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A Transdiagnostic Screening Protocol for Mental Disorder, Based on Research Domain Criteria (RDOC)

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Abstract- Research Domain of Criteria (RDOC) helps to explore aspects of mental disorders. We designed a transdiagnostic protocol for assessing mental features based on the RDOC concept. We conceptualized RDOC systems as features that are measurable in clinical research. For designing this protocol, we used observation, clinical interview, and examination for surveying the cognitive system, emotion system, social system, regulatory system, circadian rhythm, and sensory motor system. This protocol is a screening model for assessing indicators that RDOC has considered for the psychological dimensions. The protocol helps clinical research (besides clinical interview of DSM) to have a comprehensive quantitative and qualitative description, in order to perform personalized assessment. By using this protocol, we have a specific profile of features that can be used for personalized formulation.

Keywords: transdiagnostic approach, RDOC, mental disorder, transdiagnostic assessment, personalized formulation.

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A Transdiagnostic Screening Protocol for Mental Disorder, based on Research Domain Criteria (RDOC)

Hamide Ajam Zibadi [α] & Mohammad Arbabi [σ]

Abstract- Research Domain of Criteria (RDOC) helps to explore aspects of mental disorders. We designed a transdiagnostic protocol for assessing mental features based on the RDOC concept. We conceptualized RDOC systems as features that are measurable in clinical research. For designing this protocol, we used observation, clinical interview, and examination for surveying the cognitive system, emotion system, social system, regulatory system, circadian rhythm, and sensory motor system. This protocol is a screening model for assessing indicators that RDOC has considered for the psychological dimensions. The protocol helps clinical research (besides clinical interview of DSM) to have a comprehensive quantitative and qualitative description, in order to perform personalized assessment. By using this protocol, we have a specific profile of features that can be used for personalized formulation.

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I. Introduction

Transdiagnostic approach is a new way for exploring new diagnostic assessments, that suggests alternative conceptualizations of the processes implicated in mental disorder, and provides a platform for understanding of epidemiology, and clinical treatment [1]. In 2009, the National Institute of Mental Health (NIMH) created the Research Domain Criteria (RDOC) to develop new research approaches to the classification of mental disorders. In this way we can find new classification in mental disorder based on measurable features and depend on psychopath-logical mechanisms. RDOC is a translational approach that considers the important aspects of behavior based on neuroscience research[2].

The RDOC framework include: Negative valence: systems that enable response to aversive stimuli or contexts (e.g., threat, loss, aggression due to frustration); Positive valence: systems that mediate reward-related activity (e.g., approach motivation, reward responsiveness); Cognitive systems, such as attention, perception, and memory; Social processes, such as affiliation and attachment, facial expressions and other social communication, and perception and understanding of the self and others; and Regulatory systems and circadian rhythms: such as sleep-wakefulness, brain stem activation, and arousal systems[3,4] Also, Sensory motor system was added, by NIMH, later. RDOC domains are defined from genome to phenome. Actually, for every system has been defined by gens, molecules, cell, circuits, physiology, behavior, self-report, and paradigms[5]. Also, there are toolboxes and researches have been done for now (refer to the cite of RDOC)[6]. But there is no protocol for assessing all systems in clinical research. Then, the first step for using a transdiagnostic protocol in clinical research is making tools with RDOC concepts. The purpose of this article introduces a transdiagnostic protocol that we designed based on RDOC concepts that can be used in clinical research. We conceptualized features that assess each of these systems. The protocol includes clinical interview, observation, and test. Features and indicators based on emotion system (negative and positive valence), cognitive system, social system, regulatory and circadian system, and sensory motor were defined. Then, after carrying out this protocol, we can have a quantitative and qualitative variable for all of these domains.

a) *Description of Transdiagnostic Protocol that Designed*

We used observation, clinical interview and examination, for surveying cognitive system, emotion system, social system, regulatory system, circadian rhythm, and sensory motor system. In the following, we will explain how to evaluate the features of these systems:

1. *Emotion System:* Based on RDOC, emotion system is defined two parts include negative[7] and positive[8] valence systems. That each of system include sub domains (Fear, anxiety, loss, and …). Features that we considered for screening of emotion system include anxiety, fear, depression, irritability, and aggressive behavior. As well, painful situations that happened to a person, which are divided into childhood and recent traumas. This system is measured with the help of clinical interview. It

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means each of the features are assessed by clinical judgment during clinical interview.

