

# Panic Disorder and Agoraphobia Across the Lifespan

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## Abstract

This article is aimed to give a short overview over the most important features and research findings about panic disorder and agoraphobia. The diagnostic criteria will be discussed reviewing the changes in the history of the Diagnostic Statistical Manual for Mental Disorders. Epidemiology will be reviewed within development and maintenance factors. Different theoretical models will be discussed and the evidence-based treatment approach will be explained. Possible mechanisms of change are explained and the article ends with a short overview of clinical implications and future directions of research.

## Definition and Diagnostic Criteria

### Panic Disorder

Panic disorder and agoraphobia can be disabling conditions, which are associated with significant interference in occupational and social functioning (Schmidt et al., 2013). Certain degrees of anxiety are adaptive in daily life and can protect us when confronted with dangerous situations. Thus, we can think of the continuum from worry to anxiety to panic as an alarm system designed to protect us from danger. However, when this alarm system goes off even in relatively safe situations and we fear the alarm system itself, this can have a major negative impact on the individual's daily functioning.

According to the Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM-5), panic disorder refers to experiencing recurrent and unexpected panic attacks (Criterion A). A panic attack is an abrupt surge of intense fear or intense discomfort that reaches a peak within minutes, and during which time four or more of a list of 13 physical and cognitive symptoms occur (American Psychiatric Association (APA), 2013). This includes palpitations, pounding heart, or accelerated heart rate; sweating; trembling or shaking; sensations of shortness of breath or smothering; feelings of choking; chest pain or discomfort; nausea or abdominal distress; feeling dizzy, unsteady, light-headed, or faint; chills or heat sensations; paresthesia; derealization or depersonalization; fear of losing control; and fear of dying. The term 'recurrent' refers to have experienced more than one panic attack and 'unexpected' refers to the fact that no obvious trigger has elicited the panic attack. Panic attacks can even occur when the individual is relaxing or during nighttime. The distinction between expected and/or unexpected panic attacks has to be made carefully, based on open and structured questioning about the attacks and circumstances. In the United States and Europe, approximately one-half of individuals with panic disorder have expected panic attacks as well as unexpected panic attacks (Craske et al., 2010). Thus, according to the DSM-5, the presence of expected panic attacks does not rule out the diagnosis of panic disorder (APA, 2013).

However, most patients with panic disorder experience a mixture of different types of panic attacks (Schmidt et al., 2014). During the onset of panic disorder, panic attacks

occur spontaneously and unexpectedly. However, as time progresses, patients are often able to establish a link between panic and a variety of situations, which trigger their panic attacks at an earlier stage, so that panic attacks appear to be more situationally bound over the course of panic disorder.

The frequency and severity of panic attacks can vary widely and depend largely on the individual coping style and avoidance behavior. In panic disorder, experiencing panic attacks is accompanied by frequent worries about the next panic attack and the possible consequences. These consequences include the presence of a life-threatening illnesses (e.g., cardiac disease, seizure disorder) or social concerns, such as embarrassment or fear of being judged negatively by others because of visible panic symptoms and concerns about mental functioning such as 'going crazy' or losing control (Criterion B) (APA, 2013). Often maladaptive behaviors occur to minimize the occurrence of panic attacks. Examples include avoiding physical exertion, reorganizing daily life to ensure that help is available in the event of a panic attack, restricting usual daily activities, and avoiding situations, such as using public transportation or shopping. If intense fear of multiple situations is present, a separate diagnosis of agoraphobia is given.

