

Psychological interventions in the treatment of generalized anxiety disorder: a structured review

Interventi psicologici nel trattamento del disturbo ansioso generalizzato: una revisione strutturata

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Summary

Objective

Generalized anxiety disorder (GAD) is a common and distressing condition, which typically has a persistent course and is often resistant to treatment. Cognitive behavioural therapy (CBT) has long been considered the first-line psychotherapeutic option for GAD, but many patients, and especially the elderly, do not experience long-lasting benefits. The aim of this review is to summarize the strengths and weaknesses of CBT and other psychological interventions to guide the development of new approaches and encourage new controlled studies to improve clinical outcomes.

Methods

We conducted a computerized literature search through PubMed and Google Scholar using the term generalized anxiety disorder/GAD, both alone and in combinations with the terms psychological treatment, cognitive behavioural therapy/CBT, CBT Packages, new CBT approaches, third wave CBT, internet computer-based CBT, psychodynamic therapy, brief psychodynamic therapy, applied relaxation, AR and mindfulness. The identified articles were further reviewed to scan for additional suitable articles. The search took place between October 2011 and September 2012.

Background

Generalized anxiety disorder (GAD) is a common and impairing disorder, often comorbid with other mental disorders, particularly major depression, other anxiety disorders, alcohol dependence and physical illnesses¹⁻³. It is the most common anxiety disorder in primary medical care settings, with lifetime prevalence rates ranging between 4.1-6.6%, and is associated with increased use of health services⁴. Women are almost twice as likely to be affected as men⁵, with a lifetime prevalence of around 7% in women and 4% in men. Other risk factors include age greater than 24 years; being separated, widowed or divorced; unemployment, and not working outside the home⁶.

Results

Cognitive behavioural therapy has been the most studied psychological treatment and is recommended as a first choice intervention for GAD. Applied relaxation has demonstrated similar effectiveness as CBT. Novel approaches and adaptations of GAD, such as well-being therapy, have been developed to provide a wider range of therapeutic choices: although preliminary results are encouraging, further studies are needed to establish their efficacy and relative value when compared to more conventional CBT.

Conclusions

CBT, applied relaxation, psychodynamic approaches, internet-computer-based CBT, mindfulness techniques, interpersonal emotional processing therapy metacognitive model and well-being therapy have all shown beneficial effects in treating GAD. The current "gold standard" in treating GAD remains CBT, but given the nature of the disorder, clinicians should be aware of the other therapeutic options when making treatment decisions in accordance with patients' needs.

Key words

GAD • Psychotherapy • CBT • Applied relaxation • Psychoanalysis • Well-being therapy

GAD is characterized by excessive and uncontrollable worry, accompanied by psychological symptoms (such as reduced concentration, distractibility, indecisiveness, memory difficulties, restlessness, irritability and nervousness)⁷, and physical (somatic) symptoms (such as back and neck pain, upset stomach, nausea, abdominal pain, tachycardia, fatigability, chest pain, dizziness and headache)⁸; all occurring for at least 6 months. Patients with GAD are chronically anxious, apprehensive and markedly worried about everyday life circumstances (for example, job responsibilities, finances, being late) and have exaggerated health concerns for both themselves and family members⁹. Children and adolescents with GAD tend

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to worry about their abilities or quality of their performance at school or sporting competitions, even when the performance is not assessed by others. Others worry about catastrophic events such as earthquakes or nuclear wars¹⁰. According to Borkovec and Newman¹¹, individuals with GAD may use worry as a maladaptive coping strategy, in misguided efforts to help them solve problems and prevent future dangers and threats. Given its chronic course, high disability, low rates of remission¹² and impaired quality of life, there is a continued need to advance both pharmacological^{13 14} and psychological treatment options. Current management usually involves pharmacotherapy, psychotherapeutic interventions or their combination¹.

Methods

We wished to provide a comprehensive and topical review of psychological interventions in GAD. This work extends a recent dissertation on new approaches to generalized anxiety disorder (Bolognesi, University of Bologna, 2010). We conducted a computerized literature search through PubMed and Google Scholar using the term generalized anxiety disorder/GAD, both alone and in combinations with the terms psychological treatment, cognitive behavioural therapy/CBT, CBT Packages, new CBT approaches, third wave CBT, internet computer-based CBT, psychodynamic therapy, brief psychodynamic therapy, applied relaxation, AR and mindfulness. Recent textbooks on GAD mainly in the English language were inspected, and the reference lists of identified articles were reviewed to identify additional suitable articles. The search took place between October 2011 and September 2012. The principal features of the identified studies are summarized in Table I.

Results

Cognitive-behavioural therapy

The theoretical basis of cognitive-behavioural therapy (CBT) was elaborated by Aaron T. Beck¹⁵ who developed a therapeutic intervention based on an assumption that affective disorders are mediated by cognitive factors. Cognitive interventions have the purpose of modifying maladaptive cognitions and beliefs (cognitive restructuring). In the treatment of GAD, behavioural approaches based on exposure techniques seem to have only limited effects, probably because the disorder is not characterized by a specific avoidance of external sources (unlike simple phobias or social phobia)¹⁶, and anxiety and worrying appear to occur without an obvious or specific cause. There are specific cognitive-behavioural packages for GAD¹⁷⁻¹⁹. Borkovec and Ruscio²⁰ have implemented

a treatment for GAD that seems to be the most specific²¹. The specific "ingredients" in this treatment include self-monitoring, questioning, use of techniques based on imagination and relaxation techniques.

CBT has been the most studied treatment²² and is considered by many to be the first choice psychological treatment for GAD²³. According to Fisher and Durham²⁴, more than 30 clinical trials have been conducted (around half of which employed DSM criteria) in which CBT was the main focus of intervention. Among the earliest summaries is the review of Chambless and Gillis²⁵, who examined 7 studies published between 1987 and 1992, in which GAD was treated with a CBT protocol and compared with placebo, waiting list and non-directive therapy. When compared with the control groups, there was evidence for the effectiveness of CBT, with an effect size pre/post treatment of 1.69, and pre-treatment/follow-up of 1.95. However, these studies were not homogeneous relative to the control group, and all involved only small numbers of patients.

