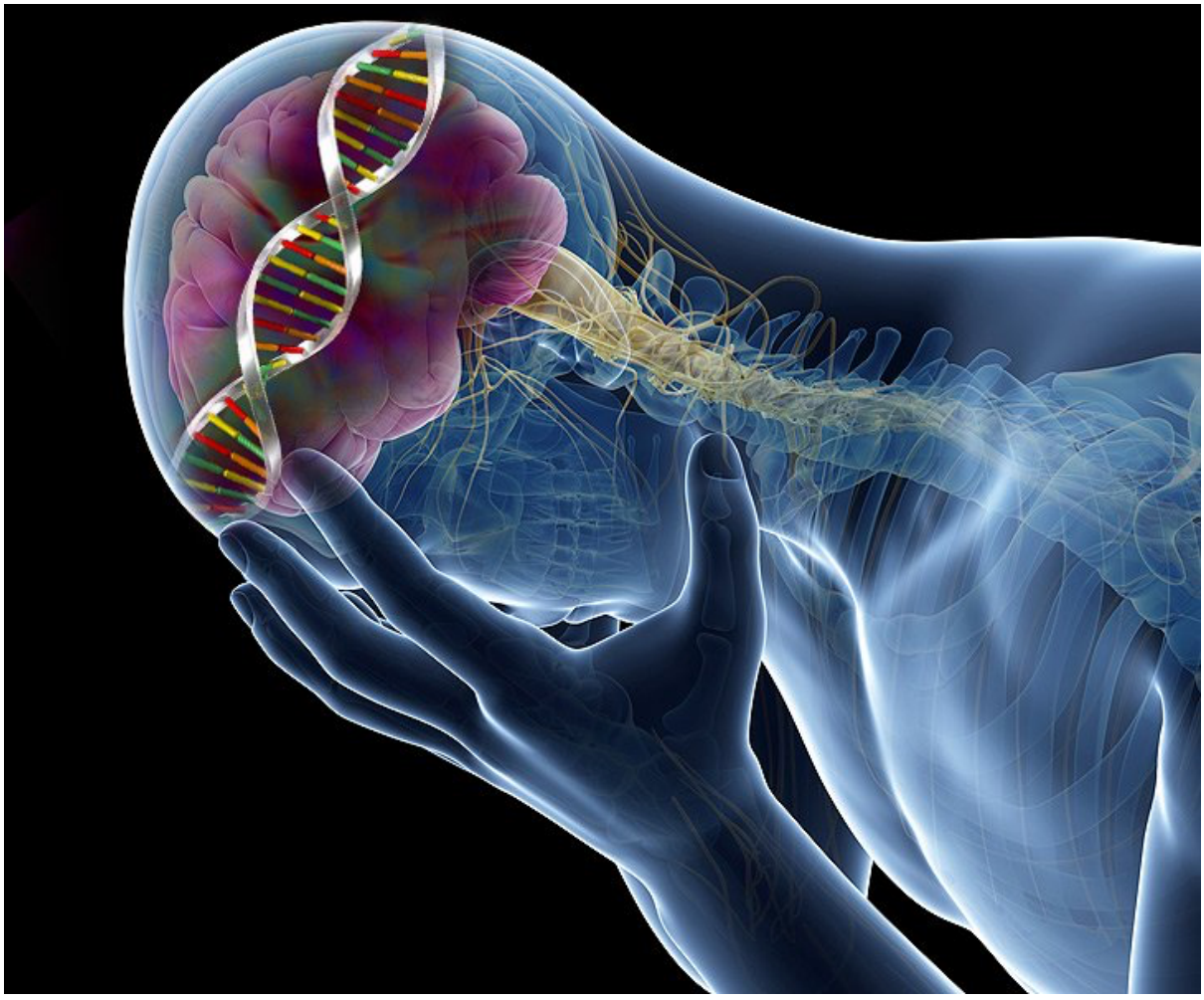

Phylogenetic origins of depression

Bachelor Thesis

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Abstract

In this bachelor thesis I examine the phylogenetic origins of unipolar depression. Depression has many economic, social and personal cost, but current treatment does not work for many people and relapse rates are high. It has been suggested that understanding the etiology and why humans are vulnerable to psychopathology in the first place can be beneficial in terms of improving treatment practices. Some evolutionary psychologist has argued that clinical depression is a discrete adaption while others argue that it is a malfunction of the adaptative capacity for low mood. I account for the arguments of each field and subsequently for behavioral genetic findings on depression and three models of genetic variation from evolutionary genetics which explain why natural selection has not eliminated susceptibility alleles for psychopathology. Next I discuss how behavioral genetics and evolutionary psychology can be used eclectically to identify ultimate causes of depression based on an analysis of the fields' similarities and differences. I argue that no incommensurable differences in meta-theory or philosophy of science exist, which would complicate the eclecticism. Moreover, if a phylogenetic explanation of individual commonalities and differences in vulnerability to depression is to be done, both fields are needed. I conclude that clinical depression is likely not an adaption in itself, but rather a result of polygenic mutation-selection balance leading to a continuum of affect reactivity interacting with adaptive time-lags and other genotype-environment interactions, to produce dysregulations in the adaptive capacity for low mood.

Introduction

The world health organization (WHO) estimates that by 2020 depression will be the second-ranking disease in terms of disability-adjusted life years (Kessler & Bromet, 2013). Because of this impact on society in terms of the economic, personal, and social cost of this disease (Kessler & Bromet, 2013), it seems relevant to continue scientific investigations into its etiology, because understanding can arguably improve treatment methods (Allen & Badcock, 2006). Furthermore, current treatment methods work for only about two-thirds of patients (Carr, 2016). Due to the above findings, I found it relevant to investigate how evolutionary psychology (EP), combined with genetic theories, can be used eclectically when it comes to an understanding of the etiology of unipolar depression. Understanding why some humans are vulnerable to developing depression can arguably help treatment practices (Nesse, 2015).

