Transsemptomatic Diagnosis as a Replacement for Transdiagnostic Approach in Psychiatry

Psikiyatride Transdiagnostik (Tanı Ötesi) Yaklaşım Yerine Transsemptomatik (Semptom Ötesi) Tanı

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ABSTRACT

Traditionally, the DSM and ICD diagnostic systems have been based on the principle that mental disorders are separate diseases with different etiologies and clinical manifestations. On the other hand, the transdiagnostic approach argues that many diseases such as anxiety and depression share a common etiology and have similar clinical features, pointing to the great overlap between different psychiatric disorders in genetic, epidemiological and neuroscience studies. In this context, the Research Domain Criteria (RDoC) project was initiated in order to create a research model and shape future classifications. Unlike traditional diagnostic classifications, RDoC assumes diseases as pathophysiology-based dysfunctions of the brain's neuronal circuits rather than symptom clusters. However, there are limitations in transdiagnostic approach studies such as complex methodologies, unclear criteria, inclusion of very different diagnoses in the same study, and insufficient inclusion of serious psychiatric diseases. In this article, the importance of correct diagnosis in psychiatry is stated by emphasizing "Trans-symptomatic diagnosis" instead of "Transdiagnostic approach".

Keywords: Transdiagnostic approach, Research Domain Criteria, transsymptomatic diagnosis

ÖZ

Geleneksel olarak DSM ve ICD tanı sistemleri mental bozuklukları farklı etiyolojileri ve klinik görünümleri sergileyen ayrı hastalıklar olduğu ilkesine dayanmaktadır. Buna karşın transdiagnostik yaklaşım genetik, epidemiyolojik ve sinirbilim araştırmalarında farklı psikiyatrik bozukluklar arasındaki büyük örtüşmelere işaret ederek anksiyete ve depresyon gibi birçok hastalığın ortak etiyolojiyi paylaştığını ve benzer klinik özellikler taşıdığını savunur. Bu çerçevede bir araştırma modeli oluşturmak ve gelecekteki sınıflandırmaları şekillendirmek amacıyla Araştırma Alanı Kriterleri (Research Domain Criteria, RDoC) projesi başlatılmıştır. RDoC geleneksel tanı sınıflandırmalarından farklı olarak hastalıkları semptom kümeleri yerine patofizyoloji temelli, beynin nöronal devrelerinin işlev bozuklukları olarak değerlendirir. Ancak, transdiagnostik yaklaşım çalışmalarında karmaşık metodolojiler izlenmesi, kriterlerin net olmaması, çok farklı tanıların aynı çalışmaya dahil edilmesi ve ciddi psikiyatrik hastalıkların yeterince dahil edilmemesi şeklinde kısıtlılıklar bulunmaktadır. Bu yazıda "transdiagnositik (tanıl -ötesi) yaklaşım" yerine "transsemptomatik tanı (semptom ötesi tanı)" vurgulanarak psikiyatride doğru tanının önemi üzerinde durulmaktadır.

Anahtar sözcükler: Trandiagnostik yaklaşım, araştırma alanı kriterleri, transsemptomatik tanı

Introduction

Psychiatry has been acting according to traditional diagnostic systems (DSM/ICD) from past to present. In this direction, a psychiatrist aims to establish a categorical diagnosis for the patient by placing diagnostic criteria at the center of psychiatric evaluation and thus to determine a treatment plan. This approach has dominated both clinical practice and health policy. However, studies mostly consist of a single diagnostic category and control group. However, those working in this field know that diagnoses and classifications in psychopathologies are not always clear. For this reason, alternative approaches are being tried against the understanding of a single diagnostic category. With the criticism that these systems are not useful, the transdiagnostic approach is presented as an option. The transdiagnostic approach, which originates from cognitive behavioral therapy, has emerged as an alternative to the categorical approach in psychiatry. The transdiagnostic approach argues that many psychopathological processes such as anxiety and depression share a common etiology and that these disorders have similar cognitive, emotional and behavioral characteristics. Suggests transdiagnostic conceptualization and intervention rather than a categorical approach (Etkin ve Cuthbert 2014, Fusar-Poli ve ark. 2019, Barch 2020, Dalgleish ve ark. 2020).

In this article, the importance of correct diagnosis is emphasized by emphasizing "Transsymptomatic Diagnosis" instead of "Transdiagnocytic approach" within the aspect of medical model in psychiatry and traditional medical approach.

