Chapter 7

Evolutionary Perspectives on Depression

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Key points:

- We classify depression into twelve subtypes.
- Different adverse life events lead to different patterns of symptoms, suggesting that different subtypes of depression arise based on the triggering factors.
- Major depressive disorder is a disease caused by features of contemporary western lifestyle: social isolation, limited physical activity, chronic stress, and unhealthy food.
- Major depressive disorder is associated with neuroinflammation.

Abstract

We propose that major depressive disorder is not a unitary disease. Instead, different triggering factors causing periods of low mood can give rise to different and sometimes even opposite symptom patterns. Some of the symptoms of depression are maladaptive; others may be psychobehavioural adaptions to solve the adaptive problem that triggered the depressive episode. It is therefore logical to subtype depressive episodes according to the triggering factors. In evolutionary psychiatry, depressive episodes can be classified into discrete subtypes that are induced by: 1) infection, 2) long-term stress, 3) loneliness, 4) traumatic experience, 5) hierarchy conflict, 6) grief, 7) romantic relationship dissolution, 8) postpartum events, 9) season, 10) chemicals, 11) somatic diseases, and 12) starvation. In hunter-gatherers and in people who have traditional lifestyles, periods of low mood only rarely turn to episodes that fulfill the diagnostic criteria of major depressive disorder. Modern lifestyles cause low-grade inflammation and an increased susceptibility to chronic stress, which introduce symptoms of sickness behaviour into reactive short-term mood changes. Therefore, features of contemporary environments may prevent normalisation of mood after adverse life events, resulting in major depressive disorder. An evolutionary approach to depression helps identify the factors in our environments and lifestyles that contribute to greater susceptibility to this debilitating disorder, which can inform both prevention and treatment of depression. We further propose that the treatment of major depressive disorder should be tailored according to the patient's depression subtype, focusing on root causes of the disorder rather than alleviating symptoms with drugs.

Key words: evolutionary psychology, evolutionary psychiatry, major depressive disorder, MDD, gut microbiota, mood change, neuroinflammation, stress responsivity, chronic stress, mismatch hypothesis

1. Introduction

Major depressive disorder (MDD) is the most prevalent psychiatric disorder. With recent developments in evolutionary psychiatry, multiple evolutionary explanations have been proposed to explain the evolutionary origins of major depressive disorder and the possible adaptive functions of its symptoms (e.g., Andrews and Thomson, 2009; Badcock et al., 2017; Nesse, 2019; Nettle, 2004). However, none of the explanations has received full acceptance and none of the explanations has, thus far, provided improvements in the efficacy of treatments. For example, 30-60% of patients with major depressive disorder are not responsive to available pharmacotherapeutic interventions, remission rate is often below 50%, and recurrence rate is more than 85% within ten years of a depressive episode (Sim et al., 2016).

We have suggested that the main reason why previous evolutionary explanations have failed to provide good explanations for MDD and why pharmacological treatments have had such low efficacy is because MDD is not a single disorder (Rantala et al., 2018). Likewise, another reason why it is difficult to provide convincing evolutionary explanations for the symptoms of depression by studying the behaviour of depressed people is that because the environment has changed from the environment in which our psychobehavioural adaptations evolved, previously adaptive behaviour might have become maladaptive (see chapter 1, this volume). If we want to understand the evolutionary functions of depression symptoms, we should understand what were their functions in ancestral humans in ancestral environments, which constitutes the main selective landscape underlying the psychobehavioural predispositions that characterise contemporary humans.

In this chapter, we argue that MDD is a disease of modern lifestyles. We also provide evolutionary explanations for each symptom that is used in the diagnostic criteria of major depressive disorder. Finally, we propose a subtyping of depressive episodes according to the proximate factors that triggered the mood changes and their possible ultimate (i.e., evolutionary) functions.

1.1 MDD as a disease of modern lifestyle

The prevalence of MDD varies greatly between countries. For example, a World Health Organization survey found that the prevalence of lifetime MDD varies from 19.2% observed in the US to 3.3% observed in Romania (Merikangas et al., 2011). The prevalence of MDD has also increased over time. For example, Chinese people born after 1966 were 22.4 times more likely to suffer from a depressive episode than Chinese people born before 1937 (Lee et al., 2007). A meta-analysis of Minnesota Multiphasic Personality Inventory data of American college (N = 63,706) and high school (N = 13,870) students found that young adults were 6–8 times more likely to meet the diagnostic criteria of MDD in 2007 compared to peers in 1938 (Twenge et al., 2010). A population study in Lundby, Sweden, found that the point prevalence of depression in 1957 was 0.8%—in 1972, it was 2.6% (Hagnell et al., 1993), and in 2009, it was 10.8% in Sweden overall (Johansson et al., 2013). It has been estimated that the total number of people living with MDD worldwide increased by 49.86% between 1990 and 2017 (Liu et al., 2020).

Anthropologists who examined hunter-gatherer societies that have lifestyles closer to those of our ancestors have reported that MDD (that fulfills the diagnostic criteria of DSM) has been very rare compared to people who have a modern lifestyle. For example, a study of the Kaluli people of New Guinea found that only one in 2,000 people interviewed met the

criteria for being clinically depressed (Schieffelin, 1986). Similar findings have been reported from the Thai-Lao of Thailand (Keyes, 1986), the Toraja of Indonesia (Hollan and Wellenkamp, 1994, 1996), and the Bushmen of the Kalahari (Thomas, 2006). Cross-cultural analyses have found that the degree of modernisation correlates with higher prevalence of MDD in a dose-dependent manner (Colla et al., 2006).

