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Biobehavioral assessment of the anxiety disorders: Current progress and future directions

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Abstract

It is difficult to accurately assess and differentially diagnose the anxiety disorders. The current system of assessment relies heavily on the subjective measures of client self-report, clinical observation, and clinical judgment. Fortunately, recent technological advances may enable practitioners to utilize objective, biobehavioral

measures of assessment in a clinical setting. The current body of literature on two of these biobehavioral tools (eye-tracking and electrocardiogram devices) is promising, but more validation and standardization research is needed to maximize the utility of these devices. Eye-tracking devices are uniquely capable of providing data that can be used to differentially diagnose anxiety disorders from both other commonly comorbid and misdiagnosed disorders. Both eye-tracking and electrocardiogram devices are able to provide change-sensitive assessment information. This objective, real-time feedback can assist clinicians and researchers in assessing treatment efficacy and symptom fluctuation. Recently developed wearable and highly portable electrocardiogram devices, like the wearable fitness and behavior tracking devices used by many consumers, may be particularly suited for providing this feedback to clinicians. Utilizing these biobehavioral devices would supply an objective, dimensional component to the current categorical diagnostic assessment system. We posit that if adequate funding and attention are directed at this area of research, it could revolutionize diagnostic and on-going assessment practices and, in doing so, bring the field of diagnosis out of the 20th century.

Key words: Biobehavioral; Assessment; Diagnosis; Anxiety; Electrocardiogram; Electrocardiogram; Eye-tracker

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Core tip: Anxiety disorders are some of the most commonly comorbidly- and mis-diagnosed disorders in the DSM-5. The current system of assessment and diagnosis depends on clinician and client report measures, which are subjective and prone to bias. Recent technological advances make it possible to utilize the biobehavioral measures from eye-tracking and electrocardiogram devices in clinical settings. These devices can provide a much needed dimensional, objective, and change-sensitive component to current diagnostic and treatment-efficacy assessment protocols. This article summarizes the

status of and outlines future directions for research on this important topic.

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INTRODUCTION

While the Diagnostic and Statistical Manual of Mental Disorders (DSM) has been the guidebook to the assessment for psychiatric disorders for more than half of a century, its system of diagnosis has been fraught with flaws, concerns, and issues since its inception. Each revision of the DSM has sought to correct the flaws of the preceding revision, resulting in so many changes that the first edition of the text bears little resemblance to the most recent edition, the DSM-5^[1]. Each of these editions have been built on the same principle: Developing a system of discrete categorical diagnoses which are determined by a list of symptom criteria—the presence or absence of which are determined by tools of client self-report, clinical observation, and clinical judgment^[2]. Once a diagnosis is determined, those three tools are used in the ongoing assessment of symptom severity to determine treatment efficacy. Despite the advances made over the past several decades, there are still serious problems with this current system of assessment. Excitingly, recent technological advances and research breakthroughs in biobehavioral tools of assessment may help address these issues to build a sounder system of diagnosis and a sensitive system for assessing the fluctuation of symptom severity, particularly in the realm of anxiety.

The DSM-5's categorical system presumes that mental disorders are discrete issues with distinct boundaries^[1], however this concept is not reflected in the research^[3]. For people with anxiety disorders having comorbid disorders may be more common than having a single, discrete disorder. For example, one study found that 89% of people with an anxiety disorder were also diagnosed with a disorder of a different category^[4]. One reason for this is that there is considerable overlap in the diagnostic criteria between some of the anxiety disorders and other categories, such as the depressive disorders^[5]. While many people who are diagnosed with dual or multiple disorders may truly have two (or more) discrete disorders, a dual diagnosis in some people can instead be due to a single underlying issue that presents in such a way to cause a dual diagnosis with the current nosology^[6]. A separate study indicated that approximately one third of participants with at least one anxiety disorder diagnosis also qualified for at least one or more additional anxiety disorder diagnosis^[7]. Comorbidity in anxiety disorders

is associated with difficulties in determining treatment path^[8] and worsened clinical outcomes related to course of treatment^[9].

While the DSM-5 was being developed, the task force considered adopting a dimensional model of psychopathology, in contrast to the current categorical system^[2,10,11]. The dimensional model looks at disorders as not having a single distinct cut off point, and allows for multiple dimensions in a diagnostic model, such as intensity, duration, and level of disruption caused by a disorder's symptoms and components^[10]. Most advocates for this system suggested the integration of a dimensional component into the categorical system to provide a fuller diagnostic picture that would be more functional for clinical application^[2,12]. Some sections of the DSM-5 diagnostic structure included a quasi-dimensional element, by including specifiers that categorize severity of symptoms as "Mild", "Moderate", or "Severe"^[1]. Unfortunately, the dimensional model was not incorporated into the DSM-5 diagnostic structure for anxiety disorders in any way, shape, or form^[1]. Since its publication, the debate has continued as to whether the DSM's categorical model should continue to be revised to a more dimensional structure^[13].

