ORIGINAL ARTICLE

Role of Microstructural White Matter Changes of Somatosensory Cortex in Stress Among Non-Clinical Population: A Diffusion Tensor Imaging Study

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ABSTRACT

INTRODUCTION: Stress is a common response by people to stressors or potential threats, resulting in physical, affective, and cognitive changes. Emotions are associated with interpretations of physiological changes, and the processing of emotions is largely dependent on the somatosensory cortex which includes the postcentral gyrus. The objective of this study was to examine the correlation between stress and alterations in the microstructure of white matter in the somatosensory cortex among healthy non-clincal population. **MATERIALS AND METHODS:** A total of 30 participants were recruited. The participants were administered the Depression, Anxiety, and Stress Scale 21 (DASS-21) questionnaire. All subjects underwent Magnetic Resonance Imaging (MRI) brain scanning, with diffusion tensor imaging (DTI) used to assess white matter integrity. The association between stress scores in DASS-21 and DTI parameters was analyzed. **RESULTS:** A significant negative relationship was observed between stress scores and fractional anisotropy (FA) values in the left postcentral gyrus (r=-0.393, p=0.032), suggesting that stress has an early detrimental effect in this region, while no significant correlation was found in the right postcentral gyrus (r=-0.300, p=0.107). **CONCLUSION:** The findings of our study indicate that stress may lead to early impairments in the microstructural somatosensory cortex, particularly in the left postcentral gyrus. These alterations were observed using DTI technique. Hence, the alterations in the microstructure of white matter in the brain prior to the onset of the disorder may play a vital role and could serve as a new and promising biomarker for the early identification and treatment of the disease in the non-clinical population.

Keywords
Stress, DTI, Somatosensory, White Matter

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INTRODUCTION

Stress is a negative psychological condition triggered by stressors or potential dangers in humans. It is a common response that involves changes to one's physical, emotional, and mental functions.[1] Stress is typically accompanied with physical symptoms. Indeed, nearly every people may encounter episodes of stress at some stage in their lives, and it has been indicated that sub-threshold stress and anxiety symptoms are commonly observed in the general population.[2] Prior research has predominantly examined the cognitive, emotional, and neurological dimensions of individuals experiencing anxiety and stress, neglecting the influence of their somatic brain networks.[3] It was suggested that emotional processing plays a crucial role in regulating behaviour, particularly decision-making.[4] All emotions are based on the body's homeostatic interpretations of changes in its condition.[5] It has been suggested that interoceptive memories and visceral emotional experiences serve as substrates for decision-making. The postcentral gyrus, which is part of the somatosensory cortex, plays a vital role in emotional processing and is often activated by physical sensations.[6]

The heightened neuronal activity in the postcentral gyrus is mostly associated with the impacts of social stress.[7] It has been demonstrated that the postcentral gyrus can be used to predict treatment responses during the analysis of pleasant facial expressions.[8] An enhanced connection between the postcentral gyrus and the amygdala indicates a heightened capacity to control emotions, while the association between the postcentral gyrus and the anterior cingulate cortex during rest is linked to negative emotional consequences.[9] Research indicates that the prefrontal cortex and limbic system have significant roles in chronic stress. However, it is suggested that more emphasis should be given to the participation of somatosensory brain regions, specifically the postcentral gyrus.[10] Therefore, it is crucial to determine how stress conditions underlie the post-central gyrus's effects.