The best evidence that the prevalence of depression is associated with modern lifestyle comes from the Old Order Amish, who still have a lifestyle resembling that of the 18th century. Egeland and Hostetter (1983) studied the prevalence of MDD for five years and found that only 41 out of 8,186 adult Amish individuals met the diagnostic criteria, suggesting that the prevalence of MDD is only 0.5%. The one-year prevalence of MDD among other Americans is 10.4% (Hasin et al., 2018). Thus, the difference in the prevalence of major MDD is at least 20-fold. However, this may be an underestimate because among other US citizens the estimate is given as a one-year prevalence, while Egeland and Hostetter (1983) gave the five-year prevalence. Naturally, the low prevalence of MDD does not mean that hunter-gatherers or the Old Order Amish do not experience periods of low mood, sadness, or grief. However, it seems that in hunter-gatherers or the Old Order Amish, such periods just do not transform into episodes of MDD that would fulfill the diagnostic criteria of DSM-5 or ICD-10.

1.2 Why does modern lifestyle increase the risk of MDD?

One evolutionary psychological explanation for the current "epidemic" of MDD in developed countries is that our bodies and minds have simply not evolved in line with the Western way of life (Rantala et al., 2018). In modern societies, there are many lifestyle factors that may increase the risk that an episode of low mood or sadness exacerbates to an episode of MDD.

We don’t exercise enough, we eat too much, we get too much energy from food but too few nutrients, we don’t spend enough time in nature, we sleep too little, our community is reduced, large families are rarer, and many suffer from loneliness even when surrounded by millions of people in big cities (Hidaka, 2012; see chapters 1 and 2, this volume). In addition, modern lifestyle has led to reduced diversity in gut microbiome (Schnorr et al., 2014). These changes have brought us such diseases of modern lifestyle as cardiovascular disease, adult-onset diabetes, osteoporosis, gastrointestinal cancers, autoimmune diseases, allergies, and many more diseases that do not exist among people who have a hunter-gatherer lifestyle (Lindeberg, 2010). Common to these diseases is that they are all associated with low-grade inflammation (Furman et al., 2019).

Low-grade inflammation does not only cause diseases of modern lifestyle, but it also increases the likelihood of developing MDD. The depressant effect of low-grade inflammation is particularly pronounced in autoimmune diseases in which the amount of proinflammatory cytokines is constantly elevated. For example, up to 70% of people with rheumatoid arthritis develop clinical depression at some point in their lives (Matcham et al., 2013). Many studies and meta-analyses have found that the concentration of circulating C-reactive protein (CRP) (a biomarker of inflammation) and proinflammatory cytokines are higher in patients with MDD than in controls (Goldsmith et al., 2016; Osimo et al., 2019). Follow-up studies have suggested that inflammation is a cause rather than simply a consequence of the illness (Khandaker et al., 2014; Zalli et al., 2016).

Experimental evidence supports the hypothesis that proinflammatory cytokines cause mood changes. For example, typhoid vaccine substantially increases the amount of proinflammatory cytokines in blood and lowers mood as soon as three hours after vaccination (Harrison et al., 2009). Symptoms of depression have also been observed in experiments in which non-depressed patients have been given proinflammatory cytokines against hepatitis C

virus (Bonaccorso et al., 2001). In addition, experiments in which healthy subjects have been administered endotoxins produced by *Escherischia coli* have shown an elevated amount of proinflammatory cytokines in the blood and an emergence of depressive symptoms (Eisenberger et al., 2010).

Further support for the hypothesis that low-grade inflammation plays a role in major depressive disorders comes from numerous studies and meta-analyses which have found that anti-inflammatory agents alleviate symptoms of depression (Kappelmann et al., 2017; Kohler-Forsherg et al., 2019). Low-grade systemic inflammation causes neuroinflammation (i.e., the inflammatory response of microglial cells), which is a key factor that interacts with the three neurobiological correlates of MDD: dysregulation of the serotonergic system, dysregulation of the hypothalamic-pituitary-adrenal axis, and alteration of the continuous production of adult-generated neurons in the dentate gyrus of the hippocampus (Troubat et al., 2021). This neuroinflammatory hypothesis of depression is supported by brain imaging studies that have found signs of neuroinflammation in depressed patients (Holmes et al., 2018; Richards et al., 2018; Setiawan et al., 2015).

It appears that as neuroinflammation affects neurotransmitters that influence mood, especially serotonin (Rantala et al., 2019), neuroinflammation prevents the normalisation of mood after an individual has experienced an adverse life situation, and it may also exacerbate the symptoms of depression (Rantala et al., 2018). In addition, the increase in the amount of proinflammatory cytokines associated with low-grade inflammation may cause the body to begin to respond to it as it does with infection—that is, to produce sickness behaviours that help save energy for the immune system to defeat the “infection” (Rantala et al., 2018).

If we want to understand why inflammation increases the risk that normal mood change turns to MDD, we must first understand, at the ultimate level, why certain symptoms associated with depression exist in the first place.

2. The function of depression symptoms

2.1 Emotional pain

Natural selection has equipped us with the ability to sense physical pain so that we do not harm our bodies. It teaches us to avoid doing the painful thing again (Williams, 2016). Pharmacologically reducing pain can be detrimental to an individual's long-term health (Rantala et al., 2017). As with physical pain, the purpose of mental pain is to make an individual avoid future activities that have led to mental pain or decreased mood in the past. Thus, mental pain, like physical pain, can be adaptive.