Two subsequent reviews^{24 26} examined studies in GAD during the period 1980-1999, using outcome scores obtained from patients with the Hamilton Anxiety Rating Scale (HAM-A)²⁷ and State-Trait Anxiety Inventory (STAI-T)²⁸ as indicators. In the first²⁶, the authors examined 14 studies in which cognitive and behavioural therapies, relaxation, biofeedback and non-directive therapy were compared. In general, in post-treatment assessment there was a reduction of 54% in somatic symptoms measured with the HAM-A and a 25% reduction in the tendency to worry with the STAI-T. The most robust results were obtained with CBT and were comparable to those obtained in pharmacological treatment studies that compared anxiolytic drugs with placebo²⁹. In a subsequent review, Fisher and Durham²⁴ examined long-term outcomes (follow-up to six months) of anxious patients treated with CBT, behavioural therapy (BT), psychodynamic therapy, applied relaxation and non-directive therapy, incorporating six additional studies into the previous work. In general, at the follow-up assessment, only 2% of patients had worsened, 36% remained stable, 24% had made a symptomatic improvement and 38% had experienced remission of symptoms. Of all the treatment approaches considered, applied relaxation and CBT showed the highest remission rates (60% and 51% respectively). The authors emphasized that a proportion of patients derived no benefit from psychotherapy, and recommended longer follow-up periods.

Subsequently, Borkovec and Ruscio²⁰ reviewed 13 controlled studies in patients with anxiety disorders (GAD or panic disorder) and found significant efficacy for CBT approaches, when compared to strictly cognitive or behavioural interventions (post-treatment effect size = 0.26; follow-up = 0.54). In addition, CBT was found to be su-

perior in efficacy compared to treatments classified as “placebo”, which included psychodynamic therapy, supportive therapy and medications (effect size post/treatment = 0.71; follow-up = 0.3). Improvements obtained with CBT were maintained at follow-up (9 months), and there were only low drop-out rates. Hunot et al.³⁰ reviewed 25 studies to evaluate the effectiveness of psychotherapy in treatment of GAD, and in particular to establish whether psychological therapies classified as “cognitive-behavioural” were more effective than other forms of psychological intervention. In all studies included in this meta-analysis, CBT was compared with control groups (either treatment as usual, or waiting list) (13 studies) or other forms of psychotherapy (12 studies). CBT was found to lead to a greater reduction of anxiety symptoms after treatment compared to control conditions (46% vs. 14%); CBT was also found to reduce worrying and secondary symptoms of the disorder. However, the authors argued that the included studies did not clarify the long-term effects of CBT, possible adverse effects or the overall tolerability of psychological therapies for GAD.

More studies are needed to ascertain the potential efficacy of psychodynamic or supportive therapy in treatment of GAD compared to CBT. Covin et al.³¹ emphasized that the effect of CBT on pathological worrying has not been evaluated sufficiently, and carried out a meta-analysis on 10 studies to examine the efficacy of CBT, in the long term, to decrease pathological worrying as measured by the Penn State Worry Questionnaire (PSWQ³²). When considering PSWQ scores, a significant effect of CBT was seen compared to control conditions. However, the effect of CBT appeared to be influenced by age as younger adults responded more favourably to CBT. While many studies have shown that CBT is an effective treatment for GAD, only about 50% of treatment completers achieve high end-state functioning³⁰ or full recovery³³, and there is a need for augmentation of current CBT strategies with other approaches³⁴.

Applied relaxation

Ost³⁵ extended techniques of progressive relaxation (PR) and developed an intervention called “applied relaxation” (AR) arguing that it represents a coping strategy for tackling anxiety. Without reference to the potential role of dysfunctional beliefs and automatic thoughts, the therapist explains to the patient that he/she can learn to reduce the level of physiological arousal in specific stressful situations³⁶. In fact, a study comparing applied relaxation, cognitive therapy, the combination of both interventions (AR + CT) with a waiting list has been preformed, and the three active treatments had similar effectiveness and were more effective than being placed on a waiting list; moreover, the superiority was maintained over two years.

Borkovec and Costello³⁷ examined the efficacy of CBT compared to applied relaxation (AR) and non-directive counseling sessions (NDC) in a sample of 55 patients. After treatment, patients receiving CBT and AR improved similarly and were significantly more improved compared to those undergoing NDC. After 12 months, 58% of subjects treated with CBT had responded positively vs. 33% treated with AR and 22% with NDC.

Ost and Breitholtz³⁸ compared CT and AR in a sample of 36 patients with GAD, finding positive and similar effects for both at post-treatment and 1-year follow-up: drop-out rates were relatively low (5% for CT and 12% for AR). Some years later, Arntz³⁹ compared the same forms of treatment in a sample of individuals with GAD comorbid with other Axis I disorders (representing 78% of the total sample) which is more representative of routine clinical populations: CT and AR were similarly effective at post-treatment and follow-up (6 months). Borkovec et al.⁴⁰ analyzed the efficacy of the combination of the two approaches (AR + CT), comparing it with CT and AR, and found that all treatments led to an improvement that was maintained over time: there was no significant difference between the 3 treatments.

A more recent study by Hoyer et al.⁴¹ compared AR with one of the ingredients of CBT, namely exposure to situations that generate excessive worry (worry exposure, WE), the aim of which was to compare the effectiveness of WE as a single and independent therapeutic technique. The 73 patients included in the study were randomly assigned to 15 sessions based on WE, 15 sessions of AR or inclusion in a waiting list (WL). Post-treatment results showed significant improvements in both experimental groups compared to WL, but no difference between AR and WL. Improvements shown by patients increased after treatment (6 months) and were stable over time (follow-up to 12 months). These studies demonstrated that CBT and AR are similarly effective in the treatment of GAD, although a recent study by Dugas et al.⁴² indicated that CBT was marginally superior.

