Clinical Psychology Review 29 (2009) 623–637

Contents lists available at ScienceDirect

Clinical Psychology Review

Causal modeling of panic disorder theories ☆

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ARTICLE INFO

Article history:
Received 11 February 2009
Received in revised form 3 August 2009
Accepted 5 August 2009

Keywords:
Causal modeling
Causal theories
Panic disorder
Cognitive theory
Neurobiological theory
Psycho-dynamic theory

ABSTRACT

We compare a variety of theories of panic disorder using a neutral framework: causal modeling. The framework requires identification of key constructs and specification of their interaction. Biological, cognitive, and behavioral elements of the theory have to be clearly distinguished, as do critical past events and current trigger conditions. The theories compared were drawn from the psycho-dynamic, cognitive, and neurobiological literature. We conclude that there are substantive differences among the cognitive theories and between the biological theories reviewed. However, cognitive and biological theories appear to be compatible in principle. It is not clear whether substantive differences among theories are due to the existence of subtypes of PD or due to the predominance of multifactorial cause. It is argued that current treatment methods imply particular theories, and that particular patterns of success and failure can be understood in relation to theory through the methods we have employed.
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Contents

1. Causal modeling as a framework

Increasing work by psychologists in the clinical field has led to an explosion of theories of disorders. Unfortunately, very little work has been done in comparative evaluation of various theories, particularly when they come from different approaches: for example biological versus cognitive. Ideally, such comparisons should be done with techniques which are unbiased with respect to the nature of the

☆ The ideas in this paper were first presented to "Decision Making in Psychotherapy" in Leuwen April 23rd 2007, in a poster presented by Leonardo Fava and Lisette Hornstra. We are grateful to Ms. Hornstra for her contributions to this manuscript. Thanks are also due to Elizabeth Hill, Chris Brewin, Guinevere Tufnell, Kristin Strauss, and Nicole Krol for their comments on earlier versions.
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doi:10.1016/j.cpr.2009.08.002

competing theories. This theoretical neutrality is characteristic of what we call a *framework*, a term that contrasts with *theory* and *model*. A model is, in this way of thinking, representation of a theory within a particular framework.

The causal modeling framework was developed by Morton and Frith (1995) and Morton (2004) in order to represent theories of developmental disorders, making clear distinctions among biological, cognitive, and behavioral components of the theories. The framework has been applied to a variety of disorders, especially autism (Frith, Morton, & Leslie, 1991), dyslexia (Morton & Frith, 1993a,b, 1995, 2002), psychopathy (Blair, 1995), conduct disorder (Krol, Morton & de Bruyn, 2004) and DCD (Sims & Morton, 1998). The framework has also been particularly useful for comparison of different, often competing, causal theories of dyslexia (BPS, 1999; Frith, 1999). Here, the advantage of using the causal modeling framework has been to demonstrate that some theories that were perceived as being totally different from each other were essentially similar, differing only in the relative weighting of the primary causes. In other cases, the weakness of particular theories, for example of autism (Morton, 2004), has been highlighted following their representation in the causal modeling notation. The framework has also been beneficial in the training of education psychologists (Monsen, Graham, Frederickson, & Cameron, 1998; Frederickson & Cline, 2002) who have adapted the framework for understanding pathways of special educational needs.

A causal model of a particular theory, then, is a representation of that theory within the causal modeling framework. The techniques are particularly useful for considering theories of panic disorder since they help to clarify, in each theory, the extent to which biological and environmental factors interact with cognitive processes in determining behavior.

Use of the causal modeling framework involves creation of a directed graph in which the elements of a theory are connected with arrows. Thus, an arrow linking element A to element B will have the force of "A causes B", meaning that, in the particular theory, if A is not present, B would not be found. Note that in different theories, elements may be more or less specific. For example, one might postulate a genetic cause without specifying locus.

The model space is divided up into three components, corresponding to biological, cognitive and behavioral elements. We will also use the concept of *equivalence*. Equivalence emerges when there is both a biological element and a cognitive element to a theory which are effectively identical for the purposes of the theory. Thus, we shall see below that the hippocampus is named as the location where the context of a trauma is stored. This context would serve as a cue for the retrieval of the traumatic experience from memory. The hippocampus has a direct connection with the amygdala, and this connection is entirely in the biological domain. On the other hand, we want to represent the effect of the reoccurrence of the original context in triggering a panic attack. Such input has to be cognitive since the elements of the context have to be recognized, and interpreted, and this process is subject to a variety of cognitive influences. Thus the individual's expectations may play a role in accessing the trigger memory. In general, such cognitive processes are not specified biologically, nor would such a biological specification be relevant to PD. All the PD theory needs is that expectations influence the interpretation of the environment. It is useful in this example, then, to keep the hippocampus as the biological specification and the associative memory as the *equivalent* cognitive specification. In the Causal Model, the hippocampus would be the element linking to other biological elements, and the associative memory would be the link to other cognitive components of the theory.

In previous work, causal models have represented the history of development. In this paper, we will also use a slightly different kind of model which includes current processing. They are to be thought of as additional information to help us understand the theories and data that underlie the causal hypotheses. We also want to make a distinction between antecedent conditions on the one hand and immediate causes on the other. For example, a traumatic event will have a long-term consequence in cognitive and brain structures. This will be part of the causal model. However, there will often be a local cause of a symptomatic breakdown which need not necessarily have permanent consequences. This distinction is the same as that drawn by Roth, Wilhelm, and Pettit (2005) between distal cause and proximal cause. They consider that each of the causal theories of panic attack that they consider "presupposes that there is a *unique* underlying proximal cause, a single underlying event that is both causally necessary and *under normal background conditions* causally sufficient for a PA" (Roth et al., 2005, p. 172, their italics). They then examine falsifiability of each theory in terms of the relation between proximal cause and PA. We will not attempt to identify such a unique element, but rather, will contrast developmental history of the individual contributing to the antecedent conditions with the processing occurring at the time of an attack.

Causal modeling consists of linking elements at the same or at different levels. It can conveniently represent the influence of the environment either at the biological level, as modifying the phenotypic expression of genetic predisposition, or at the cognitive level. As such, it can be an efficient tool to represent the multicausality of disorders and to represent biosocial or bio-psycho-social theories (Kiesler, 1999). This makes it ideal for representation of theories of panic disorder.

2. Panic disorder

The key event in panic disorder is the panic attack. This is defined by Clark (1986) in the following way:

> "A panic attack consists of an intense feeling of apprehension or impending doom which is of sudden onset and which is associated with a wide range of distressing physical sensations. These sensations include breathlessness, palpitations, chest pain, choking, dizziness, tingling in the hands and feet, hot and cold flushes, sweating, faintness, trembling and feelings of unreality" (p. 461).

Normally, an individual is aware of the source of any fearful sensations they have. In panic disorder, the same types of sensation are seemingly unprovoked, unexplained and often occur out of the blue. Furthermore, the characteristic panic could be the principal symptom in terms of temporal precedence; on the other hand, it might be secondary and be seen as a severity marker of a co-morbid illness (Roy-Byrne, Craske & Stein, 2006).

It is believed that, during a panic attack, anxiety can have deleterious physical, social, and psychological consequences that extend beyond any immediate physical discomfort. That is to say, some of the observed symptoms are secondary rather than primary. Let us give an example from the clinical practice of LF. A patient was anxious about swallowing food because he was scared that the food could become stuck in his windpipe and consequently he could choke. The consequence of this was that he ate less than normal, almost only liquid food, and there was an accompanying loss of weight. From the social point of view, because he was scared of being choked, he ate very slowly, and avoided going out to dinner. Because he avoided situations that would expose his problem, he became more isolated, his habits changed and he became depressed. Clearly, treating the depression without addressing the panic disorder would be inappropriate or inadequate.

In addition, some symptoms are not specific to panic disorder, but occur in various combinations in other anxiety disorders, such as post-traumatic stress disorder and social anxiety. For example, phobic avoidance of a certain location could occur in PTSD or social anxiety as well as PD. Again, treatment of the symptom without consideration of the cause would be limited in value.

We can elucidate this point by considering the most important treatments with empirical support, pharmacotherapy and cognitive behavioral therapy (CBT) (Roy-Byrne et al., 2006). Both these treatments have positive effects on patients with PD, but in a recent review of the literature, Furukawa, Watanabe and Churchill (2006) showed that the combined treatment of antidepressant and psychotherapy (mostly CBT) was more effective than antidepressant alone or than psychotherapy alone. After treatment was discontinued, patients who had received combined treatments continued to benefit compared with those who had received medication only. Briefly, we would argue that the antidepressant suppressed some of the symptoms without affecting the underlying cause. The psychotherapy would deal with aspects of the underlying cause without ameliorating the brain condition that put the patient at risk. Finally, we are open to the idea that PD may not always have the same cause. Thus, panic disorder in three patients may have three different individual causes and the treatment of each might require a different focus. We will see how such a situation is treated in causal modeling. There are other examples of this discussed in Morton (2004) in the context of differential diagnosis.

There is a variety of current theories ranging from biological, through cognitive to psychoanalytic theories and we have not been able to find any work comparing a range of theories in terms of their causal structure and their implications for treatment. A recent review paper by Roth et al. (2005) assesses scientific rigor, and thus falsifiability of several theories, and we will refer to the conclusions of this paper in the final section. Roth et al. largely treat the theories they consider as being independent of one another, and evaluate them singly. We are more interested in their degree of overlap.

We will first discuss psychodynamic theories of panic disorder, and then we will move on to cognitive hypotheses before looking at biological models. These three types of theory encompass the full range of explanation of PD, and cover the full range of therapeutic intervention. What we have tried to do is select the most influential theories of each type rather than considering all current theories.

3. Panic disorder theories

3.1. Psychodynamic hypotheses

Most psychodynamic theories of anxiety disorders apply to the whole spectrum of anxiety disorders. In contrast to the DSM IV (APA, 1994) they do not make a distinction between panic disorders and generalized anxiety disorders. It is argued that panic and other forms of anxiety are not qualitatively different; they only differ in severity (Michels, Frances, & Shear, 1985). This relates to personality types and defensive style. Indeed, Bond and Perry (2004) showed that patients with chronic and recurrent anxiety and depressive disorders and/or personality disorders who have different defensive styles, (such as "maladaptive," "image-distorting," or "self-sacrificing"), significantly reduced their symptoms after three years of psychodynamic psychotherapy and changed their defensive style adaptively. According to this study, we might conclude that anxiety level, and therefore, according to the theory, susceptibility to PD, would be determined primarily by defensive style. However, Edelson (1988) warns "differences in the conclusions of psychoanalysis and other disciplines (e.g. in neurobiology or neuropsychology) often reflect differences in what is meant by the term 'anxiety'" (pp. 89–90).

Some psychodynamic theories of panic disorder are based on the ideas of Freud (Michels et al., 1985). In his work, anxiety played an important role. Freud used the term 'anxiety neurosis' to refer to a personality trait which involved sensitivity to excessive or inappropriate anxiety. Freud considered anxiety to be the symptom of underlying sexual conflict, the result of an accumulation of sexual tension (Michels et al., 1985). However, in more recent psychodynamic views (Busch, Milrod & Singer, 1999; Sweeney & Pine, 2004), anxiety is not necessarily a symptom of sexual conflict, but could be the result of any form of underlying conflict. For example, Shear, Cooper, Klerman, Busch and Shapiro (1993) argued that, in addition to sexual themes, social and cultural themes, such as underlying aggressive impulses or conflicts between dependence and independence, may also be the root of the crucial underlying conflict, and thus play an important role in the generation of anxiety.

