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Petril Times

NEWSLETTER

INFORMATION BULLETIN ISSUED AS A SERVICE TO THE MEDICAL PROFESSION

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A LONGITUDINAL STUDY OF ROLE OF SELF-REPORTED STRESSORS IN EXHAUSTION DISORDER RECOVERY

Introduction:

Exhaustion disorder (ED) is a stress-related disorder characterised by long-lasting physical and mental exhaustion symptoms. Although stress is required for the development of ED, little is known about the role of stressors in ED maintenance. [1] Exhaustion disorder (ED) is a criteria-based diagnosis that is used for severe cases of exhaustion caused by stressors that have been present for at least six months (for an overview of the diagnosis's development. Recovery from stress-related exhaustion can be a lengthy process, and many patients experience long-term functional impairment due to cognition and/or fatigue years after seeking treatment. According to a recent longitudinal study, one-third of patients met the diagnostic criteria seven years after being diagnosed with and treated for ED, and the majority still struggled with ongoing symptoms such as decreased stress tolerance, fatigue, and cognitive issues. [2] The study's purpose was to look into the role of work-related stressors, personal stressors, and adverse childhood experiences in long-term recovery from ED.

Methods:

A mixed methods approach was used. The design was sequential, and data analysis was done in two parts: the first was qualitative analysis of patient records, and the second was statistical analysis of the data retrieved from the qualitative coding. Work-related stressors, private-related stressors, and adverse childhood experiences were examined in the records of 150 ED patients. Two patient records were examined for each patient, one from the time of diagnosis (baseline) and one from the 7-12 year follow-up clinical assessment (follow-up). At follow-up, 51 of the 150 patients still met the diagnostic criteria for ED (ED group), while 99 no longer met the diagnostic criteria and were thus considered recovered (EDrec). Percentages in each group (ED and EDrec) reporting each stressor at baseline and follow-up were calculated, as were percentage point differences between groups, as well as 95% confidence intervals for the differences.

Results:

At baseline, significantly more EDrec patients (73% EDrec, 53% ED) reported quantitative demands and managerial responsibilities (14% EDrec, 2% ED). At baseline, there was no difference in private-related stressors. At the follow-up, significantly more ED patients (8 ED, 0% EDrec) reported managerial responsibilities and caregiver stress (child) (24% ED, 6% EDrec), and significantly more

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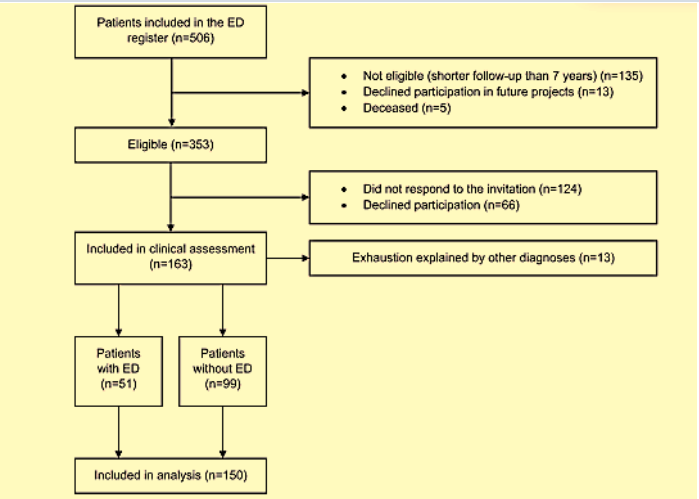
EDrec patients reported caregiver stress (parent) (6% EDrec, 0% ED). There were no differences in terms of adversity in childhood.

Discussion:

High quantitative demands at work were the most frequently reported stressor in both groups at baseline. This is consistent with previous research that identified quantitative demands at work as the most commonly reported stressor contributing to the development of ED. Furthermore, a systematic review and meta-analysis discovered that a heavy workload increases the risk of exhaustion. [3]



Flow-chart of included participants

In terms of adverse childhood experiences, there were no significant differences between the groups. According to these findings, adverse childhood experiences do not appear to be associated with the persistence of ED. There have been no previous studies examining the relationship between ED and adverse childhood experiences, so it is unknown whether adverse childhood experiences influence the development of ED.

