

The “Amygdala Hypothesis” for ME/CFS & Fibromyalgia



Written by Ashok Gupta

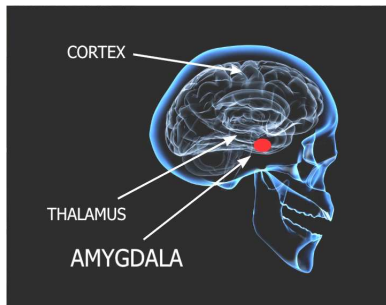
Harley Street Solutions, No.1 Harley Street, London W1G 9QD UK. info@guptaprogramme.com

Website www.guptaprogramme.com , Tel: +44 (0) 845 475 1 475

I used to suffer from ME/CFS myself around 10 years ago, when I contracted it whilst studying at University. Since then, for the last 10 years I have dedicated my life to finding an effective treatment for ME/CFS, and associated conditions such as Fibromyalgia and MCS. I have since recovered 100%, and I successfully treat patients at my clinic in Harley Street in Central London.

THE AMYGDALA HYPOTHESIS

My medical research seems to indicate that ME/CFS is a neurological condition, and may be caused by abnormalities in a brain structure called the “amygdala”,

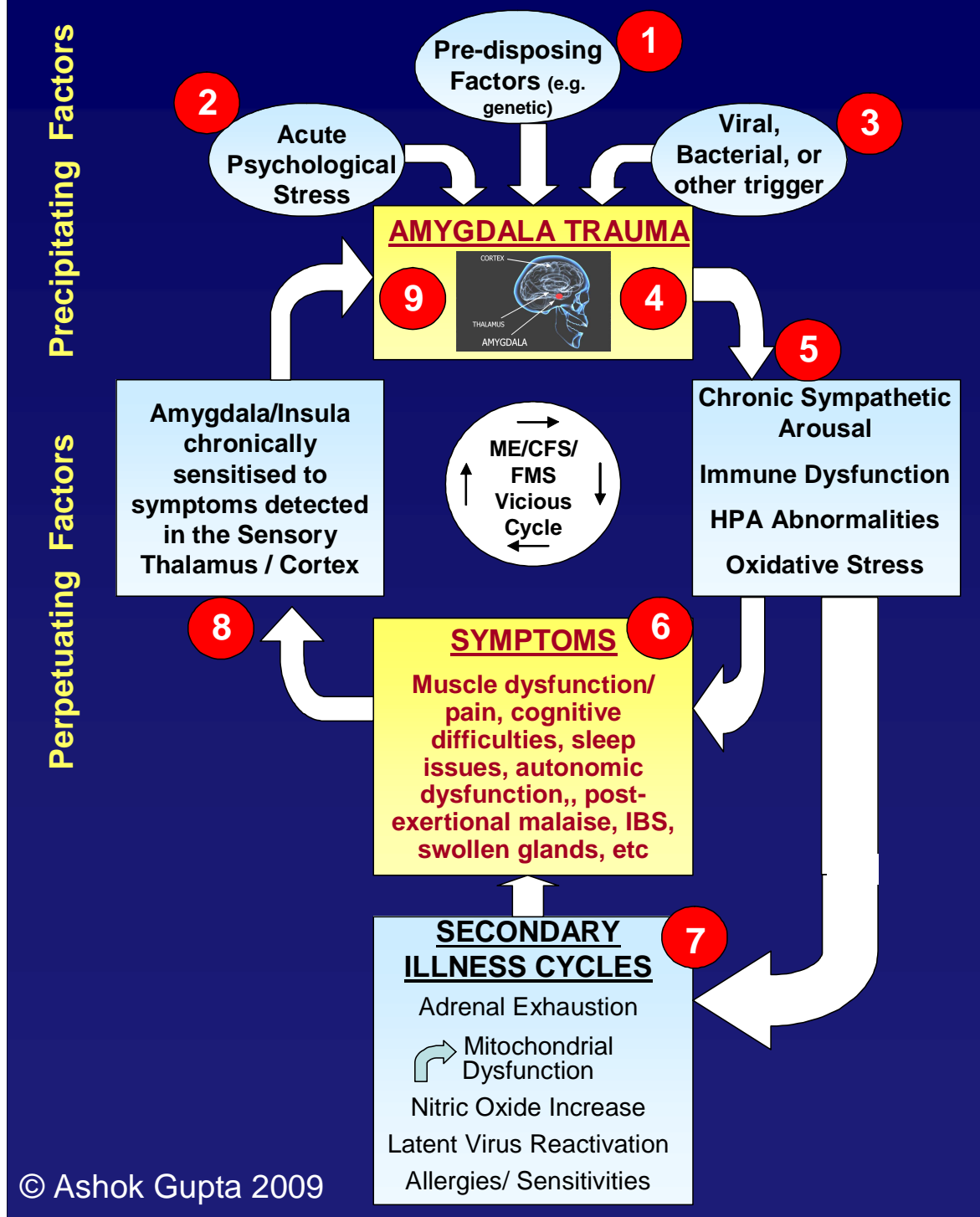


which is deep in the unconscious brain. One of the amygdala’s roles is to protect the body from potential threats. Research on the amygdala has traditionally focused on physiological or emotional threats, whereas recent research is showing that the amygdala is involved in protection mechanisms related to chemical and immunological threats as well. This hypothesis serves as a potential unifying model for the various observations in patients.

I published my hypothesis in a peer reviewed medical journal in 2002, which is available to read online here: <http://www.guptaprogramme.com/html/medicalPaper.asp>

Below, I will go through a basic explanation of the medical paper in layman’s terms using the following diagram:

THE AMYGDALA HYPOTHESIS



Right at the top, let's start with the pre-disposing factors to developing these illnesses, i.e. the risk factors (1). These may include genetic factors and environmental factors yet to be fully determined.

Then there are two other precipitating factors which contribute to these illnesses developing in someone. Firstly, the start of the illness is often accompanied by psychological or physical stress (2), as well as some kind of acute physical illness (3). In the case of ME/CFS, that physical illness might be a particularly difficult virus or bacterial infection (e.g. Glandular Fever, gut enteroviruses, etc), or another kind of illness. In Fibromyalgia, the physical trauma may be an accident, or on-going chronic pain in a part of the body. In MCS, the trigger may be heavy exposure to a toxin. There will be