2.2 Rumination

Rumination about events that triggered depression is more common in situations where the same event can be expected to recur (Keller and Nesse, 2006). Continuous rumination about the events that led to depression helps the depressed person to avoid similar situations in the future and to solve related social and psychological problems (Andrews and Thomson, 2009). However, this does not mean that rumination about negative things is adaptive in all situations, and excessive rumination can be detrimental to the person's ability to move on with their life.

2.3 Lack of concentration

Depressed people tend to perform poorly in tests that measure the ability to concentrate. They also often find it difficult to study and work because they do not know how to focus on what they are reading. Difficulty concentrating can manifest as indecision and frustration. Lack of

concentration is the result of depressed people thinking about things other than what they should focus on (Andrews and Thomson, 2009). Things that constantly come to mind are normally related to the factors that triggered the depressive episode. Lack of concentration is a by-product of rumination about the things that triggered depression, and can thus be adaptive (Watson and Andrews, 2002).

2.4 Changes in weight

Appetite can either increase or decrease depending on which factor has triggered the depressive episode. The most likely explanation for the weight gain associated with depression is related to “comfort eating”. Many depressed people experience increased cravings, especially for carbohydrate-rich and fatty foods, as eating them stimulates dopamine secretion in the brain’s reward system and causes momentary mood rise (Macht and Simons, 2000). In addition, sleep problems, often associated with depression, increase appetite and cause weight gain (Magee et al., 2009).

Loss of appetite in depression may be caused by an increase in the levels of proinflammatory cytokines caused by prolonged stress, infection, or low-grade inflammation. Proinflammatory cytokines increase the body’s production of leptin (Andreasson et al., 2007). Leptin is a satiety hormone that is released into the blood by adipose tissue. It reduces appetite and hunger. Cytokine-induced loss of appetite may be an adaptation to overcome diseases. Many animals also lose their appetite after becoming ill or injuring themselves (Exton, 1997) which reduces activity and saves energy. The reduction in appetite and fasting can enhance the functioning of the immune system in a number of ways (Wilhelm et al., 2021).

2.5 Anhedonia

Anhedonia refers to the inability to feel pleasure. Feelings of pleasure and joy are adaptations produced by natural selection: they motivate individuals to behave in ways that helped our ancestors pass on their genes to future generations (Barron et al., 2010). Depressed people typically lose interest in doing things that used to produce joy and pleasure, such as hobbies, social events, or sex. A person's appetite may decrease when eating no longer causes the same pleasure as before. Experimental studies in humans and many other animals have shown that injecting proinflammatory cytokines causes anhedonia (Rantala et al., 2018). The anhedonia caused by an infection is adaptive, as it reduces activity and conserves energy for the immune system. Anhedonia caused by neuroinflammation rather than infection, however, is often maladaptive (Rantala et al., 2018).

2.6 Sleep problems

The presentation of sleep problems may differ depending on the triggering factor of MDD. A depressed person might have problems falling asleep, wakes up at night, suffers from early-morning wakening, or sleeps too much. Increased need for sleep may occur in the types of depression where saving energy has been beneficial. For example, after losing or failing to achieve an important goal in a hierarchy conflict, it is sometimes better to sleep and save energy for a new attempt. In addition, the increased need for sleep in a disease state caused by an infection helps save energy. Winter depression is characterised by an increased need for sleep, which seems to be a maladaptive by-product of the reduced amount of light and the low-grade inflammation that cause a disruption of the circadian clock (Rantala et al., 2018).

A stressed person has lighter sleep, wakes up often, and may wake up to the slightest sound. When sleeping, a person is at their most vulnerable and unable to defend themselves. A stressed person's amygdala is overactive, raising stress hormone levels and alerting the body to danger. This is reflected in the quality of sleep. In contemporary developed societies, sources of sound at night are mostly harmless, but in our evolutionary history this was not always the case, and nocturnal sounds could have come from an approaching predator or a hostile person, making it beneficial for a stressed person to have light sleep.

Rumination about things that triggered depression causes insomnia because it keeps the mind overactive and makes it difficult to fall asleep (Watson and Andrews, 2002). For example, after a relationship ends, a person may ruminate at night about the reasons why the relationship went wrong and what should have been done differently. In these cases the brain prioritises rumination over sleep.

2.7 Exhaustion

In the context of infection, exhaustion helps to conserve the body's energy resources for use by the immune system. High proinflammatory cytokine levels resulting from peripheral low-grade inflammation or neuroinflammation may cause exhaustion, because the brain responds to them in a similar way as to an infection. Exhaustion may also result from chronic fatigue arising from sleep problems caused by stress or rumination, and as such is maladaptive (Rantala et al., 2018).

2.8 Psychomotor agitation or slowness

Some depressed people also experience psychomotor agitation or retardation. Agitation refers to anxiety accompanied by severe restlessness. It can manifest as inadvertent movements, walking back and forth, wringing of hands, constantly putting on and taking off clothes, or other similar activities. In the context of depression, psychomotor restlessness often appears to be a by-product of the associated anxiety, with no adaptive function (Rantala et al, 2018) and is often a side effect of antipsychotics (Gillies et al., 2013).

