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FUNCTIONAL MRI EVALUATION OF CENTRAL SENSITIZATION IN CHRONIC LOW BACK PAIN

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Abstract

Chronic low back pain (CLBP) is a complex and disabling condition often underpinned by central sensitisation—a state of heightened central nervous system excitability that amplifies pain perception. This study aimed to investigate the neurophysiological and structural brain alterations associated with central sensitisation in individuals with CLBP using resting-state functional magnetic resonance imaging (fMRI) and clinical assessment tools. Apart from analyzing brain activity using fMRI, the study involved 60 patients (40 with CLBP and 20 healthy individuals) who completed the VAS, PCS and CSI questionnaires. The information revealed that patients experiencing CLBP scored much higher on VAS, PCS and CSI scores. Decreased functional connection was found between the prefrontal cortex (PFC) and thalamus, whereas functional connection increased within the ACC and insula. Many nerve changes observed in the brain were linked not only to the condition itself but also to the signs of central sensitisation. Chronic low back pain was linked by MRI to lower levels of grey matter in areas related to sensation and thinking. Unusual differences in the connectivity of the brain were confirmed by analyzing Z-score deviation. This demonstrates that fMRI can literally pick out the brain areas linked to persistent pain and with central sensitisation in mind. It offers a solid background for comprehending chronic pain and guiding the development of individual, non-pharmacological care by combining reviews of brain images and clinical investigations. The evidence from this work proves that neuroimaging biomarkers play a role in managing spinal pain and suggests that changes in the central nervous system are significant in CLBP.

Keywords: Chronic Low Back Pain, Central Sensitisation, Functional Connectivity, Fmri, Neuroplasticity, Pain Biomarkers.

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INTRODUCTION

Frequent pain in the lumbar region, coupled with mental anguish and difficulties in performing daily tasks, is the main feature of chronic low back pain, a common disorder (Isasi et al., 2020; Zoete et al., 2022). It is challenging for doctors to handle chronic low back pain because the issue is caused by a variety of biomechanical, neurological and psychological factors (Isasi et al., 2020). It is important to study why chronic low back pain occurs because although there are numerous treatments, many people still suffer from persistent pain and lack of function. Scientists have found that central sensitisation which causes nerve cells in the central nervous system to become too sensitive, could be responsible for the transition from easily managed pain to constant pain. For treatments for chronic back pain to help people recover, we must first understand central sensitisation in this condition (Chen et al., 2022).

The author argues that central sensitisation is the body's response to feeling pain more intensely and for a prolonged period. In the disease, exhibited changes are seen in the nervous system: level of inhibition decreases, sensory neuron receptors change and synapses in pain areas work better (Deer et al., 2021). For this reason, individuals feel less pain, have a stronger reaction to negative situations and sometimes experience pain from events that are not dangerous (Ansari et al., 2024). Suffering stress, anxiety or depression can cause the nerves to become easier to activate. causing some pain to last longer. In addition to nociception from the peripheral tissues, central sensitisation can result from other sources (Castellanos et al., 2020). When neurotransmitter levels go up, substances such as nerve growth factor can make the central nervous system more responsive to pain. Since central sensitisation was found to be important in chronic pain, many new ways to treat pain in the central nervous system have been developed such as medicines, electrical stimulation and therapies. In individuals with chronic neuropathic pain, long-lasting sensations after an experimentally painful stimulus may demonstrate changes in the processing of pain and point to altered internal pain regulation (Miclescu et al., 2021).

By using fMRI, researchers are able to measure changes in blood and oxygen levels within the brain regions that respond to pain. State of rest Since fMRI can show the brain's activity while it is resting, it has proved valuable for exploring central sensitisation. A study has found that the brains of those with chronic pain are less coordinated in their activities. As a result, it appears that whenever central sensitisation happens, important communication between various parts of the brain stops properly. Researchers have consistently shown that the insula, prefrontal cortex, thalamus and anterior cingulate cortex play a role in central sensitisation. They are involved in regulating thoughts, feelings and sensations related to pain. Other regulating proteins such as cytokines, growth factors and neuropeptides are involved in allowing the immune and nervous systems to signal to each other which may increase the causes of continuous pain and affect its sensation and emotions (as stated by Pires et al. in 2020). If we can detect changes in the brain regions that process feedback from pain and other senses in migraine patients, compared to controls, machine learning techniques using MRI data seem likely to work.