Transdiagnostic Terminology

Transdiagnostic

From the Latin, the prefix "Trans" can mean across/from one side to the other (along, through). Transatlantic, crossing the Atlantic Ocean (adjective, crossing; sea voyage) can be given as an example of this meaning. Another usage is "beyond (the drawn border), further ". Therefore, a transdiagnostic approach in psychiatry is expected to go beyond existing categorical diagnoses and make a better classification (Fusar-Poli et al. 2019).

In another study, it has been stated that the term transdiagnostic can be used across diagnoses and beyond diagnosis (above diagnosis), but they refer to effects that are common in different psychiatric disorders (across, personal opinion). Otherwise, it is not to go above and beyond existing diagnostic categories (above and beyond, from the article) to ignore them (Gong et al. 2019).

Transdiagnostic Processes

All biological, psychological and cognitive processes that are actually mental can be included here from the point of view. Visual evoked potentials, impulsive responses to emotions, emotion regulation and face recognition processes are transdiagnostic (Fusar-Poli et al. 2019). According to the cognitive approach, they are dysfunctional processes that can play a causal role in more than one different psychiatric disease. For example, post-diagnostic cognitive processes such as attentional bias towards negative stimuli and information, repetitive negative thinking and memories, interpretation and expectation bias, working memory defects, executive dysfunctions can be seen in various diseases (Nolen-Hoeksema and Watkins 2011, Goodkind et al. .2015). The transdiagnostic approach focuses on these core dysfunctional processes so that it can help to understand the nature of psychopathology in a shorter way. In addition, it can offer process-based approaches such as disorder-specific attention control training, anxiety sensitivity treatment, and rumination-focused therapy (Nolen-Hoeksema and Watkins 2011, Dalgleish et al. 2020).

Transdiagnostic Risk Factors

For example, childhood sexual trauma is a general transdiagnostic risk factor for mood disorders, anxiety disorders, eating disorders, sexual disorders, dissociative disorders, substance use disorders, and most commonly personality disorders. Genetic transmission and especially childhood brain damage can also be considered as transdiagnostic risk factors (Nolen-Hoeksema and Watkins 2011).

Transdiagnostic Mechanisms

Impaired stress response associated with hypothalamic-pituitary-adrenal (HPA) axis activity, prefrontal cortex hypoactivity associated with impaired impulse control and emotion regulation skills, neurotransmitter systems mediating reward-seeking behavior can be considered as transdiagnostic mechanisms (Nolen-Hoeksema and Watkins 2011).). Neuronal and biochemical mechanisms underlying genetic risk factors that can also cause psychiatric diseases can be included in the transdiagnostic group (Goodkind et al. 2015).

Transdiagnostic Constructs

National Institute of Mental Health (NIHM) has introduced a research strategy based on reconceptualization by focusing on the structures that make up the specific neuronal circuits of psychopathology to accelerate the identification and treatment of psychiatric disorders. This strategy encourages the exploration and identification of these structures at various levels, from genes to physiology and behavior. Constructions are grouped into five large domains that serve to regulate closely related mental functions: negative valence, positive valence, cognition, social processes, and arousal/modulation. For example, the negative valence field consists of constructs such as fear, anxiety, threat, loss. It is envisaged that each structure is defined along the continuum from normal to pathological. Thus, healthy fear may serve a protective function under appropriate conditions, while inappropriate or excessive fear may contribute to psychopathology. Related fields and structures are independent of traditional diagnostic categories (Elmer et al. 2016).

There is literature that defines all the areas covered in transdiagnostic approach studies as construct. Accordingly, functional brain networks, dopamine synthesis capacity, brain response to visual threats, thalamic connectivity in early life stresses, ventral-striatal reactivity to reward, even homocysteine and remethylation are transdiagnostic structures (Fusar-Poli et al. 2019).

p Factor

Against the view that psychiatric disorders are distinct and categorical, the idea that many disorders are comorbid and in a continuum has been discussed. Some authors interested in this field, considering the dimensionality, persistence, co-occurence, and sequential comorbidity of psychopathology, consider psychiatric diseases first internalizing, externalizing and thought disorders and then found it appropriate to define it as the general psychopathology dimension (p Factor). This definition is similar to the g factor used in general intelligence in psychological sciences. Higher p factor scores indicate more dysfunction, higher hereditary transmission, worse developmental history, lower brain integrity, lower IQ values, higher susceptibility to different mental illnesses, and more exposure to danger in early life. According to the transdiagnostic approach, the p factor explains why it is difficult to find causes, outcomes, biomarkers, and individual-specific treatments in psychiatric diseases and facilitates research (Caspi et al. 2013, Gong et al. 2019, Barch 2020).