In this paper, depression is an example of psychopathology for two reasons: 1) On the global level, it accounts for the greatest number of years lost to disability of any mental disorder. 2) I found it pragmatic to discuss the etiology of only one type of psychopathology because of space constraints.

Thesis structure

This paper will begin with an account of some current theories about the evolutionary and genetic origins of depression. The reason for doing this is to present a theoretical basis to be used for analysis and subsequent discussion. Afterward, I will analyze how the differences and similarities between the behavioral genetic and evolutionary psychological approaches influence the prospect of using the fields eclectically. This will be done by an analysis of both the theoretical basis of the approaches and the philosophy of science behind them. This analysis is done to reflect on possible implications for using the fields to discuss the etiology of depression.

Definition of concepts

I will begin this paper by defining some relevant concepts used throughout the thesis. I will be explaining essential concepts from both EP and BG, starting with the fields themselves.

Evolutionary psychology (EP): The study of psychology from an evolutionary perspective. EP proposes that human behavior, cognition, and emotion, can be explained by internal psychological mechanisms developed through natural and sexual selection (Siegert & Ward, 2002).

Adaptationism and the adaptationist program: The Darwinian view that physical and psychological traits are evolved adaptions to natural selection rather than other evolutionary processes. The adaptationist program attempts to identify these adaptions and identify their etiology (Krasnow & Truxaw, 2017).

Behavioral genetics: The study of how genetics and environmental influences lead to individual differences in behavior. The field is made up of molecular genetics, which studies the effects of specific genes at a DNA-level, and quantitative genetics, which investigates how phenotypic variances and covariances can be separated into genetic and environmental components (Knopik et al. 2017, p. 391).

Heritability: The amount of phenotypic variation in traits that are due to genetic variation in a population. The mathematical formula for heritability is where is the total phenotypic variation and is the variation due to additive genetic effects. Additive means when the combined effects of genes are equal to the sum of the individual impacts with no interactive (epistatic) effects) (Keller & Miller, 2006; Knopik et al. 2017).

Environment of evolutionary adaptedness (EEA): A statistical composite of the selection pressures that occurred during the evolutionary period responsible for the adaptions production (Tooby & Cosmides in Buss, 2016, p. 37).

Unipolar depression: A mental disorder characterized by disturbances in affect, cognition, physiology, and behavior. Depression affects more than 350 million people worldwide with associated annual costs of €92 billion and is estimated to become the leading cause of disease burden in the world by 2030 (Giosan et al. 2014; Kessler & Bromet, 2013).

The following symptoms constitute depression:

- Persistent sad, anxious, or "empty" mood
- Feelings of hopelessness, or pessimism

- Irritability
- Feelings of guilt, worthlessness, or helplessness
- Loss of interest or pleasure in hobbies and activities
- Decreased energy or fatigue
- Moving or talking more slowly
- Feeling restless or having trouble sitting still.
- Difficulty concentrating, remembering, or making decisions
- Difficulty sleeping, early-morning awakening, or oversleeping
- Appetite and/or weight changes
- Thoughts of death or suicide, or suicide attempts
- Aches or pains, headaches, cramps, or digestive problems without a clear physical cause and/or that do not ease even with treatment (Caulfield, 2019)

Literature search

In this section, I will account for the method of literature search I have employed for the research behind this thesis.

Because I was interested in papers that might be classified as biological papers due to my research question involving psychology, biology, and genetics, I chose the inter-disciplinary database SCOPUS for my literature search.

I did four searches, first with the keywords "Evolutionary psychology AND behavioral genetics" because I was interested in any papers using the two fields eclectically. I subsequently searched for ""Evolutionary psychology" OR "behavioral genetics" AND depression" because I was interested in papers involving evolutionary theories of depression or behavioral genetic papers on depression to gain an understanding of the current knowledge of depression in both fields. Finally, I searched for "evolutionary AND psychopathology" because I reasoned that this sub-field of EP might provide evolutionary theories of psychopathology which had not been used explicitly for explaining the etiology of depression. All SCOPUS searches were done on February 14th, 2020.

Furthermore, I employed additional Google searches when I needed papers to broaden my knowledge of any of the topics I have written on. I also used a chain search method if any of the papers from my literature search mentioned any articles, I found relevant.

Etiological theories of depression

In this part of the paper, I will account for a selection of etiological theories of depression from EP and BG, beginning with a brief account of the field of evolutionary psychopathology. I will account for adaptationist theories of normal variations in low mood and an adaptationist theory of clinical depression. Subsequently, I will account for findings from BG about depression and move on to a theory of individual differences concerning psychopathology based on evolutionary theory and genetics.

Evolutionary Psychopathology

A sub-discipline of EP is evolutionary psychopathology or evolutionary clinical psychology. This field concerns itself with explaining the ultimate causes of psychopathology; that is why humans are vulnerable to developing mental illnesses as supposed to how it happens (Siegert & Ward, 2002).

A central question for evolutionary psychopathology is why natural selection has not removed psychopathology from the human species since it at face value seems to reduce fitness, both classic and inclusive (Keller & Miller, 2006). Several theories have been proposed to explain the continued and cross-cultural presence of psychopathology. I will account for evolutionary theories of depression below.