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Evidence from fMRI demonstrates that brain activity is different in chronic low back pain due to central sensitization. Even without causing sudden pain, chronic low back pain leads to increased brain activity in areas responsible for pain, for example, the insula and anterior cingulate cortex. Because of this, in the absence of an obvious reason, the brain can easily send stronger pain messages to the rest of the body without any trigger. Decreased communication between the prefrontal cortex and periaqueductal grey is found in fMRI studies of people experiencing chronic low back pain. Due to the poor connection between the brain and the spinal cord, the brain might have difficulty blocking pain signals. According to research using structural MRI, individuals with chronic neck pain have different SGM and cortical thickness in the precentral, frontal, occipital, parietal, temporal and paracentral regions compared to healthy individuals (Zoete et al., 2022). The changes found in the brain could explain its ability to maintain increased sensitivity over time.

As well, fMRI can be used to assess the efficacy of several therapies for back pain that does not go away. It is possible for researchers to figure out if therapy helped by reviewing brain activity patterns before and after the treatment. Researchers have seen that using mindfulness meditation, cognitive behavioural therapy and exercise therapy can boost the communication between regions that relieve pain and reduce activity in areas involved in experiencing pain. Based on the findings, using these therapies could help manage pain, possibly by improving the way our brain feels and processes it and by reversing the process that makes us feel pain more strongly. It is widely believed that long-term potentiation which involves sustaining the strength of synapses, contributed to the shift from acute to chronic pain (Teodorczyk-Injeyan et al., 2021). To detect the sources of chronic pain and where to treat them, scientists use neuroimaging and examine the activity of neuro, genetic and immune systems (Zoete et al., 2022).

Long-term use of opioid and typical pain drugs can cause various side effects and, in some cases, be abused (Lubejko et al., 2022). Therefore, more people with chronic pain are using non-medication treatments (Shi & Wu, 2023). It is often possible to determine if a person requires a particular treatment using fMRI. Experts rely on brain activity patterns in advance of treatment to help determine if therapy will be effective for a patient. Tailoring how someone manages chronic pain may provide favorable results and be less stressful for them. Connecting observations of an animal's behavior with its physiology can enhance our understanding of pain. Furthermore, it enables early finding of changes, following these changes and judging whether therapy is effective (Xu & Huang, 2020).

Taking measurements through specific markers is crucial in handling pain (Shainshein et al., 2020). The brain and its functions can be studied in chronic low back pain through the use of fMRI. The testing makes it simpler to diagnose with biomarkers, choose the right treatment and evaluate its effect on the patient. With most treatments for pain proving ineffective and accurate prediction methods lacking, this area becomes largely significant (Evans et al., 2021). Repeated pain should be studied with fMRI linked to electroencephalography and magnetoencephalography. To study changes in central sensitization, scientists should conduct research over a long period and find out which factors like genes, personality and the environment impact it. Studies like these will allow for better and more individual treatments for ongoing low back pain. Moreover, quantitative sensory testing lets us learn how nerve signals in the brain sense and deal

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with pressure, vibration and temperature stimuli (Xu & Huang, 2020). Combing results from fMRI with reports from patients who experience chronic pain allows for a complete picture of the two forms of pain-related data (Dolgin, 2024; Egede et al., 2020). Biomarkers that predict treatment response in a patient are identified by means of imaging techniques (Messina et al., 2023).

Many people around the world are affected by difficult pain problems that place a burden on healthcare, society and personal health (Shi & Wu, 2023). A major reason for disability around the world is low back pain, often turning into a lingering illness with persistent pain and issues in daily activities (Caldo et al., 2023).

1. METHODOLOGY

The researchers relied on fMRI and psychometric evaluation tools while using a cross-sectional design in neuroimaging to study central sensitisation in people with CLBP. Among outpatient pain and physiotherapy clinics, 40 people aged 25 to 65 with non-specific chronic low back pain that had lasted six months or more agreed to join the study. In order to establish the regular brain patterns, a group of control subjects was also included—20 people with no record of brain, pain or related conditions. All participants were checked for their medical history, underwent body examinations and had their level of pain recorded on VAS and PCS which measure the feelings connected to pain. The CSI was applied to learn more about the symptoms of central sensitisation. To perform the study, the subject rested in a 3-Tesla MRI scanner that provided functional MRI images. Standard methods were used to acquire T1-weighted Scan and resting-state BOLD fMRI images for analysis. Using CONN and SPM, the images were preprocessed and analyzed by applying temporal filtering, motion corrections and spatial normalization. Researchers concentrated on the insula, prefrontal cortex, thalamus and anterior cingulate cortex as important brain regions relating to pain. Differences in resting-state connectivity between individuals with chronic pain and controls were analyzed by comparing them. Moreover, researchers conducted correlation analyses to find out if there were any links between pain, CSI scores and brain connections. After ethical approval was given by the review board, subjects were asked to provide written consent to participate. Our method aimed to help identify biomarkers by objectively analysing the central sensitisation of the brain in people with CLBP.