One reason the dimensional model was not incorporated into the DSM-5 was the lack of a single, standard, empirically-supported, and widely-agreed upon measurement of assessment for the dimensional system for the anxiety disorders to be based upon^[10]. This issue may be tied to another problem in the current system of assessment for anxiety disorders: Dependence on accurate self-reports by the client and accurate clinical observation and judgment. Reflecting this, there was disagreement about whether a dimensional scale would rely primarily on clinician ratings or client self-ratings^[10]. Both sources of information are subjective, of course, and thus highly flawed. As but one example, client self-report and clinician-report on psychological measures do not necessarily agree with one another^[14]. Accurate self-report requires high levels of insight and complete honesty on the part of the client. Many clients cannot or will not accurately perceive their thoughts and feelings or the reasonableness of those thoughts. This is widely understood, as evidenced by the DSM-5's addition of a level of client insight specifier for disorders like obsessive compulsive disorder (OCD)^[11]. Even if clients do have a clear understanding of their symptomatology, one study found that 93% of clients purposely lie to their mental health practitioners, with the most frequent lies being about the severity of the symptoms and how badly the client feels^[15]. Additionally, there is considerable error in self-reporting for observable behaviors such as physical activity^[16], so even the reports of clients trying to be accurate with fair insight into their psychological state may be inaccurate due to biases and memory errors.

Similarly, clinical judgment is also prone to errors and biases. Clinicians are susceptible to the all common human information processing errors^[17-19]. One of the most notable information processing errors in assessment

is stereotyping^[18]. Clinicians often make decisions of diagnosis based upon how much a client resembles their own personal prototype, a mental conception for the most typical client with that diagnosis^[19]. As such, clinicians' diagnoses can be influenced by client characteristics that are not related to diagnostic criteria, such as race, sex, and occupation^[20-22]. The inflexibility of this prototypical stereotype bias can quite often lead to misdiagnosing clients^[19]. Unfortunately, the issue of practitioner information processing errors is not easily remedied; clinical judgment improves only slightly with education, training, and/or experience^[23,24]. This may partially be since it is rare for clinicians to receive timely and effective feedback about their decisions^[17]. Clinicians may engage in faulty strategies when hypothesis testing^[24], often falling prey to confirmation bias by unwittingly seeking information that confirms the accuracy of their judgment as opposed to seeking out information that would refute it^[25]. Accurate feedback may be essential to the process of learning from experience^[26], though the literature is still unclear as to whether this is true specifically for clinical judgment^[23].

The concerns of client self-report and clinician judgment extend beyond just the initial diagnosis. Disagreement between client self-report and clinical judgment occurs before treatment and at the end of treatment^[14], impacting treatment efficacy assessment. This is true for both clinical trials and individual case formulation, and can lead to erroneously continuing ineffective treatment, discontinuation of effective treatment, or prematurely terminating treatment with individuals who would benefit from further services. A more objective and change-sensitive method of assessment would provide the clinician with immediate feedback to reduce the prevalence of these treatment plan errors.

In summation, the DSM-5 used a categorical system for diagnoses whose severity and type appear to be better represented on a dimensional scale^[27,28] and the standard practice of assessment uses a variety of kinds of client self-report and clinical judgment measures, which are both highly subjective. In addition to these general issues, the problems with the current diagnostic and assessment system for anxiety disorders specifically are many and varied. This has led in part to the anxiety disorders being among the most misdiagnosed^[29]. Because of the flaws in the current system, we suggest that the development, integration, and adoption of a more objective and change-sensitive measure of diagnostic status is imperative. We propose that one or more standardized biobehavioral methods of assessment may be the solution.

Why do we use the term biobehavioral? Years of medical and psychological research have demonstrated that psychological conditions have significant physiological impacts, and vice versa^[30]. For example, many people suffering from clinical depression show cellular alterations that result in lower levels of immunity than healthy populations^[31]. Many diseases progress more

rapidly when accompanied by poor mental health^[32]. Inversely, physical conditions such as chronic pain can have deleterious effects on mental health^[33]. Integrating psychological, behavioral, and biological factors when studying or improving mental health is referred to as the biobehavioral approach^[30]. This approach affords clinicians and researchers quantitative information about an individual, and increases the resources available for treating mental health conditions.

Vast advances in a variety of biobehavioral measurement tools have been developed and refined across the last 30 years. Biobehavioral devices provide unbiased reports of physical behavior and biological processes. Electrocardiogram (ECG) and eye tracking devices are powerful and sensitive tools of biobehavioral assessment that were traditionally limited to only top of the line medical and research facilities due to their once exorbitant cost. Recently, more cost effective versions of these devices have been developed which greatly increases the accessibility and utility of such tools for clinical settings. Despite their greatly decreased cost, the sensitivity of these tools are very promising for identifying unique symptoms of anxiety disorders salient to accurate differential diagnoses^[34]. Incorporating a biobehavioral, dimensional component to the DSM's categorical system of diagnosis would make psychiatric classification more in line with other medical classification systems^[13]. For instance, hypertension is diagnosed partially based upon a doctor's clinical judgment, but is accompanied by physiological, dimensional measures, namely systolic and diastolic blood pressure reading^[13].

The purpose of this paper is to discuss the current research status of two of the most well-researched and easily accessible biobehavioral tools and suggest future research directions to be taken to validate and incorporate their use in both diagnostic assessment and treatment outcome evaluations. First, the basic characteristics of several anxiety-related disorders and commonly co-occurring disorders will be reviewed. Second, a summary of the data captured by eye-tracking technology and a description of several affordable tools that are currently available is provided, followed by a review of the available literature on the discriminative ability of eye-tracking research. Third, descriptions of the most relevant information captured through ECG devices and affordable devices available are presented, along with how this data can assist in monitoring real-time change in symptomology.

ANXIETY AND RELATED DISORDERS

The DSM-5 taxonomy is loosely based on clustering disorders by similar symptomatologic features, but not necessarily by similarities in clinical presentation such as age of onset^[13,35]. The specified DSM-5 disorders placed in the category for anxiety disorders are separation anxiety disorder, selective mutism, specific phobia, social anxiety disorder (SAD), panic disorder (PD), agoraphobia, and generalized anxiety disorder (GAD).

