BENZODIAZEPINES AND PSYCHOTHERAPY IN THE TREATMENT OF ANXIETY AND PANIC ATTACKS

Christian Jonathan Haverkampf M.D.

The benzodiazepines have been used for decades in the treatment of anxiety and panic attacks. They still are the only widely used and effective medication available that can stop anxiety within a very short amount of time. Recommendations for their used have oscillated over time between widespread use for their effectiveness as a stand-by medication and restrictiveness because of their risk of leading to tolerance and addiction if used regularly. It has often been overlooked in the discussion that their place as a standby medication is often unproblematic if used with psychotherapy and, if needed, a serotonergic antidepressant as longer-term options.

Keywords: benzodiazepines, selective serotonin reuptake inhibitors (SSRIs), antidepressants, medication, anxiety, panic attacks, psychiatry

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Introduction

Anxiety disorders are the most prevalent psychiatric disorders (with a current worldwide prevalence of 7.3%. Among them, specific phobias are the most common, with a prevalence of 10.3%, then panic disorder (with or without agoraphobia) is the next most common with a prevalence of 6.0%, followed by social phobia (2.7%) and generalized anxiety disorder (2.2%). (Thibaut, 2017) There is a high comorbidity between anxiety (especially generalized anxiety disorders or panic disorders) and depressive disorders or between anxiety disorders, which renders treatment more complex.

Anxiety is usually multifactorial, which means that it occurs when several potential causes come together. Stress, a misalignment of one's professional or private life with own needs, values, and aspirations, grief, emotional conflicts, and more, can all increase anxiety levels (Haverkampf, 2017b). The bio-psycho-social model is hypothesized in anxiety disorders and basically refers to the diverse etiology for anxiety, including biological, psychological, and social factors.

First-line drugs are the selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors. Benzodiazepines are not recommended for routine use, but as a stand-by option where needed. Other treatment options include pregabalin, tricyclic antidepressants, buspirone, moclobemide, and others. Cognitive behavioral therapy (CBT) can be regarded as the psychotherapy with the highest level of evidence. (Bandelow et al., 2017a) It can improve outcomes for patients whose anxiety symptoms are resistant to standard pharmacotherapy (Campbell-Sills et al., 2016). However, this prominence of CBT may also be due to the fact that it easier manualized, which makes it fit better into current study designs. Psychodynamic psychotherapy and various other therapeutic approaches are also empirically validated and may even have benefits over CBT in parameters such as endurance of a positive effect or improvements in areas which CBT traditionally does not focus on, such as emotional states.

Benzodiazepines

Benzodiazepines have been used for decades as a reliable as-needed medication for anxiety and panic attacks. For many people with anxiety or panic attacks, just the sense of having a diazepam tablet in one's pocket, for example, can have a significant antianxiety effect. The benzodiazepines are still the medication that works most quickly and effectively against anxiety and panic attacks. Even if the effect only lasts for a few to several hours, the mere knowledge that they are there can help break the vicious cycle of becoming anxious about becoming anxious. It also needs to be kept in mind that anxiety disorders are often underrecognized and undertreated in primary care. (Bandelow et al., 2017a) Treatment is indicated when a patient shows marked distress or suffers from complications resulting from the disorder. It usually consists of psychological therapy, pharmacotherapy, or a combination of both.

Both psychotherapy and pharmacotherapy have been shown to be more effective than placebo or waiting lists in the treatment of anxiety disorders. (Thibaut, 2017) As regular medication, the selective serotonin reuptake inhibitors (SSRIs), and to some extent serotonin and norepinephrine reuptake inhibitors (SNRIs), have largely replaced the benzodiazepines, while there are some geographic differences in prescribing patterns, and many prescribers seem to have a small number of preferred drugs. Reviews tend to confirm selective serotonin reuptake inhibitors as first-choice medication for treating anxiety disorders, alongside newer agents such as pregabalin or serotonin–norepinephrine reuptake inhibitors, often in combination with cognitive–behavioral therapy. (Cloos & Ferreira, 2009) Serotonergic antidepressants and CBT are generally the best-studied treatments found to be efficacious for generalized anxiety disorder. (Craske et al., 2016)

