A Natural Medicine Approach to Anxiety Disorders

Background to condition

Fear is a fundamental emotion expressed in all mammals, invoked by an immediate threat detected in the environment. It involves co-ordinated emotional, behavioural, and biological responses, including the classical 'fight, freeze or fight' response. In contrast, anxiety is a future oriented affective state in which the individual prepares to cope with a possible negative event in the absence of a triggering stimulus. Interestingly, neuroimaging studies demonstrate that both fear and anxiety share common neural pathways.[1]

Anxiety can offer adaptive advantages by orienting and preparing the individual for a possible threat. Whilst transient anxiety is a core component of the human experience, it becomes pathologic when this processes is prolonged, excessive or context independent and more difficult to regulate.[1]

Aetiology

Anxiety disorders are driven by a complex interplay between biological, psychological, social and environmental factors. There is evidence that highly anxious people display processing deficits in decision-making situations, which results in an increased propensity to make illogical connections between unrelated events. Anxiety disorders can be characterised by increased vigilance to situations that are perceived as threatening, with concomitant maladaptive and prolonged activation of the threat circuit.[1]

Anxiety disorders tend to run in families, with the likelihood of an anxiety disorder in a first-degree relative of an affected individual being 4 to 6 times greater than relatives of unaffected individuals. Extreme forms of adversity, particularly during childhood are associated with alterations in the neurocircuitry involved in fear and emotional processing, with a reduced activation of the fear extinction system. Parental factors associated with anxiety disorders in children include overprotectiveness; interparental conflict; perfectionism; and modelling of reaction to fearful, stressful or unpredictable situations. Therefore, it is observed that genetics and/or familial as well as environmental factors play predominant roles in the genesis of anxiety disorders.[1]

Stressful life events may play a role in precipitating emotional disorders, with stressors involving loss more typically related to the development of depression, whilst those signalling danger or threat associated with the onset of anxiety disorders. Other risk factors associated with the onset of anxiety include; childhood sexual abuse; early parental loss through death or separation; other childhood adversity and female gender.[1]

Biologically, anxiety disorders are often associated with dysfunctions in y-amino-butyric-acid (GABA) neurotransmission. GABAergic neurons and receptors play a key role in the modulation of anxiety responses both in the normal and pathological state. The level of neuronal inhibition is downregulated in pathological anxiety states and is therefore a major target of pharmacological treatment.[2]

Dysfunctions may also be present in a host of other pathways involving neuroendocrine and neurotransmitter pathways.[3]

Naturopathic treatment goals:[4]

- Reduce anxiety, worry and somatic symptoms
- Support the stress response and normalise HPA axis activity
- Educate on 'worry management' techniques
- Implement appropriate lifestyle changes
- Improve diet quality and reduce stimulants
- Implement preventive strategies to lessen chance of relapse

Clinical presentation

Generalised anxiety disorder (GAD) and social anxiety disorder (SAD) are among the most common mental health conditions. GAD is characterised by excessive uncontrollable worry in day-to-day life, whereas SAD is characterised by the persistent fear of embarrassment or negative evaluation when engaging in public performance or social interactions. There is a significant co-morbidity between the two conditions.[5]

In GAD, the focus of the worry is not restricted as it is in other psychiatric disorders. The patient may have multiple worries, which often shift over time. Common worries include; work and family responsibilities, money, health, safety, car repairs and chores. Most patients with GAD have one or more co-morbid psychiatric disorder including depression, specific phobia, social phobia and panic disorder.[6]

Worry in GAD, may also be associated with restlessness, easy fatigability, difficulty concentrating, irritability, muscle tension and disturbed sleep.[6]

Anxiety can arise suddenly (panic) or gradually over many minutes, hours or days. It can last from a few seconds to years; a longer duration is characteristic of an anxiety disorder.[5]

Anxiety presentations (DSM-V)[1]	Medical causes of anxiety[5]	Drug induced anxiety[5]
• Panic disorder • Agoraphobia • Generalised anxiety disorder • Social anxiety disorder • Specific phobia • Selective mutism • Separation anxiety disorder • Anxiety disorder due to another medical condition • Substance/medication induced anxiety disorder	• Hyperthyroidism • Pheochromocytoma • Hyperadrenocorticism • Heart failure • Arrhythmias • Asthma • COPD	• Corticosteroids • Cocaine • Amphetamines • Caffeine • Drug withdrawal (alcohol, sedatives and other illicit drugs)