A more accurate term for this group may be fear and anxiety disorders, because while these constructs are interrelated, they are different, and some of these disorders have a much more prominent fear component while others are more anxiety-based^[2,35]. Fear is an emotional, cognitive, and physiological response to and directed at a present threat^[36]. Anxiety is also a distressing emotion, but it is typically characterized by future-oriented, threat-focused cognitions and a perceived state of ambiguity or uncertainty^[36]. Both anxiety and fear states are characterized by heightened autonomic arousal which is demonstrated through multiple physiological reactions.

There is little to no research on the biobehavioral reactions of individuals with separation anxiety disorder, selective mutism, PD, and agoraphobia. For this reason, this paper focuses on GAD, specific phobia, and SAD. GAD is characterized by excessive and uncontrollable worry. The symptoms are the result of the interaction between cognitive and physiological responses to imagined or perceived threats^[37]. Individuals with GAD are consumed by monitoring and avoiding potential sources of threat and danger. Specific phobias are characterized by an immediate, extreme, and persistent fear toward an object or situation, and thus are more fear-based than anxiety-based^[1]. SAD is characterized by persistent fears of social interactions or situations in which criticism and rejection by others is possible^[1]. Individuals with SAD are extremely critical of their social performance and are anxious about whether they will be able to make positive impressions or live up to social expectations^[38].

The anxiety disorder cluster is, by no means, a comprehensive grouping of all disorders with a significant anxiety component. Several other disorders are also defined in part by extremely high levels of anxiety. Most notably, posttraumatic stress disorder (PTSD) and obsessive compulsive disorder (OCD) are comprised of symptoms that clearly denote high levels of anxiety. To qualify for a post-traumatic stress disorder diagnosis a person must experience a traumatic event and then experience intrusive dreams, memories, dissociative, distressing, and/or physiological reactions and hyperarousal that lasts for at least one month in duration after experiencing the traumatic event^[1]. Obsessive compulsive disorder is characterized by obsessions and/or compulsions. Obsessions are unwanted and intrusive images, impulses, thoughts, or ideas that are threatening, nonsensical, disgusting, or obscene^[39]. These obsessions are categorized into six categories: Contamination, violence, sex, religion, the need for exactness, or responsibility for harm^[40,41]. Each type of obsession causes distress and functional impairment. Most people with OCD also experience compulsions, the strong urge to engage in an action, whether mental or physical, to reduce the anxiety caused by the obsession^[39]. The overlap in diagnostic criteria for PD, agoraphobia, social phobia, specific phobia, GAD, OCD, and PTSD can make diagnosis

based on self-report and clinical judgment difficult. For example, a fear of dirt can either be part of a specific phobia or a component of OCD for an individual with a contamination obsession. Fear of a location could be associated with a specific phobia, be related to a fear of being unable to escape (as in Agoraphobia), tied to a traumatic event, or be due to fear of being judged by the people in that location (as in SAD). Under the current diagnostic system, accurate and thorough client self-report is imperative to correctly categorizing these symptoms into the appropriate diagnostic box, which as previously discussed, is unlikely to consistently occur.

In addition to the issue of co-occurrence and misdiagnosis within the fear and anxiety related disorders, the disorders also frequently co-occur with and are misdiagnosed for disorders from other categories. There are relatively high rates of co-occurrence between major depressive disorder (MDD) and each of the disorders mentioned above, particularly with GAD^[42]. Major depressive disorder has so much in common with GAD and PTSD, that an alternate empirically-based structure was proposed for the DSM-5 with MDD, GAD, and PTSD in a category together called "Distress Disorders", while the other disorders listed above were placed in a separate "Fear Disorders" category^[13,35]. There is also significant overlap between the anxiety disorders and attention-deficit/hyperactivity disorder (ADHD), with nearly half of the individuals with an ADHD diagnosis having a comorbid anxiety disorder^[43]. However, this is, likely, partially due to misdiagnosis^[44]. ADHD is characterized primarily by impulsivity and inattention^[1]. People with high levels of anxiety often have difficulty concentrating and maintaining attention^[45]. They may also act abruptly in ways that appear highly impulsive, due to their desire to avoid fear-inducing stimuli or, in the case of OCD, due to a compulsion to complete certain behaviors. Understanding a client's internal processes related to these behavioral symptoms is imperative to accurate differential diagnosis between these disorders. Self-report can be a helpful tool to this end, but biobehavioral measures of physiological markers through eye-tracking can provide insight into internal processes which may assist in differentially diagnosing ADHD and MDD from disorders like OCD, PTSD, GAD, SAD, and specific phobia, especially in cases where a client has a lack of insight or where there are barriers to accurate verbal communication. Eye-tracking and ECG devices can also provide clinicians with detailed and change-sensitive measures of symptomatology which can assist in evaluating the course of a disorder and efficacy of treatment.

EYE TRACKING AND ANXIETY

Eye-tracking technology has made it possible to measure certain physiological markers, that contain covert information about individuals, such as pupil dilation, eye-movements, and fixations^[46]. For example, due to the established relationship between dopamine

and blinking, blink rate has been frequently used as a marker for dopamine^[47]. Additionally, changes in pupil size when viewing sad stimuli has served as a predictor for depression^[48]. The eye has many behaviors, each one indicative of other things happening within the individual. For our purposes, there are three important behaviors of the eye that eye-trackers are successful in accurately measuring. First are saccades, those rapid eye-movements that occur consciously and unconsciously when changing fixation points^[45]. These are one of the most common types of eye-movements and the ones typically measured when using eye-tracking technology^[49].