The underlying conflict can be seen as necessary but not sufficient condition for PD to occur. Some psychodynamic views consider that the immediate cause of anxiety is unconscious mental imagery of frightening situations arising from the underlying conflict (Michels et al., 1985). In this formulation, the circumstances leading to acute anxiety start with a subject's initial appraisal of a state of affairs as dangerous (Edelson, 1988). The next stage is that of imagining the situation.

> "The state of affairs is anticipated by the subject; it does not actually exist. Thus, it is imagined, not perceived, by the subject. The subject believes […] that this imagined state of affairs will become an actual state of affairs if he acts upon some impulse of his own" (Edelson, 1988, p. 91).

Imagery of these frightening situations is provoked either by adverse "life events" (Busch et al., 1999) or by unacceptable instinctual wishes (Sweeney & Pine, 2004) though no mechanism has been proposed in either case. It can lead to one or multiple behavioral or mental response patterns, which are involved in anxiety reduction (Michels et al., 1985).

The intra psychic conflicts are more fearful for the person with panic disorder than the experience of a panic attack (Busch et al., 1999). Thus, anxiety can lead to symptoms of panic disorder in an attempt to avoid experiencing the underlying conflict. This process of internal conflict may take place in combination with the occurrence of acute stressors, which enhance the likelihood of the expression of panic symptoms (Busch et al., 1999). When defense mechanisms are repeatedly unable to inhibit the expression of symptoms, more anxiety is generated and can then become problematic (Edelson, 1988; Sweeney & Pine, 2004).

Although it is not considered in most versions of the theory, the psychodynamic framework does allow for a genetic predisposition (Busch et al., 1999; Shear et al., 1993). Thus, Shear et al. (1993) propose that an "inborn neurophysiologic irritability predisposes to early fearfulness." (p.859). Early life events, including trauma, may also contribute to development of anxiety neurosis (Bandelow et al., 2002; Shear et al., 1993). Shear et al. (1993) found that their PD patients recalled their parents as angry, frightening, critical, or controlling. They suggest that this leads to a weakness in the formation of early relationships. Such factors, then, create susceptibility for imagining of dangerous situations, related to abandonment, for example.

A generalized psychodynamic theory of panic disorder has been depicted in Fig. 1. In this we have picked out what seem to be the essential components both in terms of prerequisites and in terms of processing at the time of the panic attack. Prerequisites of the psychodynamic theories of any disorder, the antecedent cause, seem to be adverse early life events, perhaps involving the parents, possibly together with a predisposition of low anxiety threshold or particular defensive style. A full theory would have to give some causal account of such predisposition.

The combination of predisposition together with early adverse events gives rise to an unconscious underlying conflict with its attendant anxiety and a tendency to appraise situations as dangerous. The prerequisites, the history of the individual, are shown by components in oval shaded shapes connected by solid lines with solid arrows. The processing at the time of a panic attack, the immediate cause, is shown by elements in rectangular boxes joined by

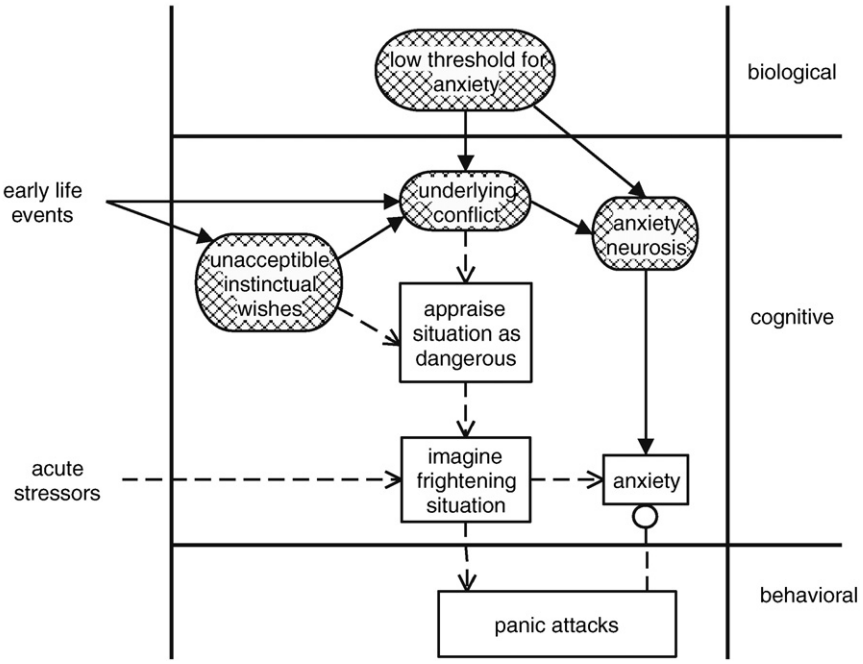

Fig. 1. A causal model for a generalized psychodynamic theory. The oval boxes, connected with solid arrows, represent the causal history of the individual — the prerequisites. The other elements, and the connecting hollow arrows, represent the processing at the time of the panic attack.

dotted lines. This starts with presence of acute stressors, when the level of anxiety produced by the underlying conflict becomes intolerable; the patient imagines a frightening situation and proceeds into a panic attack. The result of the panic attack, according to the theory, is to reduce the level of anxiety caused by the conflict. One thing missing from the underlying theories, and from the diagram, is how the system learns that panic is a way of controlling anxiety. This assumption has complex cognitive implications which need elucidation.

An alternative way of conceptualizing the patient's relation with their parents might be through the role of attachment expressed by Bowlby (1973). Bowlby conceptualized panic as an extreme form of anxiety. For him, the early lack of parent's protection would lead to exacerbation of the perception of threat later in life.

3.2. Cognitive hypotheses

There has been a number of causal theories of panic disorder within a cognitive framework. Some researchers focused their attention on identification of and subsequently modification of negative cognitions involved in the process of panic attacks (Clark, 1986; Rachman, 1994). Others were interested in identifying the role of *positive* cognitions, in order to explain the central role of coping abilities in panic disorder, with negative cognitions being relegated by them to a subordinate role (Bandura, 1988).

3.2.1. Clark

Clark's explanation of panic disorder was based on the subject's catastrophic misinterpretation of certain bodily sensations that are associated with anxiety responses.

> "A wide range of stimuli appear to provoke attacks. These stimuli can be external (such as a supermarket for an agoraphobic who has previously had an attack in a supermarket) but more often are internal (body sensation, thought or image). If these stimuli are perceived as a threat, a state of mild apprehension results. This state is accompanied by a wide range of body sensations. If these anxiety-produced sensations are interpreted in a catastrophic fashion, a further increase in apprehension occurs. This produces a further increase in body sensations and so on round in a vicious circle which culminates in a panic attack." (Clark, 1986, pp. 462–463).

Clark's model is shown in Fig. 2.

Clark (1996) focused on the importance of the repetitive nature of panic attacks. He made a distinction between the infrequent autonomic events regarded as panic attacks in the normal population, and the recurring panic attacks that typically culminate in a diagnosis of panic disorder. Bodily sensations, such as palpitations and dizziness, could arise in daily events such as exercise, walking or driving and even be caused by non-anxiety-related emotional states, such as excitement, anger, and happiness. In panic disorder, the individual cognitively misinterprets these bodily sensations as evidence of impending danger. Thus, palpitations might be misinterpreted as a signal of a heart attack, dizziness as evidence of impending loss of control. These low-level bodily sensations are what Clark means

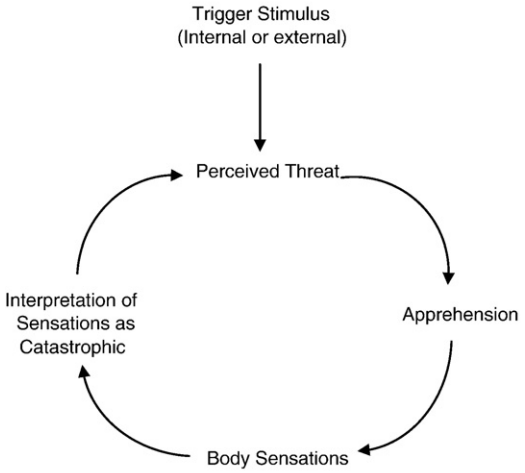

Fig. 2. The vicious circle of panic proposed by Clark (1986).

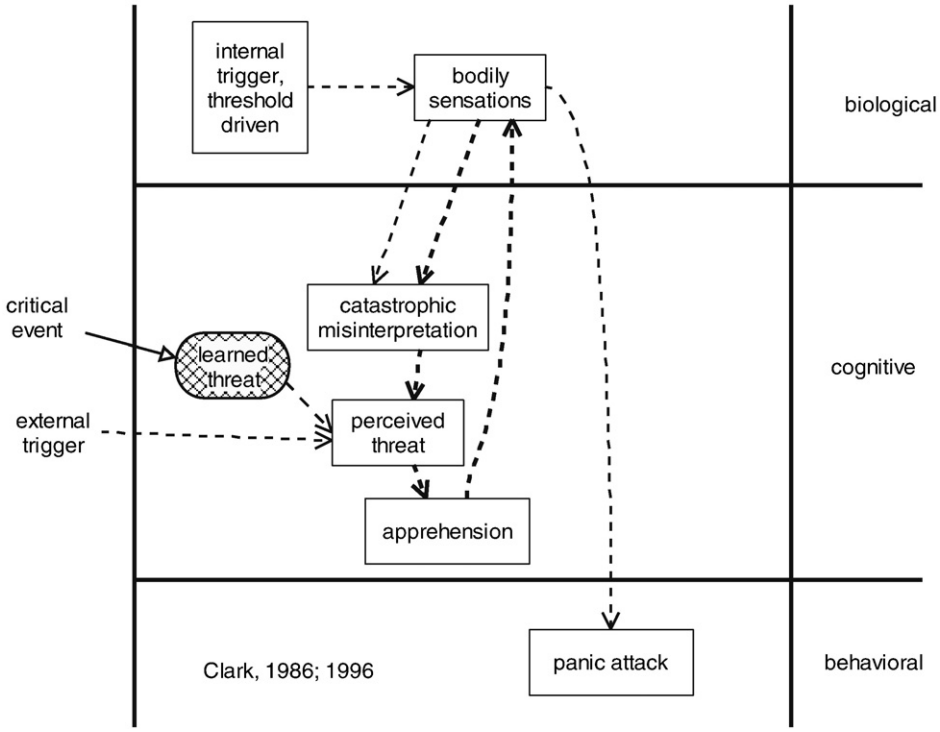

Fig. 3. Clark's (1986) theory. The learned threat is the only pre-requisite.

by "internal trigger stimuli". After the initial trigger, these bodily sensations become part of the vicious circle.

The causal model for Clark's theory is given in Fig. 3. In Clark's theory the only antecedent cause is the learned threat and this is caused by some previously occurring critical event. In the figure, the vicious circle indicated by heavy dotted lines. This can be started off either by an external trigger or by an internal trigger: an initial, relatively small variation in bodily sensations. For this, there must be a threshold level of bodily sensation above which the panic attack will be triggered. It would seem necessary that the bodily sensation threshold for a catastrophic misinterpretation and, perhaps, the connections constituting the vicious circle would also be abnormal. Clark does not elaborate on this issue.

3.2.2. Bandura

In contrast to Clark, Bandura (1988) focused on the central role of self-efficacy. By this he meant an individual's perception of their own ability to cope with threat, in this case, their own sense of panic. Self efficacy is a generative capability in which multiple sub skills must be continuously employed to manage different circumstances often containing unpredictable and stressful elements. Individuals with the same sub skills may, therefore, perform poorly, adequately, or extraordinarily, depending on their self-beliefs of efficacy, which affect how well they use the capabilities they possess. Thus, individuals who believe themselves to be inefficacious are likely to effect limited change even in environments that provide many potential opportunities. Conversely, those who have a firm belief in their own efficacy figure out ways of exercising some measure of control in environments containing more limited opportunities and many constraints.