### Agoraphobia

The essential feature of agoraphobia is marked or intense fear or anxiety triggered by real or anticipated exposure to a wide range of situations (Criterion A; APA, 2013). The diagnosis requires the occurrence of symptoms in at least two of the following five situations: (1) using public transportation, such as automobiles, buses, trains, ships, or planes; (2) being in open spaces, such as parking lots, marketplaces, or bridges; (3) being in enclosed spaces, such as shops, theaters, or cinemas; (4) standing in line or being in a crowd; or (5) being outside of the home alone (APA, 2013). When experiencing fear and anxiety cued by such situations, individuals typically experience thoughts that something terrible might happen (Criterion B). Individuals frequently believe that escape from such situations might be difficult (e.g., 'cannot get out of here') or that help might be unavailable (e.g., 'there is nobody to help me') when paniclike symptoms or other incapacitating or

embarrassing symptoms occur. 'Paniclike symptoms' refer to any of the 13 symptoms included in the criteria for panic attack, such as dizziness, faintness, and fear of dying. 'Other incapacitating or embarrassing symptoms' include symptoms such as vomiting and inflammatory bowel symptoms, as well as, in older adults, a fear of falling or, in children, a sense of disorientation and getting lost.

Fear or anxiety is evoked nearly every time the individual comes into contact with the feared situation (Criterion C). Thus, an individual who becomes anxious only occasionally in an agoraphobic situation (e.g., when standing in line on only one out of every five occasions) would not be diagnosed with agoraphobia (Craske et al., 2010; Wittchen et al., 2010).

### From DSM-IV to DSM-5

The definition and diagnostic criteria of panic disorder and agoraphobia have undergone significant changes over time in the DSM (Schmidt et al., 2014). In particular, the description of the relationship between panic disorder and agoraphobia has undergone interesting changes within the DSM. While Marks (1970) originally suggested to classify agoraphobia as a phobic disorder arising from fears of public places that may or may not occur with panic attacks, as was done in the DSM-III (American Psychiatric Association (APA), 1980), over time researchers increasingly recognized that agoraphobia can occur as a consequence of panic attacks and in the DSM-III-R and DSM-IV the relationship between these conditions was reversed. Agoraphobia was considered to be a consequence of panic attacks and thus, agoraphobic behaviors were classified more as panic-related sequelae (Frances et al., 1993; Goldstein and Chambless, 1978; McNally, 1994).

In the DSM-5 (APA, 2013), agoraphobia is classified as a distinct disorder from panic disorder. This means that patients can receive either a diagnosis of panic disorder or a diagnosis of agoraphobia, or a comorbid diagnosis of panic disorder and agoraphobia. The separation of panic disorder and agoraphobia is based on large cohort and prospective studies wherein it is shown that agoraphobia exists in individuals who never experienced any panic attacks or paniclike symptoms (Faravelli et al., 2008; Fava and Morton, 2009; Wittchen et al., 1998). For a recent review see Emmelkamp and Powers (2009). A detailed analysis of the prospective reports as well as analysis of the incidence patterns of agoraphobia indicate that a substantial percentage of individuals with this diagnosis show no history of panic or paniclike symptoms (Wittchen et al., 2008). However, fairly often, panic disorder and agoraphobia are comorbid conditions. For a more complete discussion on the diagnostic changes between DSM-IV and DSM-5 with regard to the diagnosis of panic attacks, panic disorder, and agoraphobia see Schmidt et al. (2013).

### Prevalence

The 12-month prevalence of panic disorder ranges between 1% and 3% across the United States (Kessler et al., 2012, 2005) and Europe (Goodwin et al., 2005; De Graaf et al., 2012). The 12-month prevalence of agoraphobia is approximately 1.7% in adolescents and adults (Kessler et al., 2012; Wittchen et al., 2011). Onset of agoraphobia can occur during childhood but

the most vulnerable periods to develop the disorder are late adolescence and early adulthood (Beesdo et al., 2009; Bittner et al., 2007). The gender ratio is 2:1 with females experiencing twice as often agoraphobia as men (Wittchen et al., 2010). This may be for several reasons: (1) males (especially young) tend to be less willing to openly discuss agoraphobic fears and avoidance behavior, (2) because of this desire to not appear 'weak,' they might expose themselves to the feared situations with fear reduction over time as an unintended consequence, or (3) they use other methods to enter the feared situations (alcohol/substances).