Second are fixations, purposeful stops of the eye on a specific part of the visual environment and represent where visual attention is being allocated^[45]. A fixation occurs between saccades when the eye is stationary, and are valuable for several reasons. First, they show the type of stimuli on which a person is focused (e.g., sad faces). Second, the frequency and duration of fixations can yield information about an individual's condition (e.g., fixation duration can be indicative of current mood)^[50]. Lastly, different stimuli can change an individual's fixation patterns, which can in turn influence how the stimuli are perceived by the viewer^[51,52].

The third behavior is pupillary size, which has served as an indirect measure of neurological functioning for many years in the medical field^[53]. Pupillometry, the method of recording pupil diameter, has made its way into other fields and is now commonly used as an indirect measure of cognitive load, attention, and emotional arousal in psychology^[34,54]. As previously discussed, clients are not always honest, and many times, they are unaware of certain relevant information about themselves. The pupil is a gateway to certain aspects of the brain and can make this hidden information accessible. For example, pupil diameter increases when a person is looking at emotionally arousing stimuli as opposed to neutral stimuli^[34]. This can expose how certain things may influence more emotional arousal than others, even if the client has no desire or ability to communicate these differences. Incorporating measures of pupil diameter into a treatment plan would also be beneficial in instances where a client is experiencing anxiety, but is unable to pinpoint the major sources responsible for his anxiety. Tracking his pupil dilation while looking at stressful stimuli could reveal the primary areas of struggle.

The evolution of eye-trackers has paralleled that of computers. They have transformed from machines of massive proportions and immense costs to easily portable and affordable devices. Eye-trackers today come in a wide variety of sizes, prices, and capabilities. Eye-trackers recording at the minimum of 60-Hz have been validated as capable of accurately measuring pupil dilation^[55]. Most affordable eye-trackers on the market are capable of measuring at 60-Hz and above. One of the leading companies manufacturing portable eye trackers is Tobii. This Stockholm-based company sells

small, easy to set up, portable eye trackers for as low as € 159.00. The company Smooth Eye offers an eye tracker that samples at 1000 Hz, and they can design a customized eye-tracker to meet the client's needs. Pricing varies depending on the features wanted by the client. The Pupil Headset by Pupil Labs (€ 1640) is a complete headset that the client can wear for hours at a time without worrying about wires or remaining in the same spot. It is also possible to simply make an eye tracker; many websites offer step-by-step guides to building affordable eye-trackers. These are only a sample of the companies offering affordable eye-tracking devices. There are many more and each one offers different services and software. The affordability and portability of current eye-trackers make it possible for eye-tracking to become a standard tool used in psychology, and it may almost be time to move them from the research laboratory to the clinician's office. There is a great deal of promising research wherein eye trackers demonstrate their ability to assess types of anxiety (Table 1), but a consistent method of doing so has yet to be developed.

Using eye tracking to assess type of anxiety

One of the most common and useful behaviors that eye tracking technology captures is attentional bias. Attentional bias is the tendency to attend to certain stimuli at the expense of others, and is one of the most commonly measured behaviors in mental health-related eye-tracking studies^[56]. This bias is shaped by an individual's experiences and mental states. For example, people struggling with depression tend to focus on negative stimuli, while people with PTSD tend to focus on threatening stimuli^[57,58]. Negative attentional biases often turn into a malfunctioning cycle because the mental state that developed these negative attentional biases is only receiving reinforcing feedback, thus maintaining the condition^[59]. Fortunately, maladaptive attentional biases can change through treatment, and the progress of this change can be tracked through eye movements^[60].

In addition to providing insight into cognitive aspects, eye-tracking methods can also yield useful data that can help distinguish between commonly confused conditions^[61]. As previously mentioned, there is significant overlap between certain anxiety disorders and depression. People with anxiety display an orienting bias making them faster at detecting threatening stimuli^[62]. Additionally, people with anxiety make more frequent eye movements^[62]. Neither of these features are present in depressed or healthy populations^[50]. People with GAD selectively attend to different stimuli than people with depressive disorder and nonclinical populations. Interestingly, individuals with GAD who are not depressed orient to threatening faces before neutral faces^[63-65].

Eye-tracking studies on depression have found that depressed clients with no anxiety do not display hypervigilant eye-movements, but instead have longer

Table 1 Eye-tracking differences across DSM diagnoses

Eye tracker information pertinent to differential diagnosis	Anxiety	Generalized anxiety disorder	Depression	Phobia	SAD	Post-traumatic stress disorder	Obsessive compulsive disorder	Attention-deficit hyperactivity disorder
Attentional Bias (the tendency to attend to certain stimuli at the expense of others)		Tend to focus on threatening stimuli. Selectively attend to more threatening stimuli	Tend to focus on mood-congruent stimuli (<i>e.g.</i> , SAD, negative)	Tend to avoid feared stimuli	More sensitive to faces showing emotion over neutral faces	Tend to focus on threatening stimuli	Tend to focus on aversive stimuli	
Orienting Bias (faster detection of certain stimuli)	Faster detection of threatening stimuli	Faster detection of threatening stimuli. Orientation to threatening faces before neutral faces	Slower to detect threatening stimuli (compared to anxiety or generalized anxiety disorder)	Faster orientation to feared stimulus		Faster detection of threatening stimuli		
Frequency of eye movements	Higher frequency of eye-movements	Higher frequency of eye-movements	Slower frequency of eye movements than in anxiety or generalized anxiety disorder				More fixations during a visual search task than anxiety and nonclinical populations	Higher frequency of eye movements
Engagement/disengagement of stimuli				After detecting feared stimulus, quick disengagement with the stimulus	Takes longer to disengage from a threatening facial expression than other expressions	Do not show the same type of disengagement as people with a phobias		
Stimulus avoidance			Lack of interest in positive stimuli - focus instead on mood-congruent stimuli	After detecting feared stimulus - quick disengagement and avoidance of feared stimulus	Avoidance of eye-contact and faces in general, even if faces are pleasant. Correlation between severity of SAD and the amount of gaze avoidance			
Fixations, saccades, and pupil dilation	Make less fixations (closer to nonclinical populations) than people with obsessive compulsive disorder during a visual search task		Longer fixations on mood-congruent stimuli than those who have anxiety			Greater pupil dilation in general than nonclinical populations	Longer and more frequent fixations towards aversive stimuli. Deficits in goal-oriented visual tasks (higher error rates, inaccurate eye movements for the specific task)	Premature saccades occur more frequently than in nonclinical populations. Higher error rates on anti-saccades tasks than non-clinical populations

