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Vol 2
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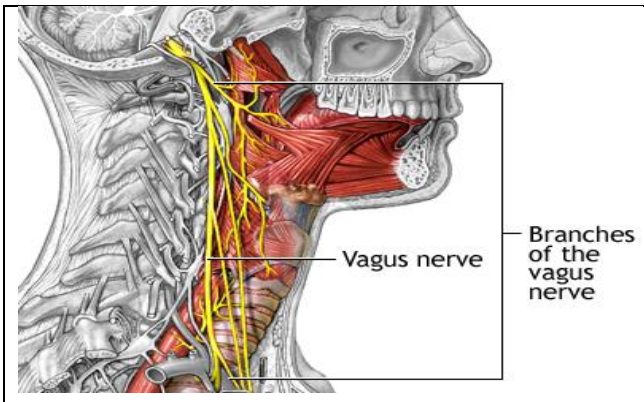
1. Assessment of the alteration of cross-sectional area (CSA) and the echogenicity of the vagus nerve among major depressive disorder patients

Introduction

Sonographic research has witnessed an increase in attention since the vagus nerves (VNs) are particularly significant in psychiatric and neurological illnesses. The parasympathetic autonomic nervous system (ANS) is fundamentally made up of the VNs. Autonomic dysfunction, which includes symptoms like palpitations, impaired sleep, hunger, and gastrointestinal functioning in neuropsychiatric illnesses like major depressive disorder (MDD), caused by a functional imbalance between diminished VN activity and the sympathetic nervous system.[1] A disease with significant effects on the individual, the medical community, and the economy is major depressive disorder (MDD). Drug therapy and other forms of therapy (such as electroconvulsive therapy) may cause treatment resistance and have side effects that include memory loss, slowed reaction time, and persistent symptoms.[2] A reliable method for examining VNs in vivo is high-resolution ultrasonography (HRUS). Previous research suggested a relationship between sonomorphological VN changes and autonomic function in healthy probands. Different neurological diseases were described as causing morphological changes to the cervical VNs.[1] So, this study analysed the VN in patients with MDD using high-resolution ultrasound (HRUS) and hypothesised that the CSA and echogenicity of the VNs were altered in comparison to healthy controls.



VAGUS NERVE

Methods

This cohort study included 50 MDD patients and 50 healthy participants. All individuals were subjected to a thorough neurological examination in order to rule out people with clinically obvious but previously undiagnosed polyneuropathy or Parkinsonism. All of the MDD group's participants were receiving psychotherapy and antidepressants at the time they participated in the study. All participants completed the Patient Health Questionnaire-15 (PHQ-15) with a focus on somatic

symptoms and the Beck Depression Inventory (BDI) to assess the severity of depression at the time of participation. HRUS was used to evaluate the echogenicity (mean on the grey scale) and the CSA of the cervical VNs at the level of the thyroid gland and both median nerves.

Results

The MDD group had significantly higher BDI and PHQ-15 scores. The present depressive episode lasted a mean of 25 weeks in the MDD group at the time of the test. The left VN-CSA was substantially greater in the MDD group during HRUS exams compared to the control group ($p = 0.045$). Both of the median nerves' (MN) CSAs and those of the right VN were comparable between groups (Table 1). Recurrent depressive illnesses were the main cause of the left VN-CSA enlargement, according to analysis of the MDD subgroup. In comparison to the control group and the MDD group, the left and right MN-CSA were similar. The echogenicity of the VN and MN did not differ between groups.

Variable		MDD group	Control group	*p*-value
VN-CSA left (mm^2)	Mean, SD	1.7 ± 0.4	1.5 ± 0.4	0.045*
VN-CSA right (mm^2)	Mean, SD	1.8 ± 0.5	1.7 ± 0.5	0.269*
MN-CSA left (mm^2)	Mean, SD	6.9 ± 1.3	6.5 ± 1.2	0.079*
MN-CSA right (mm^2)	Mean, SD	6.8 ± 1.3	6.5 ± 1.2	0.063*
VN GSM-Index left	Mean, SD	4.5 ± 2.4	5.3 ± 4.6	0.482#
VN GSM-Index right	Mean, SD	5.3 ± 4.7	6.1 ± 5.9	0.328#

*Student's *t*-test; #Mann–Whitney *U*-test; HRUS, high-resolution ultrasound; VN, vagus nerve; CSA, cross-sectional area; GSM, gray scale mean; SD, standard deviation.