Magnetic Resonance Imaging (MRI)- based diffusion tensor imaging (DTI) capability to assess the Fractional Anisotropy (FA) values of white matter tracts offers a promising avenue to explore how stress affects the brain's networks. FA values, indicative of the directional coherence of water diffusion in tissue, serve as a marker for white matter integrity. Reductions in FA are often interpreted as a sign of decreased white matter organization, potentially reflecting damage or alterations in neural pathways critical for emotional processing and cognitive function.[11,12,13] Increased activity was observed in the brain regions of the thalamus, para-hippocampal gyrus, middle frontal gyrus, and inferior temporal gyrus in the group with the mental disorder.[11] It was demonstrated notable alterations in the microstructure of cerebral cortical regions linked to mood disorders.[12] The rapid growth and subsequent reduction of dendrites and synaptic structures in certain groups of cortical neurons during specific sensory learning experiences may be responsible for the underlying microstructural alterations.[13] Despite the extensive research on the changes in brain function and structure associated with stress and stress-related disorders, there have been few studies that specifically focus on a healthy or non-clinical population. This group refers to individuals who do not have any known mental health conditions or diseases and are not currently seeking or receiving medical treatment. We hypothesized that the changes in brain function and structural integrity of the brain's white matter that precede the onset of a disorder may be crucial for the early identification and management of the illness in individuals who are not yet clinically diagnosed. The aim of this study was to investigate the relationship between early mental psychopathology and changes in the structural integrity of white matter in the brains of healthy non-clinical persons. Based on the functions of the postcentral gyrus and the somatic marker hypothesis, we hypothesised that changes in the microstructure of the white matter in the somatosensory cortex, notably the postcentral gyrus, would be linked to the level of stress.

MATERIALS AND METHODS

Participants

Thirty non-clinical healthy subjects were enlisted in total, consisting of 21 males and 9 females with a mean age of 40.83 years (range: 27–57 years). Participants were assessed for handedness, resulting in 25 right-handed and 5 left-handed individuals. Two qualified psychiatrists distributed the Depression, Anxiety, and Stress Scale 21 (DASS-21) questionnaire to the subjects. The methods were performed in compliance with approved protocols. Individuals who exhibited any movement during the scan, had neurological problems, severe psychiatric conditions, head injuries, or were pregnant or lactating were excluded from the study. Prior to the study, all participants provided written informed consent, which was approved by the Research Ethics Committee (ID -2022-047).

Instruments

The DASS-21 is a self-administered instrument designed primarily to evaluate the existence of negative emotional states, such as depression, anxiety, and stress. The tool consists of 21 items that measure levels of depression, anxiety, and stress using a Likert scale that ranges from 0 to 3. A score of 0 signifies that the state did not affect the individual in any way. A score of 1 suggests that it had some influence or occurred occasionally. A score of 2 indicates a significant impact or frequent occurrence. A score of 3 signifies a strong influence or a near constant presence. The DASS-21 is a simplified version of the DASS-42. The DASS-21 demonstrates high internal reliability, as seen by Cronbach's alpha coefficients of 0.88 for the Depression scale, 0.82 for the Anxiety scale, 0.90 for the Stress scale, and 0.93 for the overall scale.[14] The stress level of the participants in this study was assessed by utilizing the 7 stress sub-items out of the total 21 sub-items in the DASS-21 questionnaire. The scores were calculated by summing the scores for each sub-item and then multiplying by two to ensure that they may be interpreted consistently with the lengthier form of the 42 items.

Data Acquisition

The Siemens 3-Tesla MR scanner was utilised for conducting MRI scans. Subjects were given instructions to maintain full motionless while inside the scanner. In order to reduce head movement, foam pads were placed on either side of the head, while earplugs were used to decrease the noise produced by the scanner. The diffusion tensor imaging (DTI) parameter sequence were set as follows: The repetition time: 7649 milliseconds, the echo duration: 72 milliseconds, the flip angle: 90 degrees, the field of view: 240 millimetres, the matrix size: 96 x 96, the section thickness: 2.5 millimetres, there is no section gap and the number of excitations: 1.0, with the acquisition time is 4 minutes and 28 seconds. The electrostatic repulsion model was used to apply diffusion-weighting gradients along 32 noncollinear directions. The imaging consisted of 2 images with b0=0 and 32 images with b1=1000 s/mm. In addition to the DTI scan, high-resolution anatomical T1, T2, and FLAIR weighted images were also obtained for each patient.