Psychomotor retardation manifests as a slowing down of thoughts and movements. This may be a by-product of sleep problems and/or a person concentrating their cognitive resources on rumination about matters that led to depression. Psychomotor retardation is one symptom of sickness behaviour, but it can also be the pathological consequence of peripheral low-grade inflammation and/or neuroinflammation (Rantala et al., 2018)

2.9 Pessimism

Pessimism leads to a gloomy and negative worldview. Studies show that people are normally over-optimistic about future prospects and their own abilities, and failures and depression dissolve this delusion of optimism. Pessimism reduces the pursuit of achievements in situations where failure is likely. It is adaptive in situations where past failures predict future ones (Rantala et al., 2018).

2.10 Excessive guilt

An individual may feel guilty about the event(s) that triggered their depression. Feelings of guilt make one reflect upon how their actions led to that outcome, and thus help minimise the

likelihood of the same thing happening again. The greater the role played by one's own actions in the situations that led to the event that triggered the depression, the greater the sense of guilt (Keller and Nesse, 2006).

2.11 Loss of self-confidence

Because self-confidence regulates progress in social hierarchy, the loss of self-esteem that occurs as a result of a hierarchy conflict prevents one from challenging those higher in the social hierarchy and thus protects one from new problems. Traditionally, psychologists have thought that good self-esteem leads to success. However, research suggests that good self-esteem is the result rather than the cause of success in the social hierarchy (Baumeister et al., 2003). Success enhances self-esteem, and failures lower it.

2.12 Recurrent thoughts of death

Thoughts of death and suicide are common in depressed people. Although suicide sounds like an eminently maladaptive solution, suicide may have increased inclusive fitness in our ancestors as a result of kin selection (see chapter 1, this volume). Suicide can help pass on one's genes to the next generation in a situation where an individual is a burden to their close relatives and their own reproductive potential is weak. By killing oneself, an individual may contribute to the reproductive success of their close relatives and thus to the proliferation of their own genes. In such a case, one's close relatives would have one mouth less to feed and no sick individual to be looked after (Decatanzaro, 1986). Indeed, several studies have shown that suicidal thoughts and suicides are more common in those who have poor chances of

reproduction and who feel they are merely a burden to their loved ones (Rantala et al., 2018) (see Soper et al., this volume, for an alternative perspective on suicide).

In experimental studies in humans, it has been found that just injecting proinflammatory cytokines into the bloodstream causes suicidal thoughts in some healthy subjects (Capuron et al., 2002). It is highly likely that the increase in levels of proinflammatory cytokines associated with clinical depression as well as bipolar disorder produces maladaptive suicidal ideation. The brain seems to respond in the same way to acute infection and neuroinflammation. Indeed, the intensity of low-grade inflammation is directly related to suicidal ideation (O'Donovan et al., 2013; Holmes et al, 2018).

The threat of suicide is also an effective way to get attention and help from close relatives as well as community members who benefit from the existence of the individual (for example, a former spouse if the couple has children together). For a threat to be credible, a person must be serious about it, as a result of which some people may end up killing themselves (Rantala et al., 2018).

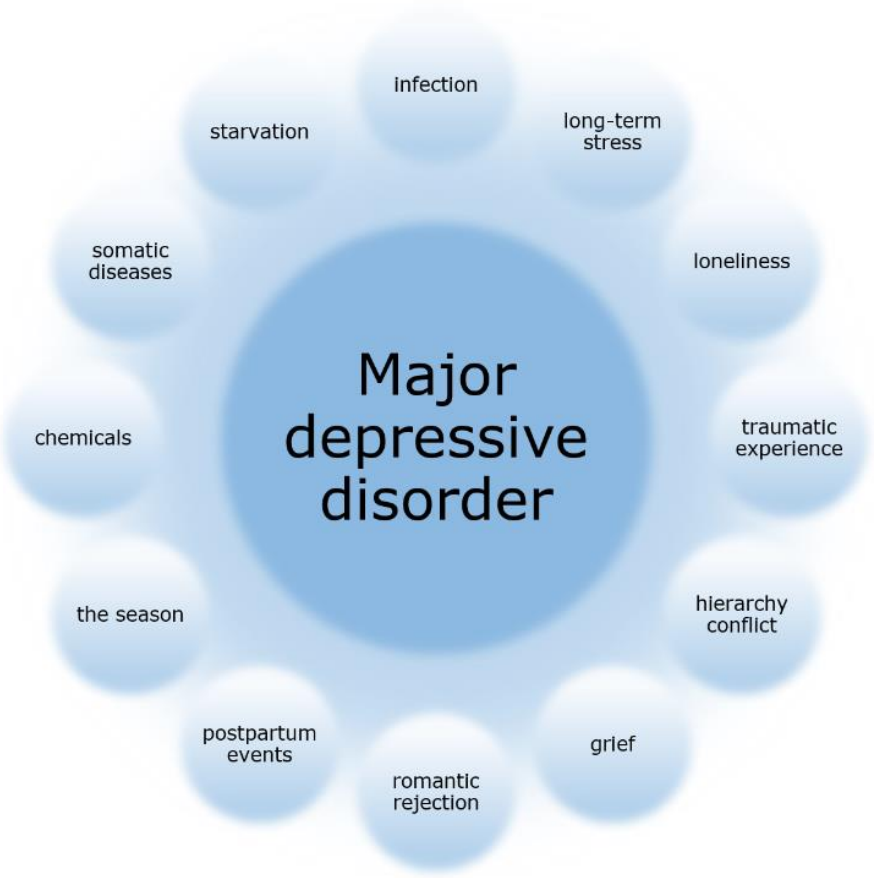
3. Subtypes of depression

A peculiar aspect of MDD is that two people diagnosed with this disorder may have completely opposite patterns of symptoms. For example, a person with depression can gain or lose weight, as well as suffer from excessive sleepiness, insomnia, or poor sleep quality. Speech and movement, in turn, can slow down or speed up. Different depressive episodes may have different symptom profiles even for the same person. Evolutionary psychologists think that symptoms of depression have evolved to solve the adaptive problem(s) that caused the depressive episode and that different adverse life events may lead to different patterns of depressive symptoms (Keller et al., 2007; Keller and Nesse, 2005). It is probable that