Table 1. Results from high-resolution ultrasound scans of MDD patients and healthy controls.

Discussion

In this investigation, HRUS allowed for the reliable assessment of tiny nerves such as the VN. In neurodegenerative diseases, including Parkinson's disease and amyotrophic lateral sclerosis, the VN-CSA was consistently found to be reduced, whereas inflammatory diseases were noted to have an expanded VN-CSA. The left VN-CSA was noticeably greater in the MDD group during HRUS exams compared to the control group.[1] According to Oura K. et al., the CSA of the VN was assessed bilaterally by ultrasonography at the thyroid gland level. In the study group, ultrasound imaging

revealed that the median CSA of the VN was considerably lower on the left side than on the right side.[3]

Conclusion

The current study concludes that the left VN-CSA enlargement in patients with MDD, and particularly in individuals with recurrent depressive illnesses, may prove to be a potential imaging biomarker.

In order to connect the gut and the brain, the vagus nerves and their afferent and efferent fibres are essential.

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2. Correlation between childhood trauma with cognitive deficit and anatomical brain changes in bipolar disorder individuals with remission

Introduction

Childhood traumas (CT) have been proposed as a potential risk factor for cognitive impairment in bipolar disorder (BD) since they have a significant impact on the cognitive function of adult BD patients and appear to have occurred less frequent among cognitively normal BD patients. Independent of psychiatric diagnosis, CT was also associated with decreased grey matter (GM) in the prefrontal cortex (PFC), with more pronounced volume reductions in patients who reported having had more CT.[1] Bipolar disorder (BD) patients experience cognitive impairments in partial or full remission in 50–70% of cases. These impairments might affect attention, processing speed, verbal learning and memory, executive skills, and many other cognitive areas. Patients with cognitive impairments have experienced decreased psychosocial functioning, which includes concerns with retaining employment, interacting with others, being less independent, and having financial troubles. However, recent research suggests that environmental stressors, including childhood trauma (CT), may also be significant. [2] This extensive MRI study aimed to investigate the neuronal association of cognitive impairment in BD, specifically their relationship to CT.

Methods

In this cross-sectional study, magnetic resonance imaging (MRI) data from 235 participants were used. To assess the structural neuronal correlation of cognitive impairment in BD patients, a cognitive evaluation and an MRI were performed. Prefrontal cortex measurements, hippocampus shape/volume, and total cerebral white (WM) and grey matter (GM) were compared between the cognitively intact and cognitively impaired BD and MDD patient groups were compared between them and healthy controls (HC).

Results

Greater childhood trauma and worse overall cognitive function were associated with cognitively impaired BD patients having a smaller total cerebral WM volume than HC. Additionally, compared

to HC, cognitively normal BD patients similarly displayed reduced adjusted GM volume and thickness in the frontopolar cortex but higher adjusted GM volume in the temporal cortex. Compared to patients with MDD, BD patients with cognitive impairment had a lower cingulate volume. Each group shared similar hippocampal measurements. There was an overall sample-wide positive connection between the total volume of cerebral WM and overall cognitive function (Figure 1). Significant connections with attention, psychomotor speed, working memory, and executive skills were found in subsequent correlation analyses of cognitive subdomain performance.

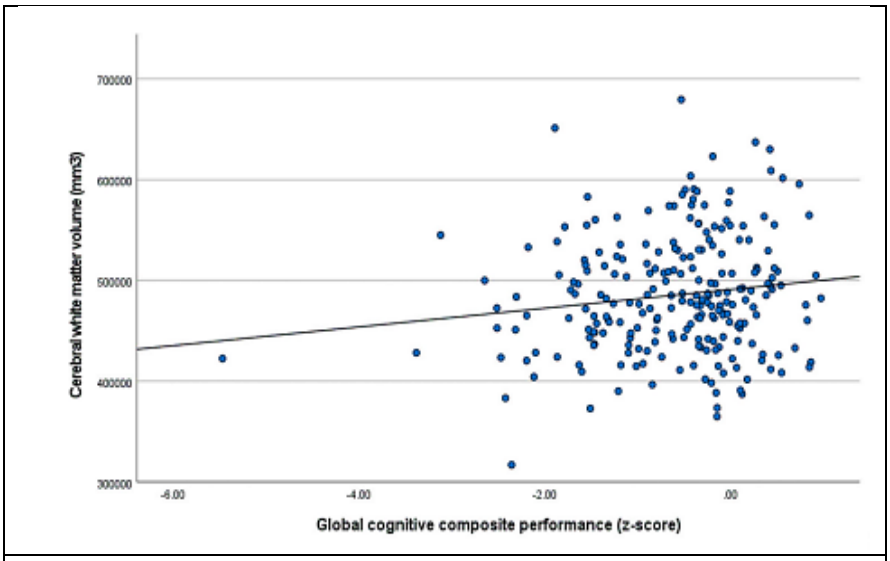

Figure 1. Scatterplot showing the relationship between the total sample's performance on the global cognition test and cerebral white matter volume