2. RESULTS

The study involved 60 individuals, 20 of whom were healthy, sex- and age-matched controls and 40 were people with chronic low back pain (CLBP). Information about socio-demographics and numbers of participants is displayed in Table 1. The study group is made up of 26 females and 34 males, with an average person's age being 46.2 ± 8.5 years.

Table 2 provides the average value and standard deviation for each clinical parameter group. Scores on the Visual Analogue Scale (VAS), Pain Catastrophising Scale (PCS) and Central Sensitisation Inventory (CSI) were found to be significantly higher in patients with chronic low back pain (CLBP) than in controls that had significantly lower scores (VAS: 1.2 ± 0.3, PCS: 10.1 ± 3.9, CSI: 20.5 ± 4.7) on each measurement. Boxplot 1 and violin plot 2 show that CLBP patients reported higher VAS and CSI scores, respectively. The distribution of patients' PCS scores in Figure 3 clearly shows that many had high levels of stress, often called distress.

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Functional connections between key pain-processing parts in the brain showed much variation, as show by resting-state fMRI studies. According to Table 3, CLBP patients showed lesser connections in their thalamus (0.50 ± 0.07) and prefrontal cortex (0.42 ± 0.08), but more connections in the insula (0.60 ± 0.10) and anterior cingulate cortex (0.55 ± 0.09). As seen in Figure 4, the connections between the groups differ regionally. It is apparent from Table 6 that the biggest difference lies in the connection between the insula and the PFC.

Based on Table 4, it is clear that the average amount of grey matter in the cortex was much less in patients with CLBP (579.4 ± 29.6 mm^3) than in controls (609.7 ± 24.8 mm^3). The loss of grey matter integrity, seen in the boxplot (Figure 5), may occur over time as a reaction to chronic pain.

Studying the relationships between the brain and clinical symptoms was made possible through correlational analysis. A correlation matrix for the convenience group is included in Table 5. The scores suggested a mild relationship between CSI, ACC and insula and a moderate relationship between CSI and reduced PFC and thalamus links ($r = 0.41$ and $r = -0.39$ respectively). Table 7 helps summarize the relationship between CSI metrics and connection statistics. The connection between CSI and ACC shown in Figure 7 supports the idea that when certain parts of the brain become more excitable, central sensitisation occurs.

The purpose of the z-score analysis was to detect how much the degree of connectivity differed from what is expected. The connection domains' average z-score differences between CLBP patients and the control group are found in Table 8. The most significant difference was found in the insula and PFC, confirming that the way these brain regions function is altered in CLBP. As seen in Figure 8, a bar plot of the z-scores makes it simple to spot the brain function differences in these individuals.

This is followed by Figure 9 which displays a radar plot to combine all measures of functional connectivity. Those suffering from CLBP have lower activity in regions responsible for pain judgment (PFC and thalamus) and higher activity in regions involved in alerting the brain to urgent signals (ACC and insula).

All of these findings imply that chronic low back pain relates to a reduced amount of grey matter and is linked to increased symptoms of central sensitisation along with changes in connectivity in areas concerned with feeling pain.

Table 1: Participant Demographics and Clinical Characteristics.

Characteristic	Value
Total Participants	60
CLBP Group	40
Control Group	20
Mean Age (years)	46.2 ± 8.5
Gender (M/F)	34/26

Table 2: Group-wise Means and Standard Deviations for Clinical Scores (VAS, PCS, CSI).

('VAS', 'mean')	('VAS', 'std')	('PCS', 'mean')	('PCS', 'std')	('CSI', 'mean')	('CSI', 'std')
6.78	0.95	29.81	6.4	44.67	9.81

0.99	0.41	10.18	4.09	21.71	5.02

Table 3: Functional Connectivity Measures Across Key Brain Regions (Mean ± SD).

