minutes. Beginning the session with genuine presence, the therapist creates a safe space for the subject to express their problems. The gaze spotting technique is used to be most suited for online platforms (Grand, 2009). Therapist asked the subject to adjust the 80-cm pointer. The therapist asks the subject to describe uncomfortable physical feelings. The therapist will ask the SUDs level of the stimulated body spot before shifting the pointer to track the accompanying sensation. The therapist pauses at the subject's triggered spot. BSP also uses biolateral sounds, which provide comfort while activating unpleasant memories. Continue until body feeling is decreased. The therapist must maintain dual attunement, even online. In the case of complete memory reprocessing (i.e., the subject reported 0 activation on a scale of 0 to 10), the therapist asked the subject to return to the initial memory to assess any changes, then used the "Squeeze the Lemon" technique (Grand, 2009) until the participant felt no residual emotional activation. This research process takes 45 to 60 minutes. The therapist checks the subject's SUDs level after the process.The HC subject had a clinical assessment and waited 210 days. Before and after treatment, PTSD patients had PET scans. 210-day PET scans were performed on HC.

Results and Discussion

Nearly all clinical assessments improved (Table 2 & Figure 1). The HAM-A pretest score was 43, which was a very severe level of anxiety, and the posttest score was 27, which was a moderate level. The DASS pretest depression score was 37, anxiety was 35, and stress was 37. All were extremely severe. After 30 BSP sessions, the DASS scores reduced to 32 for depression, 14 for anxiety, and 14 for stress.

Table 2 <Clinical Assessment (DASS, HAM-A, PCL-5 (PTSD Assessment)>

	PTSD	
	Pre-Test	Post-Test
HAM-A	43	27
DASS (Self Report)		
Depression	37	32
Anxiety	35	14
Stress	38	14
PCL-5	77	65

Figure 1 shows that the PCL-5 is a widely used DSM-correspondent self-reported evaluation of PTSD symptoms. The PCL-5 findings were described in the table and figures three before and after therapy. PCL-5's pretest score was 77, indicating very severe PTSD symptoms. Following BSP therapy, PCL-5's score dropped to 65 for very severe to severe PTSD symptoms. Even though this result had not hit the cut off or normal level, the result showed improvement in symptoms.

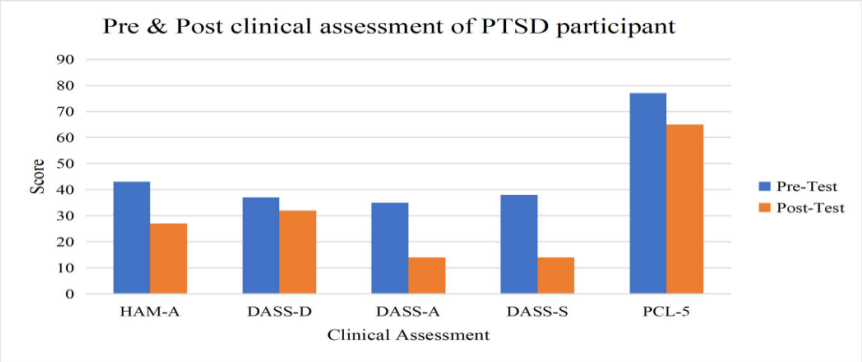

Figure 1 <Pre & Post Clinical Assessment of PTSD Participant>

Table 3 <SDMAC of Pre and Post Measurement of Healthy Control (HC) and PTSD>

ROI	SDMAC			
	Pre HC	Pre PTSD	Post HC	Post PTSD
rMFC	1,2951	-0,0447	1,3143	0,2074
lMFC	0,0196	0,5413	-1,2826	0,5609
rMTC	-0,6247	0,3263	-0,0139	-0,3124
lMTC	-0,6684	0,265	0,1454	-0,0542

Notes : rGFm = right mid frontal cortex; lGFm = left mid frontal cortex; rMAT = right anterior medial temporal cortex; lMAT = left anterior medial temporal cortex