Discussion

This study showed that the structural brain correlates of cognitive impairment was caused by a primary disease in BD and the relationship with CT. The overall volume of cerebral WM was found to be less in the cognitively impaired bipolar disorder (CI-BD) patients than in the HC.[1] According to Macoveanu J et al., cognitively impaired individuals have thicker left dorsomedial prefrontal tissue than cognitively normal patients and healthy controls. Between patient subgroups and healthy controls, hippocampal grey matter volume and shape were similar. Cognitively challenged patients had less cerebral white matter volume overall than the other groups.[3]

Conclusion

The current study concludes that structural neuronal correlates of cognitive impairment in BD may include regional frontopolar and temporal GM abnormalities, lower total cerebral WM, and lower total cerebral WM, the severity of which may be correlated with the degree of childhood trauma.

Patients with cognitively impaired bipolar disorder (CI-BD) also showed grey matter anomalies in the frontopolar prefrontal cortex (PFC) and temporal cortex, which may indicate disturbance of normal neurodevelopment or compensatory mechanisms to maintain mood stability.

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Vol 2
ISSUE 11
Petril Times
NEWSLETTER
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3. Identification of the characteristics of the theory of mind impairment among schizophrenia patients

Introduction

Schizophrenia (SCZ) is a mental illness that affects up to 1% of the world's population and can lead to serious disability. Patients with SCZ frequently exhibit both positive and negative symptoms, including motivational impairments, decreased affective function, hallucinations, delusions, and cognitive or speech difficulties. SCZ also affects social cognition, which is one of the disorder's key characteristics. The Theory of Mind (ToM), a fundamental aspect of social cognition, is the capacity of an individual to understand and communicate the causes of their own and others' mental states, including desires, beliefs, and behavioural intentions.[1] The strongest correlation between the theory of mind's (ToM) abilities and daily functioning in schizophrenia is its capacity to infer others' mental states. ToM functions as a mediator between neurocognition and functioning, and deficiencies in this area are linked to problems with productive activities and social interaction.[2] Numerous studies have established that patients with SCZ have ToM impairment; however, not much is known about this impairment's features, including its various orders (first- and second-order) and components. Moreover, no research has examined the independent relationships between this impairment and clinical symptoms.[1] This study aimed to characterise the ToM impairment symptoms in SCZ patients.

Methods

This study included 30 SCZ patients and 30 healthy controls whose age, gender, and educational level were similar. The Positive and Negative Symptom Scale (PANSS) was used to assess the clinical symptoms of SCZ patients, and the Trail Making Test, Symbol Coding Test, and Digit Span Test were used to assess the subjects' neurocognitive abilities. The Yoni task was used to assess the subjects' level of ToM impairment at several stages (first- and second-order), as well as for individual components. The prospective ToM performance types were identified and analysed using latent profile analysis and network analysis, and independent relationships between ToM impairment and clinical symptoms were evaluated.

Vol 2
ISSUE 11
Petril Times
NEWSLETTER
INFORMATION BULLETIN ISSUED AS A SERVICE TO THE MEDICAL PROFESSION

Results

Based on performance in the healthy control group and the patient group in the Trail Making Test, Symbol Coding Test, and Digit Span Test, neurocognitive abilities were considerably worse in the patient group. Significant first-order and second-order impairments were present in SCZ patients ($P < 0.05$), and complex emotional states predominated in the second-order affective ToM component ($P = 0.003$) (Table 1). ToM impairments in patients with SCZ could be divided into groups with complete, second-order, and comprehensive deficiencies, according to the results of the latent profile analysis, but it was not possible to divide the patients based on differences in the cognitive and affective ToM components. The results of the network analysis showed that the cognitive ToM component was correlated with positive symptoms, while the affective ToM component was correlated with negative symptoms.