Bandura thought that a sense of threat could be caused both by individuals' appraisal of their own coping abilities and by the assessment of perceived dangers of the environment; however, he conceptualized the role of perceived threat and danger in the process of panic attack as subordinate to the primary effect of low self-efficacy. Accordingly, reductions in panic disorder would be brought about by changes in self-efficacy rather than by reduction in catastrophic misinterpretation of bodily sensations.

The causal model of Bandura's theory resembles that of Clark, with low self-efficacy replacing learned threat. However, the only trigger in Bandura's theory is an external trigger which, in conjunction with lower self-efficacy leads to a perceived threat, and the initiation of the vicious circle which leads to the panic attack. Note that Bandura does not specify where the factor of low self-efficacy comes from (for example, whether it is a trait), or whether there are any other developmental contributions to the condition. Clearly, the complete causal model would indicate such factors. Note that the idea of self-efficacy, as Bandura uses it, is a complex factor, being the outcome of self-monitoring of performance. A component of it may be a trait, and it certainly would be subject to a variety of environmental influences, none of which have been considered here. Some of these issues were addressed by Casey, Oei, and Newcombe, (2004) in an extension of Bandura, to be discussed below.

3.2.3. Beck

Positioned between the theories of Clark and Bandura is the model of Beck (Beck, Emery and Greenberg 1985). He argued for the importance of catastrophic misinterpretation of bodily sensations that are central in the process of appraisal. However, he assumed that there were three other factors that could be involved in the panic disorder: namely, perception of the likelihood of danger, the individual level of coping abilities and rescue factors.

Beck explained that the central role in all anxiety disorder was the sense of vulnerability, defined as "a person's perception of himself as subject to internal or external dangers over which his control is lacking or is insufficient to afford him a sense of safety" (Beck et al., 1985, p. 67). He does not specify the extent to which the sense of vulnerability is under genetic influence or acquired.

The causal model for Beck's theory would essentially be the same as that for Bandura, with *vulnerability* in place of *low self-efficacy*. The reader may not think that the two terms are well differentiated. Indeed,

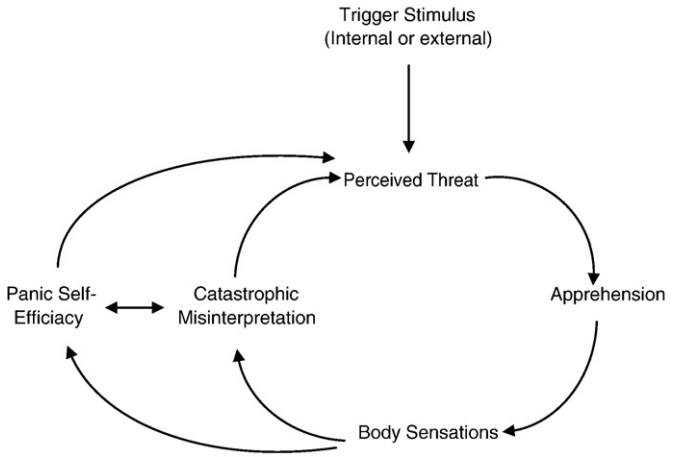

Fig. 4. The vicious circle of panic proposed by Casey et al. (2004). This is a modification of Clark's view shown in Fig. 3.

it could be that choice of one over the other could be determined by their relative effectiveness as constructs used in CBT.

3.2.4. Casey

Recently, Casey et al. (2004), drawing on the work by Clark, Bandura, and Beck, described a new Integrative Cognitive Model for panic disorder, in which both catastrophic misinterpretation of bodily sensations and panic self-efficacy independently contribute to and mediate the cognitions that are involved in the maintenance of the sequential and repetitive process of panic disorder. Casey et al. (2004) point to studies indicating that factors, such as the level of self-efficacy may affect physiological arousal. In their thinking, then, such cognitive factors should be incorporated early in the circle of panic disorder. For example, a very low level of self-efficacy could in itself result in sufficiently high arousal to start the panic disorder cycle. Casey et al. (2004) depict their model as in Fig. 4, in terms of a variation from Clark's model which we showed in Fig. 2.

The main focus in CBT based on this work is on development of self-efficacy. This usually results in the reduction of the probability of a panic attack (Casey et al., 2004). Furthermore, as one can see in Casey's model, self efficacy may influence perceived threat at the beginning of the vicious circle. CBT, then, acting at this level, may positively change the perception of some situation which otherwise could create the condition for starting the vicious circle of panic. However, according to Casey, such self-efficacy also interacts with and influences the next steps of the vicious circle. Indeed, this positive cognition may directly affect both body sensation and catastrophic misinterpretation. The influence of positive cognition brought about by CBT, would be especially important for the stage of catastrophic misinterpretation. Instead of a particular sensation being interpreted in such a way as to set the whole panic process in motion, the influence of the positive cognition would be to change the interpretation completely. This in turn could create the conditions for an enduring new interpretation of body sensations, finally creating a deletion of this circle.

The causal model for Casey et al. (2004) is given in the next figure (Fig. 5). This differs from Bandura's theory in two main ways. The first is the role of low self-efficacy in increasing physiological arousal which then initiates the vicious circle. The second is the link from low self-efficacy to catastrophic misinterpretation. This link has a circle on it indicating the inhibitory nature of the relationship between the two, with the plus sign indicating that it is the rise in self-efficacy which leads to the reduction in catastrophic misinterpretation. In the model, the role of self-efficacy becomes clear both in triggering the vicious circle in the first place, and then being the means of inhibiting the circle when it becomes the target of therapy. The multiple causes are clarified, and the importance of a combined treatment becomes clear.

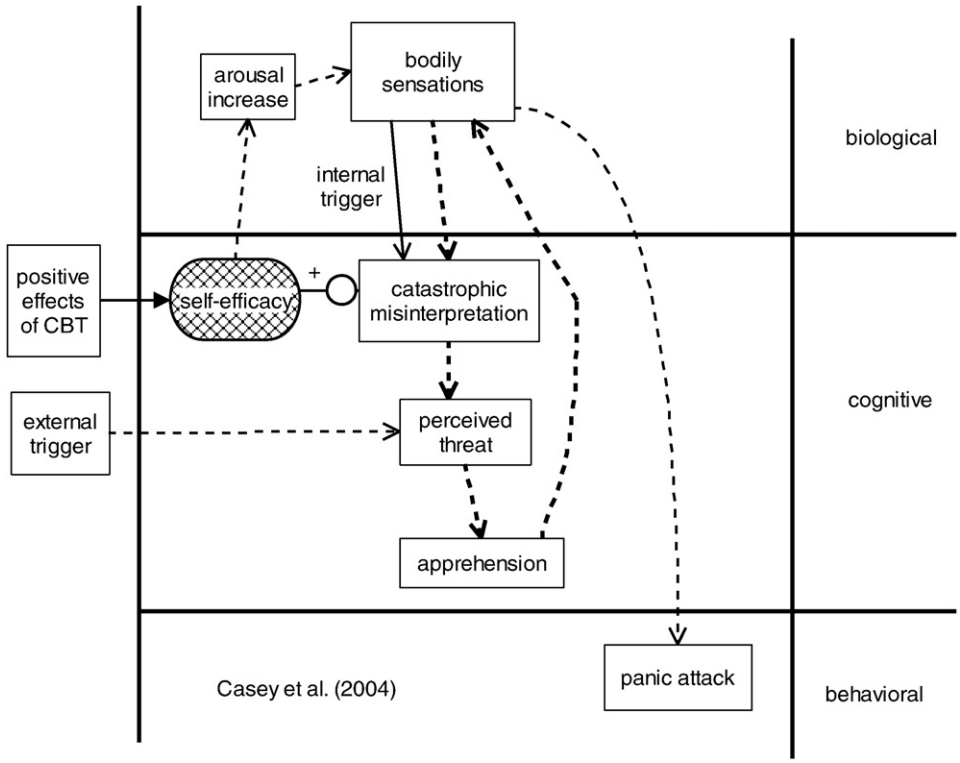

Fig. 5. Casey et al.'s (2004) theory of panic disorder. Low self-efficacy is postulated as a key element on the grounds of the effectiveness of CBT targeting this factor. Low self-efficacy is meant to lead to increase in arousal, and increase in self-efficacy is meant to inhibit the catastrophic misinterpretation.

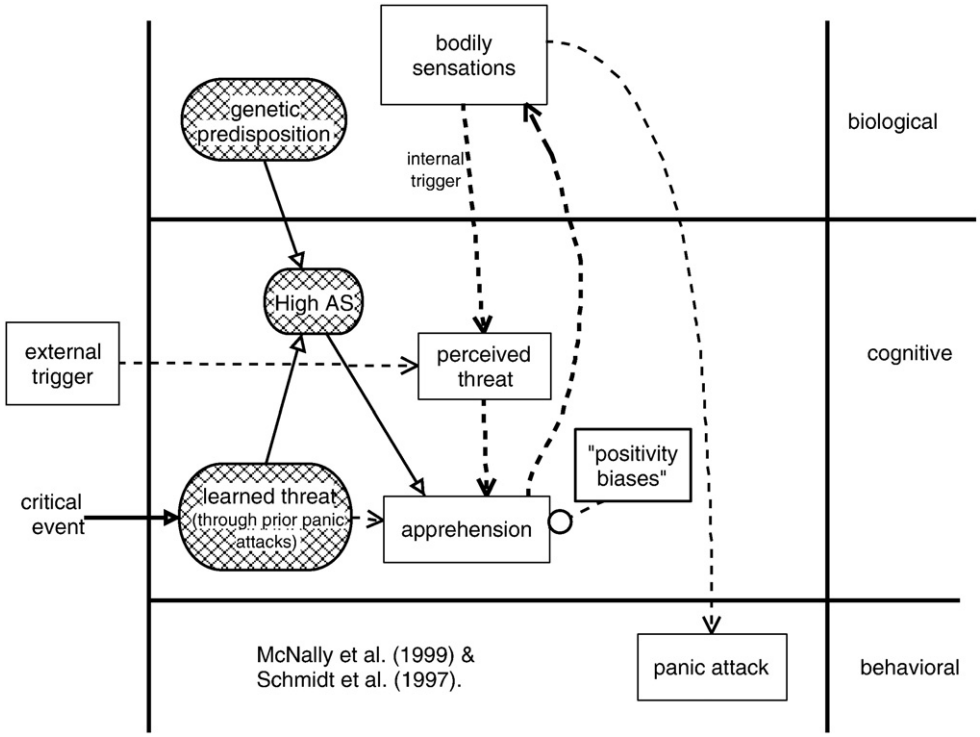

Fig. 6. Causal model for McNally et al. (1999) and Schmidt et al. (1997). High AS (anxiety sensitivity) is a risk factor for the development of panic attacks, and thus the learned threat.

3.2.5. Other cognitive theories

In a different vein, some authors (McNally & Foa, 1996; Reiss & McNally 1985) have focused their attention on the role of anxiety sensitivity (AS) in the process of panic disorder. AS refers to fear of anxiety-related sensations and is measured by the Anxiety Sensitivity Index (ASI). Some studies (McNally & Foa, 1996; Struzik, Vermani, Duffin & Katzman, 2004; Sturges, Goetsch, Ridley & Whittal, 1998) found that anxiety sensitivity is a dispositional variable which is especially elevated in people with panic disorder. The most important finding was that ASI scores predict panic symptoms in response to biological challenges (e.g., carbon dioxide inhalation) that provoke feared bodily sensations. McNally (1994) contrasted AS theory with the cognitive model of panic (Clark, 1996; Wells, 1997, Salkovskis, 1998; Clark and Salkovskis, 1989), emphasizing the fact that AS is the fear of the anxiety/arousal sensations which are actually occurring and not the catastrophic misinterpretation of those sensations that is at the centre of the other cognitive hypotheses. We have interpreted such statements as an indication that, for McNally, catastrophic misinterpretation is not in the vicious circle that typifies PD (though, of course, it may still take place). The resulting Causal Model is shown in Fig. 6.