The current study discovered that patients with long-term exhaustion and recovered patients had similar adverse childhood experiences. In clinical practise, this means that the prognosis for people suffering from ED should not be determined by their childhood adversities. The non-recovered group reported more stress from being a caregiver for a child with a psychiatric disorder or chronic illness. This finding emphasises the significance of identifying this subset of patients in clinical practise and addressing their difficult situation during treatment. This study also suggests that this stressor may worsen over time, resulting in a lack of recovery from ED.

This study looked into some of the many possible factors that could be linked to long-term exhaustion. Several other factors, including personality traits, may be related to long-term exhaustion and should be investigated. Thus, a recent study from our research group discovered that obsessive-compulsive personality disorder (OCPD) was significantly more common in patients with ED who had not recovered 7-10 years after diagnosis compared to former ED patients who had recovered. [4]

Conclusion:

The study's main finding is that neither adverse childhood experiences nor any of the stressors at baseline are linked to long-term ED. A subset of patients who still meet the criteria for ED seven years after diagnosis report stress from caring for a child with chronic disease or psychiatric disorder, which may contribute to long-term exhaustion in some of these patients. The data suggest that in clinical practise, the emphasis should be on reducing current stressors. Caring for a child with psychiatric disorders or chronic disease should be approached with caution, as this stressor has been linked to long-term exhaustion.

The main finding is that neither adverse childhood experiences nor any of the baseline stressors are linked to long-term ED. Long-term exhaustion may be associated with ongoing stressors related to having responsibility for other people, such as managerial responsibilities or caring for a child with a chronic disease or psychiatric disorder.

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CHRONIC STRESS IN BIPOLAR DISORDERS OVER TIME: THE ROLES OF THE HPA AXIS AND PERSONALITY

Introduction:

Chronic stress has been linked to the pathophysiology of bipolar disorder (BD), but the exact mechanism is unknown. Stress is associated with hypothalamic-pituitary-adrenal (HPA) axis activity in BD patients. [1] Patients with BD are more vulnerable to stress, which results in abnormal HPA axis activation. This suggests that HPA axis activity could be a biomarker for the disorder. [2] The HPA axis activity mechanism in BD, however, is more complex than previously thought, as both hyperactivity and hypoactivity of the HPA axis are linked to affective disorders. The hypothesis could explain why stress is initially manifested as hypercortisolism but is thought to contribute to the development of hypocortisolism over time. While abnormal HPA axis activity persisted in clinical remission and at the euthymic stage, this suggests that abnormal HPA axis activity is an endophenotype of the illness rather than an epiphenomenon. [3] The objective of this study was to investigate the relationship between HPA axis activity and BD symptoms in different clinical states, as well as how personality influences the process.

Methods:

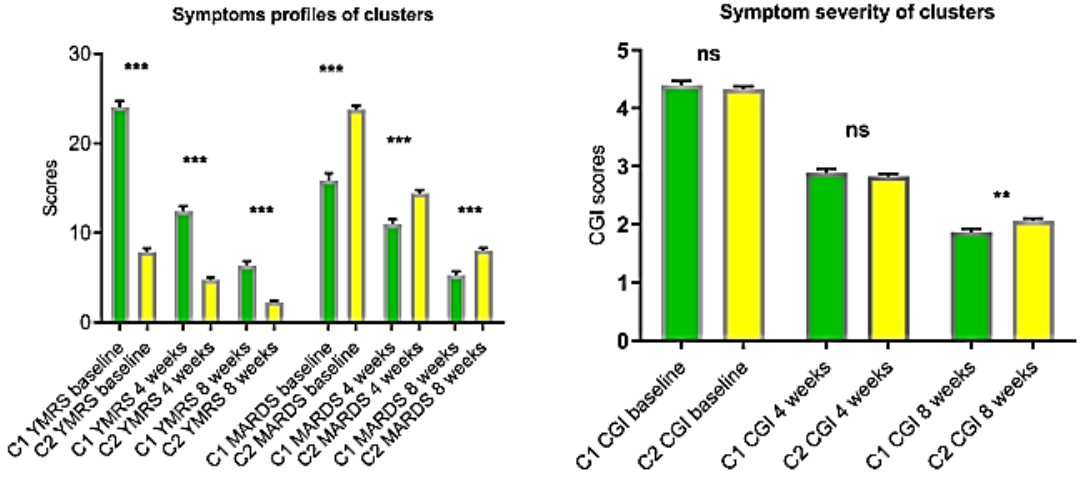
The differences in HPA axis activity among four BD states were investigated in this study. Using dynamic temporal warping (DTW) analysis and an unsupervised machine learning technique, we enrolled 813 BD patients in an 8-week longitudinal study to investigate the relationship between HPA axis activity and symptom trajectories. Furthermore, the relationship between the HPA axis, personality, and BD symptoms was investigated using mediation analyses.