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The interrelationship between anxiety and depression

Anxiety disorders can be so disruptive that depression may result. Alternatively, an anxiety disorder and a depressive disorder may co-exist, or depression may develop first, with signs and symptoms of an anxiety disorder occurring later.[5]

General approach to evaluation

An important step in the assessment of anxiety is to establish the cause, triggers, and duration of the symptoms. This can be achieved through an exploration of the nature of the symptoms (e.g. worries, somatic symptoms, and avoidance behaviours), triggers (e.g. stressful life events, medical illnesses, substance abuse, and change in medications), and the patients thoughts and beliefs regarding their anxiety. For example, anxiety about attending a social event may be due to; low mood and lack of interest (indicating major depressive disorder) or due to the fear of being negatively scrutinised by others (indicating social anxiety disorder).[1] An understanding of these patient-specific fears and concerns will assist the practitioner to formulate an individualised treatment plan and identify the need for a multidisciplinary approach to treatment.

Mental distress that occurs immediately after or shortly after experiencing or witnessing an overwhelming traumatic event are classified as trauma and stressor-related disorders such as acute stress disorder and post-traumatic stress disorder.[5]

Given that anxiety disorders are diagnoses of exclusion, it is important to rule out the contribution of concurrent medical illnesses or medication, which could be playing a role. Risk factors for a substance or medical cause of anxiety include: no previous history of an anxiety disorder, an onset of anxiety later in life, a recent change in medical health, prescribed medication, substance use pattern and the presence of atypical symptoms during a panic attack such as loss of consciousness, syncope, or loss of bladder or bowel control.[1]

Treatment of anxiety is encouraged where:[5]

- Other causes are not identified
- The anxiety is very distressing
- Anxiety interferes with daily functioning
- Anxiety does not stop spontaneously within a few days

Additional support

Cognitive behavioural therapy

Cognitive behavioural therapy is considered one of a number of first line therapies for anxiety disorders and its efficacy is well established.

A 2016 meta-analysis found large to very large treatment effect sizes from CBT in the treatment of anxiety disorders.[1]

Exercise

Exercise appears to be beneficial for people with a stress or anxiety disorder resulting in a significant reduction in anxiety symptoms. The exact mechanisms are not fully understood, however it is thought to be related to increases in brain-derived-neurotrophic-factor, improved autonomic nervous system functioning and increased release of endorphins, serotonin and other endogenous opioid neuropeptide transmitters.[34]

In addition, considering that patients with anxiety disorders have a significantly increased risk of cardiovascular disease, the benefits of exercise are likely to extend beyond the treatment of mental health symptoms.[34]

Massage therapy

Reductions in state and trait anxiety following a single dose and course of treatment respectively have been observed in clinical studies, and results have been comparable to psychotherapy.[35]

Meditation therapies

Meditation encompasses any practises in which the practitioner trains an individual's consciousness, or calms his/her mind in order to realise some benefit. The goal is often to achieve a state of 'detached observation' or 'restful alertness'. Considering the combined impact of biological, behavioural and cognitive vulnerabilities in anxiety, it is not surprising that meditation in various forms has been found to be beneficial in the management of anxiety. Abdominal breathing, commonly used in meditation, has long been used as a tool for coping with panic attacks. Meditation has consistently been shown to reduce cortisol and catecholamine levels that may otherwise trigger biologically based anxiety responses. Meditation can be thought of as a training tool to control the mind as a means to reduce anxiety, in addition to developing coping mechanisms to facilitate a calm and non-destructive response to stressful stimuli.[36]