## Development and Maintenance Factors

### Development and Avoidance Behavior

Epidemiological research has investigated potential risk factors for panic disorder. As in most psychiatric disorders, a diathesis-stress model is commonly used to explain the development and maintenance of the disorder (Roy-Byrne et al., 2006).

While panic attacks are quite common in the general population, only a small percentage of people develops panic disorder (Emmelkamp and Powers, 2010). While most people who experience a panic attack during their lifetime just go on with their life, a small percentage starts worrying about their next panic attack and their perceived consequences. There is some evidence that this panic-related apprehension is one of the key factors in developing panic disorder (Telch et al., 1989). Panic appraisal is usually considered to consist of three different aspects: (1) perceived likelihood of panic occurrence, (2) the perceived negative consequences, and (3) the perceived efficacy in panic coping (Telch et al., 1989). There are some indications that these aspects of panic appraisal are the best predictor for agoraphobic avoidance (Smits et al., 2004; Telch et al., 1989; Cho et al., 2007).

Other researchers emphasize the importance of cognitive factors in the development of panic disorder (Beck and Emery, 1985; Clark, 1986), for example, anxiety sensitivity (McNally, 2002). Anxiety sensitivity is referred to as the fear of benign bodily sensations, which is caused by anxiety – also referred to as fear of fear (Goldstein and Chambless, 1978; Reiss et al., 1986) and has long been considered a specific vulnerability of panic disorder (White et al., 2006). Anxiety sensitivity is mostly conceptualized as a trait that remains relatively stable over time; although there are more studies showing that anxiety sensitivity decreases following treatment (Naragon-Gainey, 2010; Smits et al., 2008).

Currently, it remains unclear why some individuals with panic attacks start avoiding situations while others do not (Emmelkamp and Powers, 2010). Most individuals with agoraphobia experience some panic attacks or show some signs of anxiety before the onset of panic disorder and/or agoraphobia (Fava et al., 1992). The initial onset of agoraphobia is typically before the age of 35 years. There is a latent incidence risk in late adolescence and early adulthood. The mean age for onset of agoraphobia without preceding panic attacks is between 25 and 29 years (Nocon et al., 2008; Wittchen et al., 2010). Usually the course of agoraphobia is chronic and if not treated the remission rate is low (10%) (Emmelkamp and Wittchen, 2008). With increasing severity of agoraphobic symptoms, chronicity

increases and full remission rates decrease. In the long-term, a range of comorbidity may complicate the course of agoraphobia; depressive disorders, substance use disorder and traits of personality disorders. The clinical feature of agoraphobia is relatively consistent across the life span, although situations, which trigger fear and avoidance as well as the type of cognitions, may change. For example, for children being outside their home alone is the most frequently feared situation, whereas in adults standing in line in a shop and being in open spaces are most often feared (Wittchen et al., 2010). Common cognitions in children include becoming lost while in older adults cognitions focus more on falling.

Although panic severity does not predict the development of agoraphobia, the patients' exaggerated likelihood estimation of panic occurrence in situations is the best predictor of agoraphobic avoidance accounting for almost 80% of variance in avoidance behavior (Rachman, 1994; Telch et al., 1989). In a recent trial, it was shown that initial changes during therapy in agoraphobic cognitions predict later changes in avoidance behavior (Meyerbroeker et al., 2013).

Twin studies show 40% heritability with contributions from common familial environmental effects (<10%) and unique environmental effects (>50%) (Roth et al., 1984). It has further been suggested that an anxious temperament, which is characterized by neuroticism functions as an important risk factor (Watanabe et al., 2005).

### Life Events and Stress

There is increasing evidence that life events often precede the onset of panic disorder. In a number of studies, it was found that up to two-thirds of patients with panic disorder experienced a significant personal loss in the year preceding the onset of panic disorder (Faravelli and Pallanti, 1989; Milrod et al., 2004; Pollard et al., 1989; Scocco et al., 2007). Most individuals report stressors in the months before their first panic attack, which can be interpersonal stressors, stressors related to physical well-being, or work-related stressors. Another important aspect is that childhood experiences of sexual, physical, and/or emotional abuse. These experiences are commonly reported in individuals with panic disorder (Roy-Byrne et al., 2006; Schade et al., 2004).