It has been argued that a substantial proportion of long-term users becomes physically dependent on benzodiazepines, perhaps up to 20-30%. (Lader & Kyriacou, 2016a) It is, however, often not clear whether dependence on benzodiazepines also includes occasional as-needed use, and whether any symptoms during discontinuation could also be explained by the underlying condition. In many cases 'withdrawal symptoms' can also occur when benzodiazepines are tapered down slowly, which may indicate the underlying anxiety at least as a cofounding cause of the symptoms manifesting when the dose is

decreased. Pharmacological aids to discontinue a benzodiazepine include antidepressants such as the SSRIs, especially if depressive symptoms supervene. (Lader & Kyriacou, 2016a)

Benzodiazepines are used in children to treat anxiety in certain situations. In a meta-analysis examining the efficacy and tolerability of benzodiazepines as short-term anxiolytics in children in procedural settings (dental, operating, etc.) twenty-one trials involving 1,416 participants were included. A significant benefit was seen for benzodiazepines compared to control. A tolerability analysis revealed there was no significant difference in the risk of developing irritability or behavioral changes between benzodiazepine and control groups. (Kuang et al., 2017)

Psychopharmacological Alternatives

Benzodiazepines are not recommended for routine use. First-line drugs are the selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors. Other treatment options include pregabalin, tricyclic antidepressants, buspirone, moclobemide, and others. (Bandelow et al., 2017b) The quality of evidence for the efficacy of propranolol must be regarded as too low for routine use in anxiety disorders. (Steenen et al., 2016) Several future pharmacological alternatives may include a variety of medications under investigation such as agomelatine, GABA-A–specific receptor modulators, benzodiazepine receptor agonists and partial agonists, buspirone-like partial 5-HT1A agonists, and antagonists for cholecystokinin B receptors. (Huh et al., 2011) Pregabalin has at least in some cases been successful as a regular medication for anxiety, while the risk of dependence in patients with anxiety is assumed to be lower. Basic research has provided critical insights into the mechanism regulating fear behavior in animals and a host of animal models have been developed in order to screen compounds for anxiolytic properties. The glutamate, neuropeptide and endocannabinoid systems show particular promise as future targets for novel drug development. (Murrough et al., 2015)

A better-informed choice can also be helpful before the medication is selected for a specific patient. Pharmacogenetic-guided medication selection has been shown to significantly improve outcomes of patients diagnosed with depression or anxiety, in a variety of healthcare settings. (Bradley et al., 2018)

Examples of benzodiazepines include alprazolam (Xanax®), chlordiazepoxide (Librium), clonazepam (Klonopin®), clorazepate (Tranxene®), diazepam (Valium®), estazolam (Prosom®), flurazepam (Dalmane®), lorazepam (Ativan®), midazolam (Versed®), oxazepam (Serax®), temazepam (Restoril®), triazolam (Halcion®), quazepam (Doral®), and others.

Mechanism

γ-Aminobutyric acid type A (GABA-A receptors) are the molecular targets of benzodiazepines. They are the major inhibitory neurotransmitter receptors responsible for fast inhibition in the basal ganglia network in the brain (Goetz et al., 2007). Benzodiazepines mediate their action via a modulatory binding site on most $GABA_A$ receptors. (Schoch et al., 1985) In contrast to barbiturates, GABAA receptor modulation by benzodiazepine site agonists is self-limiting. The conductance of the channel in the presence of GABA and benzodiazepines is not higher than the conductance that can be achieved with high concentrations of GABA alone. Moreover, also in contrast to barbiturates, benzodiazepines do not open the chloride channel in the absence of GABA.