Anxiety sensitivity has been established as a cognitive risk factor for the development of panic attacks (McNally, Hornig, Hoffman & Han, 1999; Schmidt, Trakowski & Staab, 1997). These results suggest that more marked interpretive biases for internal cues are evident at higher levels of anxiety. McNally et al. (1999) speculated that the presence of what they described as "positivity" biases, may protect people with high anxiety sensitivity from developing panic disorder. It is plausible, then, but not clearly established, that the anxiety indices, low self-efficacy and high AS, may be partially determined or augmented by the occurrence of a panic attack. If one wished to represent this in a causal model it would be more complex but manageable.

3.2.6. A composite cognitive theory

We can now attempt to put together these various cognitive theories in order to see the extent to which they are compatible or contradictory. The composite cognitive theory is shown in Fig. 7. The patient comes with three antecedent conditions: *lower self-efficacy* arising from early attachment problems, in the manner of Bowlby (1973), *high anxiety sensitivity*, arising from a genetic predisposition or from attachment problems, and *learned threat* arising from some early critical event. Together, these make the system underlying the vicious circle susceptible to being triggered. This can happen either externally, with a combination of the external trigger and the learned threat (the ampersand means that both the related links are needed), or internally. Internally, we have allowed low self-efficacy to lead to an increase in arousal levels, leading to bodily sensations that trigger the vicious circle. We have also allowed an option to have the circle operate without catastrophic misinterpretation, as suggested by McNally et al. (1999).

Thus far, we see that the different theories fit together in a way that leads to panic attacks being overdetermined. There are several approaches that occur to us on studying the composite:

1. To question whether all the crucial constructs are valid, namely, learned threat, high AS and low self-efficacy.
2. To ask whether certain of these constructs are themselves caused by another. For example, if someone acquires a learned threat [in Clark's terms] will they develop high AS.
3. To ask whether the three constructs correspond to distinct subgroups of PD patient or could be seen as three dimensions, with each patient having a value on each.

The next Fig. 8 is a pure causal model of the composite cognitive theory. In this figure we focus on the state on the PD sufferer, indicating the precursors for the various elements. In particular, the possible developmental relationships between high AS and low self-efficacy are shown. Such links are missing in Fig. 7, since there are no theories that postulate an interaction between these factors in the course of a panic attack. What we include in Fig. 7 but omit from Fig. 8 is the detail of the operation of the system during a panic attack. Thus, the vicious circle is here referred to simply as a state of the patient, not as a mechanism. The causal model can also be seen as a description of the patient's history.

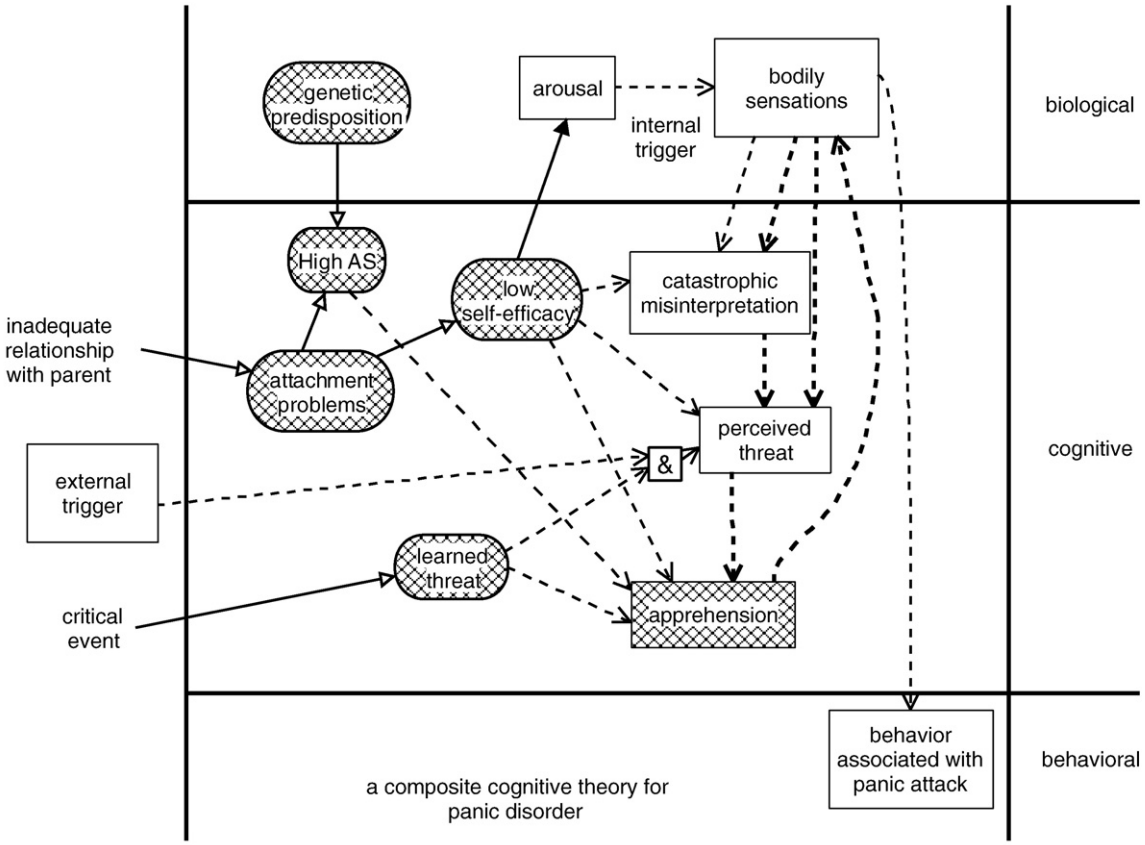

Fig. 7. A composite cognitive theory for panic disorder. As before, the oval boxes and hollow arrows represent the prerequisites, the solid arrows the current processing during a panic attack. The dotted lines indicate the vicious circle.

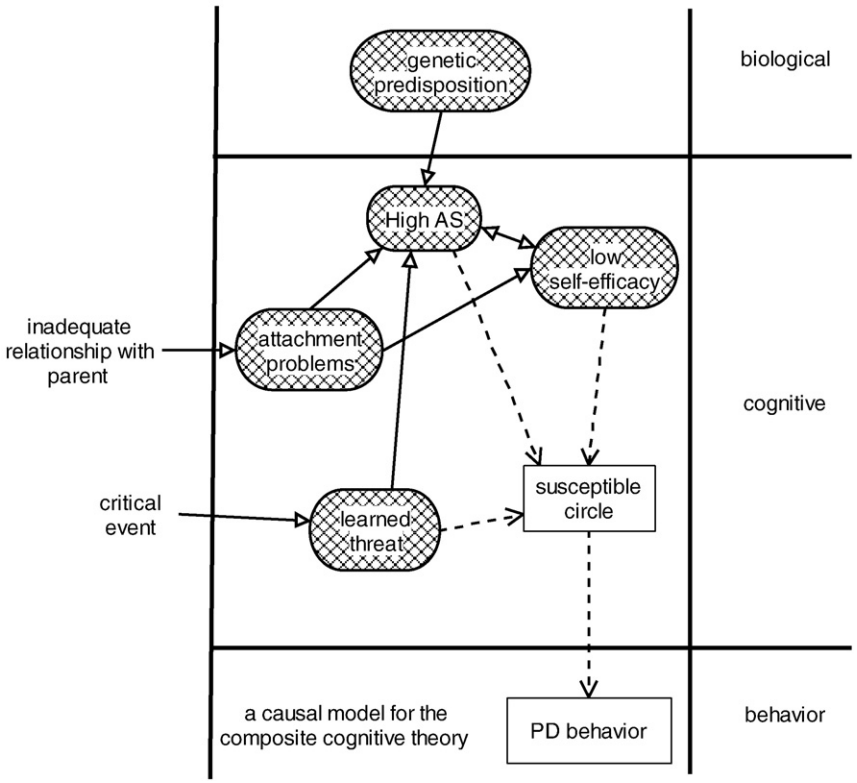

Fig. 8. A causal model for the composite cognitive theory. The one factor that has not been included is any notion of susceptibility to catastrophic misinterpretation postulated by Clark (1986).

3.3. Biological hypotheses

3.3.1. Neuroanatomical theories— Gorman

Many biologically-based causal theories have been postulated with regard either to specific anxiety disorders or to anxiety disorders in general (Gray, 1985). These theories have in common the fact that they focus on heritability and the neurological abnormalities that underlie anxiety disorders (Pine, Cohen, Gurley, Brook, & Ma, 1998). A typical theory of this sort is the Neuroanatomical Hypothesis of panic disorder (Gorman, Kent, Sullivan, & Coplan, 2000). This theory posits that the behavioral symptoms of panic disorder are mediated by a fear network in the brain, which is centered in the amygdala and includes the prefrontal cortex, insula, thalamus, and amygdala projections to the brainstem and hypothalamus. Simply put, this theory states that people with panic disorder have an extremely low threshold for the activation of the fear network in their brains. Excessive activity in this network leads to autonomic and neuroendocrine activation through the projections to the brainstem and hypothalamus from the amygdala resulting in the typical PD symptoms.

The lateral nucleus of the amygdala receives afferents from cortical regions involved in processing and evaluating sensory information. According to Gorman et al. (2000):

> "Potentially, a neurocognitive deficit in these cortical processing pathways could result in the misinterpretation of sensory information (bodily cues) known to be a hallmark of panic disorder, leading to an inappropriate activation of the "fear network" via misguided excitatory input to the amygdala" (p. 495).

We will note here that the notion of "misinterpretation" is a cognitive one, and resembles the idea that is central to Clark's theory discussed above. We will return to this point later.

Gorman et al. (2000) proposed that activation of the fear network as a result of cognitive misinterpretations, could lead to the release of certain neurotransmitters that can cause autonomic behavioral responses related to panic disorder. These responses include an increase in respiratory rate, increases in blood pressure, heart rate, defensive behaviors and postural freezing. Thus, processes at the biological level can directly lead to behavioral symptoms.