2. *Cognitive System:* RDOC defined wide range of cognitive functions in this system[9]. The features are considered as assessment of cognitive system included concentration, verbal fluency, language, and memory[10]. This system is measured by using clinical interview and parts of Addendrok's Cognitive Examination-C test (ACE[11]. In part of clinical, concentration and memory problems are assessed with questions of concentration and memory in daily life of the patient (normal=0, problem=1). And concentration, verbal fluency, language, and memory are tested based on parts of ACE that are related to concentration (…of 18), verbal fluency (… of 14), language (… of 26), and memory (… of 26).
3. *Evaluation of the Social System:* Social processes responses to interpersonal aspects of various types, including perception and interpretation of environment[12]. In this protocol, we conceptualized as features are evaluated include: relationships between person and outside environment, which includes family relationship, marital relationship, social relationship, job satisfaction, and academic achievement, and daily performance. This part is executed with questions of the patient; for example, are you have any family challenge with family and romantic relationship, have you job satisfaction, have your academic achievement in school and college. Based on the answers of patient we do scoring normal=0, problem=1, highly problem=2.
4. *Evaluation of the Sensory Motor System:* Sensorimotor dysfunction will need to consider distinct to succeed in diagnostic strategies in the identification of novel targets for psycho-pharmacological research and therapy in mental disorders[13].In this system, for screening sensory-motor system, we consider features that include energy, restlessness, psychomotor, tremor, and pain are evaluated quantitatively and qualitatively. Questions of this part include: how is your energy daily (very low=-2, low=-1, normal=0, high=1, very high=2). It needs to explain high and very high mean abnormality of energy that seems in hyper activity. Psychomotor like energy is assessed and scored. Tremor assessment includes examination of tremor in hands, legs and other parts of the body (normal=0, moderate range of tremor=1, severe tremor=2). Pain includes: do you have any pain in head and body (normal=0, sometimes=1, always=2).
5. *Evaluation of The Regulatory System*: Arousal/ Regulatory systems are responsible for generating activation of neural systems as appropriate for various contexts, and providing appropriate homeostatic regulation of such systems as energy balance and sle[14] . General indicators are considered for regulation of the body including heart rate with examination (normal=0, moderate range of heart rate problem=1, sever heart rate problem=2), blood pressure with history of blood test or examination (normal=0, sometimes high blood pressure=1, chronic hypertension=2), blood sugar with history of diabetes (normal=0, borderline blood sugar=1, diabetes=2) blood fat (normal=0, borderline blood fat=1, chronic blood fat=2) breathing (normal=0, moderate range of shortness of breath=1, severe shortness of breath=2), digestive and excretory problem with historical problem and illness like as IBS, constipation, diarrhea (normal=0, moderate =1, severe=2), and hormonal problem with history of thyroid disease, sexual hormone, cortisol and other hormones (normal=0, moderate =1, severe=2).

Also, arousal is a continuum of sensitivity of the organism to stimuli, both external and internal[15]: then we considered appetite, sexual desire, and menstrual period in females. Appetite with question of appetite and changes of weight (low appetite with low weighting=-2, low appetite=1, normal=0, high appetite=1, high appetite with high weighting=2). Sexual desire (very low=-2, low=1, normal=0, high=1, very high=2) Menstrual cycle (normal=0, irregular=1) and PMS (normal=0, moderate PMS=1, severe=2).

Homeostatic and circadian processes regulate the propensity for wakefulness and sleep[16]. Then we considered quality and quantity of sleep in this protocol; by question: do you have any problem in sleeping and awaking like as falling asleep, quality of sleep, low or over sleep (very low or over sleep or very problem in falling asleep and nightmare =2, moderate range of low or over sleep, moderate range of falling sleep, nightmare=1, normal=0).

In the table, we show the structure of this transdiagnostic protocol. It should be mentioned in all items were defined 0= normal, 1=moderate problem, and 2=severe problem

Systems	Domains	Quantitative	Description
Cognition	Concentration test	Based on ACE … 0f 18	Normal/ problem
Cognition	Memory test	Based on ACE … of 26	Normal/ problem
Cognition	clinical concentration	0,1	Normal/ problem
Cognition	clinical memory	0,1	Normal/ problem
Cognition	Verbal fluency	Based on ACE … of 14	Normal/ problem
Cognition	Language	Based on ACE … of 26	Normal/ problem
Cognition	Perception	0, 1, 2	Error/ Hallucination
Cognition	Thought	0, 1, 2	Obsession/ delusion
Emotion	Mood status	0, 1	Depressed/anxious/ irritable/ other
Emotion	Behavior	0, 1	Aggression/abnormal behavior
Emotion	Motivation	0,1,2	Death wish, suicide
Emotion	Childhood trauma	0,1,2	Severity
Emotion	Recent trauma	0,1,2	Severity
Social	Marital relationship	0,1,2	Severity
Social	Family relationship	0,1,2	Severity
Social	Academic achievement	0,1	Normal/poor
Social	Job satisfaction	0,1	Normal/no satisfaction
Social	Social relationship	0,1,2	Severity
Social	Daily functioning	0,1,2	Severity
Sensory motor	Energy of daily	-2 to +2	Very low to high
Sensory motor	Psychomotor	-2 to +2	Very low to high
Sensory motor	Tremor	0,1,2	Severity
Sensory motor	Pain	0,1,2	Severity
Regulatory	Heart rete	0,1,2	Severity
Regulatory	Blood pressure	0,1,2	Severity
Regulatory	Blood sugar	0,1,2	Severity
Regulatory	Blood fat	0,1,2	Severity
Regulatory	Respiratory	0,1,2	Severity
Regulatory	Digestion and exertion	0,1,2	Severity
Regulatory	Hormones	0,1,2	Severity
Regulatory	Appetite	-2 to +2	Severity
Regulatory	Sexual desire	-2 to +2	Severity
Regulatory	Menstruation	0,1, menopause	Normal/PMS
Circadian rhythm	Sleep pattern	0 to 2	Severity