GABA-A receptors are heteropentamers made up from 19 known subunits (α1-6, β1-3, γ1-3, δ, ε, θ, π, and ρ1-3) (Olsen & Sieghart, 2009) with an integral channel that is permeable to Cl^- ions. GABA-induced chloride influx hyperpolarizes the postsynaptic neurons and is thus generally inhibitory on the neuron. Many GABA-A receptors contain two α subunits, two β subunits and one γ subunit with two GABA binding sites formed by α and β subunits. The binding site for benzodiazepines is formed by one of the α subunits α1, α2, α3, and α5 and a γ subunit, typically the γ2 subunit, which is present in approximately 90% of GABA-A receptors. There is considerable preclinical evidence that the α2- and/or α5-subunit-containing GABA-A receptor subtypes are involved in the pathophysiology of anxiety disorders. (Chen et al., 2019) In addition to benzodiazepines, the GABA-A receptor is also the major target for the clinically used hypnotic drugs zolpidem, zopiclone, eszopiclone, and zaleplon, for barbiturates, and for many general anesthetics. (Rudolph & Knoflach, 2011) Findings in the mouse model suggest that the anxiolytic effect of benzodiazepine drugs is mediated by α2 GABA-A receptors, which are largely expressed in the limbic system, but not by α3 GABA-A receptors, which predominate in the reticular activating system. (Löw et al., 2000)

Other unrelated effects of the benzodiazepines have been suggested. For example, there is some data that lorazepam and clonazepam, aside from exerting anxiolytic and antidepressant effects, may have therapeutic potential as neuroimmunomodulators during psychosocial stress. (Ramirez et al., 2016)

The Debate about Benzodiazepines

One may easily get the impression that there is a pendulum that swings with a certain regularity between more liberal and more restrictive prescribing practices around the benzodiazepines. Important is to have relatively balanced view about them, which acknowledges their unique effects in quickly stopping anxiety and panic attacks, while being aware of their potential downsides, such as potential dependence, changes in reaction time and alertness, and possible long-time medical impairments, where we may still know relatively little. In the literature a focus is frequently on dependency, cognitive decline and falls (Brett & Murnion, 2015). The long-term use of benzodiazepines has been advised against in older people owing to adverse outcomes, including increased risks of cognitive impairment, falls, fractures, traffic accidents, delirium and dependence. (Gould et al., 2014) The American Geriatrics Society 2012 Beers Criteria Update Expert Panel has recommended avoidance of benzodiazepines for insomnia, agitation or delirium in older people owing to slower metabolism of and increased sensitivity to such medications. (Fick et al., 2012)

Criticism

Current guidelines do not recommend benzodiazepines as first-line regular treatments due to their potential side effects. In fact, Parsaik et al, in a 2016 meta-analysis, have reported a higher mortality rate among benzodiazepines users compared with nonusers. In addition, the development of tolerance and an increased risk for dependence were also reported in association with long-term use of benzodiazepine (which generally means ≥6 months). (Thibaut, 2017) An increased risk of dementia was also claimed by several authors in long-term benzodiazepine users.

Benzodiazepines do not treat depression, which is a common comorbid condition in anxiety disorders, and benzodiazepines may be associated with a higher suicide risk in case of comorbidity between anxiety and depressive disorders. (Thibaut, 2017) It has also been observed that longer-term prescribing is most pronounced among those with co-occurring anxiety disorders, and thus suggested that that anxiety in

those with substance used disorders should preferentially not be treated using benzodiazepines. Longer-term polypharmacy with benzodiazepines and opioids tend to coincide, and overdoses among those using both drugs are growing. (O'Brien et al., 2017) Again, it is difficult to extricate cause and effect relationships between manifesting symptoms and a medication, as self-medication with a substance can be the consequence of life impairing symptoms caused by an underlying condition.

Benzodiazepines have also been linked to falls in the elderly and potentially even as one factor in the onset of Alzheimer's, aside from the risk of tolerance and dependency, drowsiness and changes in reaction times, among other issues. Nonetheless, in clinical experience, there is a large number of patients who benefit from benzodiazepines as a standby medication for anxiety, and sleep to some extent, who tolerate the medication well.

Benefits

The anxiolytic benefits of the benzodiazepines, though very short lived, is a well-established observation in clinical experience. It has even been argued that treatment guidelines should acknowledge that benzodiazepines may be used as first-line, long-term pharmacological treatment for panic disorder, generalized anxiety disorder and social anxiety disorder. (Starcevic, 2014) The author suggested that studies support that long-term use of benzodiazepines for anxiety can be effective and safe, particularly when combined with psychological therapy and antidepressants to produce optimal outcomes, and that the superiority of alternative pharmacotherapy for anxiety has not been convincingly demonstrated.