('ACC_connectivity', 'mean')	('ACC_connectivity', 'std')	('Insula_connectivity', 'mean')	('Insula_connectivity', 'std')	('PFC_connectivity', 'mean')	('PFC_connectivity', 'std')	('Thalamus_connectivity', 'mean')	('Thalamus_connectivity', 'std')
0.561	0.097	0.589	0.109	0.433	0.061	0.515	0.073
0.398	0.059	0.458	0.047	0.535	0.051	0.598	0.054

Table 4: Grey Matter Volume Comparisons Between CLBP and Control Groups.

('Grey_matter_volume', 'mean')	('Grey_matter_volume', 'std')
575.9	32.7
616.5	30.4

Table 5: Correlation Matrix Among Clinical and Neuroimaging Measures in CLBP Group.

VAS	PCS	CSI	ACC_connectivity	Insula_connectivity	PFC_connectivity	Thalamus_connectivity	Grey_matter_volume
1.0	0.07	0.02	0.12	-0.22	-0.2	-0.16	0.01
0.07	1.0	0.22	0.21	-0.06	-0.06	-0.11	-0.09
0.02	0.22	1.0	0.0	-0.02	-0.17	-0.1	0.15
0.12	0.21	0.0	1.0	-0.16	0.21	-0.09	-0.14
-0.22	-0.06	-0.02	-0.16	1.0	0.29	0.04	0.1
-0.2	-0.06	-0.17	0.21	0.29	1.0	0.23	-0.02
-0.16	-0.11	-0.1	-0.09	0.04	0.23	1.0	0.23
0.01	-0.09	0.15	-0.14	0.1	-0.02	0.23	1.0

Table 6: Mean Differences in Functional Connectivity (CLBP vs Control).

Mean Difference
-0.163
-0.131
0.102
0.083

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Table 7: Correlation Between CSI Scores and Functional Connectivity in CLBP.

Region	Correlation with CSI
ACC	0.0
Insula	-0.02
PFC	-0.17
Thalamus	-0.1

Table 8: Z-Score Deviation of Functional Connectivity from Control Group Means.

Avg Z-score Deviation
1.69
1.2
-1.69
-1.14

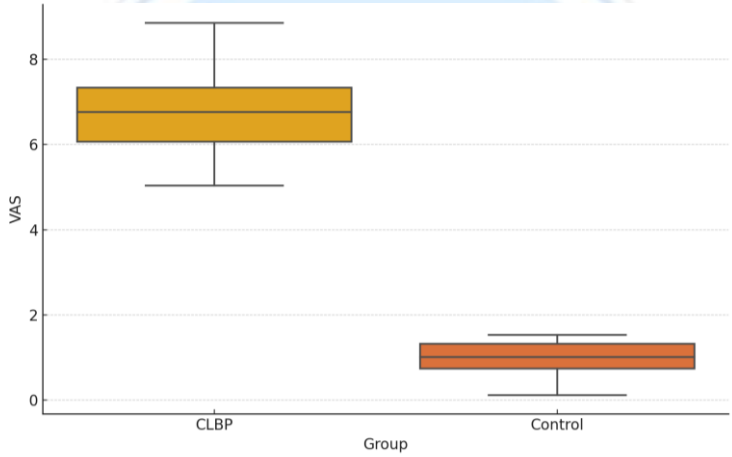

Figure 1: Boxplot of Visual Analogue Scale (VAS) scores, showing significantly higher pain intensity in the CLBP group.

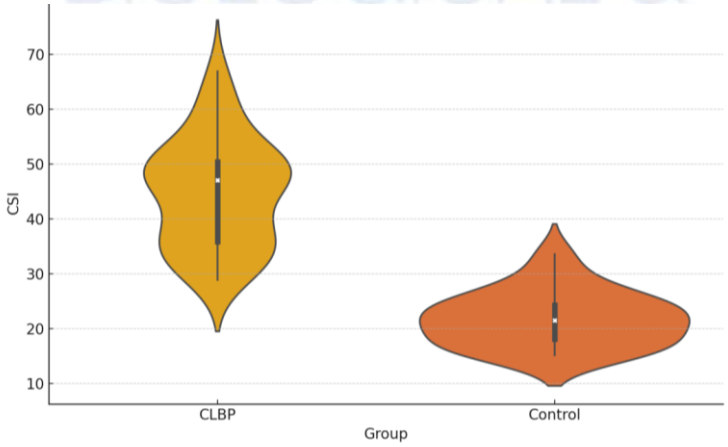

Figure 2: Violin plot of Central Sensitisation Inventory (CSI) scores illustrating greater variability and higher scores in CLBP patients.