Psychodynamic therapy

Over the past 20 years there has been growing interest in various forms of brief psychotherapy derived from psychoanalytic principles even though there is a relative absence of comparative randomized controlled trials⁴³. Some studies have indicated that psychodynamic therapy is as useful as other forms of psychological intervention⁴⁴⁻⁴⁸. The psychodynamic approaches that appear to be more promising in reducing symptoms of GAD are brief Adlerian psychodynamic psychotherapy (B-APP) and supportive-expressive psychodynamic therapy. B-APP is a time-limited psychodynamic psychotherapy (10-15 sessions lasting 45 minutes), based on Adler's

theory of individual psychology⁴⁹. The therapist attention is not primarily oriented towards problem solving, but mainly deals with deep needs expressed by the patient's suffering and existential situation, and the overall objective of treatment is to increase self-esteem and self-efficacy⁴⁶. The study undertaken by Ferrero et al.⁴⁶ involved 87 patients with GAD, assigned to one of the following treatments: 10 sessions of brief therapy-APP (n = 34), medication (n = 33) or combined treatment (n = 20): the results suggested that B-APP could effectively treat GAD both as a monotherapy and in combination with pharmacological treatment, with a reduction in anxiety and depressive symptoms maintained at 1-year follow-up.

Supportive-expressive psychodynamic therapy^{45 50} has been claimed as an effective, brief, focal and interpersonal treatment for GAD. This therapeutic approach is focused on cognitive factors such as interpersonal concerns and previous challenges, and the model is based on the supposition that worrying has a defensive function and that traumatic experiences are largely interpersonal in nature. These relational patterns are cyclical, maladaptive and comprise "core conflictual relationship themes" (CCRT), which consist of wishes for the perceived response of another person and the consequent self-response⁵¹. This approach emphasizes a positive therapeutic alliance as this is thought to provide a "corrective" emotional experience, thus allowing the patient to deal with feared situations, both psychologically and behaviourally⁴⁷⁻⁵². The effectiveness of this approach was first demonstrated in the study of Crits-Christoph et al.⁴⁵ in which 26 patients with GAD underwent 16 weekly sessions of supportive-expressive (SE) focal psychodynamic psychotherapy followed by three monthly booster sessions: patients showed improvements in anxiety and depressive symptoms, worrying and interpersonal functioning. More recently, Leichsenring et al.⁴⁷ demonstrated the effectiveness of this approach in a study in which patients with GAD were randomly assigned to receive either CBT (n = 29) or psychodynamic therapy based on Crits-Christoph therapy. Both groups showed significant and stable improvements in symptoms of anxiety and depression, though CBT was superior in measures of trait anxiety (STAI), worrying (PSWQ) and depression (BDI). The recent study reported by Salzer et al.⁴⁸ confirmed these findings. It is possible that that supportive-expressive psychodynamic therapy in GAD may be optimized by employing a stronger focus on the process of worrying.

Internet computer-based CBT (CCBT)

The development of new technologies and communication tools (computer software, Internet, messaging services and chat) has resulted in their growing use in clinical settings, in order to administer psychotherapeutic proto-

cols to an increased number of patients at lower costs. Generally, CBT protocols are included in specific computer software (e.g., "FearFighter" developed by Marks⁵³), or placed on websites to which patients can be connected and register. Alternatively, this approach may involve individual CBT techniques providing contact between therapist and patient, supported through the Internet. It has been argued that these innovations may allow access to treatment for individuals who need psychological services, but who for various problems, such as anxiety, mental health, disability or other medical complications, cannot leave their house⁵⁴.

Meta-analysis and systematic reviews⁵³⁻⁵⁷ of Internet and computer-based CBT (CCBT) for the treatment of anxiety disorders have shown these new techniques are superior to placebo and placement on a waiting list, and to be substantially equivalent to standard CBT. However, these techniques have been applied mainly to patients with panic disorder, obsessive-compulsive disorder and post-traumatic stress disorder, and few studies have determined the potential efficacy of Internet and computer-based CBT in reducing autonomic symptoms and worrying.

A recent study⁵⁸ introduced a computer programme focused on treatment of the most common anxiety disorders (GAD, panic disorder, social phobia and post-traumatic stress disorder [PTSD]) in primary care services, establishing its potential feasibility in routine clinical practice. This programme, called "coordinated anxiety learning and management" (CALM) provides some psychoeducational modules relevant for treatment of all four anxiety disorders, and more specific modules for each disorder. The findings of this preliminary work indicate that clinicians consider this programme to be helpful and easy to use.

Mindfulness based approaches and other novel approaches

Over the last 10-15 years, developments of CBT have become widely adopted, including mindfulness-based stress reduction (MBSR), mindfulness-based cognitive therapy (MBCT), meta-cognitive therapy, acceptance-based CBT, interpersonal therapy and well-being therapy: all have shown promising results in the treatment of GAD³⁸.

Mindfulness-based stress reduction (MBSR)

The mindfulness-based stress reduction (MBSR) programme was devised by Kabat-Zinn and colleagues⁵⁹, with the goal to help individuals in developing "mindfulness" through intensive training in mindfulness meditation. Mindfulness has been defined as "paying attention, in a particular way, on purpose, in the present moment, with acceptance"⁶⁰. It is usually achieved through a regular daily discipline including both formal and informal exercises. A typical MBSR programme includes 8 weekly

group therapy sessions, a half-day meditation retreat after class 6, daily home practice based on audio CDs with instruction and daily record keeping of mindfulness exercises. Formal mindfulness exercises include the body scan, namely sitting meditation with awareness of breath; mindful movement and informal practice involve mindful attention to selected routine, day-to-day activities.