crossovers in symptoms between these three conditions according to the theory. The theory predicts that the pattern of symptoms in the body will be different, but that the underlying cause may be the same. The theory still holds if there is a gradual onset versus a specific onset (see medical paper for further details).

The combination of these precipitating factors changes the circuitry of the amygdala, making it continually over-stimulate the body (4). During the trauma, the amygdala learns to be hyper-reactive to any symptoms detected in the body, in association with the “insula” (another brain structure). This conditioning happens unconsciously without a person actually realising it is happening.

From then on, the amygdala continually over-stimulates the sympathetic nervous system directly (5) (the sympathetic nervous system is the emergency response of the body to threats, and when triggered, the parasympathetic nervous system (bodily repair, detoxification, digestion, etc) is switched off and energy is diverted to the emergency). It over-stimulates the hypothalamus and the whole HPA (Hypothalamic-Pituitary- Adrenal) Axis, which subsequently downgrades as a result, making it difficult for the body to respond to stress. The amygdala also over-stimulates the whole brain, keeping many brain circuits in a state of hyper-arousal. This adversely affects the levels of neurotransmitters in the brain including serotonin and dopamine. There may also be conditioning in the immune system; this means that aspects of the immune system are inappropriately re-triggered in a unique pattern individual to each patient. Finally, this over-stimulation causes higher levels of oxidative stress in the body, and a compromised immune system.

A continual unremitting stimulation can cause symptoms which can severely affect every single organ and system in the body, including the endocrine (hormonal) system, and the immune system. **(PLEASE SEE THE APPENDIX TO THIS ARTICLE FOR A DETAILED EXPLANATION OF HOW SYMPTOMS ARE CREATED)**. Furthermore, it can cause secondary effects in the body, which then lead researchers to think that those physical observations are the cause of the condition, whereas they are simply symptoms of a deeper underlying brain abnormality.