Evolutionary theories of depression

An adaptationist framework for depression has been suggested by multiple authors. There seems to be a consensus about the idea that the normal human non-clinical depression response is an adaption to cope with and adjust to various sources of loss, but a debate about whether clinical depression could also be an adaptation (Allen & Badcock, 2006). I will account for theories of low mood, and an adaptationist theory of clinical depression below.

Low mood as an adaptation

In the following, I will account for the hypothesis of low mood as an adaptation, or a set of adaptations and Keller & Nesse's (2004/2006) situation-symptom contingency hypothesis. In this paper, low mood will refer to any non-disordered kind of depression. These theories propose that even long periods of low mood with symptoms consistent with those of depression can be adaptive as long as they are warranted by the situation individuals find themselves in (Keller & Nesse, 2004/2006; Stevens & Price, 2016).

Steven & Price (2016) propose that low mood relates to the punishment and reward system of humans, and functions to adjust to altered circumstances. The symptoms of low mood serve to discourage behavior that might decrease reproductive success in the individual's circumstances.

The universality of low mood across cultures suggests adaptation (Steven & Price, 2016). As Nesse & Williams (1995) writes: "*If there is little chance of a pay-off, it is best to sit tight rather than waste energy*" (in Steven & Price, p. 65). From an evolutionary psychopathology perspective, low mood is an adaption that is activated by cues signaling fitness losses, with the severity proportional to the loss (Keller & Nesse, 2004). Allen & Badcock (2006) classifies these theories into those theorizing that low mood is an adaptation designed to conserve resources and energy after defeat, those proposing it is an adaptation to loss concerning social competition and those hypothesizing it is a response to loss of and/or lack of attachment figures. According to these authors, the theories are not mutually exclusive.

From this approach, the context of low mood is what is essential as opposed to relying on arbitrary cut-offs between low mood and clinical depression (Keller & Nesse, 2004; Stevens & Price, 2016). Furthermore, it has been proposed that different adverse situation leads to various symptoms of low mood, selected for to solve the challenges specific to each case. This is called the situation-symptom congruence hypothesis. According to this hypothesis, each symptom of low mood serves a function (Keller & Nesse, 2006, p. 316).

The social navigation hypothesis

In the following section, I will account for Watson & Andrews' (2002) social navigation hypothesis (SNH), which is an adaptationist theory of clinical depression claiming that

clinical depression is a discrete adaptation. Because there are too many evolutionary theories of clinical depression to account for here, I will focus on an etiological theory of depression that focuses on its relation to social relations. I chose the social navigation hypothesis because this theory articulates the adaptationist perspective of clinical depression most clearly and has also been reviewed specifically by individual difference theorists (e.g. Nettle, 2004; Allen & Badcock, 2004; Keller & Miller, 2006).

The SNH posits that the onset of clinical depression is related to significant social problems. According to Watson & Andrews (2002), clinical depression is adaptive for two reasons: social rumination and a social motivation function. Social rumination is thought to improve an individual's ability to focus on by creating cognitive changes that enhance focus on and ability to solve crucial social problems. It is hypothesized that decreasing hedonic interest and increasing focus on social information, consistent with the symptomology of depression, is adaptive for solving social problems. This proposition is supported by evidence of the superior performance of depressives for solving certain social problems and assessing personal control over outcomes than non-depressives (Watson & Andrews, 2002). Secondly, the social motivation function is proposed to enhance reluctant social partners with a fitness interest in the depressive to provide fitness-enhancing investments through honest signaling of the high cost of depressive symptoms or passive fitness extortion (Watson & Andrews, 2002). Passive fitness extortion works because caring for the depressed individual is less costly than suffering the continued cost of the depression (Allen & Badcock, 2006).

The adaptationist theories of low mood and the SNH attempt to explain what is theorized to be common to all individuals. However, these theories cannot explain why natural selection has not eliminated individual differences in vulnerability to clinical depression (Keller & Miller, 2006). This is what the "individual difference theories" I will account for below attempt to do.

Depression, individual differences and BG

In the following, I will account for relevant behavioral genetic findings on depression and some complementary theories from evolutionary genetics on how genetic variation is maintained in the gene-pool of a species.

Current findings from BG indicate that the heritability of unipolar depression lies around .37 (Knopik et al. 2017). Evidence suggests that more severe depression could be more heritable, with one twin study showing a heritability of liability of 70 percent (Knopik et al. 2017). Furthermore, evidence indicates that the most significant risk factor for developing the first episode of depression is having a first-degree relative with an affective disorder (Nettle, 2004).

Also, severity and recurrence show familiality for major depressive disorder (Knopik et al. 2017, p. 224).

In terms of environmental influence on the vulnerability to depression, it has been found that the shared environment explains roughly zero percent of the variance with the non-shared environment, measurement error included, explaining the rest (Knopik et al. 2017). Finding significant non-shared factors for basically any trait has proven very difficult. As such, none has been significantly associated with developing depression, very possibly because these are stochastic and idiosyncratic (Plomin et al. 2016, p. 13).

Finding specific genes associated with depression has been challenging, and only a handful with small effect sizes has been found (Knopik et al. 2017). The reason for these results is most likely that complex traits are highly polygenic, which means that many genes of small effect contribute, very likely thousands (Plomin et al. 2016). Because the current genetic technology used to map and identify genes have limited power to detect the small effects of single genes even with sample sizes in the hundredths of thousands, only the most common genes with the most significant effects has been identified (Plomin, et al. 2016). While this is problematic for identifying the etiology of the individual differences in vulnerability to depression, models of genetic variability from evolutionary genetics can help with this (Keller & Miller, 2006). I will account for those relevant to low mood and depression below.