MBSR appears to be useful in the treatment of GAD and panic disorder⁶¹⁻⁶⁴, prevention of relapse in depression⁶⁵ and psychological distress in both clinical and healthy but stressed populations⁶⁶. Kabat-Zinn et al.⁶⁷ found that an 8-week group intervention based on mindfulness meditation significantly reduced anxiety and depressive symptoms in individuals with DSM-III criteria for GAD and PD, which were maintained at a 3 years of follow-up⁶². Lee et al.⁶³ showed a significant reduction in anxiety symptoms and hostility, but not in depressive symptoms, in GAD and PD patients treated with MBSR compared to an education programme group. The recent study reported by Vollestad et al.⁶⁴, found that in patients with GAD, PD or social anxiety disorder, mindfulness training had sustained beneficial effects compared to a waiting list control condition.

Mindfulness-based cognitive therapy

Mindfulness-based cognitive therapy (MBCT) is a group treatment derived from MBSR that incorporates additional cognitive strategies. It has been found to be effective in prevention of relapse in patients with major depression⁶⁵. The programme requires that the therapist teaches patients strategies to release themselves from dysfunctional thoughts, such as depressive ruminations in depressed patients and excessive worrying in patients with GAD. A typical MBCT package consists of 8 weekly group sessions, each lasting two hours. In the first 4 sessions, the therapist teaches a deep relaxation technique called the "body scan", where it passes through the various parts of the body using the contraction and relaxation of muscles, breath and imagination. In addition, patients should fill in a complete diary at home and continue to practice relaxation. In the last 4 sessions, when patients have learned the relaxation technique, they learn to "dismiss" any dysfunctional thoughts.

An open study by Evans et al.⁶⁷ suggested the efficacy of this technique in decreasing anxiety, tension, worrying and depressive symptoms in patients with DSM-IV diagnosed GAD. A further open study reported by Craigie et al.⁶⁸ highlighted the effectiveness of this approach in GAD patients with an Axis I comorbidity. In a more recent study⁶⁹, MBCT was compared to an anxiety disorder education programme (ADEP) in patients who met GAD and PD, defined according to DSM-IV criteria. The MBCT group demonstrated significantly greater decreases than the ADEP group

across all anxiety and depression scales. However, there were no significant differences between groups in terms of somatization, interpersonal severity, paranoid ideation or psychoticism subscale scores of the SCL-90-R. Because of the limitations of this study, the authors emphasized the need for additional controlled studies with more patients and a broader range of outcome measures.

Acceptance-based behaviour therapy

Acceptance-based behavior therapy (ABBT) for GAD⁷⁰ incorporates elements of CBT⁷¹⁻⁷², acceptance and commitment therapy⁷³, mindfulness CBT⁶⁵ and dialectical behavior therapy (DBT)⁷⁴⁻⁷⁵. According to its proponents, patients with GAD have difficulties in accepting their emotional experiences and their physiological activity, show excessive worry for future situations or to the possible negative consequences of their decisions, are intolerant of uncertainty, constantly seek confirmation and reassurance, tend to avoid potential dangerous situations and have thoughts with negative content. A typical therapeutic approach consists of 16 sessions, delivered weekly (4 of 90 minutes and 12 of 60 minutes). The main phases of this treatment⁷⁶ are psycho-education, mindfulness and monitoring, relaxation and mindfulness techniques and mindful action. A preliminary study in GAD suggested that acceptance-based behavior was associated with considerable improvements in anxiety, worrying and depression at the conclusion of treatment, with benefits persisting at 3 months follow-up⁷⁷. More recently, Roemer et al.⁷⁸ examined the potential efficacy of this approach in a crossover study in which patients were randomized to receive either ABBT immediately, or to be placed on a waiting list to receive it later. ABBT was more effective in decreasing anxiety and depressive symptoms. In patients who completed the protocol (including those initially on the waiting list), ABBT was associated with an improvement in the skills of mindfulness and in reduced avoidance. At follow-up, 78% of patients no longer met criteria for GAD and benefits were maintained over a further 9 months. The effectiveness of ABBT in reducing GAD symptoms has recently been confirmed⁷⁹.

Metacognitive model

A "metacognitive model" has also been proposed⁸⁰⁻⁸². According to this model, GAD sufferers have positive, rigid and deep-rooted beliefs about the efficacy of worries such as coping strategies to deal with threats, which contrast with negative beliefs about the uncontrollability of these concerns and the danger of their consequences for physical, psychological and social functioning. These concerns are defined as "type 2", or "worry about worry", and are associated with dysfunctional cognitive strategies such as seeking reassurance, mental avoidance and at-

tempts at suppressing negative thoughts. The core feature of the model is the change of positive and negative beliefs about worry and the development of alternative strategies for assessment and management of threat, using verbal and behavioural procedures⁸³.

The meta-cognitive therapy process is structured in the following way: 1) modification of beliefs about the uncontrollability of worry; 2) modification about positive convictions of worry; and 3) presentation of alternative strategies for assessing threat. Meta-cognitive therapy aims at altering the beliefs about the uncontrollability of worry, modifying the positive convictions about worry and introducing alternative coping strategies for dealing with worry. Specific techniques incorporate case formulation, socialization, discussion regarding the uncontrollability of worry, the danger of worry and positive worry belief. The efficacy of this model has been shown in two studies. A preliminary uncontrolled study⁸⁴ involving 10 consecutive patients with GAD included assessments before and after metacognitive therapy, and at 6 and 12-month follow-up visits. Patients showed significant improvements in worry, anxiety and depression; recovery rates were 87.5% at the end of treatment, and 75% at 6 and 12 months. A more recent study⁸⁵ included 20 patients with GAD defined according to DSM-IV-TR who were randomly assigned to either metacognitive therapy or applied relaxation (AR). Metacognitive therapy was superior to AR at the end of treatment and at 6-month and 12-month follow-up appointments, with particular benefits on reducing trait-anxiety, worrying and metacognitions.