### Comorbidity

High comorbidity rates have been found in individuals with anxiety disorders for substance abuse, especially alcohol abuse (Grant et al., 2004). In patients with an alcohol-related substance use disorder, an overall rate of more than 42% was found to have a comorbid anxiety disorder (Schneider et al., 2001). Most prevalent were social phobia (14%), agoraphobia (13%), and panic disorder (5%). The relationship between substance abuse and panic disorder and agoraphobia seems to be reciprocal (Emmelkamp and Powers, 2010). Individuals are often convinced that the use of alcohol reduces their anxiety and substance abuse might be attributed to anxiety as a form of self-medication (Zimmerman and Chelminski, 2003). On the other hand, symptoms of panic and anxiety are common symptoms during withdrawal and should be distinguished from primary anxiety disorders (Emmelkamp and Vedel, 2006).

### Medical Conditions

Panic disorder is commonly associated with numerous medical conditions and symptoms such as dizziness, cardiac arrhythmias, apnea, hyperthyroidism, asthma, COPD, and irritable bowel syndrome (APA, 2013). However, it remains unclear, what the exact nature of this relation is (cause or effect) and it might be that some physical symptoms just overlap and are due to the medical condition.

### Theoretical Background

Depending on theoretical background, different models have been developed to explain the development and maintenance of panic disorder and agoraphobia. Although, different theoretical background often lead to different treatment models. In panic disorder and agoraphobia in general the treatment consists of the same basic components.

### Cognitive Model

As in most anxiety disorders, the appraisal of threat is central to the cognitive theory of panic disorder and agoraphobia (Beck and Emery, 1985; Salkovskis et al., 2007). One possible explanation is that panic occurs because individuals are appraising normal somatic symptoms of anxiety as excessively threatening (Clark, 1986). According to the cognitive model of panic disorder, panic can be classified as an anxiety, which focuses on somatic sensations, which are usually increased while experiencing anxiety (Salkovskis, 2007). According to this view, the cognitive hypothesis of panic is based on the premise that individuals who are experiencing recurrent panic attacks do so because they have a tendency to misinterpret bodily sensations as dangerous or life threatening. Thus, in long-term individuals fear their fear.

### Behavioral Model

In panic disorder, the pairing of intense fear and experiencing bodily sensations at the same time is central to develop the disorder in the classical conditioning paradigm. According to a classical conditioning model, the occurrence of one of the symptoms (e.g., palpitations) leads 'automatically' to the other (anxiety: 'I might have a heart attack') thus provoking a full panic attack. According to the conditioning paradigm, the same holds true for the development of panic disorder and agoraphobia. In the comorbid condition, panic attacks are correlated with certain situations, which in the long run lead to more paniclike symptoms leading to a situational-bound panic attack. The maintenance of anxiety disorders in general can be explained by operant conditioning when leaving the feared stimulus leads to reward (Emmelkamp et al., 1995).

Different theories have been discussed to explain the major effects of exposure therapy in anxiety disorders (Telch et al., 2014). It has been argued that exposure can be explained by means of habituation (Marks, 1978). According to Wolpe (1958), the effects of exposure therapy can be explained by means of reciprocal conditioning: the central idea is that fear could be eliminated by pairing a patient's fear response with

a physiological response, which was incompatible with the fear response (e.g., relaxation), and which would lead to inhibition of the original fear response. In experiments all over the world, it was shown that relaxation was not a necessary component to achieve meaningful fear reduction (Emmelkamp, 1982). In more recent views, treatment success is explained in terms of a learning paradigm (Bouton, 2000; Craske et al., 2008).

### Biological Model

As in most other psychiatric disorders, multiple gene interactions are central to the biological models (Craske and Barlow, 2008). It is suggested that relatively broad or nonspecific genetic factors influence the vulnerability to panic and anxiety. This gene interaction probably explains why panic disorder and agoraphobia tend to run in families. For a recent review, concerning the debate about gene–environment interaction in panic disorder see Battaglia (2013).