We see that the concepts can be used interchangeably in the transdiagnostic literature and can also be diversified such as transdiagnostic symptoms (Buckholtz and Meyer-Lindenberg 2012), models (Nolen-Hoeksema and Watkins 2011), marker (Gong et al. 2019). Instead of "risk factors", "processes" (Nolen-Hoeksema and Watkins 2011) and "mechanisms" can be preferred as "features" (Dalgleish et al. 2020). In addition, it is stated that the transdiagnostic factor frequently defines the p factor (Gong et al. 2019, Barch 2020). Finally, the brain area examined in transdiagnostic studies can be defined as "structures" and the function considered as "processes" (Fusar-Poli et al. 2019). At this point, it is understood that both concepts, in fact many of them, are intertwined and there are no clear distinctions.

Transdiagnostic Approach

Traditional psychiatry is based on the principle that mental disorders are separate categories exhibiting different etiologies and clinical manifestations. On the other hand, there are patients who clearly show signs of psychopathology or show partial criteria of more than one category together, but do not fully comply with the definition of any diagnostic category. In addition, it is known that comorbidity is common in psychiatry, and a significant proportion of patients who meet the diagnostic criteria for one disorder can also meet the criteria for at least one other disorder. Therefore, within current diagnostic systems, it may not be possible to define precise boundaries between the different categories, especially in some cases. A growing number of genetic, epidemiological and neuroscience studies point to great overlaps between different psychiatric disorders (Insel et al. 2010, Ozdemir 2012, Gong et al. 2019, Ma et al. 2019, Marshall 2020).

Similar gene groups and environmental risk factors can cause different diseases from various diagnostic categories, including schizophrenia, depression, obsessive-compulsive disorder (OCD), and post-traumatic stress disorder (PTSD). These data suggest that each disorder can be understood as combinations of specific diagnoses and transdiagnostic features or mechanisms in the conceptualization of psychiatric disorders. An exemplary research model focuses on a transdiagnostic factor, the p factor, that may predispose to psychopathology. If a transdiagnostic factor underlies more than one psychiatric disorder, then there may be a common neuroanatomical basis and/or a marker across different diagnostic categories. Thus, the development of transdiagnostic interventions that can reduce the risk of emergence of psychopathology can be facilitated (Etkin and Cuthbert 2014, Gong et al. 2019).

Neuroscience research has challenged the view that psychiatric disorders are separate entities. In fact, evidence has shown that abnormalities in brain function are often similar across disorders. Accordingly, the findings map for specific symptoms or clinical disruptions rather than describe a specific disease and point to dimensional differences in the functioning of brain systems. Psychopathology not as separate diseases; defines boundaries as definable areas. The transdiagnostic approach attempts to dimensionally classify mental disorders based on observable behaviors and neurobiological measurements. As a dimensional system, it places psychiatric disorders on a continuum from normal experiences to the most severe, and thus aims to make them more understandable (Ozdemir 2012a, Aktif and Cuthbert 2014, Badcock and Hugdahl 2014).

Transdiagnostic Classification and Research Domain Criteria (RDoC)

As the largest research institution to fund mental health research in the United States, the National Institute of Mental Health (NIMH) has established the Research Area Criteria to establish a long-term research framework and shape future classification schemes, particularly for genomics and neuroscience"Research Domain Criteria (RDoC)" project. In addition to advances in disease-based classifications, it is also aimed to consolidate data on pathophysiology, develop new treatments, and use research findings more in clinical practice. RDoC aims to develop new methods to diagnose psychiatric disorders based on more objective data, with reliability and validity (Insel et al. 2010, Cuthbert and Insel 2013, Cuthbert and Kozak 2013, Dalgleish et al. 2020).

Unlike traditional diagnostic classifications, RDoC treats diseases as pathophysiology-based dysfunctions of the brain's neuronal circuits rather than symptom clusters. Thus, it assumes that dysfunction, varying degrees of deviation from normal, in relevant neuronal circuits can be identified with clinical neuroscience tools, including electrophysiology, functional neuroimaging, and new methods. RDoC examines a wide range from normal to abnormal and approaches psychopathology dimensionally in various types and degrees (Cuthbert and Insel 2013).