Image Processing

The diffusion imaging data was reconstructed using the DTI technique, in combination with the MRI Converter version 2.1.0 and DSI Studio software (http://dsi-studio.labsolver.org/). Initially, the DICOM data for each participant was imported using MRI Converter in order to convert the file format from DICOM (.dcm) to NIfTI (.nii). Subsequently, the converted files were opened in DSI Studio to generate the ".src" file. The ".src" file was subsequently reconstructed, yielding "fib" data, which was then used to obtain the FA value. The DSI Studio fibre tracking algorithm is a modified version of the deterministic tracking algorithm that utilises quantitative anisotropy as the termination criteria.[15] The deterministic technique was employed as the principal orientation of the tensor, aligning with the primary direction of the fibres and adhering to the most suitable pathway. The information provided reflects the predominant alignment of fibres inside each voxel. This approach seeks to illustrate the optimal balance between valid and incorrect connections.[16]

Region of Interest (ROI)s Localization

An expert radiologist assessed the postcentral gyrus on both the left and right sides of the brain, and manually designated a region of interest (ROI) on each side. Subsequently, using the program's auto-detection tool, the postcentral gyrus is automatically discovered on both sides of the brain (Figure 1) with the same ROIs. Minor adjustments were made to the automated selection of the ROIs for each unique case, taking into account the size and form of the postcentral gyrus. The FA values were obtained and analyzed after localising the ROIs.

Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) software. Quantitative data were described by calculating the means and standard deviations with p-values <0.05 considered as statistically significant. The Pearson correlation test was used to assess the relationship between the FA-value of post-central gyrus and stress score in DASS-21 sub-items.

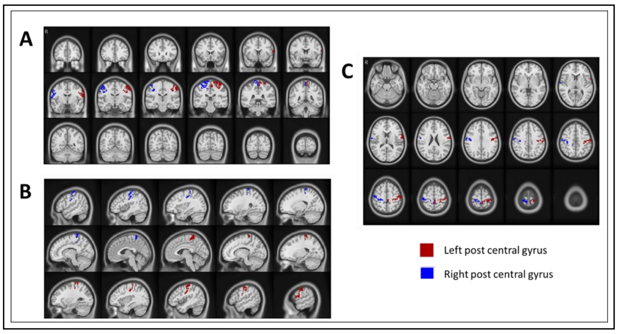

Figure 1. White matter tracts from the different cut sections; A) coronal view, B) sagittal view, C) axial view. FA values are extracted from the ROIs and analyzed in this work.

RESULTS

Clinical Variables

A total of 30 participants was enrolled in the study (21 males and 9 females; mean age=40.83, range=27–57 years). The results of the study showed that the average score ± standard deviation of the stress score of DASS-21 was 15.13 ± 7.34 (Figure 2).

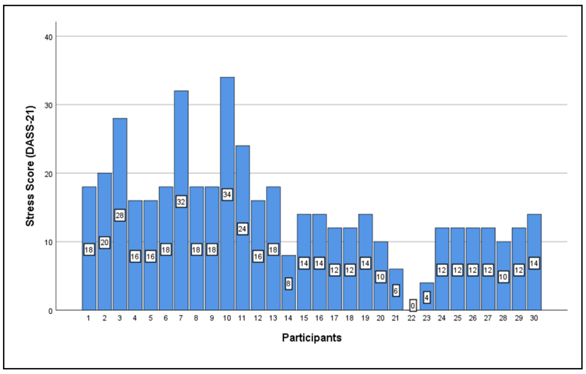

Figure 2. The distribution of the Stress Score in the healthy non-clinical participants.

Correlations Between FA-value of Postcentral Gyrus and Stress Scores

Our study has found that the MR-DTI FA value of the left post-central gyrus was negatively correlated with stress score (r=-0.393, p=0.032) (Figure 3), while no significant correlation was found between the MR-DTI FA value of the right postcentral gyrus and the stress score (r=-0.300, p=0.107) (Figure 4).

Table I: Brain regions with correlations between MR-DTI FA-value and Stress score

Brain Region	N	Mean FA value	r-value	p-value
Left post-central gyrus	30	0.208 ± 0.021	-.393	0.032*
Right post-central gyrus	30	0.179 ± 0.021	-.300	0.107

*Correlation is significant at the 0.05 level (2-tailed).