One of the techniques of the neuroanatomical approach to panic disorder is to attempt neuroimaging on the brain regions which are supposed to be involved during the panic attack. While there are several technical problems relating to neuroimaging and emotion (Fox & Raichle, 1987; Gorman et al., 2000), there are studies which have demonstrated the importance of certain structures in the fear brain network. Thus, Fredrikson, Wik, Fischer and Anderson (1995) used PET to look at changes in the brains of healthy subjects during aversive classical (fear) conditioning. They demonstrated significant increases in rCBF in several sub cortical structures implicated in the fear network, including the thalamus and the hypothalamus. More

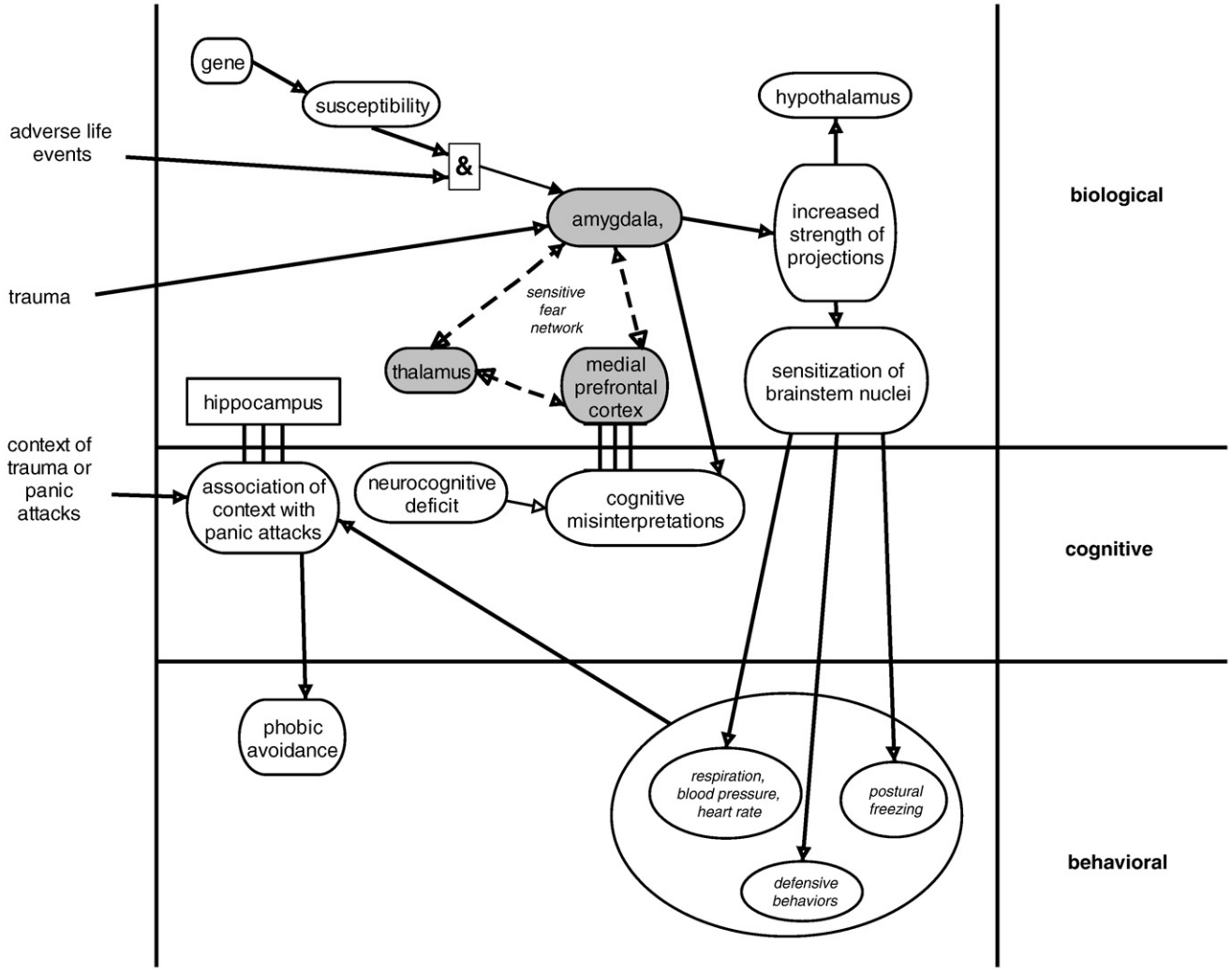

Fig. 9. A representation of the causal aspects of Gorman et al. (2000) neuroanatomical theory. Note that Gorman et al. (2000) include two cognitive constructs in their theory, each of which has an anatomical equivalent.

recently, fMRI has been used with healthy subjects, who had increased activation of the amygdala and periamygdaloid cortical areas during conditioned fear acquisition and extinction (LaBar, Gatenby, Gore, LeDoux & Phelps, 1998). In addition, several investigators have shown specific activation of the amygdala in response to the presentation of affectively negative visual stimuli (Grodd, Schneider, Klose and Nagele, 1995).

Conditioned learning has an important place in this theory. The amygdala receives direct sensory information from brainstem structures and the sensory thalamus. This enables a fast response to what are seen as potentially threatening stimuli. According to the Neuroanatomical Hypothesis, contextual information from any frightening situation is stored in memory in the hippocampus which is linked directly to the amygdala. Accordingly, people with panic disorder associate these contextual factors with previous panic attacks, so the reoccurrence of that context leads to activation of the fear network and phobic avoidance (Gorman et al., 2000). We briefly note that there are many purely cognitive theories of memory that consider the same phenomenon without reference to conditioned learning (Brewin, Dalgleish, & Joseph, 1996).

Research has shown that panic disorder is highly familial. However, there is no conclusive evidence that panic disorder is heritable. Gorman et al. (2000) assume that susceptibility to panic and not panic disorder itself is inherited. At the environmental level, adverse life events, mainly disruptions in early attachment to primary caregivers and traumatic events during childhood, can contribute to the onset of panic disorder through the creation of a neurocognitive deficit. Furthermore, there are animal studies that have shown that disruptions in attachment to the mother causes changes in the infant's hormonal and physical responses to stress that endure throughout lifetime (Anisman, Zaharia, Meany & Merali, 1998). There are several authors who have postulated a link between the disruption of early mother–child relationships and later separation anxiety. There are also studies linking separation anxiety to panic disorder (Preter & Klein, 2008). We are aware of no theory that traces the causal link between early relationships and stress, and mark this as something which is in need of work.

The Neuroanatomical Hypothesis of panic disorder has been depicted in Figs. 9 and 10. In Fig. 9 we have attempted to give the causal model of Gorman et al.'s hypothesis (2000). On the model there are three different kinds of connections between the elements:

1. Causal connections, shown with open arrows.
2. Equivalence indications — shown by three lines without arrows. Thus the hippocampus is where there is association of context with panic attacks, and the mPFC is proposed to be the site of cognitive misattributions of threat (called "learned threat" in most of the cognitive models).
3. Interconnections within the fear network shown with dashed lines.

In the model, we depict there is a genetic origin to some susceptibility which, in conjunction with adverse life events leads to the development of a sensitive fear network. This, in turn, leads to an increased strength of projections from the amygdala to the hypothalamus and various brain stem nuclei. Sensitization of these nuclei gives rise to a variety of behavioral consequences which become associated in the hippocampus with the current context. This association can lead to phobic avoidance when the context is next encountered.

The major element missing is the learning of cognitive misattributions in the mPFC. Gorman et al. (2000) as already quoted, suggest

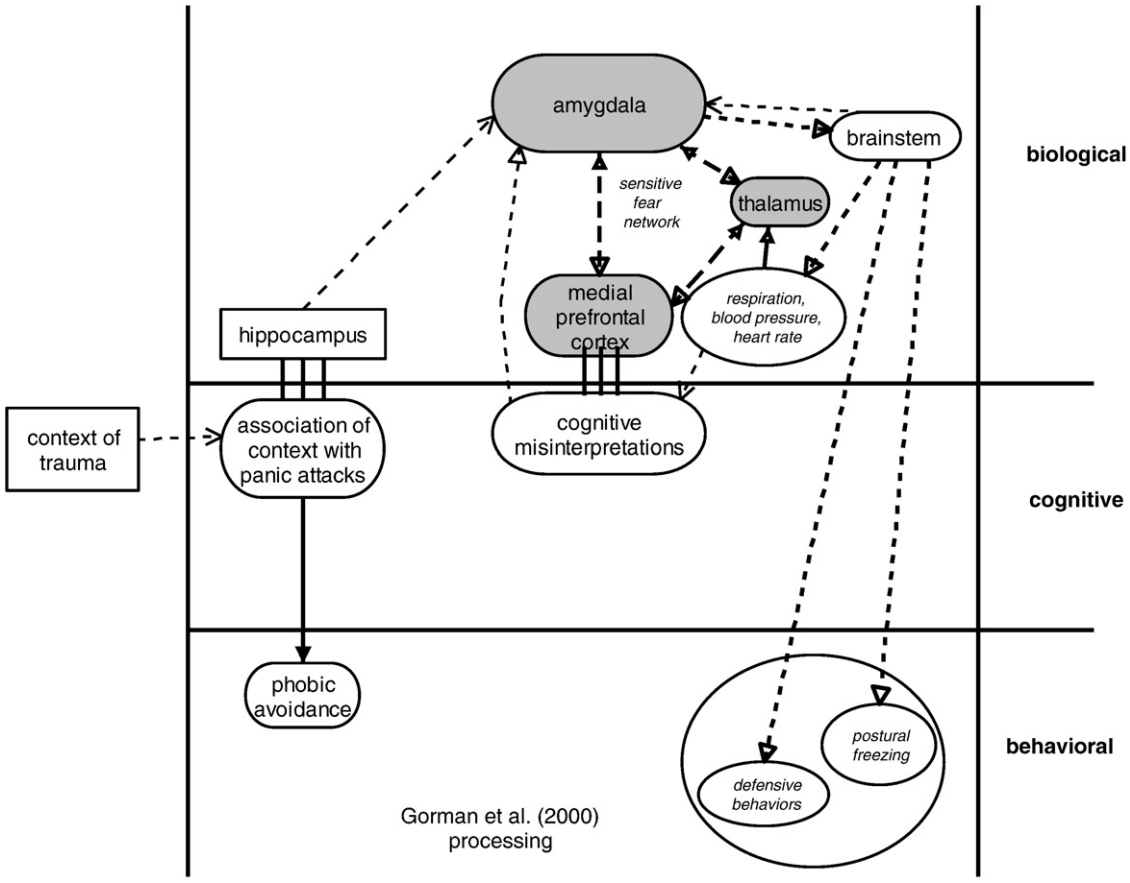

Fig. 10. The processing model underlying the theory of Gorman et al. (2000) in Fig. 9. In the theory there are two ways of triggering a panic attack. One is through the misinterpretation of visceral afferents (respiration, etc.) and the other is through the occurrence of the context of previous panic attacks.

some "neurocognitive deficit" in this area, but make no suggestions as to the nature of the deficit or the mechanism of its creation.

Finally we have the role of trauma. Gorman et al. (2000) comment that "it is not at all clear that panic disorder or any other anxiety disorder except posttraumatic stress disorder (PTSD) involves prior exposure to any aversive stimulus" (p.494) but do not discuss trauma any further. However, there is a need to show the role of trauma in those cases it does occur. In the figure, we have assumed that trauma has a direct impact on the fear network, leading to its sensitization.

Note that in this theory the hippocampus functions normally. It stores material normally and accesses this information when the appropriate cue occurs. The problem is with the content of the memory, particularly with respect to the information signaling "affect," that is sent to the amygdala. It is the interpretation of this signal in the amygdala that leads to an increase in arousal.

Fig. 9 is a causal model which gives the antecedent conditions for PD. In Fig. 10, we have represented the various processes that could be active in the course of a panic attack, according to the Gorman et al. (2000) hypothesis. The fear network would be triggered either by visceral afferents or by context. Taking the visceral afferents, Gorman et al. (2000) comment that "many patients with panic disorder are unbearably sensitive to relatively trivial somatic sensations such as mild dizziness, increase in heart rate, or slight tingling in a limb" (p. 502).

In the Gorman et al. (2000) model, such sensations enter the fear system through the thalamus. The second trigger point is through the hippocampus, in which have been stored the contextual associations of previous panic attacks or, where relevant, of the originating trauma. The hippocampus projects to the lateral nucleus of the amygdala, which, in turn, is connected with the central nucleus, the part of the amygdala that is in the fear network. When the PD patient encounters this context, the fear network could be triggered. Alternatively, the patient, anticipating the context, might avoid it.