Interpersonal emotional processing therapy

One of the more common forms of worry described by GAD patients relates to interpersonal situations, a concern that is worsened in the presence of comorbid social phobia^{29 86}. In an attempt to increase the effectiveness of CBT, a protocol of integrative therapy^{87 88} has been developed, which combines, in a sequential manner, CBT techniques with techniques targeting interpersonal problems and emotional avoidance, known as interpersonal emotional processing therapy (IEPT). Techniques used in this protocol include⁸⁹: 1) functional analysis of interpersonal behaviour and emotions; 2) analysis of the possibility or not that the old habitual behaviour can help the patient to meet his/her needs; 3) development through traditional behavioural methods such as social skill training (for example, assertiveness or empathetic behavior) that can promote more flexible alternative behaviours; and 4) the practice of new behaviours through role-play therapy. When undertaking this form of treatment, the therapist monitors any signs of weakening or breaking of the therapeutic alliance, as these problems are significantly and negatively correlated with clinical outcome⁹⁰. In a pre-

liminary uncontrolled study⁸⁸, 18 participants undertook 14 sessions of CBT plus IEPT, and 3 participants (for training and feasibility purposes) received 14 sessions of CBT plus supportive listening. Integrative therapy significantly decreased GAD symptomatology and interpersonal problems, and these benefits were maintained at 1-year follow-up. Comparison with the findings of other studies²⁰ suggests that the effect size for IEPT is higher than the average effect size of CBT for GAD.

Well-being therapy

A novel contribution to the treatment of GAD²¹ has emerged from the field of "Positive Psychology"⁹¹ with the development of "well-being therapy" (WBT)^{91 92}. WBT has common elements with CBT, such as the use of a diary, homework assignments and interaction between therapist and patient; however, the focus is on psychological well-being⁹³. The model includes 6 dimensions: autonomy, environmental mastery, personal growth, positive relationships with others, purpose in life and self-acceptance. These dimensions are often suboptimal in patients with affective disorders^{91 94}, and the therapist's aim is to encourage improvement in these dimensions through a well-structured treatment protocol, the main purpose being modification of more deleterious beliefs and attitudes to encourage and strengthen all behaviours that may enhance well-being⁹¹. In a preliminary study^{92 94}, 20 patients with GAD (according to DSM-IV criteria) were randomized into two groups, the first undertaking 8 sessions of CBT, and the second sequential treatment incorporating 4 sessions of CBT followed by 4 sessions of WBT, with a 1-year follow-up. Sequential approach CBT/WBT was associated with a significant improvement in anxiety symptoms, both at the end of treatment and at follow-up, and with an increase in the dimensions of psychological well-being compared to CBT. This study had some limitations (including its preliminary nature and small sample size), and further larger studies are needed. Sequential treatment involving CBT with WBT was found to be beneficial in a case study of a young woman with GAD⁹⁶: after 10 sessions of CBT, the patient reported feeling better with a reduction in anxiety symptoms and increased assertiveness, her involvement in a subsequent WBT protocol comprising 6 sessions, was associated with full symptomatic remission and restoration of psychological well-being, with persistence of benefit over 12 months, without evidence of symptomatic relapse⁹⁶.

Conclusions

The aim of this review is to provide an updated literature review of the available psychological treatments of GAD. Cognitive behavioural therapy (CBT) has been the

most studied treatment and it is still considered to be the first choice psychological treatment for GAD. Given the particular characteristics of GAD, some specific packages that directly target worry have been developed¹⁷⁻¹⁹. However, only about 50% of patients achieve high-end state functioning³⁰ or full recovery³³⁻⁴². Applied relaxation (AR) has shown good results in tackling anxiety, teaching the patient how to reduce the level of physiological arousal in specific stressful situations. Most studies suggested similar effectiveness of CBT and AR in treating GAD. In the last 20 years, there has been growing interest in brief psychotherapies stemmed from psychoanalytic principles. In particular, brief Adlerian psychodynamic therapy (B-APP) and supportive-expressive psychodynamic therapy have shown promising results even though there is a scarcity of randomized controlled trials. In order to find more effective treatments, new approaches such as MBSR (mindfulness-based stress reduction), MBCT (mindfulness-based cognitive therapy), ABBT (acceptance-based behaviour therapy), metacognitive therapy, IEPT (interpersonal emotional processing therapy) and WBT (well-being therapy) have been developed. The aim is not to replace standard CBT treatment, but to provide a wider range of choices. Preliminary results are encouraging, but further studies with more representative and larger samples are needed to evaluate their efficacy and efficacy compared to standard CBT. The first three treatments (MBSR, MBCT and ABBT) are based on mindfulness principles, helping the patient to become more mindful and accepting reality. MBSR is based on a regular daily discipline including formal (body-scan, breathing, mindful movement) and informal (mindful attention and day-to-day activities) exercises. MBSR appears to be useful in the treatment of GAD, panic disorder, prevention of depressive relapse and psychological distress. MBCT is a treatment based on MBSR with the incorporation of cognitive approaches. The goal of this therapy is to teach patients some strate-

gies to release themselves from dysfunctional thoughts, combined with adoption mindfulness techniques. In addition to mindfulness elements, ABBT integrates other components stemming from CBT, acceptance commitment therapy and dialectical behaviour therapy. According to this model, GAD patients struggle in accepting their emotional experiences and physiological activity, and tend to worry too much. Given the similarities between MBCT and ABBT, it will be important to define the exact temporal course of change and the mechanisms of action among these paradigms. Metacognitive therapy aims to change the positive and negative beliefs about worry by developing new strategies for assessment and management of threat, using verbal and behavioural procedures. Interpersonal emotional processing therapy and well-being therapy have been tested as sequential treatment options with CBT, and both have demonstrated their superiority to CBT. Interpersonal emotional processing therapy combines CBT techniques and others that target interpersonal problems and emotional avoidance, while well-being therapy shares the same elements of CBT although its main focus is to fully restore psychological well-being. Given that GAD is a heterogeneous disorder where onset, type and intensity of worry differ from person to person, each patient requires individualized treatment. In many patients, it may be necessary to combine treatment with pharmacotherapy. An important limitation of this review lies in the fact that we have not specifically considered the role of pharmacotherapy and its combination with the different psychotherapeutic strategies. Despite this, our narrative review confirms that well established treatments such as CBT as well as new psychotherapeutic approaches are available for the effective treatment of GAD. Clinicians should therefore be aware of the range of treatment options and help GAD patients in identifying the best therapeutic option, based on their individual needs.