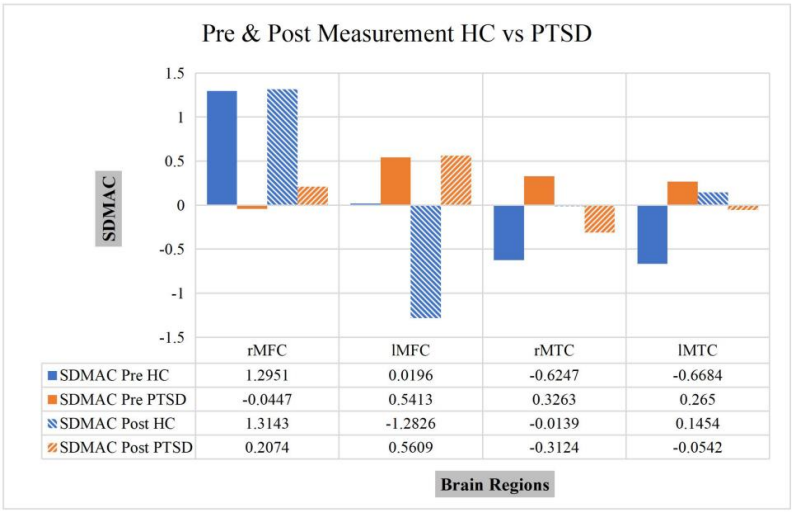

Figure 2 <Pre & Post Measurement HC vs PTSD>

Results Table 3 and Figure 2 showed that there were notable changes in glucose metabolism in some areas, either a decrease or an increase, in PTSD subjects when compared with HC at post measurement. Particularly in the right MFC, there was a significant increase in glucose metabolism after treatment of PTSD subjects. The right MFC SDMAC of PTSD subjects appears lower on pretest measurement compared to HC, indicating hypometabolism and reaching hypermetabolism after 30 sessions BSP, while left MFC remains stable hypermetabolism and never has noticeable changes. Both MTC of PTSD SDMAC showed decreased significantly after treatment, where the MTC SDMAC pretest of PTSD was higher than HC. This indicates hypermetabolism on the pretest and hypometabolism of PTSD after treatment. These findings indicate that the treatment has varied effects on the brain glucose metabolism of

PTSD subjects. This research also demonstrated varied results of HC. The left MFC SDMAC HC decreased, and the bilateral MTC SDMAC HC increased.

These findings indicate that BSP has a number of effects on brain glucose metabolism, and is thus quite effective at improving PTSD symptoms. All clinical assessment results indicated an improvement in PTSD symptoms, yet not all reached normal levels. These findings are in line with the findings of Hilderbrand et al. (59), even though the trauma symptoms did not completely decrease after just three sessions but rather after 30 sessions. Since this is a preliminary study, the results will provide an alternative therapy to deal with PTSD via an online platform and to give a new perspective of neurophysiology of BSP.

The right MFC seemed to have significant alterations in glucose metabolism as they transitioned from hyporeactivity to hyperactivity. Studies show that the MFC is thought to be involved in cognitive control, emotion, pain perception, and episodic memory in PTSD (Vega et al., 2016; Moreira et al., 2016) which is responsible for top-down processing. The MTC glucose metabolism seems to have hypoactivity significantly after BSP treatment. When fear is regulated, the frontal cortex becomes more active (Bremner, 2003, Ramage et al., 2015, Etkin et al., 2010. Fitzgerald et al., 2008) and the limbic regions, especially amygdala which is a structure in the medial temporal lobe become less active (Shin et al., 2009). It seems BSP improved regulation due to BSP attunement, which lowered brain and body stimulation. The viewer's peripheral vision generates the most neural stimulation and physical activity, which may have helped the subject process previously inaccessible painful information (Grand, 2013). This also explains how BSP promotes the brain in gaining access to the subcortical and cortical brain (Corrigan & Grand, 2013; Hildebrand et al., 2015).

Despite the small sample size (n), this study demonstrates a method in which neuroimaging is used to corroborate clinical judgment in determining the efficacy of psychotherapy methods for PTSD patients. These results, while preliminary, will shed new light on BSP's efficacy in treating PTSD symptoms and present therapeutic options for handling PTSD cases via an online platform. Study also demonstrated varying healthy control findings. Interestingly, the left MFC SDMAC showed decreased or hypometabolism, and the bilateral MTC SDMAC was hypermetabolic after 210 days waiting. We were unaware of the mechanism behind the substantial activation. This was possibly due to heightened levels of fear and stress during the pandemic situation when the scan was taken, where most people afraid went to hospital. We did not conduct a physical examination for healthy control before doing the 18FDG PET scan.

Conclusion

The findings and limitations of this study need to be taken into consideration for further research, which should include studying a larger number of brain regions and participants, and increasing the participant population so that the findings may be generalized. It is advised that a design that uses mixed methods be used in order to systematically characterize how and what changes are made in the mechanism of glucose metabolism as a result of this treatment. Utilizing additional neuroimaging techniques may also assist in establishing a deeper understanding of brain metabolism in patients with PTSD. To prevent bias in further studies, it is suggested that the control group receive a physical examination and regular health updates before receiving a PET scan.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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