different adverse life events trigger different psychological adaptations that are crafted by natural selection as responses to the adaptive problems in question. Thus, from an evolutionary psychological viewpoint, it is logical to subtype depression episodes according to the triggering factor(s). We therefore present a classification of depressive episodes into 12 subtypes based on the proximate mechanisms and ultimate functions that trigger the mood change which leads to depression (Rantala et al., 2018) (Fig. 1).

Figure 1.

Subtypes of depression based on evolutionary psychiatry (Rantala et al., 2018).



3.1 Infection-induced depression

Owing to selective pressures caused by parasites and pathogens, natural selection has equipped us with an immune system and many other adaptations to combat parasites and pathogens (Schmid-Hempel, 2011), including the behavioural immune system (Schaller and Park, 2011). One of these adaptations is sickness behaviour, which includes somatic, cognitive, and behavioural changes that help individuals overcome infection by conserving metabolic resources for the use of the immune system, thus avoiding further infections (Anders et al., 2013). Symptoms of sickness behaviour include anorexia, psychomotor retardation, sleep disturbances, anergia, anhedonia, weakness, malaise, listlessness, hyperalgesia, and impaired concentration (Dantzer, 2001). All of these symptoms seem to be adaptations against infection, helping the immune system function more effectively (Anders et al., 2013). If the infection is contagious, the social withdrawal caused by sickness behaviour may reduce the likelihood that an individual will infect their kin—a behavioural feature which increases an individual's inclusive fitness (cf. Gardner and West, 2014). Social withdrawal caused by anhedonia, fatigue, hypersomnia, and psychomotor retardation reduces mobility and helps to conserve energy for immune defence (Anders et al., 2013). It is important to note that in contemporary humans, elevated low-grade inflammation in the body that is caused by an unhealthy lifestyle can lead to similar psychopathological consequences as infections.

3.2 Depression induced by long-term stress

Short-term stress can be beneficial due to its performance-boosting effect, but if it becomes chronic, it may cause numerous health problems, including depression (Yang et al., 2015). In our evolutionary history, stress was statistically associated with a higher probability of being wounded and thus some parts of our immune system are designed to be upregulated as a response to stress, while some parts are downregulated (Slavich and Irwin, 2014). Chronic

stress causes endocrine and immune system dysfunction that contribute to sustained low-grade inflammation, causing neuroinflammation that influences neurotransmitter levels and mood (Berk et al., 2013). The symptoms of depression induced by chronic stress include reduced mood, fatigue, self-blame, appetite problems, concentration problems, suicidal ideation, sleep problems, psychomotor problems, and anhedonia. Psychomotor problems (289%) and interest loss (217%) showed the largest increases and suicidal ideation (146%) and sleep problems (52%) the smallest increases with stress, suggesting that stress affects depressive symptoms differentially (Fried et al., 2015).

Prolonged stress is also known to upregulate the immune system by causing the gut to leak non-pathogenic commensal microbes into peripheral circulation, which activates the immune defence and causes an increase in proinflammatory cytokines in blood (reviewed in Miller and Raison, 2016). This increase in proinflammatory cytokine levels triggers sickness behaviour and may lead to MDD.

Chronic stress does not have to be caused by a life-threatening danger; even modern-day working life or financial or social problems may be stressful enough to cause a state of chronic stress response that leads to depression. This subtype of depression can manifest as burnout (Bianchi et al., 2021). This subtype of depression is a maladaptive by-product of prolonged stress response, occurring because of a mismatch between the current and the ancestral environment (Rantala et al., 2018).

3.3 Depression induced by loneliness

Loneliness is the result of a person's desired number of social contacts not qualitatively or quantitatively corresponding to the state that person desires (see Dunbar, this volume). A

feeling of loneliness is an adaptation produced by natural selection that causes an individual to seek out the company of others.

Man is a highly social primate. Separation from a social group has been a life-threatening danger in our evolutionary environment, as surviving alone at the mercy of nature has been difficult and often impossible. An evolutionarily salient facet of loneliness is that it is impossible to reproduce alone. Because of this, a person unknowingly perceives loneliness as a threat, which is reflected in the activation of the amygdala and increased stress hormone levels. If the stress reaction caused by loneliness persists for a long time, it causes neuroinflammation that leads to MDD that does not help a person to seek the company of others (Rantala et al., 2018).

3.4 Depression induced by traumatic events

Most people experience some traumatic events in their lifetime. For some, the traumatic memories of the event come back as flashbacks or nightmares and cause anxiety and fear. Such people may begin to avoid objects, places, and people that remind them of the traumatic event. They may also begin to isolate themselves from other people and suffer from emotional numbness. Constantly going through traumatic events often causes symptoms such as constant alertness, frightfulness, and irritability. In psychiatry, such people are classified as suffering from post-traumatic stress disorder (PTSD).