### Mechanisms of Change

#### Panic Appraisal

There seems to be preliminary evidence for cognitive mediation during cognitive behavioral therapy (CBT) in panic disorder (Hofmann et al., 2007). In a randomized controlled trial, 91 subjects were allocated to receive CBT alone, imipramine alone, CBT plus imipramine, or CBT plus placebo. Individuals who received one of these interventions were assessed before and after acute treatment, and after a 6-month maintenance period. It was shown that changes in panic-related cognitions-mediated changes in panic severity only in treatments that included CBT. This is in line with the findings of Fernandez-Arias et al. (2013) who argued not to combine psychological treatment with pharmacological treatment. First results are promising, but more research is needed to investigate the assumed mechanisms of change in exposure-based treatments in panic disorder. Panic appraisal has been found to play an important role in the development and maintenance of panic disorder and agoraphobia, but more research is needed to replicate and further extend these findings and investigate whether these findings are specific for panic disorder and agoraphobia or whether anxiety appraisal might be a more general factor across anxiety disorders.

#### Anxiety Sensitivity

From a cognitive perspective, anxiety sensitivity can be considered a significant factor in the development and maintenance of panic disorder (Barlow, 2002). Several other studies suggest that anxiety sensitivity mediates improvement in the treatment of panic disorder (Cho et al., 2007; Hofmann et al., 2007; Smits et al., 2004). For example, one study suggested that changes in anxiety sensitivity fully mediated improvement in patients with panic disorder after CBT when compared to a wait list control condition and partially mediated improvement in patients with agoraphobia (Smits et al., 2004). These results were stable at 6-months follow-up (Cho et al., 2007). In another study, it was shown that reductions in anxiety sensitivity preceded reductions in panic symptoms (Smits et al.,

2008), thus meeting the temporal precedence criteria as a mediator of change in panic disorder. Anxiety sensitivity is associated with most anxiety disorders, but a particularly strong relationship between panic attacks and anxiety sensitivity has been demonstrated (Bentley et al., 2013). Anxiety sensitivity has also been shown to predict spontaneous panic attacks (Maller and Reiss, 1992; Plehn and Peterson, 2002).

In a large recent treatment study with 361 individuals with panic disorder, effect sizes showed that the greatest changes in anxiety sensitivity occurred at early treatment stages (Gallagher et al., 2013). Additionally, it was shown that anxiety sensitivity predicted changes in panic disorder symptoms, thus indicating that anxiety sensitivity might be a mechanism of change, which is particularly important during the early stages of treatment.

In terms of transdiagnostic approaches, anxiety sensitivity might be a marker across anxiety disorders. There is more research needed to investigate whether the above-mentioned findings can be replicated in other anxiety disorders. These findings are interesting in times of unified protocols and more dimensional perspectives of mental disorders. The above-mentioned findings are important for understanding the mechanisms of change in specific anxiety disorders, but research has also shown that anxiety sensitivity plays an important role across other anxiety disorders (Vanden Bogaerde and De Raedt, 2011).

### Evidence-Based Treatment Approaches

#### Guidelines

According to the NICE guidelines (National Institute for Health and Clinical Excellence, 2011), there is a consensus that empirically supported psychological treatments are the treatment of choice for panic disorder and agoraphobia. This can be combined with pharmacological treatments, which can produce better results in reducing relapse rates and improving maintenance of gains (Barlow et al., 2000; Otto et al., 2005), although this has been questioned recently (Fernandez-Arias et al., 2013; Hofmann et al., 2007). Please see also the section about pharmacological treatment and the paragraph about mechanisms of change.