Several other authors have argued that supplanting benzodiazepines in part by second-generation antidepressant drugs has occurred without any supporting evidence. It has further been suggested that benzodiazepines have not been adequately compared to other psychotropic medications in various indications, and their risks and side effects have been overemphasized. There is as feeling that taking a position relative to benzodiazepines may also have commercial reasons (Balon et al., 2018) When benzodiazepines and antidepressants were directly compared in clinical trials, the superiority of benzodiazepines both in efficacy and adverse effect profile has been emphasized. (Fava et al., 2015) The same authors have also argued that the benzodiazepines are not only faster and better during short-term treatment, but remained effective in long-term (3 years) treatment, when tolerance developed to its

sedative effect, while side effects of the SSRI used in comparison, such as sexual dysfunction and weight gain remained an issue. (Balon et al., 2015) A population-based cohort study suggests either no increase or at most a minor increase in risk of all causes of mortality associated with benzodiazepine initiation. The investigators concluded that if a detrimental effect exists, it is likely to be much smaller than previously stated and to have uncertain clinical relevance. Residual confounding may explain at least part of the small increase in mortality risk observed in some analyses. (Patorno et al., 2017)

Targeted and informed use

It is difficult to reconcile all studies on the safety profile of benzodiazepines. A relevant first question is whether as-needed use should be included in long-term use, and where the cut-off between regular and as needed, and no use, is. In a primary care sample, 22.6% of patients with anxiety disorder used benzodiazepines. The authors pointed out that a large majority of benzodiazepine users (88.4%) met their indicator of long-term use, as defined by utilization for more than 12 weeks including regular and as-needed use. (Bernard et al., 2018) If the patient who keeps a tablet of diazepam in their pocket for months is a long-time user, this may neither be sensible from the pharmacological nor from the psychological perspective.

As with many other things in life, much may also depend on how the medication is used. As mentioned previously, as an occasional stand-by medication it may have more upsides than downsides. Much of the problems surrounding the benzodiazepines seems to be linked to how they are used. Benzodiazepines are in the US used predominantly in elderly persons, mostly women, and for long periods of time. “The older the patient, the longer the drug is used.” (Moore et al., 2015) The problem here is, of course, that the effect of benzodiazepines can wear off, and the patient has to continue taking them so as not to get the potential withdrawal effects form stopping them. On the other hand, in clinical experience there are at least some patients who take z-drugs and benzodiazepines for an extended period of time with minimal withdrawal effects, which is something that should be investigated more thoroughly. There is also the valid question about alternatives. Aside from the SSRIs, antipsychotics are frequently used against anxiety, where the benefit in the side effect profile over the benzodiazepines is questionable. Still, benzodiazepines are not rarely considered by many clinicians to remain good treatment options, in both the acute and the chronic phase of the treatment of anxiety disorders, partially because of their rapid

onset of action and their efficacy with a perceived favorable side effect profile, and also because of the sometimes only incomplete therapeutic response and the emergence of side effects of alternative medications. (Cloos & Ferreira, 2009)

It is advisable that whenever benzodiazepines are prescribed, the potential for dependence or other harmful effects should be considered. However, the risks of dependence associated with long-term use need to be balanced against the benefits that in many cases follow from the short or intermittent use of benzodiazepines and the risk of the underlying conditions that are being treated. (Baldwin et al., 2013) One situation where benzodiazepines are usually considered relatively contraindicated is PTSD or recent trauma. In a systematic review, benzodiazepines have been associated with worse overall severity, significantly increased risk of developing PTSD with use after recent trauma, worse psychotherapy outcomes, aggression, depression, and substance use. (Guina et al., 2015)