TABLE I.

Summary of studies included in the present review. *Sommario degli studi inclusi nel presente articolo.*

Study	Participants	Design	Number	Duration	Measurements	Outcome
CBT Chambless and Gillis, 1993 ²⁵	Patients met criteria of generalized anxiety disorder according to DSM-III and DSM-III-R	7 studies have been included in a meta-analytic summary. A Beck and Emery version of CBT (1985) was combined with one or more additional behavioural techniques, most commonly progressive relaxation training and more rarely self-control desensitization or electromyogram biofeedback	Not given	Not given	<ul style="list-style-type: none"> - Hamilton Anxiety Scale (Hamilton, 1959) - Zung Self-Rating of Anxiety (ZSRI) (Zung, 1971) - Beck Anxiety Inventory (Beck and Steer, 1990) 	In all seven investigations, CBT was more effective than waiting list or pill placebo at post-test

(continues)

Table I - continued

Study	Participants	Design	Number	Duration	Measurements	Outcome
Fisher and Durham, 1999 ²⁴	GAD patients according to DSM-III-R and DSM-IV criteria	6 randomized controlled trials of psychological therapy	404	Varied between studies	- STAI-T (State-Trait Anxiety Inventory, Spielberger, 1983)	A recovery rate of 40% was found for the sample as a whole with 12 of 20 treatment conditions obtaining very modest recovery rates of 30% or less. Two treatment approaches – individual cognitive behavioural therapy and applied relaxation – do relatively well with overall recovery rates at 6 month follow-up of 50-60%
Hunout et al., 2007 ³⁰	GAD patients according to ICD 9 and ICD 10 criteria (WHO 1992) or DSM-III (APA 1980), DSM-III-R (APA 1987) and DSM-IV criteria (APA, 1994)	All the studies used a CBT approach, and compared CBT against treatment as usual or waiting list (13 studies) or against other psychological therapy (12 studies). The psychological approaches are: 1) Psychodynamic therapy 2) Supportive therapy	1305	The duration of trials ranged from 4 weeks (Lindsay, 1987) to 24 months (Barlow 1992, Dugas, 2003)	The most frequently used clinician-rated outcome measure used for anxiety symptoms was the HAM-A (13 studies), and the most commonly used self-report scale was the Trait subscale of Spielberger STAI-T (16 studies). Ten studies used the Penn State Worry Questionnaire (PSWQ), nine studies used the Beck Anxiety Inventory (BAI) and the ZSRI was used in eight studies. To measure depression, 10 studies used the clinician-rated Hamilton Rating Scale for Depression (HAM-D), and 14 studies used the self-report Beck Depression Inventory (BDI). Quality of life was measured in three studies only	Psychological therapy based on CBT principles is effective in reducing anxiety symptoms for short term treatment of GAD. The body of evidence comparing CBT with other psychological therapies is small and heterogeneous, which precludes drawing conclusions about which psychological therapy is more effective. Further studies examining non-CBT models are required to inform health care policy on the most appropriate forms of psychological therapy in treating GAD
Applied Relaxation (AR) Borkovec and Costello, 1993 ³⁷	GAD DSM-III-R Criteria	- ND Nondirective therapy - AR Applied Relaxation - CBT Cognitive Behavioural Therapy	55	12 sessions twice per week 6 months follow-up 12 months follow-up	- Anxiety Disorders Interview Schedule-Revised (ADIS-R; DiNardo et Barlow, 1988) - Hamilton Anxiety Rating Scale (HARS; Hamilton, 1959) - Assessor Severity of GAD Anxiety Symptoms (a scale ranging from 0-8 points; Barlow et al., 1984) - Reactions to Relaxation and Arousal Questionnaire (RRAQ, Heide and Borkovec, 1983) - STAI-T - ZSRA - PSWQ - The Diary Episodes measure (Barlow et al., 1984) - HAM-D - BDI	The 3 conditions did not differ on several process measures, and ND created the greatest depth of emotional processing. Follow-up results indicated losses in gains in ND, maintained gains in the other two conditions, especially CBT, and highest end state functioning for CBT