DOSAGE GUIDELINES	
THERAPEUTIC	**RECOMMENDED DOSE**
Lavender, Skullcap, Lemon balm, Zinc and Vitamin B6 (CP)	3 capsules daily
Valerian, Hops, Passionflower (NES)	2 capsules daily, 30–60 minutes before bed
Rhodiola, Siberian ginseng, Withania (RC)	2 capsules daily
Multivitamin with B complex (BT)	2 capsules daily
Activated B complex (BB)	1–2 capsules daily
Curcumin C3 Complex® (CF)	1–2 capsules once to three times daily
Curcumin C3 Complex® with rutin, quercetin, bromelain, and co-factors (BF)	2 capsules once to three times daily
Cinnamon, magnesium, zinc, chromium, vitamin B6 and manganese powder (CT)	1 teaspoon twice daily
Chaste tree, Saffron, zinc, vitamin B6, magnesium, selenium and iodine (BE)	1 capsule twice daily
Chamomile, Lemon balm, Fennel, Caraway, Globe artichoke (IB)	1 capsule three times daily with food
Glutamine, Slippery elm, probiotics and prebiotics (EC)	1 heaped teaspoon twice daily
Multi-species probiotic (TF, PF)	1 capsule daily
Magnesium (M, MFB, MFC, MDB)	1–2 tablets 2–3 times daily, or, 1–2 teaspoons daily, or 1–2 scoops daily
High dose vitamin C with bioflavonoids and co-factors (CM, CC)	1–2 capsules once to twice daily, or, 1 teaspoon once or twice daily
Bacopa, Ginkgo, phosphatidylserine (CG)	2 capsules daily

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CORE SUPPORT

A COMBINATION OF LAVENDER, SKULLCAP, LEMON BALM, ZINC AND VITAMIN B6 TO PROMOTE HEALTHY NEUROTRANSMISSION AND TO MODULATE THE SLEEP/WAKE CYCLE AND THE STRESS RESPONSE SYSTEM (CP)

Lavender oil – Anxiolytic, antidepressant and spasmolytic. Oral administration of lavender oil has demonstrated significant efficacy in reducing anxiety symptoms in generalised anxiety disorder including restlessness, tension and sleep disturbances.[23]

Skullcap – Nervine tonic and demonstrates anxiolytic and mood enhancing properties in human RCT.[24]

Lemon balm – Reduces tension, agitation and overall anxiety.[25]

Zinc and Vitamin B6 – Essential co-factors involved in healthy neurotransmission and production of GABA.

ASSESS FOR POTENTIAL CONTRIBUTING FACTORS

Assess need for stress management techniques or psychotherapy including:

- Mindfulness/ meditation
- Massage
- Cognitive behavioural therapy
- Psychology/counselling

Implement exercise regime.[7]

SUPPORT THE HPA AXIS AND THE STRESS RESPONSE

Disruption of the HPA axis due to significant stress and/or childhood trauma predisposes individuals to psychopathology.[8]

THERAPEUTIC CONSIDERATION

- **Withania, Siberian ginseng, Rehmannia, vitamin B5, vitamin C, zinc (AR)**
- **Rhodiola, Siberian ginseng, Withania (RC)**
  HPA axis modulators with herbal adaptogens and tonics may help to restore HPA axis function and sensitivity.
- **Multivitamin with B complex (BT)**

Or

- **Activated B complex (BB)**
  B vitamins are essential for healthy HPA axis and nervous system function.

ASSESS FOR GASTROINTESTINAL DYSFUNCTION

Gastrointestinal dysfunction can precede or be a consequence of psychological disturbances through independent gut-to-brain, or, brain-to-gut pathways.[28]

THERAPEUTIC CONSIDERATION

- **Chamomile, Lemon balm, Fennel, Caraway, Globe artichoke (IB)**
  Herbal GIT support regulating inflammation, motility, visceral sensitivity and psychological disturbances.
- **Glutamine, Slippery elm, probiotics and prebiotics (EC)**
  Broad-spectrum gastrointestinal support for a healthy mucosal barrier. Glutamine also functions as a precursor to GABA.
- **Multi-species probiotic (TF, PF)**
  Broad-spectrum probiotic to support a healthy microbiome.

Educate on gradual adoption of whole-food nutrient dense eating habits. Broths, soups and stews and other easily digested and assimilated meals may be beneficial.

Encourage healthy eating patterns with appropriate time to 'rest and digest'.

Encourage consumption of fibre rich foods for maintenance of a healthy microbiome.