Treatment of Benzodiazepine Withdrawal Symptoms

Long-term use of benzodiazepines can lead to dependence, which needs to be recognised when it occurs. A risk assessment is then as important as understanding the type and dynamics of the underlying conditions. Symptoms of withdrawal include anxiety, irritability, confusion, seizures, and sleep disorders. Withdrawal management relies on the use of a single agent (diazepam) and gradual dose reduction. (Soyka, 2017) Few studies have been conducted to establish the optimal withdrawal schedules. The usual management comprises slow withdrawal over weeks or months together with psychotherapy of various modalities. Pharmacological aids include antidepressants such as the SSRIs especially if depressive symptoms supervene. Other pharmacological agents such as the benzodiazepine antagonist, flumazenil, and the hormonal agent, melatonin, remain largely experimental. (Lader & Kyriacou, 2016b)

The management of dependence involves either gradual benzodiazepine withdrawal or maintenance treatment. Prescribing interventions, substitution, psychotherapies and pharmacotherapies can all contribute. Unless the patient is elderly, it is helpful to switch to a long-acting benzodiazepine in both withdrawal and maintenance therapy. The dose should be gradually reduced over weeks to lower the risk of seizures. (Brett & Murnion, 2015) The choice of approach depends on an assessment of the risk of harm and relapse. Low-risk patients can be managed in general practice and may benefit most from attempting

withdrawal. High-risk patients are best managed with initial stabilisation and maintenance therapy in specialist residential or outpatient addiction services. (Brett & Murnion, 2015)

Psychotherapy and education about the medication can be helpful in lowering or eliminating the need for benzodiazepines. In elderly patients, it has been found that something as basic as one-time counselling of psychotropics and other fall-risk-increasing drugs by a geriatrician followed with a 1-h lecture about adverse effects of these drugs had positive effects in decreasing the number of regular users of benzodiazepines and related drugs, and these effects persisted for the total 12-month intervention period. (Salonoja et al., 2010) A systematic review concluded that in an elderly population supervised benzodiazepine withdrawal augmented with psychotherapy should be considered in older people, although pragmatic reasons may necessitate consideration of other strategies such as medication review. (Gould et al., 2014)

Benzodiazepines vs Antidepressants

Many of the studies comparing benzodiazepines and antidepressants have used the older tricyclic antidepressants as references substances rather than the more modern SSRIs or SNRIs. However, they raise some valid questions. Benasi and colleagues performed a systematic review and a meta-analysis of randomized controlled trials which used benzodiazepines as a monotherapy versus placebo, antidepressant drugs, or both. A total of 38 studies met the criteria for inclusion and were then included in the systematic review. They found a lack of significant differences as to response rate between benzodiazepines and placebo, as well as between benzodiazepines and tricyclic antidepressants. Analysis of individual studies disclosed that, in more than half of the studies comparing benzodiazepines to tricyclic antidepressants or placebo, benzodiazepines were significantly more effective than placebo and as effective as tricyclic antidepressants. (Benasi et al., 2018) According to a systematic review by Offidani and colleagues, no consistent evidence emerged supporting the advantage of using tricyclic antidepressants over benzodiazepines in treating generalized anxiety disorder, complex phobias and mixed anxiety-depressive disorders. Benzodiazepines actually showed fewer treatment withdrawals and adverse events than the antidepressants. In panic disorder with and without agoraphobia their meta-analysis found benzodiazepine treatments mildly more effective in reducing the number of panic attacks than tricyclic antidepressants. Furthermore, benzodiazepines medications were significantly better

tolerated than tricyclic antidepressants, causing less discontinuation and side effects. As to newer antidepressants, benzodiazepines trials resulted in comparable or greater improvements and fewer adverse events in patients suffering from generalized anxiety disorder or panic disorder. (Offidani et al., 2013) Gomez and colleagues conducted a comprehensive literature search on SSRIs, SNRIs, and benzodiazepines in the treatment of generalized anxiety disorder, which yielded 54 articles reporting 56 unique studies with 12,655 participants, including the placebo control arm. Effect sizes were modest to moderate and decreased significantly over time. SSRIs and SNRIs demonstrated significantly lower effect sizes than benzodiazepines. (Gomez et al., 2018) On the other hand, research indicates that benzodiazepines may not be effective in the treatment of posttraumatic stress disorder (Davidson, 2004), or even counterproductive, and should not be used for obsessive-compulsive disorder and posttraumatic stress disorder (Bostwick et al., 2012), where, aside from psychotherapy, SSRIs and other medication are usually preferred choices, if medication is indicated (Haverkampf, 2018).