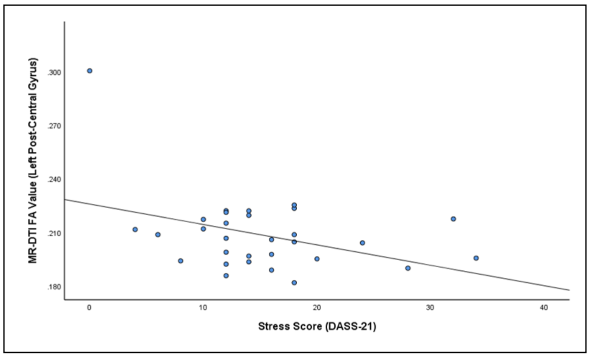

Figure 3. Correlation between MR-DTI FA value of left postcentral gyrus and stress score (r = -0.393, p = 0.032)

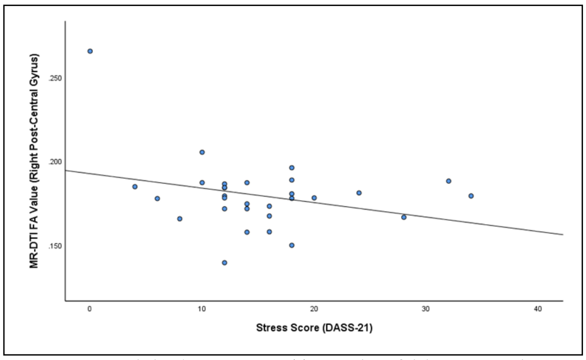

Figure 4. Correlation between MR-DTI FA value of right postcentral gyrus and stress score (r = -0.300, p = 0.107)

DISCUSSION

The aim of this study was to emphasize the significant involvement of the somatosensory cortex (specifically the postcentral gyrus) in response to stress among the groups of individuals who do not have any known mental health conditions or diseases and are not currently seeking or receiving medical treatment. This was achieved by examining the relationship between the structural alterations in the white matter of the postcentral gyrus and stress levels.

Consistent with our hypothesis, this study found that the somatosensory cortex, specifically the postcentral gyrus, which is part of the body-loop circuit, has a critical function in stress. Additionally, there is a notable inverse relationship between stress and the FA value of the left postcentral gyrus. Stress-related physical sensations can be linked to the postcentral gyrus in the somatosensory processing during stress exercises. This region is responsible for perceiving and analyzing the physiological alterations that are often induced in the body by stress.

Research has shown that the left somatosensory cortex has a greater influence on sensorimotor integration than the right somatosensory cortex.[17] The influence of handedness on brain structure and function has been well-documented with handedness can affect the lateralization of brain functions, including those related to sensory processing and stress responses.[17] In our study, the majority of participants were right-handed, which may have contributed to the observed lateralization effects.

Right-handed individuals often show stronger left-hemispheric dominance for motor and sensory functions, which could explain the significant association found between stress scores and the left postcentral gyrus.

Individuals experiencing high levels of stress tend to exhibit heightened sensitivity towards daily occurrences and stimuli, resulting in a state of perpetual vigilance and exaggerated reactions to stimuli. A plausible explanation for the association between the postcentral gyrus and stress is that individuals experiencing stress need to engage in increased brain activity in order to effectively manage stress and avoid developing pathological anxiety.[18] It was demonstrated that emotion perception is one of the functions of the somatosensory regions.[19] The postcentral gyrus, which forms connections with the frontal and parietal lobes, has been physically associated with cognitive functions such as control, memory, and attention.[20] The postcentral gyrus is a crucial component of the brain responsible for the recognition of basic emotions.[21] It is involved in the processing of somatosensory information, voluntary movement, and the regulation of emotions.[22] It was also explored that applying transcranial magnetic stimulation to the somatosensory cortex can influence the way people perceive emotions when performing social face recognition tasks.[23] Another study that looked at teens under emotional stress found that there was an alteration in the gray matter volume of the postcentral gyrus.[24]

The heightened neural activity observed in the postcentral gyrus during periods of stress, which has been associated with structural injury, could potentially indicate a rearrangement of its functional capabilities. Prior studies employing functional MRI (fMRI) in both people[25,26] and animals[27] have explored the functional reorganization of the central nervous system. According to these studies, the normal cortex undergoes substantial reconfiguration to compensate for the limitations of the affected area, resulting in behavioural adaptations. The greater extent of cortical activation, as indicated by the stronger fMRI response of the brain cortex, can be attributed to a bigger number of neurons and synapses involved in carrying out neurological function. These findings indicate that the extent of functional reconfiguration following stress, namely in the post-central gyrus region, may be influenced by the level of microstructural damage. Our study found a negative correlation between the FA value of the post-central gyrus and the subjects' higher stress levels, which might be explained by the increased neuronal activity to induce neuroplastic changes in the brain, such as axonal sprouting, dendritic growth, or synaptic remodeling. These processes may alter the organization and coherence of white matter tracts, leading to decreased FA values in DTI.