THERAPEUTIC CONSIDERATION

- **Curcumin C3 Complex® (CF)**
  Early human clinical trial data supports the use of curcumin in managing anxiety in individuals in an inflammatory state (obesity).[9]
- **Curcumin C3 Complex® with rutin, quercetin, bromelain, and co-factors (BF)**
  Broad anti-inflammatory formula which targets the 8 major inflammatory pathways.
- **High strength fish oil (OE)**
  Human clinical trials demonstrate anti-anxiety effect from fish oil supplementation.[10,11]

ATTENUATE INFLAMMATORY PATHOPHYSIOLOGY

Pro-inflammatory markers have been shown to directly modulate affective behaviour. Inflammatory cytokines are released as a result of the activation of the stress response, creating a vicious cycle.[12]

Implement anti-inflammatory diet, stress reduction techniques – where appropriate – and an exercise regime.

ASSESS FOR MUSCULOSKELETAL TENSION AND PAIN

THERAPEUTIC CONSIDERATION

- **Magnesium (M, MFB, MFC, MDB)**
  Magnesium may assist with healthy muscle contraction and relaxation.

Progressive muscle relaxation may be of value to release built up muscle tension. In addition, muscle relaxation techniques have long been recognised to improve anxiety symptoms.[29]

ASSESS FOR HORMONAL IRREGULARITIES

THERAPEUTIC CONSIDERATION

- **Cinnamon, myo-inositol, magnesium, zinc, chromium, vitamin B6 and manganese powder (CT)**
  Stress and insomnia significantly affect glucose homeostasis.[13] Assess requirements for blood sugar stabilisation.
- **Chaste tree, Saffron, zinc, vitamin B6, magnesium, selenium and iodine (BE)**
  Address HPO axis dysregulation for anxiety associated with pre-menstrual symptoms.

Implement low glycaemic load diet in combination with exercise regime.

ASSESS FOR INCREASED NUTRITIONAL REQUIREMENTS

THERAPEUTIC CONSIDERATION

- **Magnesium with co-factors (M, MFC, MFB, MDB)**
  Magnesium plays a role in both neurotransmission and regulation of the HPA axis. Supplementation has been shown to attenuate anxiety symptoms in multiple clinical trials.[30]
- **High dose vitamin C with bioflavonoids and co-factors (CM, CC)**
  Supplementation has been shown to significantly reduce anxiety scores in stressed high school students, possibly by regulating HPA axis function.[31]
- **Zinc, magnesium and B6 complex (BZ)**
  Zinc, magnesium and B6 act as essential co-factors in neurotransmitter synthesis and transmission.

Promote whole food sources of key nutritionals for long-term management.

Magnesium – nuts, legumes, whole grains, soy, parsnips, molasses, cocoa mass, corn, peas, leafy greens.

Vitamin C – paw paw, oranges, rockmelon, broccoli, brussel sprouts, tomatoes, grapefruit, cabbage, strawberries.

Zinc – oysters, wheat germ, meats, liver, whole grains, nuts, meat.

SUPPORT HEALTHY SLEEP PATTERNS

Evidence suggests a bi-directional relationship between insomnia and anxiety, in which insomnia predicts and is predicted by anxiety and depression.[27]

THERAPEUTIC CONSIDERATION

- **Valerian, Hops, Passionflower (NES)**
  Herbal hypnotics to improve sleep onset and maintenance.
- **Rhodiola, Siberian ginseng, Withania (RC)**
  Regulation of daytime cortisol secretion and circadian rhythm.

EDUCATE ON SLEEP HYGIENE

- Lighting
- Use of technology
- Avoidance of stimulants
- Sleeping environment
- Evening ritual

PRESENCE OF CO-MORBID DEPRESSION

Approximately 50% of patients suffer from a co-morbid depressive disorder.[14]

Mindfulness based cognitive therapies or other psychotherapies may be beneficial.

THERAPEUTIC CONSIDERATION

- **Rhodiola, Siberian ginseng, Withania (RC)**
  Rhodiola has shown promising results in clinical trials for both anxiety and depression.[15-19] Withania also exerts anxiolytic, and antidepressant effects.[20,21]
- **Curcumin C3 Complex® (CF)**
  Targets the inflammatory pathophysiology of depression. Curcumin found to be as effective as some SSRI's in RDBPCT's.[22]

ASSESS FOR ALTERED COGNITIVE FUNCTION

Anxious patients exhibit improved perception of environmental changes at the expense of more complex cognitive functions, including working memory.[32]

THERAPEUTIC CONSIDERATION

- **Bacopa, Ginkgo, phosphatidylserine (CG)**
  Bacopa possesses both anxiolytic and cognition enhancing properties.[33]