Genetic models of variation

To lay the foundation for my later discussion of the evolutionary and genetic etiology of depression, I will account for three popular models from evolutionary genetics that attempt to explain why natural selection hasn't eliminated susceptibility alleles for common heritable mental disorders. These theories are ancestral neutrality, balancing selection, and polygenic mutation-selection balance (Keller & Miller, 2006).

Ancestral neutrality

The theory of ancestral neutrality proposes that the fitness effects of susceptibility alleles for psychopathology were equal to the non-susceptibility alleles in ancestral environments, which has enabled them to persist. According to this theory, the susceptibility alleles have only become harmful recently (Keller & Miller, 2006)

Balancing selection

The second theory is balancing selection. The fact that mental disorders seem to lead to below-average fitness doesn't necessarily mean that they wouldn't lead to above-average fitness-effects under other conditions (Keller & Miller, 2006). Balancing selection leads to the maintenance of two or more alternative alleles because their net fitness effects balance each other out. That is because they can have positive results under one condition and harmful in other circumstances (Keller & Miller, 2006). Balancing selection can happen in various ways, with those being relevant to depression being temporal or spatial variability in fitness landscapes or antagonistic pleiotropy (Keller & Miller, 2006).

Temporal and spatial variability means that the fitness effects of alleles have oscillated over evolutionary time and space. For this to happen concerning susceptibility alleles for mental disorders, these alleles would have had to be advantageous in about half of every population location or during about half of the evolutionary time (Keller & Miller, 2006).

A second reason for balancing selection is antagonistic pleiotropy. Since complex traits do not rely on mutually exclusive genes, most genes affect more than one trait, which is referred to as pleiotropy (Keller & Miller, 2006). Antagonistic pleiotropy happens when an

allele increases one trait's fitness result but simultaneously reduces the fitness result of another trait (Keller & Miller, 2006).

Polygenic mutation-selection balance

The last of the popular theories is polygenic mutation-selection balance. The proposal of this theory is that because it takes a while for harmful mutations to disappear from the gene-pool, the persistence of heritability of traits related to psychopathology may be due to large numbers of deleterious alleles, very rare at any given locus of the population, but collectively common across loci (Keller & Miller, 2006). This theory explains that mental disorders really are maladaptive and have always been so.

Hence, Keller & Miller (2006) propose that significant variance in psychopathology is due to mutation load. They illustrate this with a watershed analogy in which "down-stream processes", or broadly defined mechanisms integrating many processes rely on "upstream processes", or narrowly defined mechanism. Mutations at certain loci disrupt upstream processes, which leads to "noise" in down-stream processes. If enough noise is present, this may lead to malfunctions such as psychopathology (Keller & Miller, 2006, p. 398).

Since the mutation target size of the brain is large with 55 percent of coding DNA likely expressed in the brain (Sandberg et al. 2002) and double that in non-coding DNA, the 500 to 2000 slightly harmful older mutations in each individual (based on conservative estimates) is likely disrupting brain processes and behavior to some extent (Keller & Miller, 2006; Prokosch et al. 2005; Fay et al. 2001; Sunjaev et al. 2001).

Summary

In the previous sections, I have accounted for adaptationist theories of low mood and the social navigation hypothesis. The former posits that the capacity for symptoms of low mood is an adaptation activated by fitness-relevant defeat or loss. The latter claims that clinical depression is discrete adaption in itself functioning to produce cognitive changes serving social problem solving and/or to motivate, through honest signaling or passive extortion, fitness partners to provide further investment in them. While the adaptationist theories

attempt to explain what is common to all humanity, the individual difference theories posit explanations for why individuals differ in their vulnerability to depression. Findings from behavior genetics show that depression is moderately heritable with a liability of heritability of .37. The shared environment explains no variance in susceptibility to depression, while and non-shared factors have not been consistently replicated. Finally, I have accounted for the argument that mutation load disrupts processes leading to endophenotypes related to psychopathology.

The eclectic use of BG and EP

To identify the possible evolutionary and genetic etiologies of clinical depression, I will argue that it is beneficial to use BG and EP eclectically. The reason for this is that both fields are needed if one is to explain both similarities and differences between individuals in vulnerability to psychopathology (Keller & Miller, 2006).

Although genetic methods are mentioned in EP literature for testing hypotheses (Buss, 2016), the research done based on EP and BG is sparse, especially in the field of evolutionary psychopathology (Siegert & Ward, 2002; Keller & Miller, 2006).

Several authors have called for greater integration of the fields (Buss, 2000/2006; Keller & Miller, 2006; Scarr, 1995), but issues present themselves when trying to use the fields eclectically. This is primarily due to differences in "intellectual geography" (Scarr, 1995), outdated views of the other field from researchers within the respective fields, different goals, terms, assumptions, and methods (Keller & Miller, 2006). With the prospect of eclectic use of these fields to discuss the evolutionary and genetic etiologies of depression in mind, I will analyze the relevant differences and similarities between BG and EP. I do this to review possible implications for using the fields together to discuss the etiology of depression.

Similarities between EP and BG

First of all, both EP and BG are grounded in general evolutionary theory described above. Both fields agree that evolution happens by gradual changes in the genome of species

(Buss, 2016; Knopik et al. 2017). It is, therefore, also agreed that behavioral traits have their basis in biology. Of course, this does not mean that phenotypes are directly equal to genotypes. Behavioral characteristics are affected by environmental factors, be they direct ecological or epigenetic effects, which are accepted as important factors in both fields (Buss, 2016; Knopik et al. 2017). In sum, it can be stated that the first level of analysis in both fields is general evolutionary theory.