Clinical studies have found a correlation between a decrease in the volume of the somatosensory cortex and the presence of depression and other mental health disorders.[28,29,30] Glial cells, including astrocytes and oligodendrocytes, play crucial roles in supporting and maintaining the function of neurons. Preclinical research indicating significant glial atrophy in mental illnesses suggests that alterations in glial cell function or structure may be involved in the pathophysiology of these disorders.[31] Additionally, post-mortem investigations have found lower neuronal cell size and glial cell counts in individuals with mental disorders, further implicating cellular changes in the brain's structure.[32, 33] Reduced FA values are often associated with disruptions in white matter integrity, which can occur due to various factors, including changes in axonal structure, myelination, and fiber organization. The observed decrease in FA value in the postcentral gyrus (part of the somatosensory cortex) could be partially explained by reductions in cortical volume and supporting neuron cells. This implies that alterations in the microstructure of the somatosensory cortex, including changes in neuronal and glial cells, may contribute to disruptions in white matter integrity within this region, leading to decreased FA values.

Our findings revealed a significant negative correlation between stress scores and FA values in the left postcentral gyrus, whereas no significant correlation was observed in the right postcentral gyrus. This contrasts with previous studies that identified the right postcentral gyrus as being associated with stress scores in larger samples. For example, Li et al. (2019) found that state anxiety was linked to alterations in the right somatic brain network, including the postcentral gyrus.[34] Similarly, Kropf et al. (2019) reported that the right somatosensory cortex plays a crucial role in emotional regulation.[35] These inconsistencies may be attributed to several factors such as differences in imaging techniques, data analysis methods, and the specific measures of stress used. For instance, our study used DTI to assess white matter integrity, while other studies might have employed different neuroimaging modalities or analytical approaches. Furthermore, lateralization of stress-related changes in the somatosensory cortex may vary across individuals. Factors such as genetic predispositions, environmental influences, and individual differences in stress perception and processing could lead to variability in which hemisphere shows stronger associations with stress.[36] The dominance of the left hemisphere in our predominantly right-handed sample could explain why we observed significant findings in the left postcentral gyrus.

Our study had certain limitations. The primary constraint was the limited population size, which impeded the ability to assess the variable degree of stress among healthy individuals. The findings from this study serve as preliminary evidence that can inform and justify the need for larger-scale studies. By demonstrating significant associations in a smaller sample, we provide a foundation for future research to build upon, potentially with larger and more diverse populations. Besides, this study only examined the somatosensory cortex. It is crucial to do additional research to examine other regions that are indirectly associated with stress. Furthermore, the study did not impose any age restrictions on the subjects, which means that the results may have encompassed brain deterioration associated with aging. In order to obtain precise prognostic forecasts for various age groups, it would be essential to have a bigger sample size. In addition, we did not assess the long-term impact of stress on the somatosensory cortex. Longitudinal studies would be necessary to investigate alterations in brain imaging and the relationship between stress and the somatosensory cortex. Lastly, the smaller subset of left-handed participants in our study did not provide sufficient data to examine potential differences based on handedness robustly. Future studies should include a more balanced representation of handedness to explore its impact more comprehensively.

CONCLUSION

In conclusion, we found that the stress eventually affected the integrity of the white matter in the postcentral gyrus. This may provide some insight into the mechanism of stress, as abnormal activity in the postcentral gyrus might affect decision-making and other activities. Individuals who experience stress exhibit emotional and cognitive processing biases that increase their susceptibility to bodily symptoms of stress, as compared to the normal population. Our research findings indicate that stress may lead to early damage in the microstructural somatosensory cortex, particularly in the postcentral gyrus, as observed using the DTI technique. Hence, the alterations in the microstructure of the brain's white matter prior to the onset of the ailment may play a vital role and could serve as a new and promising biomarker for the early identification and treatment of the disease in individuals who are not yet clinically diagnosed.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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