The RDoC framework, given below, is divided into five domains and each construct within itself:

1. Negative value field; acute threat (fear), potential threat (anxiety), constant threat, loss, lack of expected reward.

2. Positive value domain; motivational behavior, initial response to reward, sustained response to reward, reward learning, habit.

3. Cognitive systems; attention, perception, working memory, verbal memory, language behavior, cognitive (effortful) control.

4. Systems of social processes; belonging and attachment situations, social communication, self-understanding and perception, understanding and perceiving others.

5. Alertness/regulation systems; wakefulness, biological rhythms, sleep-wake (Cuthbert and Insel 2013, Badcock and Hugdahl 2014, Dalgleish et al. 2020).

These structures can be analyzed in different units as genes, molecules, cells, circuits, physiology, behavior, self-report, and paradigms. Based on the available data for each unit, RDoC summarizes hallucinations in relation to cognitive/inhibitory control disorders as follows:

Genes; heritability estimates for striatal and cortical dopamine,

Molecules; striatal dopamine increase, Glutamate hyperactivation, GABA hypoactivation,

Cells; Changes in orbito-frontal cortex (OFC) density and/or structure,

Circuits; Prefrontal-cinguloparietal-subcortical system, Posterior Medial OFC-subcortical loop,

Physiology; decreased neuronal activation to real sounds in patients with auditory hallucinations, failure to inhibit and suppress "sounds",

Behaviour; Difficulties or dysfunctions in inhibition; false alarm rates- reality confusion, Self-report; decreased sense of control, eg control of sounds, degree of real-time control,

Paradigms; Repeated continuous recognition memory tasks, Forced-attention dichotic listening task (Insel et al. 2010, Badcock and Hugdahl 2014, Dalgleish et al. 2020).

From this perspective, let's consider a table in an RDoC survey in question. The columns of the table may consist of one or more variables that progress from the genetic, molecular, and cellular levels to the circuit level, as suggested above. The rows represent the various constructs identified according to the research objectives. For example, working memory, selective attention, general memory are associated with the structure of "Cognitive systems". It can examine transdiagnostic processes involving cognitive performance and dorsolateral prefrontal cortex neuroimaging with a genetic polymorphism. He can pick up patients from the psychotic disorders service. With the RDoC classification approach, the sample can be selected from both groups containing more than one DSM diagnosis and the non-clinical population. A fear circuit study can be performed that covers all anxiety patients and examines the relationships such as startle and strain scores and symptom severity. Rows may also focus on measures from broad functional areas such as the individual, family environment, and social context.

Thus, at all these levels, both the biology and psychology of mental illness can be studied (Insel et al. 2010, Dalgleish et al. 2020).

Examples where clinically relevant models of circuit-behavior relationships point to practical use in the future include fear, reward, executive functions, and impulse control. For example, the future practitioner can complete the clinical assessment of what we now call an "anxiety disorder" in a manner similar to what is routinely done in many other areas of medicine, based on data from functional or structural imaging, genetic sequencing, and laboratory-based testing of fear conditioning and damping to determine prognosis and appropriate treatment. (Insel et al. 2010).

Transdiagnostic Findings

Transdiagnostic approach studies have focused on detecting common neuronal pathology in disorders such as schizophrenia, bipolar disorder, major depression, anxiety disorders and substance addictions, rather than a specific etiology for each disease in psychiatry. For example, some authors have argued that reduced gray matter volume as a trandiagnostic common finding is associated with cognitive impairments for many forms of psychopathology. In this respect, in order for any neurobiological factor to be defined as a transdiagnostic feature, it must be detectable in more than one diagnosis group, not in a single disease. In a study examining decreased reward response (anhedonia) in patients with major depression, bipolar disorder, and schizophrenia, the decrease in functional connections in the nucleus accumbens, which plays a similar role in dopamine release in all groups, was defined as a transdiagnostic finding (Goodkind et al. 2015, McTeague et al. 2017, Barch 2020). , McTeague et al. 2020).