Although different theoretical background often leads to different treatment models, in panic disorder and agoraphobia in general the treatment consists of the same components: (1) psychoeducation about the nature and causes of panic disorder and agoraphobia, (2) cognitive restructuring, which targets the negative cognitions associated with panic, and (3) exposure to interoceptive bodily sensations and agoraphobic situations. Sometimes, this program is completed with breathing skills training and relaxation but in clinical practice these have been largely abandoned given findings that they do not enhance outcome (Schmidt et al., 2000).

Dismantling studies of the various components of CBT for panic disorder and agoraphobia have had inconsistent findings (Craske and Barlow, 2008). On one hand, it was found that cognitive therapy as a component may be effective (Williams and Falbo, 1996) even when it is conducted without exposure and other behavioral components (Salkovskis et al., 1991). On the other hand, it was found that cognitive therapy does not have an additional value above exposure in

patients with agoraphobia (Craske et al., 1997; Ost et al., 2004). In more recent research, it was found that exposure-based interventions are usually superior to cognitive interventions in agoraphobia (Moscovitch, 2009; Sanchez-Meca et al., 2010).

### Psychoeducation

The first phase of treatment for panic disorder and/or agoraphobia usually includes psychoeducation about the nature and causes of panic disorder and agoraphobia. This information usually consists of making a more detailed and clear distinction between anxiety and panic. Further, the relationship between experiencing anxiety, panic-related bodily symptoms, and cognitions is explained (e.g., the vicious circle of panic, (Craske and Barlow, 2008)). Detailed analyses of recent panic attacks often help the patient to become aware of these relationships. If appropriate, the relationship with agoraphobic avoidance behavior is further explored in collaboration with the patient. To obtain objective information in treatment sessions, it is important to let the patient record their panic attacks and the correlating symptoms, feelings, and thoughts.

### Exposure *in vivo*

Marks (1978) has argued that exposure therapy works through emotional habituation. Habituation is defined as a decrease in fear reactions in response to repeated exposure to the feared stimulus. In panic disorder and agoraphobia, exposure targets fear of bodily sensations (interoceptive exposure) and agoraphobic situations (Emmelkamp and Powers, 2010; Meuret et al., 2012).

Meta-analyses and reviews of exposure for panic disorder and agoraphobia (Mitte, 2005; Sanchez-Meca et al., 2010) show that exposure *in vivo* has a substantial effect size for reducing agoraphobic symptoms. Additionally, exposure-based interventions (including virtual reality exposure, Meyerbröker, 2014) show strong effect sizes in reducing agoraphobic avoidance behavior (Meyerbroeker et al., 2013; Moscovitch, 2009). Interestingly, therapist guidance during exposures appears important (Gloster et al., 2011). This large Randomized Control Trial showed that guided exposure *in vivo* was more effective than exposure without therapist guidance in reducing the number of panic attacks, avoidance behavior, and improvement in global functioning.

### Interoceptive Exposure

Because individuals with panic-related symptoms usually misinterpret their bodily sensations and therefore panic even worse, one important aspect in the treatment of panic disorder is interoceptive exposure. The aim of the exposure is twofold: first, one can tolerate uncomfortable bodily sensations and second that these symptoms will decrease over time without any intervention. Thus, the patient will learn to tolerate the symptoms without misinterpreting the symptoms as resulting in the feared consequences. Additionally, the patient can compare the provoked paniclike symptoms and compare them to the recently, nonprovoked symptoms, and panic attacks.

### Cognitive Restructuring

Cognitive restructuring is often introduced in combination with the recording of the panic attacks over the early therapy sessions. The purpose of cognitive restructuring is to investigate together with the patient what thoughts and possible misinterpretations they experience along with panic attacks. Often, these thoughts or misinterpretations come along with negative emotions, which in turn can strengthen the symptoms (e.g., vicious circle of panic). By having a closer look together with the therapist at these thoughts and emotions, the patient might become more aware of certain thoughts. These thoughts – automatic thoughts – are important in panic disorder because they often generate negative behavior due to the misinterpretation of the symptoms. When patients have identified these automatic thoughts, they can be challenged with more rational alternatives.