Studies conducted in emergency response units measuring stress hormone levels immediately after a traumatic event or an accident have found that patients with the lowest stress hormone levels immediately after a traumatic experience were more likely to develop a traumatic stress disorder than those with high stress hormone levels (Aardal-Eriksson et al., 2001; Mouthaan et al., 2014). It suggests that those who respond to a traumatic event with a

fight-or-flight reaction do not develop post-traumatic stress disorder. The essential question is: why does a different response to a traumatic situation cause PTSD for those who do not respond to a traumatic event with elevated stress hormone levels?

A fight-or-flight reaction that raises stress hormone levels is not the only possible human reaction to danger. If a person experiences a danger that they cannot overcome with a fight-or-flight response but instead has to freeze or is otherwise unable to intervene, it will be better for them to avoid situations and places where the danger may recur. Natural selection has favoured individuals who effectively remember such an experience and thus avoid being in a similar situation again. Thus, PTSD appears to be an evolved adaptation to avoid situations that have traumatic qualia associated with them (Rantala et al., 2018).

In people with contemporary western lifestyle(s), PTSD is often associated with symptoms of depression. For example, a large meta-analysis composed of 57 studies reported a MDD comorbidity rate of 52% among both military personnel and civilians suffering from PTSD (Rytwinski et al., 2013). Although PTSD is associated with hypocortisolism (Bicanic et al., 2013), PTSD patients have an elevated concentration of proinflammatory cytokines (Gill et al., 2009), which explains why PTSD often takes on features of sickness behaviour and leads to depression. It seems that contemporary western lifestyle and low-grade inflammation change previously adaptive PTSD into a non-adaptive state of major depressive disorder by incorporating symptoms of sickness behaviour with PTSD, probably aggravating PTSD symptoms (Rantala et al., 2018). This hypothesis is supported by a study on Turkana warriors from Kenya, which found that in Turkana warriors, traumatic events led to fewer PTSD symptoms associated with depression than in western soldiers (Zefferman and Mathew, 2021). The important point to note is that Turkana warriors practice nomadic pastorialism, a lifestyle that is very different from that of contemporary western people. In contrast to people with contemporary western lifestyles, Turkana warriors have excellent

cardiometabolic health (Lea et al., 2020), suggesting that they do not suffer from low-grade inflammation. The hypothesis is also supported by findings showing that smoking, obesity, and low physical activity increase the risk of chronic PTSD (Buckley et al., 2004; Olff et al., 2006), while micronutrient intake may decrease it (Rucklidge et al., 2012). Thus, although PTSD *per se* seems to be an adaptation caused by natural selection to avoid the cause of the trauma, it seems that the depression triggered by PTSD is a pathological consequence caused by modern western lifestyle (Rantala et al., 2018).

3.5 Depression induced by hierarchy conflict

In many social species, defeat in hierarchy conflict causes depressive-like behaviour and physical responses that are similar to those seen in depressed humans (Rygula et al., 2005; Shively et al., 1997). In a defeated person, depression works as a sign of forfeit and as an honest signal that the defeated individual is no longer a threat to the winner. This submissive status may prevent the defeated person's expulsion from the group. Decreased self-esteem prevents the defeated individual from re-challenging the winner, thus helping the individual to conserve their bioenergetic resources (and possibly save their lives) in a situation where winning is unlikely. While clear physical hierarchy conflicts are rare in contemporary societies, conflicts still occur in the form of bullying at school or workplace and may lead to this type of depression (Rantala et al., 2018).

In this subtype, a person does not react to conflict in social hierarchy with a fight-or-flight response—instead, they give up. This subtype is therefore characterised by adrenocortical hyporesponsiveness and hypocortisolism, which indicates a down-regulated stress response. This has been demonstrated in mice where social defeat leads to elevated stress hormone levels in most individuals, but a subset give up and become depressed after

repeated social defeat and show adrenocortical hyporesponsiveness and hypocortisolism (Bowens et al., 2012). Although depression induced by hierarchy conflict is an adaptation, it does not mean that it is always adaptive in contemporary societies; instead, it is possible that low-grade inflammation may change it into a maladaptive state of MDD (Rantala et al., 2018).

3.6 Depression induced by grief

Animals generally grieve after the death of their pups, parents, or reproductive partners. They may also mourn a member of their social group with whom they have spent a lot of time. The grief triggered by the loss of loved ones does not appear to be an adaptation produced by natural selection, as it does not appear to increase an individual's fitness in any way—at least not in non-social species. Depression caused by loss is more likely to be a by-product of the ability to form long-term attachment relationships. Grief is the price we have to pay when the attachment relationship is finally broken. This assumption is supported by the fact that a person may also experience symptoms of depression as a result of the death of their beloved dog, horse, or other pet. The stronger the attachment, the longer the symptoms of depression last. On the other hand, the knowledge of the pain caused by the loss of an important person or pet makes us take more care of the people or pets that are important to us (Rantala et al., 2018).

In humans, losing a partner causes a sharp increase in stress hormone levels (Buckley et al., 2012). The increase in stress hormone levels and the resulting increase in proinflammatory cytokines in the blood may explain why grief can lead to major depressive disorder. A study on individuals whose spouses had recently passed away found that those with the highest level of proinflammatory cytokines in their blood (suggesting severe low-

grade inflammation) had the strongest symptoms of grief and the highest probability that grief and low mood turn to MDD (Fagundes et al., 2019). This suggests that western lifestyle and the resulting increase in chronic stress and low-grade inflammation increase the likelihood that normal grief and the associated decline in mood will turn into major depressive disorder (Luoto et al., 2018).