In a meta-analysis of studies examining impaired emotional processes in patient groups such as schizophrenia, bipolar disorder, depression, anxiety disorders, and substance use disorders using functional neuroimaging, hypoactivation in the medial and lateral prefrontal regions and hyperactivation in the hippocampal/parahippocampal gyrus were shown (McTeague et al. 2020). Also, abnormal brain activation patterns became more pronounced in the face of unpleasant stimuli. Based on these data, it has been suggested that emotional reactivity and dysregulation in psychiatric diseases can be formulated as dysfunctions in key brain regions and neuronal networks in terms of transdiagnosis. Again, putamen volume enlargement, which is seen in proportion to symptom severity, was presented as a transdiagnostic finding in a study conducted in patient groups with different diagnoses such as OCD and PTSD. Considering the role of the putamen in the integration of high-level cognitive, motor and limbic processes, it has been stated that the disruption of these processes in psychiatric diseases may represent a transdiagnostic feature. Thus, related processes can be used in the development of new transdiagnostic interventions aimed at reducing the risk of psychopathology in many psychiatric diseases (Dalgleish et al. 2020).

According to the genetic transdiagnostic model, the common symptoms seen in psychiatric diseases are due to dysfunctions of the same neuronal networks. The model can be summarized as follows: The common genetic risk factor for psychopathology (pleotropic) creates a predisposition for diseases A and B. This factor can lead to disruptions in the CD neuronal network. These deteriorations can lead to symptoms such as Sa-Sb-Sc...Sh-Si. While some of these symptoms (Sa, Sb) are categorically in the A diagnostic criteria, they may not be in the B diagnostic criteria. On the other hand, some other symptoms (Sh,Si) are diagnostic criteria for B but not for A. However, many (transdiagnostic) symptoms (Sc, Sd, Se, Sf, Sg) may overlap with both disease categories. Based on this, the idea that functional impairment in common neuronal networks formed by genes that pose a risk for psychiatric diseases may be responsible for both cognitive and other symptoms can be supported (Buckholtz and Meyer-Lindenberg 2012).

The important role of genes in the regulation of circadian rhythms, which is associated with many psychiatric diseases, especially mood disorders, is known. Some CLOCK gene polymorphisms have been found to be associated with sleep disorders seen in bipolar disorder and major depression. In addition, certain other related gene regions have been found to be associated with seasonal affective disorder. However, the relationship between circadian genes and non-affective psychiatric diseases such as attention deficit hyperactivity disorder, schizophrenia/schizoaffective disorder and alcohol use disorder has also been reported. Sleep processes can be described as transdiagnostic as they can be seen in a wide range of psychopathology. There may be common mechanisms between these processes and psychiatric disorders. The transdisgnostic perspective, in which sleep disorders can be a candidate, may be beneficial for clinical practice (Harvey et al. 2011).

Limitations of Transdiagnostic Studies

From a comprehensive study reviewing transdiagnostic approach studies, some of the studies conducted in this area mixed symptoms and diagnoses, followed complex methodologies, the transdiagnostic criteria were not clear, many different diagnoses were included in the same study, and serious psychiatric diseases such as schizophrenia and bipolar disorder were not included or included very few. It has been reported that there are limited number of longitudinal and more cross-sectional studies, the number of samples varies widely and they consist of small groups. In addition, it was stated that a significant proportion of the studies did not report whether structured interviews were conducted to clarify the diagnoses or speculated on the relative benefits of the transdiagnostic approach according to the diagnoses without the use of ICD/DSM (Fusar-Poli et al. 2019).

Transsymptomatic Diagnosis

In this article, the importance of correct diagnosis in psychiatry is emphasized by emphasizing "Trans-symptomatic Diagnosis" instead of "Transdiagnocytic approach". An example of this approach is conducting an etiological study for a child who presents with fever, considering infectious and noninfectious causes. If the etiological differential diagnosis of the symptom is made, the treatment will be carried out in line with the prominent diagnosis. However, if a clear diagnosis cannot be determined as a result of the evaluation, the management of the disease may be based on the symptoms and empirical treatment may be required for the symptoms.

Clinical evaluation can proceed in line with a good anamnesis, psychiatric, neurological and physical examination together with laboratory examinations. The time of onset of symptoms, other accompanying complaints, past illnesses, medications, substance use, head trauma and family history should be questioned in detail. In order to understand behavioral changes, it may be necessary to interview relatives and to use some psychometric tests such as sentence completion to determine the content of thought.