Second, both fields can be argued to be based on the same ontology, which is mechanistic materialism. From this ontology, reality precedes the subject, meaning reality is independent of human consciousness, and humans are products of the external. Humans are products of innate, unchangeable properties, and conditions (Sonne-Ragans, 2013, p. 224). For EP, this ontology can be seen in the first two theoretical tenets of the field identified by Tooby & Cosmides (1997): 1) The brain is a computer designed by natural selection to extract information from the environment. 2) Individual human behavior is generated by this evolved computer in response to information it extracts from the environment.

In the above tenets, the brain is seen as something that has been designed by an external process (natural selection). The function of the brain is to extract information from another external thing (the environment). From this, it can be argued that assumptions behind EP are that there is a physical reality independent of the subject. This reality precedes consciousness and human brain are products of it. Brains are seen as computational devices that generate behavior. This fits with the assumption that humans are products of innate, unchangeable properties, and conditions (evolved psychological mechanisms that have their basis in genes and are activated by information extracted from the environment.).

For BG, a reality precedes human consciousness and subjectivity because the theory proposes that genes are the basis of behavior. After all, behavior depends on biology, which depends on genes, which rely on the environment. (Knopik et al. 2017, p. 151). Humans must be products of external if human behavior depends on genes, and genes are products of molecules from the environment. Additionally, if genes are only changed by copying error (Knopik et al. 2017), humans must be products of "innate, (nearly) unchangeable properties and conditions". All the above assumptions fit with those of mechanistic materialism.

The two fields differ from strict mechanistic materialism in their proclamations to avoid arguments of genetic determinism and reductionism. This is done by emphasizing the impossibility of genetic effects without environmental input, how knowledge of evolutionary mechanism creates opportunities to change behavior (Buss, 2016, p. 16-17) or by merely stating that different levels of analysis provide answers to different questions. Accordingly, the issue of the reducibility of behavior to biology is an different one, which is why there is an emphasis on considering any relationships correlational until proven causal (Knopik et al. 2017, p. 151).

Fourth, the two fields arguably have roots in a mechanistic view of the subject, where the subject is a conscious, sensing machine. From this view, the subject is reduced to the product of physical and chemical laws (Sonne-Ragans, 2013). However, the nature of consciousness is scientifically unclear as it is in any other field. Still, the working assumptions in the fields is arguably that consciousness is either an adaption "*arisen in concurrently in neural evolution as ways to elaborate and extend the potential reach of instinctual urges to generate adaptive responses to the environment*" (Panksepp, 2006, p. 782) or as an epiphenomenon of complex cognitive adaptions (Robinson et al. 2015).

Fifth, both fields can be argued to have the same view of knowledge, which is an "objectivism". Here knowledge can cast light on causalities and relations in this independent nature, the subject and the object is meant to be separated from each other, knowledge can come from inductive and hypothetically deductive methods, falsification is a scientific ideal, the methods are primarily quantitative and strict methodological demands are followed (Sonne-Ragans, 2013, p 189-190). This can again be seen in the basic tenets of EP and BG's methods, which is highly statistical and attempts to separate nature from nurture to explain the biology underlying complex behavior.

Sixth, in terms of epistemology, the two fields share similarities. However, as pointed out by Sonne-Ragans (2013), in modern science, it is hard to find pure versions of epistemologies because they are often "mixed and matched". Therefore, I will simply point out similarities in traits from each epistemology.

The fields are grounded in empiricism in the sense that they rely on empirical data to test theoretical predictions, and that collected empirical data is what falsifies or supports

hypotheses. Knowledge can hence be a posteriori. Moreover, inductive methods are used in both fields (Buss, 2016; Knopik et al. 2017).

Second, the fields are rationalistic in the sense that they are also based on hypothetico-deductive methods in addition to their inductive methods. Theoretical deductions based on general evolutionary theory is common to both fields, but especially in EP's reverse-engineering process (Thornhill, 1997).

Finally, an implication of evolutionary theory is arguably empirical support for a transcendental epistemology. Natural selection works by improving survival and reproductive value over time and not necessarily for improving the accurate perception of reality (Pinker, 2002). It could arguably lead to cognitive constructs like those experiential categories proposed by Kant (Kant (1963) In Sonne-Ragans (2013)). Moreover, EP and BG are two of the firmest fields in the rejection of the mind as a blank slate (Pinker, 2002). Thus, like transcendentalism, EP, and BG accept the possibility of both a priori and a posteriori knowledge (Buss, 2016, p. 43).

Despite the fields many similarities, there are essential differences between them, which I will account for in the following section.

Differences between EP and BG

EP and BG differ in their focus on adaptationism. EP mostly has an explicit focus on identifying psychological adaptation that constitutes human nature, which is adaptations that have reached fixation in the human genome. The focus of BG is mainly on how genetic and environmental factors lead to individual differences in behavior. Although, adaptationism is implicit in BG, to the degree it is implied by general evolutionary theory (Knopik et al. 2017, p. 9-11).

The prevalence of the adaptationist program underlies further differences between EP and BG. The theory to data ratio is higher in EP than in BG (Siegert & Ward, 2002). This is arguably a consequence of the necessity of using reverse-engineering methods to identify psychological adaptions since it is not possible to study original ancestral populations directly. Also, there has only been a small amount of research carried out between EP and more empirical fields like BG (Keller & Miller, 2002).

Another difference between the fields is the focus of individual differences versus human nature. Thus, genes for traits that have reached fixation have traditionally not been of much interest to BG (Keller & Miller, 2006; Scarr, 1995). On the other hand, individual differences have been largely ignored in EP due to the focus on evolved psychological mechanisms (Keller & Miller, 2006).