3.7 Depression induced by romantic relationship dissolution

A brain imaging study on recently dumped individuals found that they had the same areas activated that are activated in people with cocaine withdrawal symptoms (Fisher et al., 2010). Because romantic love is a form of addiction where love causes dopamine bursts in the brain, its withdrawal symptoms are also similar to those of drug addiction (Bode et al., 2021). Although some of the symptoms associated with romantic relationship dissolution may be withdrawal symptoms, some symptoms seem to be adaptations caused by natural selection. For example, ruminating on the cause of the relationship dissolution can help an individual avoid repeating the same mistakes in future relationships (Andrews and Thomson, 2009). On the other hand, a drop in self-esteem causes a person to lower the aspirations they have for potential mates to better correspond with their own market value. Depression can also serve as a signal for the abandoner that the relationship was important to the abandoned person. It may arouse so much empathy in the abandoner that they return to the relationship (Rantala et al., 2018). It is possible that unhealthy factors inherent in western lifestyles or traumatic childhood experiences that are known to be associated with increased stress responsiveness may contribute to chronic stress caused by romantic relationship dissolution, leading to MDD in the most vulnerable individuals (Rantala et al., 2018). Inflammation also plays a role in

relationship problems: troubled marriages are linked with heightened inflammation, and hostile marital behaviour increases inflammation in couples (Kiecolt-Glaser, 2018).

3.8 Postpartum depression

Postpartum depression occurs in 10–15% of women in the six months following childbirth (Brummelte and Galea, 2010). In addition to regular depressive symptoms, mothers who suffer from postpartum depression typically feel a loss of interest in their baby and may even develop harmful intentions towards them. Other symptoms include crying, suicidal ideation, bouts of anger, and hopelessness (Brummelte and Galea, 2016).

Postpartum depression is linked to the mother feeling that she is receiving inadequate support from the father or from kin. This can lead to the feeling that she cannot cope with her parental duties (Myers and Emmott, in press). In our evolutionary past, it would have been catastrophic for a lone mother to be left to care for a child on her own. If a woman continued investing in a child whose survival was unlikely, she would have had fewer offspring than a woman who ceased her investment and postponed reproduction. As a healthier child has a higher likelihood of survival, it is not surprising that poor health in the child predicts postpartum depression in the mother (Rantala et al., 2018).

It appears that the primary function of postpartum depression is not the desertion of the child. Rather, postpartum depression may function as a signal to kin and the spouse that the mother needs more support. It seems that postpartum depression is an adaptation which might not be adaptive in all cases due to the environmental mismatch between our evolutionary environment and modern conditions (Rantala et al., 2018).

3.9 Season-related depressions

Winter depression

In temperate and northern latitudes, winter depression is the most common seasonal affective disorder (SAD). In winter depression, symptoms often begin in autumn and abate in spring and summer, during which mild hypomania may occur. In SAD, symptoms typically intensify in the afternoon. Features of SAD include general fatigue, decreased libido, increased need to sleep, and increased appetite, especially for carbohydrates and starchy foods (Rantala et al., 2018).

It appears that winter depression is a maladaptive by-product of the failure of a person's circadian rhythm to match the reduced daytime length (Rantala et al., 2018). Since inflammation and chronic stress may disrupt circadian rhythm (Mavroudis et al., 2013), it seems that western lifestyle may increase the risk of winter depression (Rantala et al., 2018). This hypothesis is supported by the finding that winter depression is much lower among the Old Order Amish than in other populations in the same latitudes, despite the lack of electric lighting in the Old Order Amish (Raheja et al., 2013).

Spring depression

In contrast to winter depression, some individuals feel more depressed during spring and early summer. They sleep less, wake up earlier, and their mood is worst in the morning; they also have decreased appetite and weight (Boyce and Parker, 1988). In a temperate climate, the prevalence of suicides peaks in spring / early summer and suicide rate is the lowest during the period of winter depression (Reutfors et al., 2009). The possible proximate mechanisms underlying spring depression are allergenic reactions to pollen that increase low-grade inflammation and the increase of sunlight in spring that elevates the brain's serotonin levels to an excessive degree, exacerbating depressive and anxious symptoms in individuals who have an upregulated serotonergic system due to chronic stress (Rantala et al., 2018). Thus,

spring depression seems to be a maladaptive by-product of seasonal changes in the amount of daylight and/or allergens.

3.10 Chemically induced depression

Depression may be caused by substance abuse, or it can be a side effect of medication (American Psychiatric Association, 2013). Over 40% of alcoholics meet the criteria for major depressive disorder and as many as 70% of these are classified as substance-induced depression in DSM-5 (Schuckit, 2006). Unlike in many other subtypes of depression, alcoholics suffering from depression are not depressed all day every day (Schuckit, 2006). They therefore may not fulfill the DSM-5 criteria for major depressive disorder. Unlike with other depression subtypes, the symptoms of substance-induced depression decrease or disappear with abstinence (Schuckit, 2006), making the identification of the subtype easier. In addition to changing neurotransmitter functioning, one way in which alcohol may cause depression is by causing the leak of non-pathogenic commensal bacteria from the gut into the peripheral circulation, which triggers the production of proinflammatory cytokines and leads to symptoms of sickness behaviour (Rantala et al., 2018).