	SCZ (n=30), Mean (SD)	HC(n=30), Mean (SD)	F(Controlling physical conditions)	P	η^2
First-order cognition ToM	0.67(0.332)	0.89(0.176)	8.469	0.005**	0.129
First-order effective ToM	0.65(0.286)	0.87(0.140)	12.375	0.001**	0.178
s-order cognition ToM	0.47(0.251)	0.67(0.227)	5.569	0.022*	0.090
s-order effective bToM	0.53(0.234)	0.63(0.232)	3.590	0.063	0.089
s-order effective aToM	0.53(0.243)	0.73(0.188)	9.581	0.003**	0.144

* means p<0.05, ** means p<0.01

Table 1. Comparison of the ToM accuracy between the patient group and the control group under various Yoni task conditions

Discussion

In this study, the patient group's performance in terms of neurocognitive abilities was significantly lower than that of the healthy control group. Positive symptoms were correlated with the cognitive ToM component, whereas negative symptoms were correlated with the affective ToM component.[1] Hajdk et al. revealed that the connections between neurocognition and social functioning were discovered to be mediated by the theory of mind. Interventions to enhance social functioning could possibly focus on theory of mind.[3] According to Yilmaz G et al., individuals with schizophrenia showed a larger and more significant decline in theory of mind and neurocognitive functions than the patients with social anxiety disorder and healthy controls.[4]

Conclusion

The current study concludes that patients with SCZ demonstrated various order levels, ToM deficits, and defect types. Additionally, there was a correlation between ToM and clinical symptoms in SCZ, with the cognitive and affective ToM components being connected to positive and negative symptoms, respectively.

Theory of mind therapies and training should be increased in clinical settings to promote the rehabilitation of individuals with schizophrenia (SCZ).

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4. Anxiety and depression as earlier symptoms in patent foramen ovale and acute hypoxia- A case report

Introduction

Anxiety disorders are the most prevalent type of mental illness in China. The WHO ranked anxiety disorders as the ninth-leading health-related cause of disability due to their high prevalence, comorbidity, and chronicity. The probability of anxiety disorders is significantly influenced by environmental and genetic variables. Numerous investigations using brain imaging have also revealed structural changes in the medial temporal, prefrontal cortex, and cingulate regions in anxiety disorders. The pulmonary circulation typically cannot pass through thrombi, air, fat, and other emboli

Vol 2
ISSUE 11
Petril Times
NEWSLETTER
INFORMATION BULLETIN ISSUED AS A SERVICE TO THE MEDICAL PROFESSION

from the venous system. Unless aberrant cardiac channels (such as a patent foramen ovale) exist, it will not enter the systemic circulation to cause embolism.[1] A probe-patent foramen is discovered at autopsy in 15–35% of the general population, making a patent foramen ovale (PFO) a frequent condition. The PFO permits blood to flow directly from the right to the left atrium, bypassing the pulmonary circulation and preventing the septum primum and septum secundum from ever forming a complete partition in utero.[2] In the present case, a patient with significant depression and anxiousness experienced abrupt systemic hypoxemia brought on by right-to-left shunting through the PFO.

Case Presentation

A 52-year-old female was hospitalised after experiencing anxiety, depression, and a worsening of dizzy symptoms for 4 days. The symptoms started five months after she experienced considerable work stress. A number of symptoms were mentioned, including agitation, restlessness, nervousness, worry, apprehension, being easily alarmed, melancholy, loss of energy, diminished interest, sleeplessness, tension headache, shortness of breath, dizziness, nausea, and poor appetite. As a result, depression and anxiety were identified. After receiving venlafaxine 225mg once daily, the patient feels better. However, the patient experienced dizziness, nausea, vomiting, sweating, uneasiness, panic, increased anxiety, and gradual shortness of breath after the medicine was abruptly stopped four days earlier. The patient had no medical history of mental illness, high blood pressure, diabetes, or coronary artery disease. The patient had cyanosis, however, and was discovered to be hypoxic with a 94.48% oxygen saturation in room air. The oxygen tension in the arterial blood was 65.64 mmHg. Prolactin concentration was 42.86 ng/mL, and D-dimer quantitation was 0.6 mg/L (0-0.55). Mild mitral, tricuspid, and aortic regurgitation on echocardiography. A positive echocardiogram with agitated saline contrast was obtained (RLS grade 1).