The model makes it easy to appreciate the action and limitations of medication that Gorman et al. (2000) discuss, notably SSRI medication. There are three methods of operation suggested by Gorman et al. (2000):

1. An increase in 5-HT inhibits excitatory cortical and thalamic inputs to the amygdala, preventing the amygdala from being activated.
2. The projections from the central nucleus of the amygdala to the brainstem and hypothalamus have been inhibited.
3. SSRIs produce inhibition of the brainstem sites, locus ceruleus or parabrachial nucleus, either directly or through an effect on the amygdala.

In all these cases, it is clear from the model that autonomic and neuroendocrine activation would be affected. However, in the third case there would still be projections to the hypothalamus with resulting arousal, and in both the second and third cases the fear network itself would still be activated. In these cases, the effect of amygdala and MPFC activation on cognitive misattribution would still take place. In the first of the three cases, however, the fear network would not be activated. In all three cases, the activity of the hippocampus would be unaffected. Thus, one would still expect to find phobic avoidance. This is what Gorman et al. (2000) report.

3.3.2. Klein

Another theory with a strong physiological component is the suffocation false alarm theory (SFA) of Klein (1993). At first sight, this is a specific variation on Clark's theory. Clark talks about catastrophic misinterpretation of bodily signals, which would include those related to respiration. The main difference seems to be that Klein posits a "physiologic suffocation alarm signal" which is "erroneously triggered" (Preter & Klein, 2008, p. 603). While in Clark's theory there is a cognitive misunderstanding of an accurate biological signal, in Klein's theory there is a correct cognitive understanding of an erroneous biological signal. Preter and Klein (2008) review the theory and the related evidence, particularly in relation to smoking and pulmonary complaints. They, then, note that childhood separation anxiety and sudden loss are antecedents of PD, as other theorists have observed. Such antecedents do not fit well with the unadorned SFA theory, so

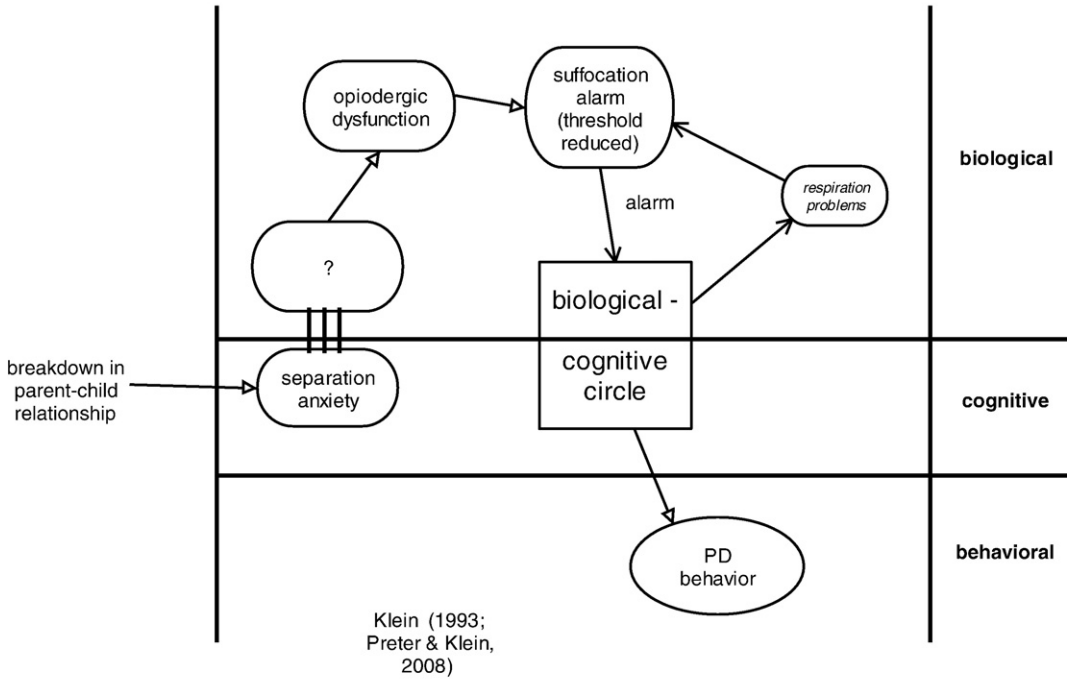

Fig. 11. A causal model for Klein's (1993; Preter & Klein, 2008) suffocation false alarm theory of panic disorder. The link between separation anxiety and the opioidergic dysfunction is not specified in the theory. We assume that the maintenance of a panic attack requires some cognitive/biological circle as in other theories, though this is not specified in Preter and Klein (2008).

Preter and Klein argue that the suffocation alarm threshold is reduced as a result of opioidergic dysfunction. This, they argue, by reference to the work of Panksepp (1998), is brought about by early, presumably extensive, separation anxiety. Their argument is complex and we will not attempt to summarize or evaluate it.

We have represented Klein's theory in Fig. 11. One element that is missing is a trigger for an individual attack. Preter and Klein (2008) talk about "spontaneous" panic (their quotation marks) with the assumption that the trigger from the alarm signal follows from a combination of normal variations in biological indicators, together with the lowered suffocation alarm threshold. We will comment on this in the discussion. Our inclination is to regard separation anxiety as a cognitive entity, since it is influenced by such cognitive factors as a feeling of loss. There will be some mechanism whereby this affects the opioid system, but this is unspecified. We have labeled it with a question mark.

In the absence of any alternative we have assumed that once the panic attack is triggered it is maintained by the same kind of interaction between cognitive and biological elements as in the other theories.

4. Causal modeling of panic disorder

In Figs. 12 and 13 we have attempted to summarize and combine the ideas in the theories we have reviewed. Fig. 12 indicates the components possibly active at the time of a panic attack. Fig. 13 reviews the proposals for the causal histories of the elements on Fig. 12. There are five main points.

1. Most theories find it necessary to postulate some sensitivity. This factor is usually seen as having a genetic contribution, possibly in combination with early adverse experiences or trauma. This component is variously termed as low threshold for anxiety, high anxiety sensitivity, a sensitive fear network, "anxiety neurosis" and low suffocation alarm threshold. Apart from the latter, which is very specific, these elements can be thought of as being substantially the same as each other, whether they are thought of as biological or cognitive. So AS [McNally/Schmidt] can be seen simply as an index of a property of the sensitive fear network. Accordingly, we have left it off Figs. 12 and 13 as being a construct without independent explanatory force, although, clearly, important from the point of view of diagnosis and treatment. For similar reasons, we have not included anxiety neurosis as a separate element, regarding it, rather, as a label for the activity of certain biological and cognitive elements.
2. From Fig. 12, it is clear that there are at least three ways of moderating activity in the sensitive fear network during a panic attack. First its activity could be dampened chemically. There is always the problem that such solutions tend not to be selective in their operation, and there does not seem to be evidence that it leads to any changes in the system. That is, once the medication ceases, the problems return. The other two approaches are

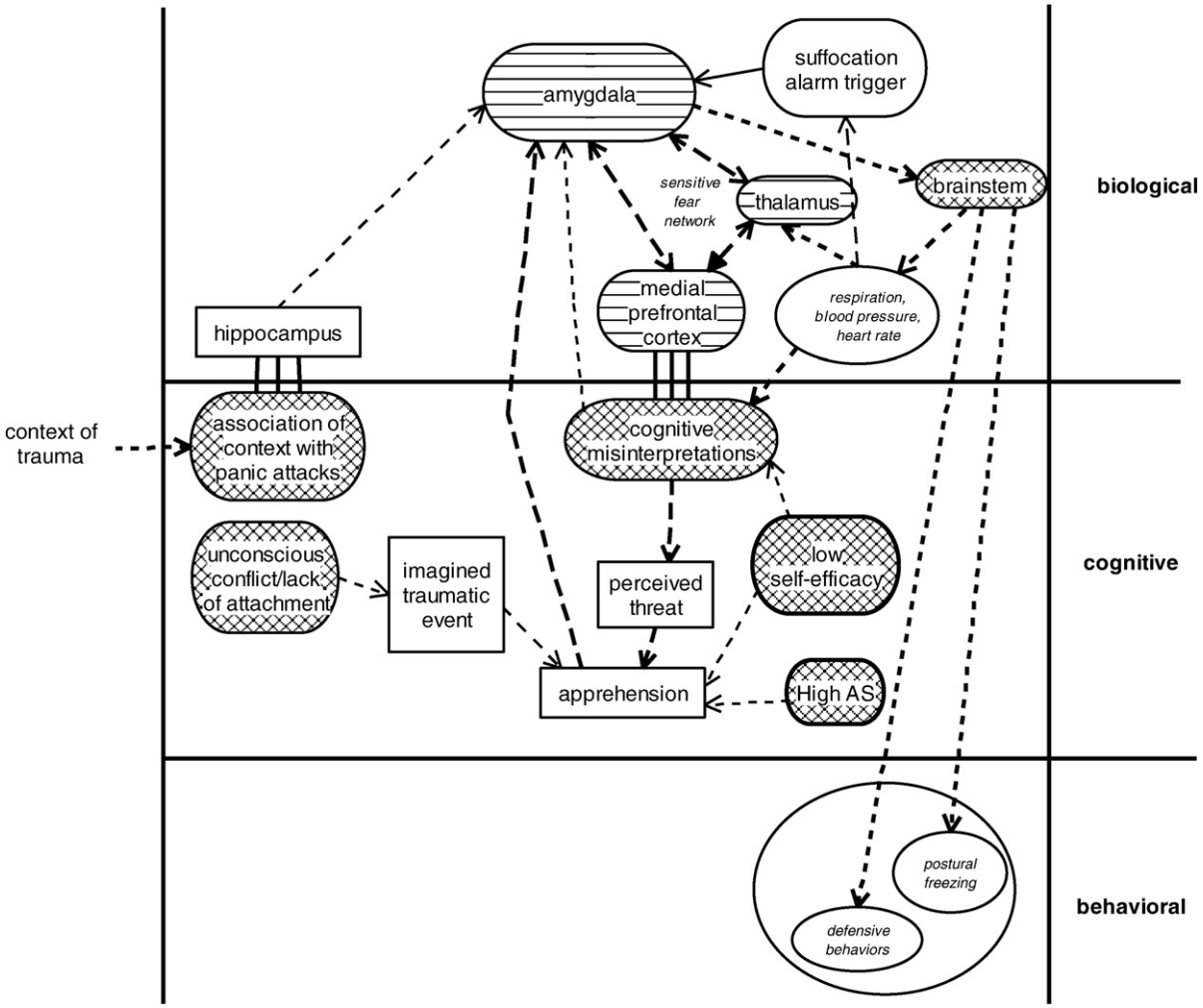

Fig. 12. A summary of the components proposed in various theories as being active during a panic attack. Pre-existing states and conditions are indicated by oval, cross-hatched forms. The sensitive fear network is shaded.