Results:

ANOVA analysis revealed that glucocorticoid cortisol (CORT) and adrenocorticotropin (ACTH) levels did not differ significantly among the four clinical states of BD. The DTW integrating clustering analysis revealed that the two clusters were optimal, with cluster 1 characterized by severe manic symptoms that then improved and cluster 2 by milder manic severity that also improved. ACTH levels differed between the two clusters, and logistic regression analysis revealed a slight positive association between ACTH levels and cluster 1. In addition, the mediation analysis revealed that ACTH influences curative efficacy through conscientiousness.

Discussion:

The current study looked at the relationship between HPA axis activity and BD symptoms in different states. In addition, the role of personality in the relationship between HPA axis activity and symptoms was investigated. There was no statistically significant difference in CORT and ACTH plasma levels between the four clinical states. DTW analysis and an unsupervised machine learning technique were used to create two clusters with distinct manic symptom trajectories over an 8-week period, and ACTH levels varied between the two clusters. The higher the ACTH level, the worse the manic symptoms, indicating a link between HPA axis activity and short-term BD curative efficacy.



Symptom profiles of the two clusters.

The current study used DTW analysis and an unsupervised machine learning technique to identify two distinct manic symptom trajectory clusters: cluster 1, which had more severe manic symptoms over the 8 weeks, had a higher ACTH level than cluster 2, which had milder manic symptoms. Furthermore, the logistic regression analysis revealed that ACTH was a short-term predictor of manic symptom trajectory. Consistent with evidence that long-term CORT levels were higher in BD and were related to the number of manic episodes. [4]

Furthermore, this is the first study to look at how personality influences the relationship between HPA axis activity and BD symptoms, and our findings show that an ACTH-Conscientiousness-CGI changing scores mediation model was established, indicating that conscientiousness personality traits mediated the effect of ACTH on BD curative efficacy over an 8-week period. Depressive symptoms were associated with conscientiousness, whereas manic symptoms were associated with increased extraversion and decreased agreeableness. In BD patients, extensive reviews have revealed amygdala, hippocampus, and cortical prefrontal changes. [5]

Conclusion:

A higher level of ACTH was found to be associated with more severe manic symptoms, indicating a chronic stress response in BD patients. Furthermore, ACTH levels influence short-term BD curative efficacy via conscientiousness mediation, indicating that psychotherapeutic interventions targeting personality to improve the stress response would favour clinical outcome prediction.

In conclusion, a higher level of ACTH was found to be associated with severe manic symptoms, indicating a chronic stress response in BD patients. Furthermore, ACTH levels influence short-term BD curative efficacy via conscientiousness mediation, providing a psychotherapeutic strategy direction for BD.

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OBSESSIVE COMPULSIVE SYMPTOM DIMENSIONS IN A COMMUNITY SAMPLE OF YOUTH ARE ASSOCIATED WITH ALTERED WHITE-MATTER MICROSTRUCTURE.

Introduction:

Obsessive Compulsive Disorder (OCD) is a common, often debilitating mental illness that imposes a significant personal and societal burden. Clinical OCD affects up to 2.7% of the population; another 6-10% of people over the age of 13 have subclinical obsessive compulsive symptoms (OCS). Obsessions and compulsions are examples of OCS (repetitive behaviors, such as checking or praying). In school-aged samples, population-based studies show a continuum between subclinical and clinically severe OCD. [1] Factor analytic studies suggest several dissociable dimensions of OCD and OCS, including preoccupations with symmetry, contamination, and intrusive 'bad thoughts.' [2] Adult OCD research has revealed a "deficit" pattern of white matter abnormalities, most notably in the cingulum bundles, corpus callosum, orbitofrontal cortex, and anterior limb of the internal capsule. [3] OCD has been associated with white-matter abnormalities, but the white matter correlates of OCS in the developing brain are unknown. Some OCS (or OCD diagnosis) correlates may be transdiagnostic or even general psychopathology factors.