Hyper-arousal of the body then causes the symptoms at (6). Furthermore, the over-stimulation of the body can create secondary illness cycles at (7). Over-stimulation can cause adaptation in receptors so that systems are down-regulated, or certain systems may simply exhaust due to over-stimulation, as is the case with the adrenal glands. Nitric oxide levels may rise (as per the observations of Professor Martin Pall), which can cause a whole host of secondary effects and symptoms in the body, including mitochondria dysfunction, perpetuating the entire vicious circle. Because the immune system is responding inappropriately, opportunistic viruses such as HHV-6 have the opportunity to flourish, increasing symptoms. Finally at (7), secondary allergies and chemical sensitivities can occur due to the hyper-sensitivity of the entire system.

(Where I differ from Professor Martin Pall's Nitric Oxide hypothesis, is that in the Nitric Oxide hypothesis, the Nitric Oxide effects are mainly local, but I do not believe that this could explain such a pervasive illness with such wide-ranging symptoms. Instead I believe that the Nitric Oxide theory reflects yet another secondary illness cycle which exacerbates symptoms, rather than the underlying cause of the condition).

Sympathetic over-activity means that sleep rhythms are affected, so the restorative “delta” sleep required for bodily repair is not effective. This has also been shown in Post Traumatic Stress Disorder, an illness where the amygdala has also been heavily implicated. This causes a patient to feel un-refreshed the next morning, causing severe exhaustion, and contributing to pain in Fibromyalgia.

At (8), these symptoms are detected by the sensory thalamus/cortex and the insula cortex (the parts of the brain that receive incoming information from the senses), and incoming signals are magnified by the amygdala, which keeps the brain and nervous system in a state of hyper arousal. The insula may be involved in interpreting the emotional meaning of the symptoms, and passing that representation onto the amygdala. The amygdala is traumatised to any symptoms at (9) that it detects in the body, and instantly re-stimulates bodily systems at (4) again.

(This central nervous system sensitivity (and resultant abnormal sensory processing causing heightened pain awareness) is gradually becoming a more accepted hypothetical model in Fibromyalgia).

This then perpetuates into a vicious circle as in the diagram. If the circle becomes particularly vicious, a patient can become bed-bound. If the cycle is milder, the patient may be able to function to a varying degree. The symptoms in each patient will depend on three factors:

- the **severity** of the conditioning effects in the amygdala and associated brain structures
- the **specificity** of the conditioning, i.e. what symptoms and what reactions were going on in the body at the time of the original trauma.
- The specific **timing** of the trauma – although symptoms can change over time

Due to the secondary effects of the condition on the body, food intolerances can develop, as well as general sensitivities. This is because when the brain and body are on high alert, the amygdala (in association with other brain structures) is prone to learning new responses to stimuli it would not normally care about. When the sympathetic system is aroused, digestive and detoxification systems are turned down or switched off, which may explain why many patients complain of feeling “toxic” inside.

A patient will also find that stress can exacerbate the symptoms simply because it “speeds up” the vicious circle, and the body does not have sufficient resources to deal with that stress. The stress can be mental, emotional or physical. With some patients, the conditioning effects are not particularly severe, which is why some patients seem to regain their health through general changes in lifestyle. For others, the conditioning in the brain is severe and causes chronic long term illness.

RETRAINING THE AMYGDALA

I wish to emphasise that I do believe that ME/CFS, Fibromyalgia and MCS are real physical conditions, and are in no way psychological. The sensitivity conditioning mainly occurs unconsciously. Gulf War Syndrome may represent a combination of all 3 illnesses to varying degrees, as at the time there was exposure to immunisations, toxins, and physiological stresses all at the same time.

Currently, I do not believe that there are any pharmaceuticals which could target such a specific reaction in the brain. Most pharmaceuticals or supplements target the symptoms rather than the underlying cause. If the conditioning effects are mild, successful treatment of symptoms may bring full recovery, but in the majority of cases, this will probably not occur.

This unconscious brain reaction is not normally under a patient's control, but I believe that some novel unique “brain retraining” techniques derived from NLP (Neuro-Linguistic Programming), breathing, meditation techniques, and others, can target the reaction and control the amygdala. Luckily the amygdala constantly communicates with other parts of the brain, and that's where retraining can take place.

In animal models, it is understood that the amygdala can be controlled with new neurones being formed, connecting from the pre-frontal cortex to the amygdala, to subdue and control its reactions. Some studies have shown that patients with ME/CFS have lower grey matter volume in this part of the brain (pre-frontal cortex). Other studies have shown that regular meditation can increase the volume of this part of the brain, showing that “brain” exercises can physically alter the structure of the brain.