Using EP and BG eclectically

While BG and EP can already be said to be eclectic fields, I will use this section to analyze how the fields themselves can be used together. My aim here is to analyze how the differences and similarities between the fields influence the prospect of using them eclectically.

First of all, because general evolutionary theory is the foundation of both fields and the genetic basis of complex behavioral traits are accepted, it should logically follow that evolved psychological mechanisms has their base in the human genome and should, therefore, be able to be studied with quantitative- and molecular genetic methods. Moreover, evolutionary psychological theories can be used to develop research questions for BG and explain research findings theoretically (Segal & MacDonald, 1998; Zietsch et al. 2015).

Second, since evolutionary theory posits that evolution occurs because of heritability, variation, and differential reproductive success, the meta-theory should allow EP to deal with interpersonal trait variation. BG methods such as twin- and adoption studies can be used for this purpose, without any meta-theoretical or philosophical complications. Also, EP theories and hypotheses can be used as bases for behavior genetic research (Buss, 2016). As Scarr (1995) argues, because of intellectual differences, the two fields rarely come together. Still, there is no barrier between using either field to study the general and variation, since the two fields are linked at all levels of analysis (p. 69).

Summary

I conclude that there is no vital theoretical or philosophical basis for not being able to combine EP and BG. As argued by Keller & Miller (2006), non-adaptationist theories can be

just as evolutionary as adaptationist ones. Next, I will evaluate the etiological theories of depression I have accounted for with an eclectic use of behavior genetics and EP.

Evaluation of etiological theories of depression

In this section, I will attempt to evaluate the etiological theories of depression by using EP and BG approaches. This is done to identify the etiology of depression from an evolutionary and genetic perspective.

I will begin by evaluating the theory that clinical levels of depression have an adaptive function.

As previously noted, there are two views in terms of the adaptiveness of depression, the first being that clinical levels of depression are a malfunction of the adaptive nature of low mood. The second that clinical levels in themselves are an adaption (Watson & Andrews, 2002). The question here becomes whether or not depression, or to what degree depression can be classified as a disorder.

To evaluate the question of an adaption, I to clarify what a disorder is (Wakefield, 1992). To this end, I will use Wakefield's (1992) definition of disorder as "harmful dysfunction". This definition incorporates both dysfunctions of systems evolved through natural selection but also what is culturally and socially maladaptive (harmful), though not necessarily a disorder in the evolutionary sense (Wakefield, 1992).

I will discuss the relevance of this definition to depression below.

Adaptive versus clinical depression

If we accept the definition of disorders having to include dysfunction criteria as Wakefield (1992) argues, it is still possible to say that there are both adaptive types of depression and depression in which the mechanism of adaptive low mood is dysregulated. Wakefield & Horwitz (2013) propose that if an individual is living under miserable circumstances, it is not necessarily dysfunctional to show signs of major depression. They write, "*In clinical depression, you have something continuous with the normal emotional range, but that nonetheless becomes categorically different* (…)" (p. 565). That is, depression becomes

something different when it becomes extremely severe, or the depressive response is harmful and dysfunctional concerning the triggering situation.

The authors' perspective seems to imply that the depressive response can be disordered at any degree of depression. Although, point exists where there is no situation in the world which could warrant an adaptive response so severe that one becomes "*paralyzed, non-functional and utterly useless to oneself and everyone around*" (Wakefield & Horwitz, 2013, p. 565). Hence, depressogenic mechanisms can dysfunction and be considered harmful by the individual, or others, in terms of current social values. For the depression to be a disordered one, it will have to satisfy both criteria (Wakefield & Horwitz, 2013; Wakefield, 1992).

With this distinction made, I will proceed to evaluate claims of adaptationism concerning low mood and clinical depression, starting with the strengths and weaknesses of the theories.

Depression as adaptation

Strengths of adaptationism concerning depression

Here I will account for the strengths of adaptationist theories of depression concerning understanding its etiology.

The SNH has good explanatory value for the symptoms of depression. It explains both physical and psychological symptoms based on the social rumination and motivation function. The authors suggest that the anhedonia, pessimism, orientation towards negative social cues, hopelessness, cognitive deficits, self-reproach, and rumination all serve to discover solutions to social difficulties with high fitness costs, especially in times of desperation (Watson & Andrews, 2002). Symptoms signaling the high fitness costs of depression such as sadness, suicidal ideation and/or attempts, lack of energy, and the symptoms of the social rumination function, could also work as a passive fitness extortion tactic to motivate reluctant social partners to invest in the individual (Watson & Andrews, 2002).

Furthermore, the SNH explains the continuity of low mood and depression, but again as a function of the environment (Watson & Andrews, 2002).

The heterogenicity of depressive disorders can also be explained by the SNH since the theory predict that individual depressions should be "tailored" to the specific environmental challenges of the affected individual (Watson & Andrews, 2002). For low mood and adaptive depression, heterogenicity is explained by the situation-symptom contingency hypothesis (Keller & Nesse, 2004).