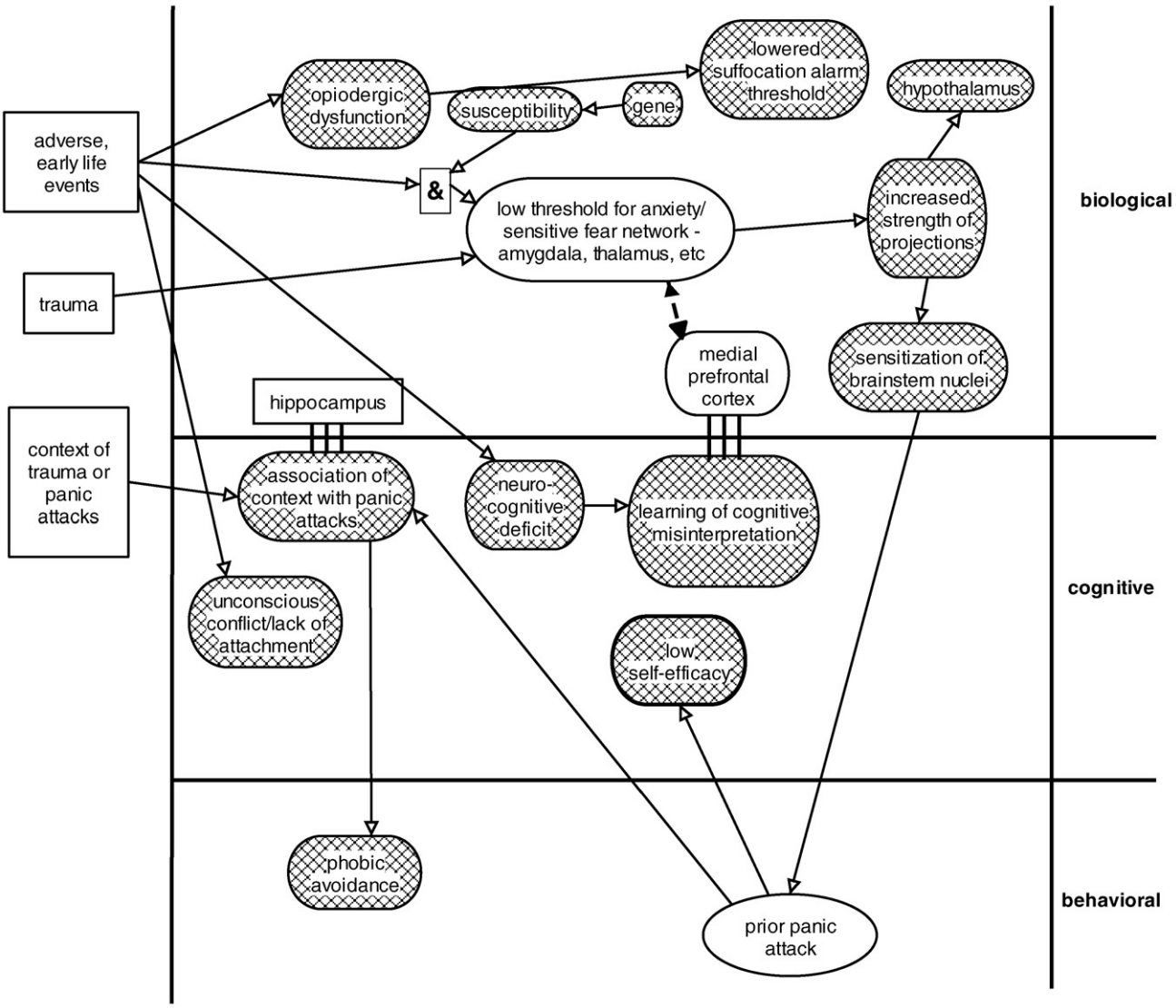

Fig. 13. A review of the various proposals for the causal histories of the elements on Fig. 12. At the biological level, the effects of external events or of the genetic contribution are to increase the sensitivity of various components.

cognitive and concentrate either on reducing the cognitive input into the fear network, or finding ways to negate the effects of the output from this network. To avoid having an over-complex diagram, these have not been diagrammed in the summary figure, but can be found in earlier figures. One example of the former would be to concentrate on reprogramming the learned threat. An example of the latter is focusing on improving self-efficacy, which, according to Casey et al. (2004) affects the cognitive misinterpretations.

3. There are two kinds of historical environmental input shown in Fig. 13. There is the specific one of an inadequate relationship with parents leading to attachment problems. There are also the more general "adverse life events" of Gorman et al. (2000) and the more specific "critical event" which leads to a "learned threat" in some of the cognitive models. Note that, in addition, it has been shown that certain "life style" aspects of the environmental appear to facilitate the development of panic disorder. Recently, research by Johnson et al. (2000) as well as Kaiya, Umekage, Harada, Okazaki & Sasaki (2005) indicated that such factors as like/dislike of physical exercise, drinking, smoking, coping skills to stressors and dietary habits as well as environmental factors including weather conditions could play a partial role in the development of panic disorder. Further research would demonstrate how such factors operated, either by affecting biological factors or cognitive ones. Most obviously, smokers would be more likely to trigger the suffocation alarm, and weather conditions could affect self-efficacy. With a model as comprehensive as that in Fig. 13, there is no temptation to try to constrain all influences into a single channel or to imagine a single cause. We deem it a strength of a causal model of this kind that it might encourage clinicians to think in terms of multiple determinants of complex disturbed behavior. This is a property of the models that has been exploited extensively by Frederickson and her colleagues (Frederickson & Cline, 2002; Frederickson, Webster & Wright, 1991) in the context of clinical assessment of children with special needs. Frith (1999) has made a similar point in relation to dyslexia.
4. There are several states or traits postulated to account for the sensitivity of some people. These include low self efficacy, which for Casey et al. (2004) could by itself lead to an increase in arousal which triggers the panic process. In some cases there is also the *learned threat*, in the cognitive theories, which can be seen as having the same function as the "association of context with panic

attacks" found in Gorman et al. (2000). However, Gorman et al. (2000) are quite explicit in believing that panic disorder is not related to other types of past "aversive stimuli." This is a substantive difference between Gorman and the majority of cognitive models but is ultimately an empirical issue. The cognitive constructs related to the learned threat can be viewed as equivalent to hippocampus function, as indicated in the figure. The structure of the theories is very similar, and we see no reason to think that Gorman et al. (2000) are talking about a different condition from the one described by the cognitive theorists. There could, of course, be an issue of clinical sampling.

5. All theories require a trigger, either internal or external, to initiate a panic attack. The external triggers can either be an event resembling a traumatic one in the past, or the context for such an event. In the psychodynamic model, there is a similar triggering input to the circle, but one in which the event is wholly imagined. The internal triggers can either be generalized anxiety triggers, which kick start a positive feed-back loop that proceeds without cognitive mediation, or some specific autonomic event which is misinterpreted cognitively. In all cases, we have diagrammed these triggers as affecting "apprehension," the construct used by Clark (1996), Beck and Clark (1997), Bandura (1988) and Casey et al. (2004). This appears an odd choice to us, since the construct is ill defined at best, and possibly ambiguous as to its cognitive/emotional versus autonomic constitution. However, it seems suitable as a holding term until some more appropriate one can be devised.

In review, Fig. 12 represents the variety of events that might be occurring at the time of a panic attack. Fig. 13 reviews the proposals for the causal history of the various constructs in Fig. 12. One of the aims of our analysis has been to see whether or not there are any fundamental differences among the theorists and whether or not they are competitive and/or cooperative in explaining PD. We have already discussed some of the similarities. There are differences which relate firstly to the cause of the sensitive fear network, and secondly to the conditions for triggering an attack. What is not clear to us is whether the differences are due to the existence of subtypes of PD or due to the predominance of multifactor causes. Thus, it may be that susceptibility is a function of negative attitude to oneself (low self-efficacy) brought about by problems of attachment, or by unconscious conflict of some kind, together with some genetic (trait) component. These might interact, and each could be self-sufficient.

Inasmuch as treatments focused on one theory or another are concerned, their success could be because of the specificity of the approach applied to a subgroup of patients, or could be because the current treatment programs all contain some general therapeutic component that improves the ability of the system to regulate itself cognitively.

5. Conclusion and clinical implications

By using the causal modeling framework we have been able to compare a variety of different theories and models of PD by expressing them in the same notation. From this, the differences and similarities have been highlighted and the crucial comparisons have become apparent. Unlike Roth et al. (2005), we have not attempted to assess the scientific status of the various theories.

As the joint model makes clear, the same system can be triggered both by internal and external triggers. We would add that the same system can be triggered both by known, consciously marked cues, as with the agoraphobic, or by cues that the patient does not consciously associate with the trauma (Brewin et al., 1996). Indeed, as we can see for the integrated cognitive model in Fig. 7, there are both internal and external triggers that might influence the onset and the maintenance of the disorder. For instance, patients with panic disorder with agoraphobia are characterized by an anxiety of either being in places or in situations where it could be difficult or awkward to get out, or where there was no likelihood of any kind of aid in the case of an unexpected panic attack. The typical threats in PD with agoraphobia include being outside alone, being in a line at the supermarket, for example, being on a bridge or traveling with bus or car.

Factors, such as agoraphobia, should be taken more into account when a clinician is planning a treatment since for this kind of patient the external triggers are more relevant. On the other hand, for patients with panic disorder without agoraphobia, the internal triggers derived from physiological changes and the associated bodily sensations are predominant in their pathology (Vincelli et al., 2000). This consideration is already taken into account partially by the CBT, where the treatment for patient with and without agoraphobia is developing in a different way. For patients with agoraphobia the treatment is more based on behavioral techniques, such as exposure to the threatened situation. For patients with PD without Agoraphobia, the CBT treatment is more cognitive, basically focused on the cognitive reorganization of the association between bodily sensation and cognitive misinterpretation (Bakker, van Balkom, Spinhoven, Blaauw & van Dyck, 1998). The differential impact of these two kinds of treatment can be clearly traced in Figs. 7, 12, and 13. In contrast, Barlow, Levitt and Bufka (1999) and Wilson (1996a,b) claim that clinicians have a tendency to use a fixed therapy protocol for all patients who have been diagnosed with a specific disorder.

We should also consider here the fact that the pharmacological treatments have short term effects, and improvements do not persist after the end of the therapy. On the other hand, CBT has a long term effect (Roth & Fonagy, 1996). Pharmacological treatments would affect the sensitive fear network and so dampen down the vicious circle. So the panic attack would not be maintained. On the other hand, it is clear in Fig. 13 that the underlying cognitive cause of the PD would be unaffected, so that on ceasing the medication, the network would return to its previous state and would still be susceptible to being triggered. In principle, CBT, for instance, while not affecting the networks, would also dampen down the operation of the circle, by affecting the "misunderstanding" and "apprehension" components but, in the long term would also reduce the chance of the circle being triggered in the first place. So the pharmacological and psychological treatments should be considered as complementary. In principle, the medication affords rapid symptomatic relief, but a psychological treatment is necessary to achieve an underlying resolution of the problem and to allow the medication to be withdrawn. The converse can also be the case: it is possible that a cognitive approach might not work because the fear network or the anxiety sensitivity is over-activated and the patient cannot work at cognitive level. In this case the therapeutic program will need to reestablish a "normal" biological level before cognitive work would be fruitful.

As we described above (particularly Figs. 7, 12 and 13), the use of the causal modeling framework in bringing together a variety of theories of PD has clarified the possible different roles of various internal variables and has highlighted the point that onset of a panic attack could be caused either by external triggers or by internal ones. We hope that the explicit characterization and combination of the theories in this way will help clinicians to re-conceptualize PD. On the one hand, the multi factorial nature of PD is manifest in Fig. 12, and, on the other hand, the relations among the factors become manageable. It becomes clearer which ones might interact and which pairs are likely to be independent. These aspects of the method might encourage clinicians to assess the nature of the internal variables and the kind of trigger responsible for initiating the panic attacks for each patient individually in order to set up the most effective treatment for an individual with this disorder. Indeed, we can see an argument for thinking of panic disorder as a symptom rather than as a diagnostic category.

References

Anisman, H., Zaharia, M. D., Meaney, M. J., & Merali, Z. (1998). Do early-life events permanently alter behavioral and hormonal response to stressors? *International Journal Developmental Neuroscience*, *16*, 149−164.

American Psychiatric Association, (1994). *The diagnostic and statistical manual of mental disorders*, (4th ed.). Washington, DC: Author.

Bandelow, B., Späth, C., Tichauer, G., Broocks, A., Hajak, G., & Rüther, E. (2002). Early traumatic life events, parental attitudes, family history, and birth risk factors in patients with panic disorder. *Comprehensive Psychiatry*, *43*(4), 269−278.