II. Discussion

Exploring and discovering between mental aspects and biology are essential requirements. While classifications of mental disorders based on DSM, are heterogeneous in laboratory studies[17]. As well, imaging and genetic meta-and mega analysis studies conducted on very large samples have not been able to reach specific neurobiology and structural foundations of mental disorders based on DSM classification[18],[19].

So, a transdiagnostic approach is necessary for discovering neurobiology of mental condition in the laboratory [20]. RDOC integrate a wide range of features into the field of mental condition [21]. RDOC helps us for modeling and formulization in the laboratory for finding new assessment and tailoring treatment. Also, according to the World Health Organization (WHO), domains that compose good mental health overlap with RDOC domains. Mental aspects are considered by WHO include: Mental health literacy, attitude towards mental disorders, self-perceptions and values, cognitive skills, academic/occupational performance, emotions, behaviors, self-management strategies and social skills, family and significant relationships, physical health, sexual health, meaning of life, and quality of life [22]; These are related with concepts of RDOC systems.

So, for considering transdiagnostic assessment in mental condition, we need to have a comprehensive and multidimensional view of mental features. This transdiagnostic protocol was designed in order to help conceptualize mental aspects in clinical research. This protocol can provide a screening model for assessing the mental features. For example, for two patients that were diagnosed with Major Depression Disorder, according to this protocol, there may be differences in the features of the five systems (for example: concentration, memory, trauma, sleep, energy, or other features).If personalization is considered, it can lead to a new personalized assessment and subsequently a new formulation. And we can assess various aspects of mental features. In continuation, we will discuss all of the systems.

1. *Emotion System:* Emotional dysfunction and deregulation are considered as the important criteria in mental disorders [23]. We need a transdiagnostic procedure for emotion dysfunction [24]. In DSM, depressed mood is a major symptom that is associated with depression disorders, and anxious mood is a major symptom that is associated with anxiety disorders. But, in clinical practice, changes of mood between depressed and anxious or other mood are usually seen, along 3 to 6 months' duration or even less. Also, there are common dysfunctions of moods between DSM diagnosis (for example: mood disorder/obsessive disorder/anxiety disorder and others).Then we examine mood and childhood trauma and recent trauma. So, if mood dysfunction and trauma exist, we should consider in the formulation and process of treatment. These features are aspects of phenomic symptoms; there is much evidence that cortical[25] and subcortical[26] regions are involved in mood dysfunction. Also, functional and structural abnormalities in cortical and subcortical regions are seen in patients that experienced trauma [27],[28].Regarding basic structures, we can use these features in clinical research with imaging protocol and other laboratory studies.
2. *Cognitive System*: Cognitive dysfunction is significantly associated with mental disorders. Clinically, concentration and short-term memory are major complaints by patients. Cognitive dysfunctions are common in mental disorders[29], such as depressive disorder[30], anxiety disorder, obsessive disorder[31] and other disorders [32]. In this protocol, we assess concentration and memory problems, as well as concentration, verbal fluency, language, and memory with the ACE test. Also, we assess obsessive thought and obsessive behavior, perception, based on clinical interview. Phenomes of cognitive systems and emotion function are related with common networks like Default Mode Network (DMN [33], Central Executive Network (CEN)[34], Salience Network [35] (SN).Also structures of frontal lobe [36], parietal lobe [37], and limbic system[38] are involved in cognitive function and emotion function. Then we can see when emotion function has a problem, cognitive problem can see; so common networks or structures influence each other. Then assessment of cognitive problems can help for formulation in process of treatment and track biological basis in mental studies.
3. *Social System:* Communication, achievements, and daily functioning are important factors for mental health care. Challenges in communication and social support and achievements can affect mental health [39]. In this protocol, family and marital challenges, job satisfaction, academic achievement, social communication, and daily functioning are defined as features of the social system. The consideration of social features can help for formulation of mental health care. Neurobiological evidence expresses that neurotransmitters play an important role in the social system[40]. Also, cortical region, subcortical region, and limbic system are involved in social communication [41], job achievement, academic achievements, and social functioning [42].
4. *Regulatory System:* that system works in order to stabilize homeostasis of the body. There is evidence that dysfunctions in the regulatory system are related to mental conditions. Studies show metabolic syndromes impact mood, appetite, sleep, and mental health[43]. Hypo of hyperthyroidism[44] and sexual hormones[45],[46] interact with depressed and anxious moods or other mental conditions. Diabetesis related to emotional dysfunction[47] and mental condition[48]. And other metabolic syndromes such as hypertension[49], heart rate problem[50], and blood fat [51] impact on mental health. Also, digestion[52] and excretion[53] are accompanied with mental problems, like Irritable Bowel Syndrome (IBS).In this protocol, the important features are considered; that include heart rate, blood pressure, blood sugar, blood fat, digestion and excretion, respiratory, and hormones. Regulatory system is related with Autonomic Nervous System [54] (ANS) (include sympathetic, parasympathetic, and enteric nervous system), hypothalamus- pituitary-thyroid[55] and –adrenal[56] circuits, pineal[57] and melatonin [58], and subsets of these are involved. Considering the regulatory system can help formulation of psychotherapy and pharmacotherapy. We should train the management of chronic disease (likes diabetes) and consider the prescription of medication. Also, most resistance treatments usually have problems in the regulatory system, for instances, cortisol hor[59], or hyper/hypothyroidism[60], then should be considered in the process of treatment. Sleep problems are one of the major complaints in patients with mental disorders[61]. The patients suffer from appetite problems with low or over being weight along with mental disorder[62]. Also, problems in sexual desire or sexual dysfunction[63] are seen. As well, menstrual problem scan relate to mental disorders[64]. So, features that were defined for regulatory system and circadian rhythm can help to personalized formulation. Also, using these features in clinical research can help to find basic biology in mental disorders.
5. *Sensory and Motor:* In this protocol, energy, psychomotor problem, restlessness, pain, and tremor are considered. Based on evidence, anatomy that controls sensory motor system include cortical and subcortical cortex [65], [66], autonomic nervous system [67], and neurotransmitters [68], [69]. Sensory motor system in treatment should be