Weaknesses of adaptationism concerning depression

A major weakness of all adaptationist theories of clinical depression is that they cannot explain individual differences since their implication is directional selection unless they explicitly credit the functions to balancing selection (Keller & Miller, 2006).
Directional selection cannot maintain the polygenic polymorphisms, which would cause the individual differences under balancing selection or ancestral neutrality (Keller & Miller, 2006). Thus, the SNH does not explain why susceptibility alleles for depression have not fixated or gone extinct but implies instead that the genes underlying depression has fixated. Hence, it is only a matter of environmental differences that some individuals become clinically depressed, while others do not. So the theory does not account for biological vulnerability for depressive disorders.
Finally, adaptationisms' vulnerability to "just-so" stories (Gould & Lewontin, 1979) is relevant. This weakness is the ease with which one can pose adaptationist explanations for current functions based on EEA's (Siegert & Ward, 2002). Thus, the minimal direct empirical evidence of the SNH and situation-symptom contingency hypothesis is problematic.
Finally, there are weaknesses of reductionism, whether ontological or methodological. Concerning etiology, a relevant criticism is that some causal mechanisms or variables may be emergent, which is more than the sum of the parts. Hence these may only come into existence at a certain level of complexity and not be candidates for reductionistic analyses (Siegert & Ward, 2002).
With these general strengths and weaknesses in mind, I will continue this paper by discussing whether clinical depression is an adaptation.

Is clinical depression an adaptation?

To evaluate the "depression as adaption" theory, I will discuss what the human genome would look like if depression is an adaptation. To this end, I will make use of the three evolutionary theories of how genetic variation can be maintained by natural selection. Keller & Miller (2006) explain that balancing selection has been a favored explanation of mental disorders because it is an evolutionary genetic theory that keeps natural selection as a cause for genetic variation. However, balancing selection would predict that susceptibility alleles for psychopathology should provide benefits that outweigh the costs of disorders (Keller & Miller, 2006). They argue that this is unlikely since, according to them, no such benefits have been identified. Considering the high fitness cost of depression, these benefits should arguably be easily identified, especially if maintained by antagonistic pleiotropy. These benefits would likely be found in the affected individual or the individual's environment if maintained by temporospatial variation.

Furthermore, Nettle (2004) argues that it is doubtful that clinical depression is adaptive for several reasons. Adaptions, in general, tend to show four characteristics 1) they show a lack of heritable variation. 2) they generally show evidence of good design. 3) they are evoked by appropriate triggers, and 4) fitness level is reduced in its absence (Nettle, 2004). According to Nettle (2004), depressive disorders show none of these hallmarks because they show evidence of heritability, recurrence without reliable triggers, inefficient symptoms of depression for achieving posited functions of the proposed adaptation, and finally lack of evidence for reduced fitness in its absence.

Findings from BG clearly show heritability greater than zero for depressive disorders (Nettle, 2004). Fisher's fundamental theorem states that traits under the strongest selection should show the lowest heritability. Several studies have found that the total additive genetic variability of highly polygenic traits under strong selection is higher than for traits under weaker selection (Keller & Miller, 2006). Thus, the heritability of the clinical depression's polygenic traits might not show that clinical depression is not an adaptation.

Concerning good design, the symptoms of depression should be efficient at achieving the proposed functions (Nettle, 2004). According to Nettle (2004), the social rumination function and the social motivation of the SNH are not backed up empirically. He argues that

there are as many studies suggesting superior performance of depressives for problem-solving, social and non-social, as there is showing the opposite. Furthermore, many cognitive deficits have been associated with depression in processing speed, memory, learning, and attentional shifting. It is not clear that these serve the social rumination function posited by the SNH (Nettle, 2004).

The social motivation function can be challenged by findings that depressive symptoms lead to rejection and hostility from others, tend to lead to less social support and are predictors of marital failure (Nettle, 2004). The SNH predicts that the majority of depressives should be better at eliciting social support, and according to Nettle (2004), there is no supportive evidence for that.

Depression is also supposed to be evoked by appropriate triggers. While some studies have demonstrated a relationship between social stress and depression, the direction of causality is unclear (Kessler, 1997; Weissman & Steiner, 1986; Weissman, 1986 in Nettle, 2004). The relation between adverse life events and depression has also been called into questions by several studies showing that depressive relapses can become only weakly or even totally unrelated to life events. And can thus be entirely unrelated to appropriate triggers (Bondolfi, 2002; Mitchell et al. 2003; Paykel, 2002; Post, 1992 in Nettle, 2004). Also, the chronicity and recurrence of depressive disorders call into question the appropriate trigger criterion, since depressive symptoms should stop when the triggers are no longer present (Nettle, 2004).

Finally, people who cannot become depressed should exhibit reduced fitness compared to the general population (Nettle, 2004). It seems that the capacity for becoming clinically depressed is absent in most people. Compared to the general population, those with depressive disorders have impaired psychosocial function, worse physical health, and higher mortality rates (Allen & Badcock, 2006). Thus, it is hard to identify what fitness-relevant traits this group with the lack of clinical depression capacity should be missing (Allen & Badcock, 2006; Nettle, 2004).

Even though clinical depression arguably does not meet the criteria for a discrete adaptation, the social rumination and social motivation function may reflect dysregulated mechanisms of low mood. I will be discussing the adaptationist position of low mood in the next section.

Adaptations of low mood

Wakefield's (1992) definition of mental disorders as harmful dysfunctions will, be used as the definition for when the low mood becomes a depressive disorder. But to identify dysfunction, it is necessary to identify the natural function which is malfunctioning (Wakefield, 1992). As argued by Keller & Nesse (2004), low mood is an adaption that evolved to adapt to various fitness losses, with the various symptoms differing based on the respective fitness loss.

Although I have argued that clinical depression does not seem to be an adaption, it could be that clinical depression is a dysfunction of the adaptive capacity for situation-symptom congruent low mood. Low mood capacity is ubiquitous and, hence, a more likely candidate for an adaption (Keller & Nesse, 2004/2006; Nettle, 2004; Allen & Badcock, 2006; Badcock et al. 2017).