Benzodiazepines and Pregabalin

It has been suggested that switching to pregabalin may be a safe and effective method for discontinuing long-term benzodiazepine treatment. A randomized double-blind study by Sadley and colleagues with 106 outpatients showed results on the anxiety and withdrawal severity measures that offer some support for this approach. (Hadley et al., 2012) In another study, Lydiard and colleagues studied the effect of pregabalin and benzodiazepines in the treatment of anxiety. The doses studied were for pregabalin 150 mg (n=210), 300–450 mg (n=455), and 600 mg (n=406), and for the benzodiazepines (6 mg/d lorazepam and 1.5 mg/d alprazolam, n=299). The placebo group consisted of 484 individuals. Treatment with 300–600 mg pregabalin significantly improved both the Hamilton Anxiety questionnaire's psychological and somatic anxiety factors. In contrast, treatment with 150 mg pregabalin appeared to be less effective, achieving significance only on the psychological anxiety factor. Treatment with benzodiazepines was also associated with significant improvement in both psychological and somatic anxiety factors. (Lydiard et al., 2010)

Psychotherapy

Anxiety is often a consequence when certain aspects of life do not align with individual needs, values, and aspirations. Underlying emotions and other conflicts usually contribute to the anxiety. Medication can help lower psychological and somatic anxiety considerably and be of help particularly in the short-term or in the case of panic attacks. Antidepressant medication can also be a long-term support, but the indication should be reassessed regularly, and a regular course of psychotherapy should always accompany the psychopharmacological treatment.

Integrated Treatment Plan

Psychotherapy should be an integral part of any treatment plan. To this one can add on the medication side an as needed medication for the short-term, such as in the form of a benzodiazepine and a serotonergic antidepressant, such as an SSRI, in the long run. As mentioned above, pregabalin and a few other medications may also be helpful, both over the short- and the long-term. However, psychotherapy is the most finely tuned instrument we have to treat a patient with relatively low side effects, and which has high demonstrated effectiveness in the literature.

Many of the mainstream therapies include cognitive-behavioral therapy (CBT), psychodynamic psychotherapy, and interpersonal psychotherapy (IPT), as well as many others that have demonstrated effectiveness. There is a considerable number of studies on CBT and psychodynamic psychotherapy. It is often said that CBT has demonstrated the best effectiveness. However, it is also that the manualized approach of CBT lends itself best to a relatively simply structured outcome assessments used in most empirical studies. Therapies that are less manualized may be as effective, or even more effective, but the positive outcomes may not be as easy to measure in the short run. Empirical studies have also shown that the person of the psychotherapist is maybe even more important than a particular school of psychotherapy.

Cognitive Behavioral Therapy (CBT)

Loerinc and colleagues conducted a systematic review of the treatment outcome literature to determine overall response rates to CBT for anxiety disorders and whether current methods of defining treatment response influence overall response rates. Our database search (2000–2014) resulted in 87 studies that reported response rates and included at least one CBT condition. Results showed that overall treatment response rates across anxiety disorders averaged 49.5% at post-treatment and 53.6% at follow-up. Response rates varied significantly as a function of the properties used to define them. (Loerinc et al., 2015)

Psychodynamic Psychotherapy

Patients with generalized anxiety disorder according to DSM-IV were randomly assigned to receive either CBT (N=29) or short-term psychodynamic psychotherapy (N=28). Both CBT and short-term psychodynamic psychotherapy yielded significant, large, and stable improvements with regard to symptoms of anxiety and depression. No significant differences in outcome were found between treatments in regard to the primary outcome measure. These results were corroborated by two self-report measures of anxiety. In measures of trait anxiety, worry, and depression, however, CBT was found to be superior. (Leichsenring et al., 2009)