SAD: Social anxiety disorder.

fixations on mood-congruent stimuli (*e.g.*, sad faces), and show a lack of interest in positive stimuli^[50,66,67].

Some researchers refer to these tendencies as the double attentional bias, increased attention to sad faces along with decreased attention to happy faces^[68]. Clients with comorbid anxiety and depression pay attention to both types of stimuli^[66,67].

Phobics show specific orienting biases as well. People with phobias are faster at detecting their feared stimulus than normal populations^[69]. Unlike in people with PTSD, people with phobias tend to disengage with the threatening stimulus and avoid looking at it. While this behavior can occur in people with other types of anxieties, it is most pronounced when an individual with a phobia is presented with the feared stimulus^[50].

Gaze avoidance, or not looking at a stimulus, is easily measured with an eye-tracker, and is a physiological response that can consistently discriminate SAD from other disorders. Socially anxious individuals avoid making eye contact and looking at faces, whether a face is happy, negative (e.g., angry or sad), or neutral^[70]. Despite this consistent avoidance, these individuals rate these smiling faces as pleasant. This discrepancy between self-reported information and biobehavioral observable reaction exemplifies the unfortunate difficulty experienced by clinicians relying on self-report.

People with SAD avoid eye contact when receiving feedback whether it is positive or negative, a behavior not seen in people with GAD, depression, or PD^[71]. Although people with SAD avoid eye contact, they are more sensitive to faces showing emotion than neutral faces, and take longer to disengage attention from threatening facial expressions, such as faces expressing disgust^[72] and anger^[73]. Additionally, there is a correlation between the severity of SAD and the amount of gaze avoidance, making it possible to determine a client's level of social anxiety through eye-tracking tests^[63].

Eye-tracking studies show that people suffering from PTSD orient faster to threatening stimuli and show greater pupil dilation than nonclinical populations^[74]. People with PTSD show an attention bias towards trauma-related stimuli over general threatening stimuli, a bias not seen in healthy populations^[74]. For example, one study showed that people with a PTSD diagnosis made more initial fixations to threatening words than people who had experienced a trauma but did not qualify for a PTSD diagnosis^[51]. Pupil dilation differences in PTSD populations have also been reported, but more research is necessary for consistency. One study reported that people with severe symptoms of PTSD showed greater change in pupil dilation when viewing negative versus neutral images, followed by people with mild symptoms of PTSD, with nonclinical populations showing the least amount of change in pupil dilation^[75]. Another study failed to replicate this result, and found that people with a clinical diagnosis of PTSD had greater pupil dilation when viewing both neutral and threatening images than people who had experienced trauma but did not have enough symptoms for a PTSD diagnosis. There were no differences in baseline pupil dilation

between groups, indicating higher levels of autonomic arousal in the PTSD group^[51], which can be measured using pupil dilation as a marker.

There are inconsistencies in the research on the type of attentional biases displayed by populations with PTSD. Three different types have been reported: Facilitated attention (attending to threatening stimulus first), delayed disengagement (difficulty disengaging from threatening stimulus), and/or attentional avoidance (avoiding the threatening stimulus after it has been detected)^[76]. While some have found evidence for attentional avoidance, most studies have seen facilitated attention and delayed disengagement^[75]. A likely reason for this divide is the different experimental methods used in the studies. The inconsistencies in the methodology, type of stimuli, and type of task performed by participants are a likely reason for this disparity. Eye-tracking studies using similar methodologies have seen more consistent results^[74].

People with OCD have shown deficits in performance on goal-oriented visual tasks in eye-tracking studies, particularly higher error rates and inaccurate eye movements^[77]. Populations with OCD also tend to make longer and more frequent fixations towards aversive stimuli, a finding that could help identify obsession-type for clients^[78]. Another eye-tracking study by Toffolo *et al.*^[79] found that participants with OCD searched for longer and made more fixations during a visual search task than either participants with anxiety or a control group, a finding that helps differentiate the diagnosis of OCD and other anxiety disorders with biobehavioral data.

ADHD and anxiety disorders can often look similar at first glance. This can lead to mistakes in diagnoses and inefficient treatment plans for clients. Some of the deficits experienced by ADHD sufferers can be seen using eye-tracking methods. Eye-tracking studies have consistently found that people with ADHD make premature saccades more frequently and have higher errors on anti-saccades tasks than normal populations^[80,81]. These patterns reflect difficulties with inhibition, which is reciprocally related to impulsivity, and could be used to help avoid misdiagnosis.