Methods:

The study used a hierarchical analysis of fixel-based white matter measures in relation to OCS and general psychopathology to investigate these questions in a large sample of typically developing youth (N = 1208). In an age-dependent manner, general psychopathology was associated with abnormalities in the posterior corpus callosum and forceps major, implying delayed maturation (specifically, hypermaturation in younger subjects).

Results:

A unidimensional measure of OCS did not correlate with any white-matter abnormalities, but separate OCS dimensions (derived from factor analysis within this sample) revealed the 'Bad Thoughts' dimension to correlate with white-matter abnormalities in the dorsal parietal white-matter and descending corticospinal tracts, and the 'Symmetry' dimension to correlate with anterior corpus callosum abnormalities. Repetition/checking and Symmetry OCS were also linked to posterior abnormalities that overlapped with general psychopathology correlates. There were no white-matter correlates for contamination symptoms. Secondary fractional anisotropy (FA) analysis revealed

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distinct white-matter abnormalities, implying that fixel-based and FA analyses identify distinct white-matter features relevant to psychopathology.

Discussion:

The investigators used FA and fixel-based analyses to investigate the white matter correlates of OCS and general psychopathology in a large, representative sample of children, adolescents, and young adults. The study discovered no significant associations between white matter measures and OCS in any of the previously identified ROIs using FA.

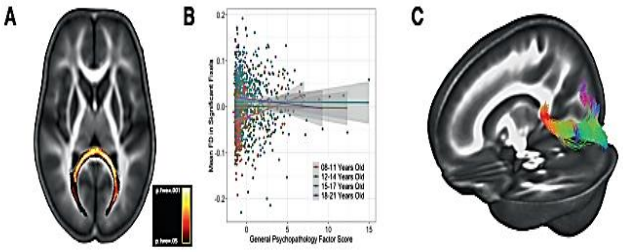

Fig. 1 Fixel correlates of general psychopathology. There was an age-dependent association between p-factor scores and FD in the splenium of the corpus callosum. Panel (A) shows the significant effect mapped on an axial plane, with the heatmap representing family-wise error corrected p-values ranging from 0.05 to 0.007 (brighter values are more significant). Panel (B) demonstrates the post-hoc visualization of the interaction effect, with age ranges defined by quartiles. Panel (C) displays a tractogram to further characterize the anatomy of the results; the significant ROI was used as a seed region and probabilistic tractography was used to construct the tractogram.

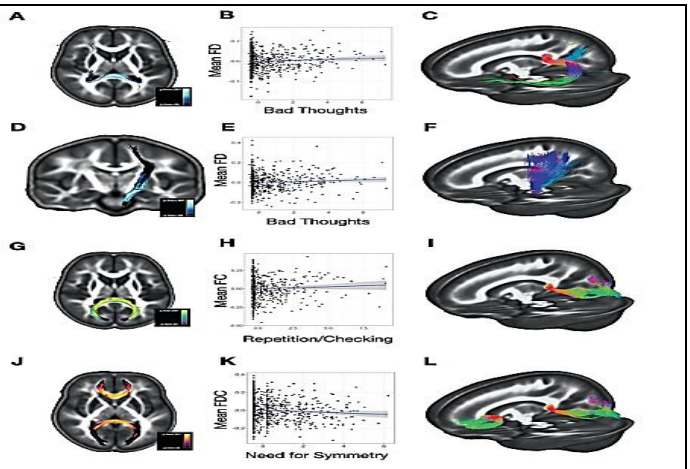

Fig. 2 Fixel correlates of OCS dimensions. Panels in the left column (A, D, G, J) display the significant regions of association for main OCSfixel findings. The center column (B, E, H, K) presents scatterplots of the assocation between each respective trait (x-axes) and the fixel-based value (y-axes). Scatterplots of these effects were generated post-hoc, and should not be interpreted as correlations. The right column contains tractograms that further characterize the anatomy of these results (C, F, I, L); each significant ROI was used as a seed region and probabilistic tractography was used to construct the tractograms.