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Table I - continued

Study	Participants	Design	Number	Duration	Measurements	Outcome
Ost and Breitholz, 2000 ³⁸	GAD DSM-III-R Criteria	- AR Applied Relaxation - CT Cognitive Therapy	36	12 weeks 1 year follow-up	- BAI - STAI-T - Cognitive and somatic Anxiety Questionnaire (CSAQ; Schwartz, Davidson and Goleman, 1978) - PSWQ - BDI	The results showed that there were no differences between the treatments Limitations: no control group The patients were not drug free
Arntz, 2003 ³⁹	GAD DSM-III-R Criteria	- AR Applied Relaxation - CT Cognitive Therapy	45	12 weeks 6 months follow-up	- Use of a Diary to indicate the average level of anxiety - A Dutch Version of Spielberger's State-Trait Anxiety Inventory (van der Ploeg, Defares and Spielberger, 1980) - SCL-90 (Arrindell and Ettema, 1981) - The Fear of Fear Questionnaire (van den Hout, van der Molen, Griez and Lousberg, 1987) - Bouman Depression Inventory (Bouman, 1987)	The results confirm that both CT and AR are effective treatments for GAD
Reger and Gahm, 2008	Various diagnosis of anxiety disorders	19 randomized controlled trials were identified and subjected to fixed and random effects meta-analytic techniques	1170	Not given	The main questionnaires adopted were: - BDI - Montgomery-Asberg Depression rating Scale - Body Sensations Questionnaire - Beck Anxiety Inventory - Fear Questionnaire - Impact of Event Scale	The results of this meta-analysis provide preliminary support for the use of Internet and computer-based CBT for the treatment of anxiety. The benefit of CCBT were superior to waitlist or placebo assignment, although the number of placebo studies was small (n = 7)
MBCT Evans et al., 2007 ⁶⁷	GAD DSM-IV	MBCT No Control Group	11	8 weeks	- BAI - PSWQ - Profile of Mood States (POMS, McNair, Lorr and Droppleman, 1971) - Mindfulness Attention Awareness Scale (MAAS; Brown and Ryan, 2003) - AMNART (Grober and Sliwinsky, 1991)	Significant decrease in anxiety, tension, worry, depressive symptoms
Cragie et al., 2008 ⁶⁸	GAD DSM-IV + additional diagnoses	MBCT No Control Group	23	8 weeks plus 1 session	- PSWQ - Depression Anxiety Stress Scales - short form (DASS21; Lovibond and Lovibond, 1996) - BAI - Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q; Endicott, Nee, Harrison and Blumenthal, 1993) - Reactions to Relaxation and Arousal Questionnaire (RRAQ; Heide and Borkovec, 1983)	Consistent with the study of Evans et al., 2008

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Table 1 - continued

Study	Participants	Design	Number	Duration	Measurements	Outcome
Kim et al., 2009 ⁶⁹	GAD PD according to DSM-IV	- MBCT (n = 32; GAD = 5, PD = 19) - ADE (anxiety disorder education program) (n = 31; GAD = 6, PD = 16)	46	8 weeks	- HAM-A - HAM-D - BAI - BDI - Symptom Checklist-90-Revised (SCL-90-R; Derogatis, 1983)	MBCT group demonstrated significantly more improvement than the ADE group according to all anxiety and depression scale scores. However no significant improvement was observed in the MBCT group versus ADE group in terms of the somatisation, interpersonal severity, paranoid ideation or psychoticism subscale scores of SCL-90-R
MBSR Vollestad et al., 2011 ⁶⁴	GAD PD SAD diagnostic criteria (not specified, see article) psychoticism subscale scores of SCL-90-R	- MBSR - Waiting List	76	8 weeks	- BAI - PSWQ - STAI-T - BDI - SCL-90-R - Bergen Insomnia Scale (BIS) (Pallesen et al., 2008) - Five-Factor Mindfulness Questionnaire (FFMQ) (Baer, Smith, Hopkins, Krietemeyer and Toney, 2006)	Mindfulness training has sustained beneficial effects on anxiety disorders and related symptomatology compared to WL
Lee et al., 2007 ⁶³	GAD PD DSM-IV Criteria	- MBSR - Education programme	46	8 weeks	- HAM-A - STAI-T - HAM-D - BDI - SCL-90-R	The reduction of anxiety symptoms and hostility in anxiety disorders is bigger in MBSR group
Miller et al., 1995 ⁶²	AD PD DSM-III Criteria	MBSR	18	3 years follow-up	- HAM-A - Hamilton Rating Scale for Panic Attacks - HAM-D - Beck Anxiety Inventory - Mobility Inventory for Agoraphobia -Accompanied and Alone	MBSR is an effective treatment to reduce anxiety disorders
Well-Being Therapy (WBT) Ruini et al., 2006 ⁹⁵	GAD DSM-IV	- CBT (4 sessions) + WBT (4 sessions) - CBT (8 sessions)	20	8 weeks A year follow-up	- The Clinical Interview for Depression (CID, Paykel, 1985) - Psychological Well-Being Scales (PWB, Ryff, 1995)	The sequential approach CBT/WBT has determined to a more significant improvement in anxiety symptoms both at the post-treatment and follow-up and an increase in the dimensions of psychological well-being when compared to CBT

(continues)

Table 1 - continued

Study	Participants	Design	Number	Duration	Measurements	Outcome
CBT + Interpersonal Emotional Processing Therapy Newman et al., 2008 ⁸⁸	Principal Diagnosis of DSM-IV criteria GAD	<ul style="list-style-type: none"> - CBT + Interpersonal Emotional Processing Therapy (18 participants) - CBT + Supportive Listening (3 participants) 	21	14 sessions of CBT + I/EP or SL 6 months and 1 year follow-up	<ul style="list-style-type: none"> - Anxiety Interview Schedule-IV (ADIS-IV; Brown, Di Nardo and Barlow), the - HAM-A - the Structured Clinical Interview for DSM-IV Axis II Personality Disorder (First, Spitzer, Gibbon, Williams and Benjamin, 1994) - Assessor Severity of GAD Anxiety Symptoms (0-8 point scale) - STAI-T - RRAQ - PSWQ <p>Secondary Outcome Measures</p> <ul style="list-style-type: none"> - The Inventory of Interpersonal Problems Circumplex (IIPC Alden et al., 1990) 	Results showed that the integrative therapy significantly decreased GAD symptomatology, with maintenance of gains up to 1 year following treatment. In addition it has been showed a clinical significant change in GAD symptomatology and interpersonal problems with continued gains during the 1-year follow-up
Leichsenring et al., 2009 ⁴⁷	GAD DSM-IV criteria	<ul style="list-style-type: none"> CBT (n = 29) STPP (Short Term Psychodynamic Psychotherapy) (n = 28) 	57	30 sessions 6 month follow-up	<ul style="list-style-type: none"> - HAM-A - PSWQ - STAI-T - BAI - BDI - Inventory of Interpersonal Problems 	Both CBT and short-term psychodynamic psychotherapy yielded significant large and stable improvements with regard to symptoms of anxiety and depression. However CBT was found to be superior in measures of trait anxiety (State Trait Anxiety Inventory), worrying (Penn State Worry Questionnaire), and depression (BDI)
Crits-Christoph et al., 1996 ⁴⁵	Mainly DSM-III-R	16 weekly sessions of Supportive-Expressive (SE) focal psychodynamic psychotherapy followed by three monthly booster sessions	26	16 weeks + 3 monthly booster sessions	<ul style="list-style-type: none"> - Structured Clinical Interview based on DSM-III-R (SCID-P; Spitzer, Williams, Gibbon and First, 1990a) - Structured Clinical Interview for DSM-III-R Personality Disorders (SCID-II; Spitzer, Williams, Gibbon and First, 1990) - HAM-A - HAM-D - BAI - BDI - PSWQ - Inventory of Interpersonal Problems (IIP; Horowitz, Rosemberg, Baer and Ureno, 1988) - Opinions About Treatment (OAT, Borkovec and Mathews, 1988) - Treatment Expectations an adaptation of the Treatment Expectations Form: Elkin, Shea, Watkins and Imber, 1989) - Adherence/Competence (a modified version of Penn Adherence/Competence Scale for SE therapy (Barber and Crits-Christoph, 1996) 	The results of this investigation indicate that brief Supportive-Expressive psychodynamic psychotherapy is a promising new treatment of generalized anxiety disorder