Depressed individuals often self-medicate low mood and anxiety with alcohol and other drugs—even if alcohol per se did not induce the depressive episode. Substance use typically does not help address the adaptive problem that led to the original mood change, although alcohol and other drugs may temporarily improve mood and reduce anxiety. Substance use can instead have hazardous long-term consequences for mental health (Leeies et al., 2010). Consuming alcohol may change the previously adaptive mood change to a

maladaptive state of major depressive disorder as it increases the production of proinflammatory cytokines that cause symptoms of sickness behaviour (Rantala et al., 2018).

3.11 Depression induced by somatic diseases

Many somatic diseases are commonly comorbid with major depressive disorder. For example, neurological conditions like Alzheimer's disease, Parkinson's disease, migraine, epilepsy, stroke, and traumatic brain injury, as well as several neuroendocrine conditions, such as Cushing's disease and hypothyroidism, are associated with an increased risk of MDD (Bulloch et al., 2015; Kim et al., 2015). A particularly salient example is multiple sclerosis—an inflammatory, demyelinating disease of the central nervous system—in which the lifetime prevalence of depression may exceed 50% (Beal et al., 2007).

Major depressive disorder is commonly comorbid with cancer. The risk of major depressive disorder is 5.4 times higher in cancer patients than in the general population (Hartung et al., 2017). There are three main reasons why cancer may induce depression: 1) receiving a cancer diagnosis may lead to a state of chronic stress and anxiety that can trigger major depressive disorder; 2) chemotherapy, radiotherapy, and surgery can result in depression induced by sickness behaviour; or 3) cancer itself can raise proinflammatory cytokine levels, triggering sickness behaviour. There is substantial evidence for all of these causes (Rantala et al., 2018). In many cases, depression induced by somatic diseases appears to be a maladaptive state as it impairs recovery from illness and increases mortality (Pinquart and Duberstein, 2010).

3.12 Starvation-induced depression

Starvation-induced depression can be seen as a psychological adaptation that helps to overcome famine. During starvation, the body begins to save energy by reducing investment in bodily functions and behaviours that are not necessary for immediate survival, like growth, immune function, and reproduction. At the beginning of starvation, physical activity increases, leading to a higher probability of finding food (Exner et al., 2000). However, prolonged starvation leads to apathy and social withdrawal in order to save energy. Starvation lowers mood, causes irritation and anhedonia, diminishes sexual interest, and reduces the ability to concentrate on tasks that require major cognitive processing because the starved individual is obsessed with finding food (Keys, 1950).

4. Problems with the current diagnostic criteria of depression

The current way of diagnosing major depressive disorder based on the number and duration of symptoms is problematic when viewed from an evolutionary psychological perspective. The current distinction between a person with major depressive disorder and a healthy person is based on the *number* of symptoms, and as such is completely arbitrary. In addition, the current diagnostic criteria automatically assume that all symptoms of depression are bad for the patient and should be eliminated. Whether depression causes harm to an individual's normal life does not in itself, from the perspective of evolutionary psychiatry, justify classifying depression as a disorder that should be pharmacologically treated. For example, fever caused by the flu is harmful to everyday life, although it is a naturally produced adaptation to overcome the disease and as such is beneficial to the patient (Williams and Nesse, 1991). From an evolutionary psychological perspective, a reactive short-term mood change turns into a maladaptive period of depression that requires intervention when a patient's symptoms no longer serve the purpose for which natural selection has shaped them,

or when the symptoms are more intense than what would serve the adaptive function (Rantala et al., 2018).

It is an even more complicated situation when a person experiences many different negative life events, triggering more than one subtype of depression, as a result of which the future combination of symptoms may no longer be a helpful response to any factor that led to the decline in mood. Symptoms can become too severe as a result of several different negative events, chronic stress, or low-grade inflammation caused by the novel conditions of western lifestyle—therefore, they no longer serve their adaptive purpose. In such cases, the symptoms may produce a condition that can be classified as pathological depression (Luoto et al., 2018).

Conclusions

The prevailing artificial classification of MDD should be radically reviewed and efforts made to assess on an individual basis whether a state of depression is a reactive response to an adverse life event or a consequence of neuroinflammation (Erjavec et al., 2021; Luoto et al., 2018; Rantala et al., 2018; Troubat et al., 2021). In order to provide the best treatment, efforts should also be made to assess whether the state of depression has become maladaptive. On the other hand, it is worth remembering that even if a certain behavioural response to adversity has been adaptive in our evolutionary environment(s), it may be maladaptive in contemporary life (see Troisi, this volume).

In diagnosing a patient's depression, it is essential to consider what is the adaptive benefit, if any, of the patient's depressive symptoms in the patient's life context. If the symptoms help solve the adaptive problem that triggered the depressive episode, pharmacologically treating the symptoms may not be beneficial for the patient. From the

point of view of evolutionary psychiatry, a more effective way can be to counsel the patient on how to overcome the adaptive problem and encourage lifestyle changes so that reactive depression does not turn into a maladaptive depression (Luoto et al., 2018; Rantala et al., 2018).

Since stress and low-grade inflammation may cause neuroinflammation and symptoms of sickness behaviour, and since they may strengthen the adaptive symptoms of reactive short-term mood change to maladaptive levels, it would be important to also alleviate stress and low-grade inflammation. Thus, we propose that rather than trying to alleviate all the symptoms of depression with just drugs, the treatment of depression should also be based on various forms of psychotherapy and lifestyle interventions that are targeted at alleviating stress, inflammation, and other proximate mechanisms behind depression (Luoto et al., 2018).

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