Eye-tracking data have also demonstrated an impressive predictive ability. Several studies have found that difficulties disengaging visual attention predicts negative affect^[82,83]. Difficulty disengaging visual attention, especially from negative stimuli, is characteristic of people suffering from depression or dysphoria^[84-86]. Another study found that the eye-movements of anxious teenagers were more successful in predicting depression two years later than their own self-reported symptoms^[82]. While additional research is needed, these promising findings on predictability show yet another potential component of eye-tracking methodology.

Eye-tracking research is beginning to shed light on new ways to differentiate diagnoses. However, there are contradictions in the literature that merit focused

attention and more research. For example, some studies have found that people with anxiety were slower in naming words related to their anxieties when compared to words that had nothing to do with their anxieties^[59,87]. This contradicts the more common notion that people are faster at detecting stimuli related to their anxiety. Although these findings are contradicting, they still show that differences exist between participants with anxiety and healthy controls. It is necessary to conduct more research so that consistent findings can allow for the implementation of eye-tracking techniques in clinical settings.

HEART RATE VARIABILITY RESEARCH

The autonomic nervous system (ANS) regulates adaptive behavioral and physiological responses to environmental stress. Individuals with mood and anxiety disorders exhibit dysfunctional ANS regulation. The heart is an ideal and widely measured organ for assessing the influence of the ANS^[88], with heart rate variability (HRV) having been studied extensively. HRV is the variation of heart period over time, measured by ECG, and is a physiological indicator of cardiovascular health, predictor of mortality, and an important biomarker of psychological well-being^[89]. There are several heart rate frequencies and each of them are influenced by different factors^[90]. High-frequency HRV (HF-HRV) is associated with respiratory rhythm and it is regulated by parasympathetic neuroanatomical structures^[91]. HF-HRV is reduced in participants with anxiety disorders compared to healthy controls^[92].

Higher resting HF-HRV is associated with greater ability to regulate stress, attention, and emotional arousal^[93,94]. Low levels of HF-HRV regulation indicate poor social and emotional regulation, and in some cases have been associated with psychiatric disorders^[95]. For example, children with behavioral problems have lower HF-HRV, while children with reliable and stable HF-HRV display fewer behavioral problems, decreased negative affectivity, and better social skills^[96]. Higher HF-HRV has also been correlated with greater affect expressivity^[97]. Outside of mental health, physical factors including cardiovascular risk^[98], diabetes, and obesity are related to low HF-HRV^[99].

The 12-lead electrocardiogram has been used for diagnosis of heart disease and cardiac screening measure for over 100 years^[100]. However, a smaller number of ECG leads are sufficient to gather the required information to guide clinical practice and decisions. Advances in wireless technology and mobile communications enables real-time ECG recording directly from smartphones and tablets without the need for ECG machines, cumbersome leads, or trained professionals. Currently, there are several small cost-friendly devices that can record, monitor, and transmit ECG signals. These devices allow the possibility to record ECGs outside the laboratory in cost-efficient and timely manner. These mobile ECG work without

electrodes attached to the skin and burdensome experimental demands on the participant.

The AliveCor (\$99) device consists of a bipolar electrode case that fits on a smartphone to record cardiac electrical activity and software to process the information from the single lead ECG. The QardioCore (\$449) is a wearable ECG strap that is worn below the chest. The QardioCore records ECG measurements and sends them directly to a user-friendly application for mobile devices. The Cronovo (\$150) is a smartwatch with the capability of recording ECG and translates the data in real time for the consumer. The Lief Smart Patch (\$229) is a device that is worn directly on the skin that is capable of continuously recording HRV and providing direct biofeedback relaxation exercises.

The AliveCor can record accurate baseline measurements and detect cardiac abnormalities^[100]. Furthermore, participants preferred the mobile ECG devices to conventional 12 lead ECG because it less burdensome and allows data to be shared directly with their healthcare providers. Mobile ECG acquisition is more cost-friendly, faster, less burdensome, and allows clinicians to review data remotely. The mobile technologies make it easier to record ECG at any time and allows for clinical studies to be conducted on a new scale. It is now possible to collect ECG data from individuals from several different countries and populations quickly and cheaply. However, some of the devices are unable to continuously record ECG data, but those devices would dovetail nicely with ecological momentary assessment studies and provide an objective measurement along with self-report. Several of these devices have not been fully vetted by empirical studies. Therefore, future research is necessary to support the usage of these devices for diagnostic assessment and treatment outcome.

The wearable health and fitness device market is growing; it is estimated that 19 million people will be wearing this technology in the next 5 years^[101]. In October 2014, the FDA approved the use of smartphone ECG, before devices were restricted to heart rate and activity monitoring. Future technological advancements in wearable health monitoring will more than likely include continuous ECG recording.

Clinical applications of measuring HRV

Coupling mobile HRV with biofeedback is an effective treatment for anxiety disorders^[102,103]. HRV biofeedback reduces autonomic hyperactivity and helps the individual learn how to regulate homeostatic mechanisms. HRV biofeedback promotes relaxation and increases vagal activity^[104]. Mobile biofeedback devices are beneficial because they provide patients with an objective measure of their physiology, rather than only relying on subjective self-report.

In the anxiety related disorders there are symptoms that denote the involvement of the ANS^[105]. These include rapid breathing, suppressed digestive processing, pupil dilation, endorphin release, heart palpitations, and reflex acceleration^[104,106]. These

physiological responses prepare the body for action and are adaptive responses when real danger is present, but this response system is maladaptive when no actual danger is present, as often occurs in the anxiety disorders^[106]. Individuals with clinical levels of anxiety exhibit less suppression of HF-HRV^[107]. Poor HF-HRV regulation in adults has also been associated with greater social anxiety^[108]. The close link between HF-HRV and anxiety disorders has been examined in PD^[109,110], in GAD^[111,112], SAD^[110], and PTSD^[113].