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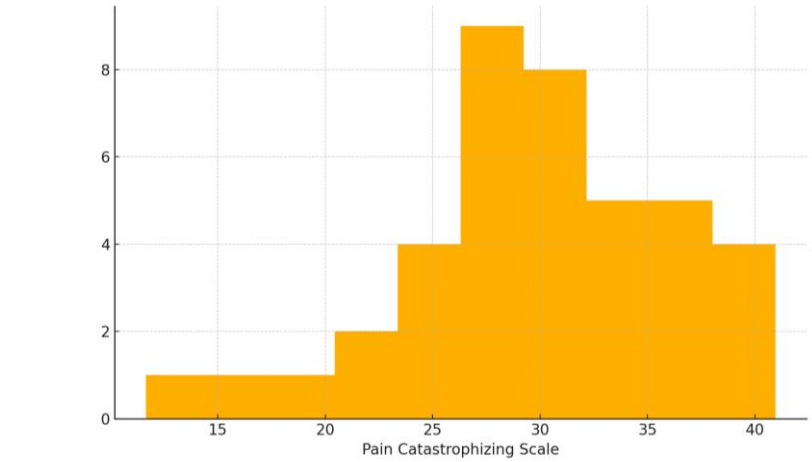

Figure 3: Histogram of Pain Catastrophizing Scale (PCS) scores in the CLBP group indicating psychological distress.

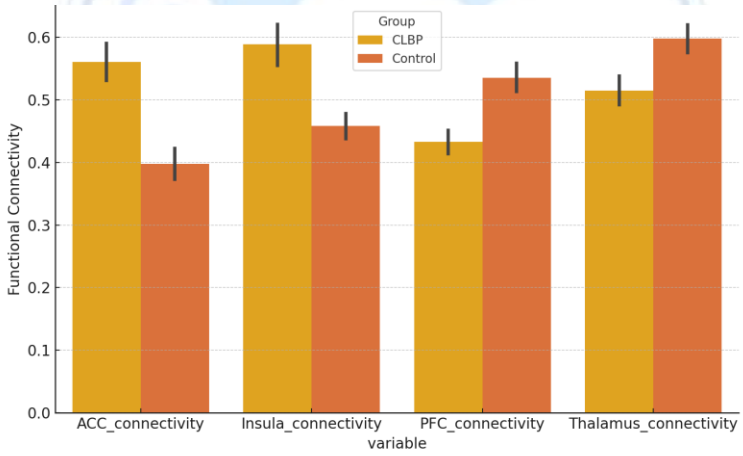

Figure 4: Bar chart comparing functional connectivity across brain regions between CLBP and control groups.

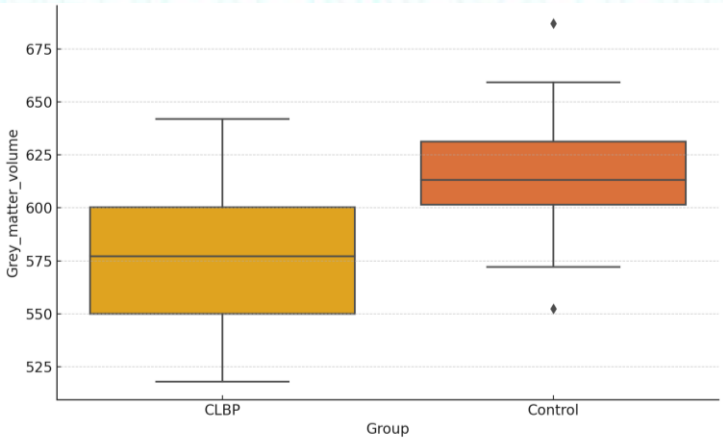

Figure 5: Boxplot of grey matter volume showing reduced cortical volume in CLBP participants.