The investigators first looked at the white matter correlates of general psychopathology. P-factor scores were associated with fiber density in the splenium of the corpus callosum in an age-dependent manner: higher fiber density was associated with psychopathology in younger adolescents/children, but lower fiber density was associated with the oldest age group. The effect was found in the splenium's medial region, which connects the bilateral occipital lobes via the forceps major. This age-dependent association could be explained by early hypermaturity followed by a later growth deficit. [4]

The general psychopathology factor (Fig. 1), as well as the OCS dimensions of Bad Thoughts, Repetition/Checking, and Symmetry (Figs. 2A, G, J), are all associated with white-matter abnormalities in the posterior corpus callosum.

The findings of the study are consistent with a recent report of an inverse relationship between genetic (SNP-based) psychopathology risk and forceps major white matter connectivity in both a developmental sample (the PING study; N = 678) and adults. [5]

Finally, the Bad Thoughts dimension was associated with fibre density (FD) in a more dorsal region of the splenium that connects the bilateral precuneus and bilateral temporal lobes, suggesting that changes in these white matter pathways disrupt networks that coordinate self-related or self-reflective processing.

There were no significant associations with a general OCS factor score that captured shared variance across all 16 OCS items, according to the study. This implies that the structural correlates of different OCS dimensions are meaningfully different. According to a recent hierarchical taxonomy of psychopathology (HiTOP) report, some OC symptoms are most correlated with a "fear" spectrum, while others have significant cross-loadings on a "thought disorder" spectrum. [6]

Although several of the study findings overlap with recent evidence from large multimodal imaging studies of OCS/OCD in adolescence, it is important to note that the study findings do not align with dominant contemporary models that link OCD pathology to dysconnectivity in frontostriatal pathways.

Conclusion:

Finally, the study found that white matter disruptions associated with general psychopathology are visible in early adolescence and age-dependent. Furthermore, we describe an OCS dimension-specific pattern of white matter changes in pathways supporting interhemispheric processing as well as visual and sensorimotor integration. These findings imply that distinct dimensions of OCD-spectrum psychopathology can be distinguished from a risk index for transdiagnostic psychopathology and are dissociable at the level of white matter biomarkers. This study could help explain how specific neural network disruptions during adolescence contribute to heterogeneity in OCD-spectrum psychopathology.

These findings suggest that OCS dimensions correlate with dissociable white matter abnormalities, implying separable networks. Future research should look at these white-matter signatures over time.

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A CASE REPORT ON THE 3 YEAR NEURORADIOLOGICAL SCREENING OF A PATIENT WITH FIRST-EPISODE PSYCHOSIS

Introduction:

The majority of cases of first episode psychosis are caused by early onset schizophrenia. Early-onset schizophrenia is most common between the ages of 15 and 25. Very early onset schizophrenia is defined as occurring before the age of 13, and it is extremely rare. Almost all practise guidelines recommend neuroradiological screening to rule out reversible causes of first episode psychosis, particularly if they are operable. [1] There are some barriers to carrying out the neuroradiological screening part of the practise guidelines for managing first episode psychosis. If a neuro-radiological finding is suspected to be an etiological factor, whether surgical intervention is recommended or not, it is necessary to monitor the consequences of the finding's progression. [2] Ultrasonography was a recommended procedure for the foetal brain during this patient's pregnancy in some cases, including this case report. The presence of a chronic cyst in this case adds another layer of complexity due to the possible role of infection in both the stenosis of the foramen of Monro and the development of first episode psychosis.

Case Report:

A 20-year-old female patient of Middle Eastern descent presented to the outpatient clinic with her family after an eight-month period of mental deterioration in which she developed paranoid delusions of persecution accusing her family of spying on her, poisoning her food and drink, and having perceptual abnormalities in the form of auditory hallucinations giving running commentary about her. The structural MRI revealed a large chronic cyst in the right lateral ventricle, measuring 8.4 cm anteroposterior x 5.7 cm side to side x 4.6 cm craniocaudally, with cyst content following CSF signal intensity. A dilated right temporal horn and right occipital horn were also present, indicating outflow obstruction due to an obstructed foramen of Monro.

The cyst was stretching the right lateral ventricle and crossing the midline, compressing and narrowing the left lateral ventricle and third ventricle, with radiological indicators of the cyst's chronicity, such as the absence of surrounding edoema and the presence of a thin capsule. Despite the massive size of the dilated lateral ventricle, the neurological examination by a senior consultant neurologist was completely normal. She was followed for 36 months. A few weeks after her symptomatic recovery, the patient planned a traditional marriage, and after counselling the patient

and her family, medications were gradually discontinued so that before her wedding day, she was completely free of Risperidone.