(continues)

Table 1 - continued

Study	Participants	Design	Number	Duration	Measurements	Outcome
Metacognitive Therapy (MCT) Wells and King, 2006 ⁸⁴	GAD DSM-IV criteria + 50% of them had additional diagnoses 30% major depressive disorder 10% social phobia 10% depression not otherwise specified and social phobia	MCT No control group	10	The range of treatment sessions offered was 3-12 6-12 month follow-up	- BAI - BDI - STAI-T - Anxious Thoughts Inventory (AnTi: Wells, 1994, 2000)	Patients were significantly improved at post-treatment, with large improvements in worry, anxiety, and depression. Recovery rates were 87.5% at post treatment and 75% at 6 and 12 months. The treatment appears promising and controlled evaluation is clearly indicated
Wells et al., 2009 ⁸⁵	GAD DSM-IV-TR et or additional diagnoses	MCT (Metacognitive Therapy) AR (Applied Relaxation)	20	8-12 weekly sessions 6-12 month follow-up	- STAI-T - PSWQ - BAI - BDI - Metacognitions Questionnaire (MCQ: Cartwright-Hatton and Wells, 1997)	MCT was superior to AR at post-treatment, at 6-month follow-up and at 12 months. This was evident on measures of trait-anxiety, worry, and metacognitions and in the terms of the degree of clinical improvement and recovery. MCT was superior at post-treatment in reducing depressive symptoms and BAI scores but these differences were not significant at follow-up The present results extend the findings of an open trial (Wells and King, 2006) and indicate stability in change obtained with MCT over a longer follow-up
Acceptance-Based Behaviour Therapy (ABBT) Roemer and Orsillo, 2007 ⁷⁷	GAD-DSM-IV or MDD plus GAD. The most common additional diagnoses were: social anxiety disorder, specific phobia, MDD, dysthymia, and panic disorder with agoraphobia	ABBT No control group	16	4 sessions (lasting 90 minutes) 2 sessions (lasting 60 minutes) (from weekly to every other week) 3 month follow-up	- Anxiety disorders interview schedule for DSM-IV-Lifetime version (ADIS-IV Di Nardo et al., 1994) - PSWQ - DASS-21 - BDI-I-A - Quality of Life Inventory (QOLI; Frisch, Cornwell, Villanueva and Retzlaff, 1992) - Action and Acceptance Questionnaire (AAQ; Hayes, Strosahl, et al., 2004) - Affective Control Scale (Williams, Chambless and Ahrens, 1997)	These preliminary findings from an open trial investigation of an acceptance-based behaviour therapy for GAD suggest that this approach may be a promising one for treating this chronic anxiety disorder, although further development of the treatment is needed
Roemer et al., 2008 ⁷⁸	GAD-DSM-IV criteria	ABBT (n = 15) WL (waiting list, n = 16)	31	4 sessions (lasting 90 minutes) 12 sessions (lasting 60 minutes) the last 2 sessions tapered (from weekly to every other week) 3-9 month follow-up	- ADIS-IV - PSWQ - Depression Anxiety Stress Scales-21-item version (Lovibond and Lovibond, 1995) - BDI - An abbreviated version of the Quality of Life Inventory (QOLI; Frisch, Cornwell, Villanueva and Retzlaff, 1992)	Acceptance-based behaviour therapy led to statistically significant reductions in clinician-rated and self-reported GAD symptoms that were maintained at 3 and 9 month follow-up assessments; significant reductions in depressive symptoms were also observed Given the preliminary nature of this study, there are several limitations. (for further information see the study)

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Table 1 - continued

Study	Participants	Design	Number	Duration	Measurements	Outcome
Treanor et al., 2011 ⁷⁹	GAD-DSM-IV criteria	ABBT (n = 15) WL (waiting list, n = 16)	31	16 sessions of ABBT for GAD 3-9 month follow-up	<ul style="list-style-type: none"> - The Affective Control scale (ACS) - The Difficulties in Emotion Regulation Scale (DERS) - The Intolerance of Uncertainty Scale-English Version (IUS) - The Anxiety Control Questionnaire-Revised (ACQ-R) - Anxiety Disorders Interview Schedule for DSM-IV-Lifetime Version - PSWQ 	Clients treated with ABBT reported significantly fewer difficulties in emotion regulation and fear of emotional responses, as well as greater tolerance of uncertainty and perceived control over anxiety than individuals in the WL control group. These effects were maintained at 3 and 9 month follow-up assessment

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