I recently conducted an initial Clinical Audit on the techniques, and the study seems to show that over 90% of patients significantly improved as a result of the treatments, and that two-thirds of patients (67%) reached a full recovery or very close to that mark within one year. The average number of years with the illness was 10.5 years. This paper has been submitted for peer review and will be published in a medical journal later in 2009. There was no control group, and this was simply an initial pilot to stimulate funding for a larger randomised controlled trial.

The Amygdala Retraining techniques are now available as an interactive DVD recovery programme, which can be used at home. They come with a money back guarantee that if no improvement is noticed within 6 months, they can be returned for a refund.

If you are interested in finding out more about the hypothesis, you can view videos online at YouTube which cover the hypothesis in depth:

SESSION 2: PART 1

<http://www.youtube.com/watch?v=SEtyMHbf08U>

SESSION 2: PART 2

<http://www.youtube.com/watch?v=OYuOXdjaSJY>

SESSION 2: PART 3

<http://www.youtube.com/watch?v=8GKA3h56VWc>

SESSION 2: PART 4

<http://www.youtube.com/watch?v=JU-rOvhTZxA>

SESSION 2: PART 5

<http://www.youtube.com/watch?v=1YhI9eXkTic>

SESSION 2: PART 6

<http://www.youtube.com/watch?v=01srRrDqj54>

Further Information:

Website:

www.guptaprogramme.com

Email:

info@guptaprogramme.com

Tel: +44 (0) 845 475 1 475

APPENDIX:

HOW THE ME/CFS/FMS SYMPTOMS ARE CREATED

Physical Symptoms:

Muscular Fatigue & Pain, Tender Points, Aching Joints : The stress response is sometime known as the "fight, flight or freeze" response. These responses, including excessive adrenaline, keep the muscles tense, and are only designed to be triggered for minutes at a time. Relaxed muscles are in a state called tone, which is a state balanced between relaxation and contraction. Prolonged tension in muscles upsets tone and allows the chemicals of fatigue (e.g. lactic acid) to temporarily accumulate and disperse, causing aches and pain. Prolonged tension is initiated and maintained by the stress response, as the muscles are primed for reaction to dangerous stimuli. This is why you may suffer

from aching limbs that seem to feel heavy and drag, but there may be nothing actually physically wrong with the muscles.

A few patients have found that magnesium supplements tend to help muscle tension. This is because magnesium acts as a muscle relaxant, and can be found in green leafy vegetables as well.

Exhaustion from sleep problems: Several studies have shown that insomniacs cannot get to sleep mainly because they are worrying about something, even if they are very tired. Studies also show that the amygdala is partly responsible for keeping people awake at night due to unconscious stress. ME/CFS/FMS patients have the same problem: their minds are constantly being bombarded by thoughts telling them that there is an ever present danger that is unresolved, and so they find it difficult to get to or stay asleep.

When a mind and body is tense, sleep is interrupted and fragmented during the night. Studies have shown that interrupted sleep causes further aches and fatigue the next day. Overall, a prolonged stress response causing an interrupted sleep has adverse reactions on the body clock, and indeed some studies have shown a mismatch between temperature rhythms and melatonin secretion in patients. The mismatches in patients have been shown to be very similar to those suffering from stress and sleep deprivation, as well as PTSD. Furthermore, it is the hypothalamus that regulates sleep rhythms, and it is precisely this brain structure which is being bombarded by signals from the amygdala.

Post-Exertional Malaise, Adverse reaction to exercise: Some studies have also shown that patients do not respond correctly to exercise, in terms of inadequate release of a stress hormone called cortisol. This is because the severe stress response means that the stress glands may eventually get depleted (e.g. adrenal exhaustion), or they downgrade and adapt to chronic stress, and whilst the signals still exist to release cortisol, the response no longer occurs. Furthermore, the system may have cut back on supplying cortisol, because it has been over-stimulated in the past. Because muscles are already exhausted from being tensed up all day, they also find it difficult to respond to exercise.

There may also be a whole host of hormonal changes in the body which mean that the body cannot respond effectively to physical, mental or emotional stresses. If the brain and body has been stimulated continually, it cannot perform appropriately because as far as it is concerned, it already has "been performing" for long periods of time, and exhaustion easily sets in.