Patient became pregnant very early in her marriage, and during the second months of her first trimester, she developed paranoid delusions coloured by her new social status, accusing her mother and sisters of plotting to steal her husband and acting on this by becoming more possessive of him.

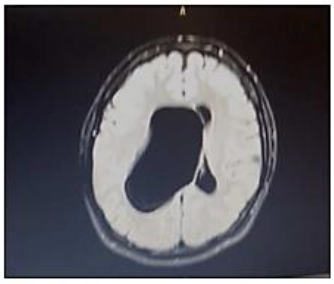

Figure 1. Chronic thin walled intraventricular cyst crossing the midline and occupying the lateral ventricle.

She gave birth to a healthy girl who was bottle fed and reached the normal developmental milestone of 24 months. As her insight improved throughout the process, the patient was eager to continue on the same antipsychotic regimen. During her follow-up, there was no evidence of risk posed to her baby as a result of negligence or disturbed behaviour, and she provided reasonable care for her baby. Risperidone 4 mg orally and Paliperidone 150 mg monthly injection were used to manage her symptoms.

She gained weight gradually, which could be attributed to the antipsychotic medication and a combination of other social factors such as a lack of exercise and having maids do her household chores for her. Fortunately, she had gastric sleeve surgery and lost eighteen kilogrammes in the two months preceding her most recent check-up. Her most recent follow-up visit revealed that she was taking Palioeridone 150 mg and Risperidone 2 mg orally. She was in stable complete remission with no evidence of relapse symptoms. Her performance at home was described as satisfactory. Her father reported that a few days after the injection, her eyes rolled up in a noticeable way, which is not painful but lasts for a few days. This was brand new and had never been reported before. The doctors' plan was to restart the anticholinergic twice daily for better results, reduce Risperidone by 1 mg/week over two weeks until she was only on the long acting injection, and then reevaluate her need for the anticholinergic before discontinuing it. The onset of the oculogyric crisis coincided with the patient's weight loss after bariatric surgery.

Discussion:

Several authors have described brain abnormalities in adult schizophrenic patients, including medial temporal lobe reduction, lateral and third ventricle enlargement, lower brain volume, basal ganglia enlargement, and thalamic abnormalities. The most commonly replicated finding is lateral ventricle

enlargement. The majority of first-episode psychosis patients will not have identifiable disorders with etiological relevance on neuroimaging, and only 3% of first-episode psychosis is organic in origin. Following the onset of symptoms, neurodevelopmental pathology may progress further. The neurodegenerative theory is supported by faster tissue loss in schizophrenia patients compared to controls. In schizophrenia, the term neuroprogression refers to neurodegeneration, apoptosis, and decreased neurogenesis/neuroprotection.

There is an apparent overlap with the infection theory aetiology in this case report, as this is relevant to possible aetiology for stenosis of the foramen of Monro and viral infectious theory of schizophrenia. Both have a neurodevelopmental origin, but it is unclear whether this overlap is relevant. It is also important to note that other colleagues encountered a case with schizophrenia-like symptoms that was the only manifestation of an arachnoid cyst in the temporal fossa with full recovery and no relapse following neuro-surgical intervention resulting in brain decompression with full psychosis remission without antipsychotic medications.

Conclusion:

Neuro-radiological screening is an important investigation that must be performed in order to screen for first episode psychosis. The discovery of neuro-radiological finding/s will aid in patient management and necessitates further investigation. The causal relationship between the neuro-radiological finding and a first episode of psychosis is still being studied. Discovering the possible relationship(s) between a neuro-radiological pathology or brain changes and the development of first episode psychosis will not only shed light on the various possible etiologies of first episode psychosis, but will also shed light on possible ways to manage first episode psychosis or predict its development and intervene earlier based on newer knowledge about its development. It is always important to remember that association does not always imply causation. Accumulating knowledge and findings in first episode psychosis, including neuro-radiological findings, will be more beneficial if these data are pooled together in a single international scientific body for better data extrapolation.

Neuro-radiological screening is an important investigation that must be performed in order to screen for first episode psychosis. The discovery of neuro-radiological finding/s will aid in patient management and necessitates further investigation.

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