Bandura, A. (1988). Self-efficacy conception of anxiety. *Anxiety Research*, *1*, 77−98.

Bakker, A., van Balkom, A. J. L. M., Spinhoven, P., Blaauw, B. M., & van Dyck, R. (1998). Follow-up on the treatment of panic disorder with or without agoraphobia: A quantitative review. *Journal of Nervous and Mental Disease*, *186*, 414−419.

Barlow, D. H., Levitt, J. T., & Bufka, L. F. (1999). The dissemination of empirically supported treatments: A view to the future. *Behavior Research and Therapy*, *37*, 147−162.

Beck, A. T., Emery, G., & Greenberg, R. L. (1985). *Anxiety disorders and phobias: A cognitive perspective.* Basic Books: New York.

Beck, A. T., & Clark, D. A. (1997). An information processing model of anxiety: Automatic and strategic processes. *Behaviour Research and Therapy*, *35*(1), 49−58.

Blair, R. J. R. (1995). A cognitive developmental approach to morality: Investigating the psychopath. *Cognition*, *57*, 1−29.

Brewin, C. R., Dalgleish, T., & Joseph, S. (1996). A dual representation theory of posttraumatic stress disorder. *Psychological Review*, *103*, 670−686.

Bond, M., & Perry, J. C. (2004). Long-term changes in defense styles with psychodynamic psychotherapy for depressive, anxiety, and personality disorders. *American Journal of Psychiatry*, *161*, 1665−1671.

British Psychological Society, (1999). *Dyslexia, literacy and psychological assessment: Report for the British Psychological Society by a working party of the Division of Educational and Child Psychology*. Leicester: Author.

Busch, F. N., Milrod, B. L., & Singer, M. B. (1999). Theory and technique in psychodynamic treatment of panic disorder. *The Journal of Psychotherapy Practice and Research*, *8*, 234−242.

Bowlby, J. (1973). *Attachment and loss*, *Vol. II*. New York: Basic Books.

Casey, M. L., Oei, P. S., & Newcombe, A. P. (2004). An integrative cognitive model of panic disorder: The role of positive and negative cognitions. *Clinical Psychology Review*, *24*, 529−555.

Clark, D. M. (1986). A cognitive model of panic. *Behavior Research and Therapy*, *24*, 461−470.

Clark, D. M., & Salkovskis, P. M. (1989). *Cognitive therapy for panic and hypochondriasis.* Oxford: Pergamon Press.

Clark, D. M. (1996). Panic disorder: From theory to therapy. In P. M. Salkovskis (Ed.), *Frontiers of cognitive therapy* (pp. 318−344). New York: Guildford Press.

Edelson, M. (1988). *Psychoanalysis: A theory in crisis.* Chicago: The University of Chicago Press.

Fox, P. T., & Raichle, M. E. (1987). Cerebral blood flow and oxidative metabolism are focally uncoupled by physiological activation: A positron-emission tomography study. In M. E. Raichle & W. J. Powers (Eds.), *Cerebrovascular diseases* (pp. 129−138). New York: Raven Press.

Fredrikson, M., Wik, G., Fischer, H., & Andersson, J. (1995). Affective and attentive neural networks in humans: A PET study of Pavlovian conditioning. *Neuroreport*, *7*, 97−101.

Frederickson, N., & Cline, T. (2002). *Special educational needs, inclusion and diversity: A textbook.* Buckingham: Open University Press.

Frederickson, N., Webster, A., & Wright, A. (1991). Psychological assessment: A change of emphasis. *Educational Psychology in Practice*, *7*, 20−29.

Frith, U. (1999). Paradoxes in the definition of dyslexia. *Dyslexia*, *5*, 192−214.

Frith, U., Morton, J., & Leslie, A. M. (1991). The cognitive basis of a biological disorder. *Autism. Trends in Neuroscience*, *14*, 433−438.

Furukawa, T. A., Watanabe, N., & Churchill, R. (2006). Psychotherapy plus antidepressant for panic disorder with or without agoraphobia: Systematic review. *British Journal of Psychiatry*, *188*, 305−312.

Gorman, J. M., Kent, J. M., Sullivan, G. M., & Coplan, J. D. (2000). Neuroanatomical hypothesis of panic disorder, revised. *American Journal of Psychiatry*, *157*, 493−505.

Gray, J. A. (1985). Issues in the neuropsychology of anxiety. In A. H. Tuma & J. D. Maser (Eds.), *Anxiety and the anxiety disorders* Hillsdale, NJ: Erlbaum.

Grodd, W., Schneider, F., Klose, U., & Nagele, T. (1995). [Functional magnetic resonance tomography of psychological functions exemplified by experimentally induced emotions]. *Radiologe*, *35*, 283−289 [German].

Johnson, J. G., Cohen, P., Pine, D. S., Klein, D. F., Kasen, S., & Brook, J. S. (2000). Association between cigarette smoking and anxiety disorders during adolescence and early adulthood. *Journal of American Medical Association*, *284*, 2348−2351.

Kaiya, H., Umekage, T., Harada, S., Okazaki, Y., & Sasaki, T. (2005). Factors associated with the development of panic attack and panic disorder: Survey in the Japanese population. *Psychiatry and clinical neurosciences*, *59*(2), 177−182.

Kiesler, D. J. (1999). *Beyond the disease model of mental disorder*. Westport: Praeger.

Klein, D. F. (1993). False suffocation alarms, spontaneous panics, and related conditions. An integrative hypothesis. *Archives of General Psychiatry*, *50*, 306−317.

Krol, N., Morton, J., & De Bruyn, E. (2004). Theories of conduct disorder: A causal modeling analysis. *Journal of Child Psychology and Psychiatry*, *45*(4), 727−742.

LaBar, K. S., Gatenby, J. C., Gore, J. C., LeDoux, J. E., & Phelps, E. A. (1998). Human amygdala activation during conditioned fear acquisition and extinction: A mixed-trial fMRI study. *Neuron*, *20*, 937−945.

McNally, R. J. (1994). *Panic disorder: A critical analysis.* New York: Guilford Press.

McNally, R. J., & Foa, E. B. (1996). The limitations of self efficacy theory in explaining therapeutic changes in phobic behavior. In R. M. Rapee (Ed.), *Current controversies in the anxiety disorders* (pp. 369−372). New York: Guilford Press.

McNally, R. J., Hornig, C. D., Hoffman, E. C., & Han, E. M. (1999). Anxiety sensitivity and cognitive biases for threat. *Behavior Therapy*, *30*(1), 51−61.

Michels, R., Frances, A., & Shear, M. K. (1985). Psychodynamic models of anxiety. In A. H. Tuma & J. D. Maser (Eds.), *Anxiety and the anxiety disorders* Hillsdale, NJ: Erlbaum.

Monsen, J., Graham, B., Frederickson, N., & Cameron, R. J. (1998). Problem analysis and professional training in educational psychology: An accountable model of practice. *Educational Psychology in Practice*, *13*, 234−249.

Morton, J. (2004). *Understanding developmental disorders: A causal modelling approach.* Oxford: Blackwell.

Morton, J., & Frith, U. (1993). What lesson for dyslexia from Down's syndrome? Comments on Cossu, Rossini, and Marshall. *Cognition*, *48*, 289−296.

Morton, J., & Frith, U. (1993). Approche de la dyslexiede´veloppementale par la modelisation causale. In J. -P. Jaffre (Ed.), *Les actes de la villette* (pp. 263−278). Nathan: Paris.

Morton, J., & Frith, U. (1995). Causal modelling: A structural approach to developmental psychopathology. In D. Cicchetti & D. J. Cohen (Eds.), *Developmental psychopathology. Theory and methods*, *Vol. 1*. (pp. 357−390). New York: Wiley.

Morton, J., & Frith, U. (2002). Why we need cognition: Cause and developmental disorder. In E. Dupoux, S. Dehane, & L. Cohen (Eds.), *Cognition: A critical look. Advances, questions and controversies in honour of J. Mehler* Cambridge, MA: MIT Press.

Panksepp, J. (1998). Affective neuroscience: The foundations of human and animal emotions. New York: Oxford University Press.

Pine, D. S., Cohen, P., Gurley, D., Brook, J., & Ma, Y. (1998). The risk for early adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders. *Archives General Psychiatry*, *55*, 56−64.

Preter, M., & Klein, D. F. (2008). Panic, suffocation false alarms, separation anxiety and endogenous opioids. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *32*, 603−612.

Rachman, S. (1994). Psychological treatment of panic: Mechanisms. In B. E. Wolfe & J. D. Maser (Eds.), *Treatment of panic disorder: A consensus development conference* (pp. 133−148). Washington, DC: American Psychiatric Press.

Reiss, S., & McNally, R. J. (1985). Expectancy model of fear. In S. R. R. R. Bootzin (Ed.), *Theoretical issues in behaviour therapy* (pp. 107−121). San Diego, CA: Academic Press.

Roy-Byrne, P. P., Craske, M. G., & Stein, M. B. (2006). Panic disorder. *The Lancet*, *368*(9540), 1023−1032.

Roth, W. M., Wilhelm, F. H., & Pettit, D. (2005). Are current theories falsifiable? *Psychological Bullettin*, *131*(2), 171−192.

Roth, A., & Fonagy, P. (1996). *What works for whom? A critical review of psychotherapy research.* New York: Guilford Press.

Salkovskis, P. M. (1988). Phenomenology, assessment, and the cognitive model of panic. In S. Rachman & J. D. Maser (Eds.), *Panic: Psychological perspectives* (pp. 111−136). Hillsdale, NJ: Lawrence Erlbaum Associates.

Schmidt, N. B., Trakowski, J. H., & Staab, J. P. (1997). Extinction of panicogenic effects of a 35% CO_2 challenge in patients with panic disorder. *Journal of Abnormal Psychology*, *106*(4), 630−638.

Sims, K., & Morton, J. (1998). Modelling the training effects of kinaesthetic acuity measurement in children. *Journal of Child Psychology and Psychiatry*, *39*(5), 731−746.

Shear, M. K., Cooper, A. M., Klerman, G. L., Busch, F. N., & Shapiro, M. (1993). A psychodynamic model of panic disorder. *American Journal of Psychiatry*, *150*, 859−866.

Struzik, L., Vermani, L., Duffin, J., & Katzman, M. (2004). Anxiety sensitivity as a predictor of panic attacks. *Psychiatry Research*, *129*, 273−278.

Sturges, L. V., Goetsch, V. L., Ridley, J., & Whittal, M. (1998). Anxiety sensitivity and response to hyperventilation challenge: Physiologic arousal, interoceptive acuity and subjective distress. *Journal of Anxiety Disorders*, *12*, 103−115.

Sweeney, M., & Pine, D. (2004). Etiology of fear and anxiety. In T. H. Ollendick & J. S. March (Eds.), *Phobic and anxiety disorders in children and adolescents* (pp. 34−60). New York: Wiley.

Vincelli, F., Choi, Y. H., Molinari, E. B., Wiederhold, B., & Riva, G. (2000). Experiential cognitive therapy for the treatment of panic disorder with agoraphobia: Definition of a clinical protocol. *CyberPsychology and Behavior*, *3*(3), 375−386.

Wells, A. (1997). *Cognitive therapy of anxiety disorders. A practical manual and conceptual guide.* New York: John Wiley & Sons.

Wilson, G. T. (1996). Manual-based treatments: The clinical application of research findings. *Behaviour, Research and Therapy*, *34*, 295−314.

Wilson, G. T. (1996). Empirically validated treatments: Reality and resistance. *Clinical Psychology: Science and Practice*, *3*, 241−244.