Digestive Problems, e.g. Irritable Bowel Syndrome (IBS): The digestive system has its own nervous system, sometimes called the "small brain". It becomes stimulated by the brain via the autonomic nervous system during stress, and this causes problems in the gut, and may tense muscles and generally over-stimulate the gut.

Also, when the "fight or flight" response is initiated by the sympathetic nervous system, adrenaline and noradrenaline direct the bodily energies and resources to the organs which are involved in fighting or fleeing. These are the muscles, so that they can respond quickly, and the brain, so that the mind can think quickly and concentrate on the source of the danger. Therefore, all other non-essential bodily functions are switched off, such as the digestive system. These means that food regularly passes through the gut but is not digested correctly, giving the symptoms of IBS. Furthermore, all muscles in the body are tensed, potentially including the muscles within the small and large intestines. The colon normally moves food by moderate contractions or spasms. Muscle tension upsets these rhythms giving either too many or too few contractions, leading to either diarrhoea or constipation, or both.

Food Allergies/Sensitivities: The gut can become highly sensitized to toxic elements in the diet, or at least foods which may now be perceived as toxic. The body is now in a very sensitised state, and therefore will over-protect itself to survive. Oxidative stress may cause "gut leakage", triggering sensitivity reactions.

Some patients find that changing their diet seems to help, and that is because there are certain food

types which are easier to digest. Eating foods which are difficult to digest while the digestive system is in this state, theoretically could worsen symptoms.

Immune System Symptoms, e.g. sore throat, swollen glands: The immune system is always in a state of delicate balance, ready to respond appropriately to a threat. However if the perception of that threat is overstated, there may be some aspects of a reactivated immune response that is constantly on alert. I will not go into the neurobiology of this mechanism here (it is commented upon in the medical paper), suffice to say that given that the original trauma often occurs in the presence of a severe virus/bacterial infection, it is no mystery that the body will retrigger immune defences as a way of making sure the body survives, even if no viral threat exists. This can often feel like having flu or a slight fever, as well as swollen glands and a sore throat, and may be the effects of chemicals called cytokines.

In some patients, this may result in a susceptibility to viral infections, and many of my patients report this. Others however may find that they do not have any more viruses than normal.

Latent Virus Reactivation/High Viral Titres: If the immune system is inappropriately retriggered, latent opportunistic viruses can take hold. Furthermore triggering of the stress system is known to reduce the effectiveness of the immune system, thereby allowing opportunistic viruses to flourish, causing further symptoms. Recently, Professor Nicholson showed that there were similar levels of multiple, systemic bacterial and viral infections in ME/CFS patients as there were in people with autism. Autism is a disorder where sustained amygdala hyperarousal is accepted as a model for partly explaining the disorder.

Visual disturbances: The delicate muscles which accommodate the lens of the eye are also affected by muscular fatigue, so that vision may be blurred, especially when looking near-to-far and vice versa. Eye fatigue also occurs because, when the fight or flight system is initiated, the vision sharpens and the eyelids retract so that the eyes can focus better on the source of the danger.

Autonomic Dysfunction e.g. temperature, sweating, blood pressure problems: The amygdala sends direct signals to the autonomic nervous system which co-ordinates many bodily responses including temperature and blood pressure. Therefore abnormalities in autonomic function can be directly attributable to chronic stimulation by the amygdala. Anxiety is well known to cause sweating, and even temperature changes.

Some patients may become "orthostatically intolerant", e.g. they have low blood pressure when they stand up, as tested by the tilt table test. This may be because of excessive pooling of blood in the legs, as the autonomic nervous system constricts blood vessels in the body, except in the limbs, so that a person can run away from dangers. This may cause problems when standing up like dizziness, as well as reduced blood flow to the head.

Multiple Chemical Sensitivities: The limbic system of the brain (which houses the amygdala and the hypothalamus) has been implicated in allergic responses and sensitivity responses. These systems become "over-cautious", reacting to toxins and pathogens "just in case" they represent dangers. When the amygdala is on high alert, it is prone to learning new sensitivities and threats which ordinarily would not have been reacted to.