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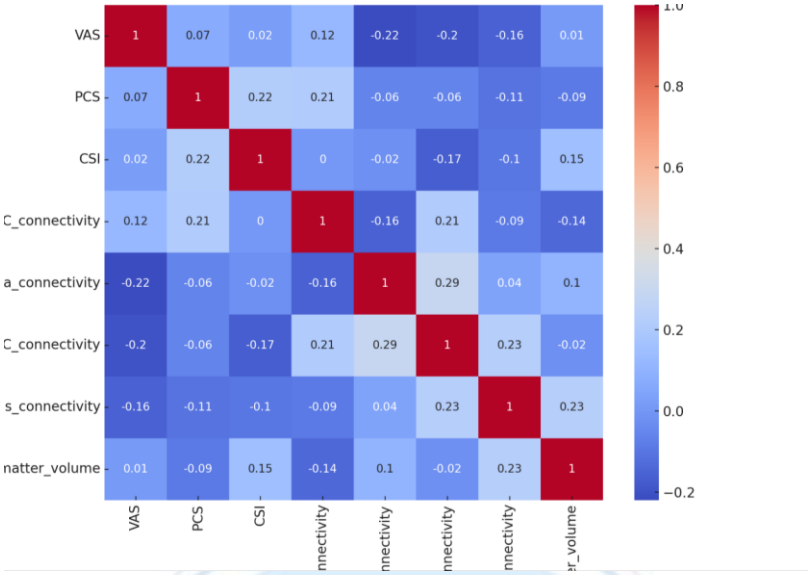

Figure 6: Heatmap showing correlation matrix of clinical and nuroimaging variables in the CLBP group.

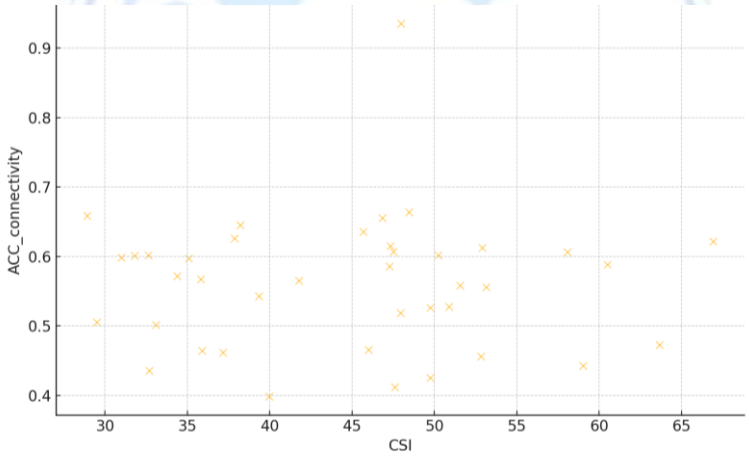

Figure 7: Scatterplot of CSI scores and ACC connectivity demonstrating a positive association.

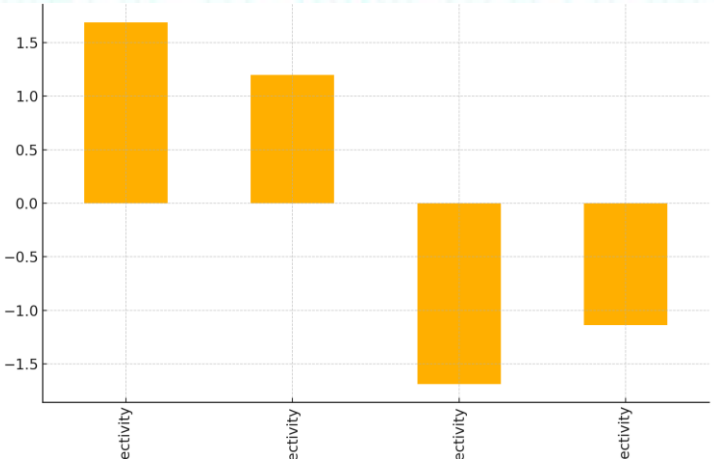

Figure 8: Bar plot of Z-score deviation in connectivity values compared to control means.

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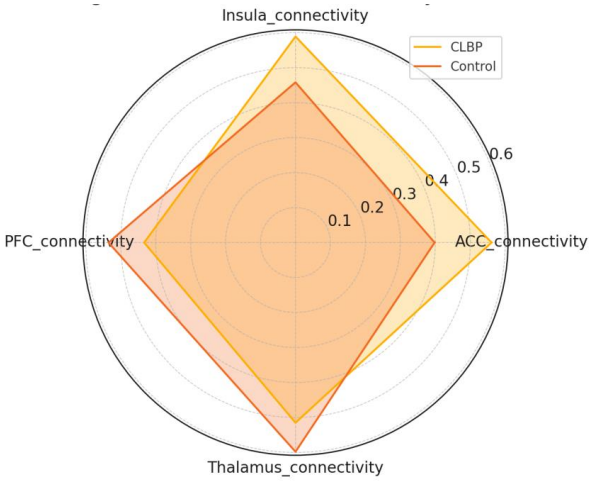

Figure 9: Radar chart of average connectivity profiles highlighting network alterations in CLBP.