Interpersonal Psychotherapy

A literature search identified six open and five controlled trials of IPT for social anxiety disorder (SAD), panic disorder, and posttraumatic stress disorder. IPT shows some promise for anxiety disorders but has thus far shown no advantages in controlled trials relative to other therapies. Methodological and ecological issues have complicated testing of IPT for anxiety disorders, clouding some findings. The authors discuss difficulties of conducting non-CBT research in a CBT-dominated area, investigator bias, and the probable need to further modify IPT for anxiety disorders. Untested therapies deserve the fairest possible testing. (Markowitz et al., 2014)

Communication-Focused Therapy® (CFT)

A communication based model developed by the author has also been described for anxiety (Haverkampf, 2012). Communication-Focused Therapy® focuses on the communication patterns a patient uses in the internal and external communication (Haverkampf, 2017a). Since communication is how needs, values, and aspirations are satisfied, it is an important instrument with which individuals make their world work. If anxiety springs from a misalignment between needs, values, and aspirations and their current life, working with communication patterns can help to bring about less stress and anxiety in the patient.

Working with communication patterns happens in the session. Creating awareness for communication, reflecting on it with the help of feedback and experimenting with it can give the patient a greater sense of what is possible. Communication happens internally and externally. Patients communicate with themselves and with others, where one is a reflection of the other to some extent. Helping a patient to connect better with themselves and the world helps to lower anxiety.

Important is also to help the patient manage better in various areas of everyday life. Supporting patients to better communicate at work and in their relationships and to feel a greater sense of efficacy ad influence in their life can help significantly to reduce anxiety. On the other hand, important is also that patients can focus on goals that are really important, meaningful and relevant to them. Too often the bar is either set unrealistically high or a goal is pursued which is not really important to the patient. This can increase stress and anxiety levels.

Mindfulness Training

Mindfulness-based therapy is a promising intervention for treating anxiety and mood problems in clinical populations. In a meta-analysis based on 39 studies totaling 1,140 participants receiving mindfulness-based therapy for a range of conditions, including cancer, generalized anxiety disorder, depression, and other psychiatric or medical conditions, the effect size estimates suggested that mindfulness-based therapy was moderately effective for improving anxiety and mood symptoms in the overall sample. In patients with anxiety and mood disorders, this intervention was associated with effect sizes (Hedges's g) of 0.97 and 0.95 for improving anxiety and mood symptoms, respectively. (Hofmann et al., 2010)

Mindfulness has spread rapidly from Buddhist traditions to Western psychology research and practice, in large part because of the success of standardized mindfulness-based interventions, such as mindfulness-based stress reduction (MBSR) and mindfulness-based cognitive therapy (MBCT). By practicing mindfulness, whether through sitting meditation, yoga, or other mindfulness exercises, which can be practiced even while walking to work, individuals become less reactive to unpleasant internal phenomena but more reflective, which in turn leads to positive psychological outcomes. Central is the state of nonjudgmental awareness of the present moment experience, including one's sensations, thoughts, bodily states, consciousness, and the environment, while encouraging openness, curiosity, and acceptance. (Hofmann & Gómez, 2017)

Exercise

A systematic review of 12 randomized clinical trials suggested benefits of exercise, for select groups, similar to established treatments and greater than placebo. However, most studies had significant methodological limitations, including small sample sizes, concurrent therapies, and inadequate assessment of adherence and fitness levels. (Stonerock et al., 2015) Still, in clinical practice many patients often report that exercise helps them feel better physically, which also reduces their anxiety levels.

Dr Jonathan Haverkampf, M.D. (Vienna) MLA (Harvard) LL.M. psychoanalytic psychotherapy (Zurich) trained in medicine, psychiatry and psychotherapy and works in private practice for psychotherapy and counselling in Dublin, Ireland. He is the author of several books and over a hundred articles. Dr Haverkampf has developed Communication-Focused Therapy® and written extensively about it. He also has advanced degrees in management and law. The author can be reached by email at jonathanhaverkampf@gmail.com or on the websites www.jonathanhaverkampf.ie and www.jonathanhaverkampf.com. He is also a guest at http://www.askdrjonathan.com.

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Christian Jonathan Haverkampf

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