Compromised Detoxification: When the body is in this sympathetic stress mode, non-essential systems are switched off, including aspects of the body's detoxification and elimination processes, and healing and repair systems. Therefore, if this reaction is prolonged, there may be accumulation of toxins in the body. Many patients complain of "feeling toxic". If the amygdala is retrained, the parasympathetic system can gradually detoxify the body in the correct way.

Alcohol Intolerance: Intolerance to alcohol has often been cited as a characteristic marker of ME/CFS. Much medical research demonstrates that alcohol actually induces the stress response by stimulating hormone release via the hypothalamus. This is exactly the response which the amygdala is conditioned to respond to, causing further symptoms. Furthermore, this reaction may malfunction due to a downgraded HPA axis and other hormonal abnormalities as a result of the stress response, causing increased sensitivity to alcohol.

Other New Symptoms: The autonomic nervous system affects all the organs and systems in the body, and that is why there are so many wide-ranging symptoms experienced. And because the amygdala is at a heightened state of awareness of all the messages coming from the body, new fears can be "learned". This means that even when innocuous signals come into the sensory neurones, these signals can be misinterpreted as dangerous by the amygdala. This happens because some patients can tend to monitor signals from their bodies, and signals can be perpetuated. This explains why patients can develop added symptoms, which can mysteriously come and go.

Cognitive Symptoms

Headaches and "Foggy" Head: Once again, these occur as a result of prolonged muscle tension in the head. The mind is particularly in a state of heightened arousal throughout the day, and becomes stressed and exhausted from so much stimulation. This can make the head sensitive and sore. Because there may be reduced blood pressure and blood flow to the head, this contributes to brain fog because there simply are not enough resources being channelled to the brain.

Inability to concentrate: The mind is on edge due to the excited state of the amygdala. Furthermore, the conscious mind is "arrested" by the amygdala, as it gets bombarded with signals about the body. Therefore, the mind finds it difficult to focus on other tasks, because it is also trying to process the signals about the body.

When patients are in the state of heightened arousal about symptoms, their memory systems are reshuffled so that knowledge and memories most relevant to the symptoms will be recalled, taking precedence over other less relevant strands of thought. This makes concentrating on anything else very difficult.

Problems with Memory: An area of the brain called the hippocampus has a dual role; in firstly providing short term memory retrieval, and secondly as a "control knob" which tries to moderate the release of the stress hormones. The hippocampus becomes damaged during a chronic stress response, and no longer is able to fulfil these dual roles well. Therefore, the formation of new memories in the hippocampus is inhibited, which means that you may have problems with short term memory formation and retrieval.

Whilst this effect may seem frightening, recovery will mean that the hippocampus can return to its normal functioning.

Emotional Symptoms:

Emotional Lability, Anxiety and Depression: The stress hormones and neurotransmitters are known to increase emotional lability and feelings of vulnerability. This causes a wide variety of added psychiatric complaints and further learned fears, especially depression and sometimes agoraphobia. Your amygdala is deliberately trying to make you feel anxious, as it is trying to warn you of danger.

Susceptibility to Stress: The long term arousal of the amygdala means that stress hormone release can become poorly controlled. Therefore, external events which have little to do with bodily symptoms, make you feel far more stressed than normal. You may perceive the world as more dangerous than it actually is, and this is made worse by the fear of increased symptoms because of stress.

Panic Attacks: Many patients become prone to panic attacks, which are known to be mediated by the amygdala. Prolonged worry may mean that the amygdala becomes trigger happy, triggering at the slightest negative signal from the body. It may detect certain bodily changes such as blood pressure increasing as a result of an external event, it prepares for a panic attack, and hence this becomes a self-fulfilling prophecy: the amygdala and the conscious mind fear a panic attack coming on, and this in itself initiates it. In general, if you experience increased external stress, this makes the symptoms even worse. This is because the stressful events impact on an already fatigued and sensitised mind and body.

Inability to Feel Enjoyment

In some patients, changes may occur in the brain's opioid system. This system becomes hyperactive. This gives the feeling of numbness, and other psychological symptoms including "anhedonia" (the inability to feel pleasure), and a sense of being cut off from life.

And Finally....

I do believe that these symptoms are temporary, i.e. they are due to systemic functional changes in the body, rather than permanent organic damage. Stopping the amygdala's hyper-reactions allows the body to trigger the parasympathetic system, meaning the body's own healing mechanisms can bring it back to balance and homeostasis.

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