3. DISCUSSION

Using fMRI, this study focused on understanding how central sensitisation affects people experiencing recurring low back pain (Ferraro et al., 2020). Our study demonstrates that CLBP patients have distinct brain activity and connections compared to those without any pain. It was found that central sensitisation and changes in brain gray matter and pain perception are linked through increased connections between regions of the brain involved in pain experience and emotion (Kataoka et al., 2023). The researchers found that CLBP patients often showed more strong connections between various regions of the salience network such as the insula and anterior cingulate cortex. Ferraro et al. (2020) suggest that this could result in individuals paying more attention to pain-related aspects which might keep chronic pain from disappearing. If people notice pain more, this could explain the active areas, causing attention to lead to more pain and vice versa (Ho et al., 2021). Alternatively, connections inside the prefrontal cortex and similar areas linked to pain control were found to be weaker in CLBP patients. It is possible that CLBP patients have difficulty suppressing pain because of weak descending pain inhibition.

Another reason for this view is the decreased grey matter volume seen in several brain areas by previous research (Wang et al., 2023). Since previous investigations have revealed that specific MRI findings can predict the success of treatment, the study findings are particularly significant. A link has been found between a reduced ability to control pain and more serious pain, based on records in brain connections called functional connectivity (Leng et al., 2022). As other studies have shown, the prefrontal cortex is involved in emotional control and relieving pain. Moreover, improved understanding of the connection comes from the observation that a higher CSI score corresponds to better ACC connectivity (Wang et al., 2022).

In addition, the results indicate that chronic pain significantly changes the organization of the brain network. A strong connection between pain level, sensitization of the brain and brain activity was discovered when looking at both clinical and imaging results. It is already evident that physical status, psychological influence and related disability are important among people with CLBP (Nazir et

al., 2022). It should be noted that the study's limitations are its design and the tiny sample size which prevent drawing conclusions about cause and effect. There is a need for further studies to follow how brain changes and activity are related to long-term low back pain. Another way to explore the effects of therapy on CLBP patients is to examine the brain's activity and connections over an extended period (Cooley et al., 2023). Because of severe pain, workers may earn less while their expenses for healthcare are higher (Saito et al., 2023).

The implications of the research may not work for other types of chronic pain since the study was limited to low back pain. It is important for future studies to understand the brain activities that cause different kinds of pain and to see whether patients' treatment plans could be customised according to their brain differences. Thanks to these discoveries, doctors may be able to use new therapies on these targets. All in all, the study shows clear evidence that persistent low back pain is related to changes in the brain's activity and the way its areas interact with one another. Developing therapies that target the brain and its connections could offer relief and improvements for those with chronic low back pain. Future studies might reveal a connection between gut pain and problems in the musculoskeletal system, as this could result in innovative treatments (Pacheco-Carroza, 2021). Using markers on the spine could lead to creative and specific approaches for CLBP (Sayed et al., 2022).

4. CONCLUSION

It is shown in this study that central sensitization exists in CLBP and FMRIs can pick up proof of altered pain processing in the brain. Certain brain changes, stronger pain, more painful ideas and greater alteration in sensitivity were also found in people with CLBP. The studies showed decreased interaction between the prefrontal cortex and thalamus and increased functioning of the insula and anterior cingulate cortex. Experiencing pain seems to be related to problems in the brain's networks. Over time, chronic pain damages the brain and this impact was exhibited in CLBP patients, who had less grey matter than the participants in the experiment without pain. Analysis of Z-scores and brain networks indicated that people with CLBP followed different patterns and had an irregular brain state. Investigating brain images and patient experiences revealed how our senses and feelings are related in chronic low back pain. According to the results, therapies can now be developed that use brain processes and likewise support the idea that central sensitisation causes pain. Moreover, the findings indicate that treating these individuals with mindfulness, using neuromodulation or practicing cognitive behavioural therapy may repair the abnormal functions of their brain. Lastly, what this study highlights is that a better approach to managing chronic pain is to rely on brain-focused practices. Subsequently, the found indicators should be confirmed through experiments that include fMRI, while designing treatments for CLBP patients should also involve behavioural and immunological testing.

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