The subjective experience of SAD is extremely distressing, as are the physiological sensations associated with the disorder (e.g., palpitations, sweating, tremors, muscle tension, blushing, diarrhea, gastrointestinal discomfort). SAD is characterized by social avoidance and disengagement, which are associated with dysfunctional autonomic processes. These dysfunctional autonomic processes are exhibited through social inhibition, emotional dysregulation, and fear. Individuals with SAD exhibit diminished HRV during baseline measures compared to healthy controls^[114].

GAD is associated with physical symptoms of restlessness, fatigue, difficulty concentrating, irritability, muscle tension, and sleep disturbance^[11]. Individuals with anxiety disorders such as GAD, do not show typical cardiac vagal activity in response to threat. Individuals with GAD display a reduction in HRV through a lack of autonomic reactivity^[115]. Individuals with GAD have high stable heart rate and low HRV^[88]. Empirical studies find that worry suppresses HF-HRV in non-anxious controls^[116]. Worrying thinking before exposure to imagery inhibits cardiovascular activity^[117]. Inducing worry suppresses HF-HRV in both non-anxious and anxious individuals^[118].

There is some variability among the anxiety disorders in physiological response. For PD there is some degree of fight-flight behavioral and physiological reaction. Individuals with PD exhibit reduced HRV^[119,120] and dysregulated respiratory system^[115-116], which suggests dysfunctional vagal activation and hyperactive sympathetic processes during challenging situations^[105]. Conversely, during non-challenging situations individuals with PD exhibit increased vagal withdrawal and hyperactive parasympathetic activation^[120]. Several studies have found conflicting results between individuals with PD and healthy controls on HRV^[105,121]. The incongruent findings may be due these studies having different methodological approaches and forms of analysis than other. Nonlinear dynamical theory may provide additional insight into the nonlinear relationship between heart rate variability and psychopathology^[121].

Specific phobias are characterized by increased heart rate and skin conductance when the individuals with the disorder are confronted with the fear object^[122]. Increased arousal is common among the specific phobias, while blood-injection-injury phobias have a unique physiological response that includes fainting. Individuals with dental phobia when exposed to phobia similar stimuli exhibit decreased HRV^[123].

Individuals with OCD are characterized by intrusive thoughts and irresistible urges to perform ritualized behavior. When individuals attempt to control these thoughts or behaviors, autonomic nervous system (ANS) activity increases. HRV has not been extensively studied in OCD and the few studies that have been performed have produced conflicting results. Some studies found increased levels of heart rate and skin conductance^[124], while other found no justifiable differences between controls^[125,126]. Using spectral analysis Slapp *et al.*^[105] found no differences between individuals with OCD and healthy controls on resting HRV. However, this study reported null findings on HRV between PD and healthy controls, which contradicts the established literature. Pittig *et al.*^[112] found that individuals with OCD exhibited diminished HRV during experimental tasks. These results need to be interpreted with caution because of a small sample size and the researchers did not account for the effects of medication. It is evident from the dearth of research on OCD and HRV that more work needs to be done to examine this relationship.

Physiological reactivity to reminders of a traumatic event is a characteristic feature of PTSD^[89]. PTSD populations have an average heart rate resting rate approximately five beats per minute faster than control groups^[127]. Higher resting heart rate and greater heart rate activity to trauma cues in individuals with PTSD have been explained as over activation of the ANS^[89,128]. The inability to regulate levels of arousal and distress is central to PTSD^[129]. The psychophysiological symptoms of PTSD include hyperarousal (e.g., excessive startle reflex, hypervigilance) and exaggerated reactions to trauma cues, which indicate a dysfunctional physiological stress system in individuals with PTSD^[130].

The role of cardiac activity in the ANS has been extensively studied in trauma research^[131,132]. Abnormalities in heart rate to trauma related a stimulus has been exhibited in a plethora of PTSD samples^[89,113,130]. Individuals with PTSD exhibit elevated tonic cardiovascular activity^[113,127] and excessive heart rate reactivity to trauma reminders^[113,128]. In contrast, some trauma-exposed individuals respond with a reduced basal HR (hypoarousal) or even dissociation when confronted with trauma cues^[133]. Individuals with PTSD compared to trauma-exposed individuals without PTSD exhibited amplified heart rate, attenuated respiration, and decreased HF-HRV^[134]. These differences are exaggerated when individuals are exposed to trauma-specific stimuli. Individuals with PTSD tend to remain physiologically aroused and fail to return to baseline levels^[113].

In summary, the majority of anxiety disorders exhibit significantly reduced HF-HRV than healthy controls during baseline measurement^[112]. Individuals with PD demonstrate the strongest differences between healthy controls on HRV^[109,112]. Individuals with GAD and SAD exhibit smaller effect sizes and exhibit less diminished HRV. Meta-analysis revealed significantly reduced HRV in individuals with PTSD, GAD, PD, SAD, and Specific Phobias compared to healthy controls^[91]. Therefore,

the anxiety related disorders exhibit unique biomarkers of psychopathology that are useful for diagnostic assessment, particularly differentiating from those without anxiety disorders. Additionally, HRV can be used effectively to objectively track treatment outcome for the anxiety-related disorders.