One of the best examples of the meta-symptom diagnostic approach in psychiatry can be the distinction between bipolar depression and unipolar depression. Both diseases show quite differences in terms of clinical and therapeutic strategies together with symptom similarities. Whenever possible, this distinction should be taken into account when dealing with practically any patient with symptoms of depression. In particular, hypomanic episodes may be overlooked, and bipolar depression may be mistakenly defined as unipolar depression. This situation may lead to delay in correct diagnosis and treatment, and seriously affect the whole life of the patient (Ozcan and Team 2021).

The same diagnosis, for example depression, may present with a wide variety of symptom manifestations. As it is known, many psychiatric diseases have been classified as different subtypes in order to better define them clinically. In addition to codes such as whether the episode was single or recurrent, the presence of psychotic features, whether complete remission was achieved in the diagnosis of DSM 5 depression, determinants with mixed features, atypical features, peripartum onset, catatonic and seasonal patterns show the diversity of symptomatology. It is thought that the same symptoms can be seen in different diagnoses and the same diagnosis can be encountered with different symptoms, making the "Transsymptomatic Diagnosis" approach mandatory.

Discussion

Since laboratory examinations used to diagnose in other branches of medicine are not yet available in psychiatry, diagnosis is made according to symptom-based criteria. These criteria are not certain for any disease. Only our clinical experience and other references, eg examinations, can mediate. Again, diagnosis has important functions in psychiatry as well as in other branches of medicine. Psychiatric diagnoses can help predict the short- and long-term treatment plan, course and outcome of the disease. In practice, diagnosis is made based on clinical judgment and experience beyond the symptom-oriented approach. For these reasons, only the symptoms may not be sufficient in the evaluation of the clinical picture (Feighner et al. 1972, Ozdemir 2012b).

Similar clinical features and similar symptoms can be seen in patients with different disorders. Therefore, it is necessary to focus on the differential diagnosis as much as possible and to determine the exclusion-inclusion criteria, especially in the first attack and suspicious cases that have not yet been diagnosed. We know that even patients with the same diagnosis do not constitute a homogeneous group in terms of clinical picture. In addition, there may be significant differences in outcomes such as complete recovery and chronic course in patients within the same diagnostic category (Feighner et al. 1972).

Transdiagnostic models of psychopathology aim to identify the underlying processes of diseases, help explain comorbid conditions, and focus on treatment options. Existing transdiagnostic approaches have difficulties in explaining the mechanisms by which psychopathology emerges. In addition, it cannot explain why individuals with the same transdiagnostic risk factor reveal different symptom clusters, for example how stress as a risk factor can lead to various diseases such as depression, anxiety and alcohol use disorder (Nolen-Hoeksema and Watkins 2011).

Although RDoC is an experimental classification approach, it is not actually a classification in the official sense. RDoC is not in a position to diagnose any patient according to any criteria. It is unclear how to set the inclusion criteria for RDoC and whether the findings are nonspecific or specific and how they relate to psychopathology. Discussions can only be speculation. However, DSM and ICD draw clear lines. Data on disease categories are clearer. It can be a guide in the next study (Cuthbert and Kozak 2013, Dalgleish et al. 2020).

Conclusion

It can be said that the transdiagnostic approach literature is not heterogeneous and even internally consistent, focuses on a limited number of psychiatric diseases, is not yet fully established in terms of standardization and concept, and as such it cannot be an alternative to existing diagnostic systems. The lack of neurobiological markers for diseases and difficulties in diagnostic classification are not related to DSM or ICD, but are due to the nature of psychiatry. We know that in medicine, problems arise with descriptive diagnostic systems made without a proper understanding of the pathophysiology. Disorders that were once considered a single disorder based on clinical presentation have been shown to be heterogeneous by laboratory testing. For example, as in different forms of diabetes mellitus; Insulin resistance to destruction of islet cells (Type1, insulin-dependent) (Type 2, treated with oral antidiabetics). From infectious diseases to subtypes of cancer, biomarkers are routinely used for different treatments. Conversely, it has been shown that clinically different manifestations may arise from the same etiology, such as syphilis and a number of streptococcal-related disorders (Insel and Cuthbert 2010).

Transsymptomatic diagnosis emphasizes etiological investigation other than the apparent diagnosis that may reveal symptoms. In addition to the psychosocial burden factors that may lead to the related picture, it reminds a comprehensive evaluation such as other medical diseases, drug use history, possibility of substance use, head trauma, childhood development history and personality traits when necessary. Ultimately, it is aimed to clarify the history confirming the diagnosis and to support it with examinations.

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