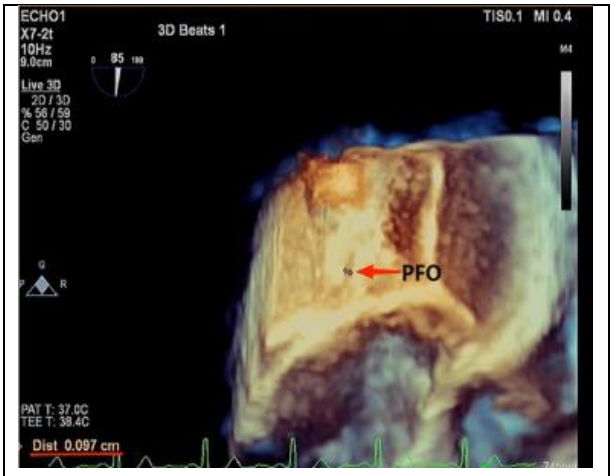

Figure 1. Transesophageal Heart Three-Dimensional Echocardiography: After the Valsalva manoeuvre, the atrial septum's ovoid fossa measured about 0.9 mm wide.

Transesophageal echocardiography (Figure 1) revealed a fossa ovoid fissure that was roughly 0.9mm broad (sometimes-stellate shunt). Additionally, an MRI picture revealed bilateral mild chronic ischemia foci in the frontal lobes (Figure 2). The overall score was 205, including 65 positive symptoms, 2.9 anxiety, 2.67 phobia, 2.33 somatization, 1.9 psychosis, 2.4 depression, 2.4 obsessive-compulsive, and 2.57 miscellaneous symptoms. Based on this, the patient was diagnosed with hypoxemia along with severe anxiety and depression (ICD-10). To treat the patient's anxiety, depression, and insomnia, paroxetine and oxazepam were recommended. In addition to helping with sleeplessness, anxiety, and depression, olanzapine helps alleviate physical symptoms, including nausea and vomiting. It is interesting to note that PaO2 improved to 89.47 mmHg only two days after symptoms like anxiety, nausea, dizziness, and shortness of breath improved.

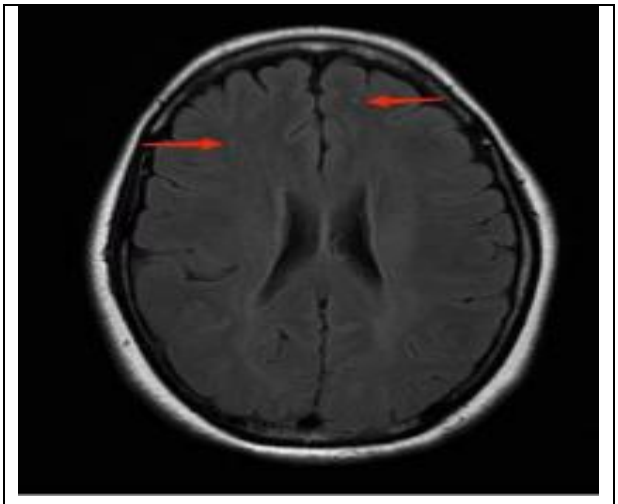

Figure 2. A bilateral modest ischemia centre in the frontal lobes was visible on an MRI T2 flare.

The patient's D-dimer levels reverted to normal, and cyanosis disappeared. The right-to-left shunt may have been minor, and acute hypoxia was gradually improved when anxiety, sadness, nausea, and other stressors were treated. After six months, the patient insisted on taking low dosages of paroxetine and olanzapine orally, felt stable, and no longer showed signs of cyanosis or hypoxia.

Discussion

Right-to-left shunting through the PFO in this case may result in acute systemic hypoxemia via a flow-driven mechanism, which may occasionally show up as cyanosis.[1] Teng P et al. revealed hemodynamic or anatomical alterations might result in right-to-left shunting through the patent foramen ovale via pressure-driven or flow-driven mechanisms.[3] Noori MAM et al. showed deoxygenated venous blood from the right atrium enters and combines with oxygenated arterial blood in the left atrium to cause PFO-associated hypoxemia.[4]

Conclusion:

Patients with acute systemic hypoxia, right-to-left shunting, severe anxiety, and depression have never been associated with a shunting mechanism or theory. It is still unknown what causes anxiety and depression in PFO patients, as well as their pathophysiology. Furthermore, the mechanisms of anxiety and sadness may be significantly impacted by patent foramen ovale.

Patent foramen ovale (PFO)-related acute systemic hypoxemia with cyanosis is caused by depression and anxiety.

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