### Relaxation and Breathing Training

Often, relaxation and/or breathing training is added to the treatment of panic disorder. The purpose is to help the patient to relax more easily when a panic attack is occurring. However, research shows that the above-mentioned treatment components are usually more effective than relaxation training (Barlow et al., 1989) and results are maintained at 2-year follow-up (Craske et al., 1991). The breathing training is often offered but not actively practiced in therapy sessions.

### Pharmacological Treatment

Generally, selective serotonin reuptake inhibitors are the medication of choice for panic disorder and agoraphobia as indicated by placebo-controlled randomized clinical trials (Roy-Byrne and Cowley, 2002). In meta-analyses, medium to large effect sizes are reported when compared to Placebo (Mitte, 2005; Bakker et al., 2002). The use of benzodiazepines is not recommended because of their physiological dependence and withdrawal (Roy-Byrne and Cowley, 2002) and because of only temporary symptom remedy (for a review about the use of benzodiazepines in combination with psychotherapy see Watanabe et al., 2007).

Recently, it has been questioned whether the combination of pharmacological treatment with psychological treatment has an additional value (Fernandez-Arias et al., 2013). It was found that in the long run, patients profited more from empirically supported psychological treatment than from psychological treatment in combination with pharmacological therapy.

### Future Directions

Although we discussed some findings on potential mediators and moderators of treatment outcome, future studies should increase our confidence in more specific targets. Further, new analysis strategies offer more powerful methods to test such mediation targets (Smits et al., 2012). For example, Kazdin (2007) outlined seven conditions to establish mediation including (1) the selection of mediators must be guided by theory; (2) treatment studies must include measures of potential mediators; (3) the timeline of the proposed mediator

and outcome must be established; (4) studies must assess more than one mediator; (5) studies must use designs that can evaluate mediators; (6) different types of studies must provide converging evidence; and (7) treatment studies must be complemented by experiments that manipulate the mediator to provide converging evidence. As more researchers use these more stringent criteria, our understanding of mediators and moderators should improve.

Future research will also likely include transdiagnostic models of psychology focusing on cognitive endophenotypes of psychopathology from an integrative cognitive psychology perspective (Emmelkamp et al., 2014). For example, emotion dysregulation (Hofmann et al., 2012) and rumination or repetitive thinking (Ehring and Watkins, 2008) are implicated across various mood and anxiety disorders. Such findings have led to transdiagnostic manualized protocols. Initial results are promising. Two open clinical trials of a transdiagnostic treatment suggest that this approach can distil common strategies and enhance the effectiveness by targeting core affective 'higher order' components, which results in substantial clinical improvement in primary and secondary disorders (Ellard et al., 2010). These findings were extended by Farchione and colleagues (Farchione et al., 2012), who treated 38 patients with a unified protocol consisting of 5 modules, which targeted key aspects of emotional processing and regulation of emotional experiences: (1) increasing present-focused emotion awareness, (2) increasing cognitive flexibility, (3) identifying and preventing patterns of emotion avoidance, (4) increasing awareness and tolerance of emotion-related physical sensations, and (5) interoceptive and situation-based emotion focused exposure (Farchione et al., 2012).

### Clinical Implications

It is important to translate research into clinically meaningful working protocols. As mentioned above, recent approaches to more transdiagnostic models of psychopathology are a promising first step into clinically meaningful results. If, for example, multiple diagnosis and specific treatment protocols can be combined, this can result in more fruitful and effective treatment planning. If this approach proves to be successful in emotional disorders, it might promote dissemination of evidence-based treatments. Another important aspect is the need for more effective studies wherein not all comorbidities are excluded. This makes studies more representative for clinical practice and might help to clarify why some treatments work for some individuals but not for others.

*See also:* Behavior Therapy: Background, Basic Principles, and Early History; Classical Conditioning Methods in Psychotherapy; Concepts and Methods of Cognitive Therapies; Epidemiology, Concepts and Methods of; Exposure Therapies and Stress Inoculation: A Brief Overview; Manual Based Treatments.

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