Heart rate variability has been extensively studied and validated as a biomarker of the anxiety related disorders^[135]. HF-HRV is a change-sensitive marker that parallels positive effects of treatment, with increases in HF-HRV following treatment for depression^[136]. Successful completion of cognitive behavioral therapy reduces psychophysiological activity in PTSD^[128,137], PD^[138,139], OCD^[140], GAD^[103], SAD^[141], and specific phobias^[142]. Therefore, HF-HRV is a potential biomarker of treatment efficacy for the anxiety related disorders^[135]. However, more research is needed to examine the efficacy of psychotherapy on HRV. Heart rate has been established as a biomarker of the efficacy of CBT on PTSD^[128,135,137]. Therefore, future research should examine the efficacy of CBT on the other anxiety disorders and if HRV can be considered a potential biomarker of treatment outcome.

DISCUSSION

Making accurate mental health diagnoses is not an easy task, especially when clinicians must rely primarily on client self-report, which can be inaccurate or misleading. Many disorders have similar symptomatology, and it can be difficult to untangle the many components to make an accurate diagnosis. Additionally, the DSM-5's categorical system can lead clinicians to make multiple diagnoses when there may be only one underlying condition responsible for the client's symptoms. While many clinicians have advocated for a dimensional model to solve these entanglements, the categorical model remains as the standard in the field. A promising solution to this quagmire would be to use biobehavioral assessments in clinical settings. The ample amount of research on heart rate variability and eye-tracking methodologies make it evident that these two measures are valuable for obtaining physiological data that is indicative of different aspects of mental health. These methods provide accurate and unbiased data (as opposed to self-report) that are useful in discriminating between disorders for diagnosis or evaluating treatment efficacy.

The multiple biomarkers that eye-trackers record provide abundant amounts of valuable data that can be used to differentially diagnose many anxiety-related disorders^[57,58,71]. ECG technology can provide clinicians with a clear visual of treatment efficacy for the anxiety related disorders^[135]. Integrating these biobehavioral devices into assessment will allow clinicians to make use of recent technological advancements in psychophysiology, years of research in biobehavioral markers, and assist clinicians in overcoming issues with self-report and human information processing errors. Using these methods could help psychological

assessment overcome the systemic flaws that have been endemic to psychological assessment and bring the system of psychological diagnosis out of the 20th century.

Imagine a common scenario, a mother brings her fidgety son, Jimmy, to her family doctor stating that he isn't doing well in school and seems distracted. She asks the physician for medication to help. Instead of the doctor asking a few hypothesis-congruent questions and prescribing ADHD medication, the physician instead asks Jimmy to put a watch on his wrist and look at a few pictures on the computer screen. A few minutes later, the doctor informs Jimmy's mom that it appears Jimmy has high levels of anxiety and is at-risk for future depression. The doctor subsequently refers Jimmy to a nearby mental health professional, who takes a closer look at the information and can see what types of attentional biases Jimmy exhibited during the assessment. Based upon this information, she can look more closely at the disorders Jimmy is most likely to have. The mental health practitioner also has information that can help her develop an accurate case formulation and determine which treatment is most likely to be effective. She also has established baseline anxiety levels that can be compared with later assessments to determine the efficacy of her treatment. This swift and objective assessment tool has the added benefit of fostering clear communication between medical professionals and mental health practitioners.

To make this vignette possible, several steps must be taken in this direction. While biobehavioral measures are becoming more prevalent, more research is needed to use these measures as resources for clinical settings. For instance, some of the research has yielded different results when analyzing the same constructs^[51,64,75,121]. One potential reason for some of the incongruent results on these studies is that each study utilized its own stimuli and methodological practices^[64]. To implement the use of these devices in a clinical setting, a standardized set of stimuli and methodology must be developed and validated. To do so, large scale studies with diverse populations comprised of clinical and healthy participants are needed. This requires funding and cooperative research relationships on a large scale. To this end, we exhort institutions to secure grants and other funding for this imperative research. Likewise, the United States Food and Drug Association (FDA) and European Medicines Agency (EMA) could encourage pharmaceutical and digital therapeutic companies to include biobehavioral measures as outcome measures when they file investigational new drug (IND) clinical plans. This could provide a more thorough picture of a treatment's efficacy and help standardize the use of biobehavioral measures in research and clinical practice.

Once a standardized set of stimuli and methodology are developed, new software would need to be developed to easily analyze the data for clinical use. It would be unrealistic to expect any general practitioner or master's level clinician considering a treatment path to painstakingly statistically analyze all the data involved

in these forms of assessment. A software program with the ability to print out easily discernible raw and standard scores would allow ECG and eye-tracker data to be interpreted in a similar manner to blood sugar readings or IQ test results.

There are several obstacles and opportunities for clinical psychology as a science and as a practice. Making these tools standard practice will be difficult, but it is possible and could resolve many of the issues currently plaguing clinical psychology. The fields of psychology and psychiatry can be serving people with anxiety disorders more efficiently and effectively, but a paradigm shift will need to occur. It would be best that as a discipline we can keep up with emerging technology instead of waiting for the current paradigm to be replaced by a better one^[143]. The process of implementing a difficult paradigm shift to incorporate the fruit of years of empirical research and technological advancement is well worth the discomfort of change and the inconvenience of validating and learning a new system of assessment.

In conclusion, many of the most troubling issues of the current system of mental health diagnosis and assessment would be greatly ameliorated by developing and utilizing a standard, objective, dimensional system through the use of eye trackers and electrocardiograms. Successfully changing the diagnostic system to include this new standard can be assisted by the concerted efforts of researchers, grant providers, government agencies, and clinicians. The benefits of including biobehavioral measures in mental health assessment far outweigh the effort it will take to make it a standard practice.

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