considered for improving activity of patients and somatic pain in psychotherapy and pharmacotherapy.

Based on this protocol, patterns of profiles can show dysfunction in two systems, or three systems, or four systems, or every five systems. For instance, one type of patient suffers from the features of cognitive systems, emotion system, and circadian system (three systems). Other type of patient suffers from the emotion system, the social system, the sensory motor, and the cognitive system (four systems). It should be mentioned, cause and effect between systems has not been determined, yet. But the features designed in this protocol have a neurobiology basis in cortical and subcortical regions, ANS, networks, hormones, and neurotransmitters; So, this transdiagnostic protocol can help in biological research strategies in mental disorders. In formulation, the features of the systems can be considered as the form of a network. Every one of the features is defined as a node in the network; So, dysfunction of the features is considered an anomaly in the mental network. The features that are considered as nodes work dynamically; for instance, at the first assessment the patient suffered from depressed mood and low sleep, but after two month he/she suffered from anxious mood, high sleep, low appetite and other features. Actually, the features may impact on together and they are dynamic, albeit biological bases may change or don't. But important aspects of mental disorder are assessed and problematic features are identified, then personalized formulation is done. Process of treatment is started and continues with the goal of improving the mental disorder. In future direction, clinical cohort study and validation of protocol are recommended.

Summary of Advantages of the Protocol:

1. This transdiagnostic protocol has a comprehensive and multidimensional view in mental aspects.
2. With using this protocol, we can assess domains of RDOC systems.
3. Although all of the features of the systems are measured by this protocol, it does not take much time, and for every clinician is accessible.
4. Also, severity of dysfunction in all of systems is visible as the forms of quantitative and qualitative features.
5. Because this protocol is done after a clinical interview based on DSM, in clinical process and study, we have no potential risk.
6. Generally, we can do personalized formulation in all of cognitive, emotion, social, regulatory, circadian rhythm, and sensor motor systems.
7. Eventually, this protocol can help to track the neurobiological basis of mental disorder.

Summary of Limitation of the Protocol:

1. This protocol needs clinical judgment, which can have different results by two clinicians.
2. This protocol can be done as clinical interview by just clinician, and it is not self-report.
3. This protocol is a suggestive model which should be valid. Also, other features might be important to add in future researches.
4. For formulation, prioritizing of features is dependent on clinical judgment of the clinician.
5. Still cannot define specific biological basis for every features.

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Conflict of Interest Statement: The authors whose names are listed certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethics Approval: This article just a suggestive protocol and there is no intervention or data sampling, then it doesn't need Ethical code.

Consent to Participate and Publication: We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication.

Availability of Data and Material: The protocol in the manuscript clearly was explained and transparency was highly considered.

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