While there is heritable variation for a trait like neuroticism, which might reflect affective reactivity, no individual's incapable of experiencing low mood, which could suggest a polygenetic adaption under stabilizing selection (Nettle, 2004). Concerning the criterion of good design, it is plausible that symptoms which are triggered reliably, have a relatively short half-life, and vanish when the trigger does function effectively to increase fitness. An example from the authors is crying as a mechanism to illicit social support and working as an honest signal of emotion (Keller & Nesse, 2006).

Low mood also shows evidence of being triggered appropriately from two studies of the situation-symptom contingency hypothesis (Keller & Nesse, 2004/2006). Furthermore, they appear consistently in response to negative situations and are seem regulated.

Lastly, groups whose capacity for low mood is deficient could be socially ostracized because they fail to learn appropriately from experience or fail to appropriately yield to dominance and status hierarchies (Stevens & Price, 2016).

Summary

I have argued that clinical levels of depression are most likely not an adaptation in itself. Though based on conventional EP procedures for identifying adaptations and arguments from several papers, the capacity for low mood arguably is. First of all, this conclusion is

based on the lack of evidence of fitness-enhancing traits associated with depression. Second, I find Nettle's (2004) argument against depression showing any of the adaptation hallmarks compelling, mainly because these criteria for identifying adaptations are generally agreed upon in EP (Buss, 2016).

Depression and individual differences

From the argument that symptoms of low mood are adaptations, which explains interpersonal commonalities, I will evaluate the strengths and weaknesses of individual difference theories concerning vulnerability to clinical depression.

Strengths of individual difference theories

A strength of the individual difference theories is that they can explain the genetics and biology of differences in vulnerability to depression by separating environmental effects from genetics, or by making predictions from genetic models. Theoretically, normal variations in low mood can also be explained by the mutation selection model.
Second, the effects of trauma, paternal age, and inbreeding on mental disorders support a mutation-selection balance model because these all affect risk for psychiatric disorders by increasing disruptions and/or mutation load and also the risk for various mental disorders. These findings support that additive effects of minor disruptions would do the same (Keller & Miller, 2006).
Third, based on behavioral genetic findings predictions about the ancestral human ecology can be made, which can help falsify of adaptationist theories.

Weaknesses of individual difference theories

A weakness of the theories is that they cannot explain commonalities as they focus on genetic variation. At another level of analysis, the mutation-induced depressogenic phenotypes responsible for individual variation in vulnerability to depression likely say nothing about possible evolutionary affective endophenotypes common to all humans, and possibly other animals (Panksepp, 2006).

Concerning the prediction that mutation load will correlate with psychopathology, the pathways between mutation and depressogenic endophenotypes are not made explicit, which is a weakness. While it is arguable that mutations at loci responsible for, say, serotonin transporters could lead to depression symptoms, much more research is needed to falsify the prediction. Thus, the specific symptoms of depression are not explained. Finally, the polygenic mutation-selection balance model can only explain the cross-cultural and historical variations in depression insofar as differences in susceptibility alleles cause it. Because this is a biological model, it is necessary to supplement with other theories to explain the variance caused by gene-environment interactions.

Neither does individual difference theories explain the chronicity and recurrence of depressive disorders directly. The theories will need to integrate with others to explain how mutation load or a high affective reactivity cause this.

In the next section, I will discuss how the individual difference and adaptative low mood theories can be supplemented by the dysregulation theories of clinical depression and evolutionary mismatch theory. The dysregulation and mismatch theories explain how proximate causes can interact with ultimate causes and lead to clinical depression.

Dysregulation, mismatches, and depression

Mismatch and depression

Evolutionary psychiatrists have proposed that mismatches between modern and ancestral environments can lead to psychopathology (Steven & Price, 2016; Li et al. 2017; Keller & Miller, 2006). Homo sapiens have spent 99 percent of their evolutionary history as hunter-gatherers. Most evolved psychological mechanisms that can be said to characterize human nature evolved under selection pressures that might be vastly different from the ones characterizing the modern environment we live in now (Buss, 2016). As Tooby & Cosmides (1997) put it, "our modern skulls house a stone-age mind." This discrepancy between the EEA and the modern environment is the basis of the evolutionary mismatch phenomenon. This term refers to the adaptive lag, which can occur if the EEA of an adaptive mechanism changes faster than the mechanism can adapt to the change (Li et al. 2018).

To make the argument of a mismatch, one will need to identify the evolved mechanism, its function, the decision rules involved, and the inputs and outputs involved in the process and products of a mechanism (Li et al. 2018). The mechanism involved in the instance of depression would be the adaptive capacities for low mood. I will use the symptom of self-reproach to exemplify. The function of this mechanism is arguably to avoid actions that could lead to similar future scenarios (Keller & Nesse, 2005) in service of adjusting to a status/dominance hierarchy when faced with defeat or loss of status (Stevens & Price, 2016). The input for this mechanism is likely a perception of a decrease in one's social status. The output of the mechanism would then be a cognitive and/or affective change through self-reproach leading to behavioral changes that ensured adjustment to the status/dominance hierarchy.

Thus, a mismatch scenario for this mechanism would be if the mechanism was inappropriately activated through perceptions of status-loss the mechanism was not designed to handle (e.g., constant access to photoshopped pictures of impossibly attractive individuals causing "Facebook depression" (see Blease (2015))). Similarly, many mismatch scenarios have been proposed to be related to depression such as higher population densities (Li et al. 2018; Stevens & Price, 2016), disruptions of community-based bonds, modern social constellations disrupting various attachment needs (Stevens & Price, 2016) and many more. For reasons of space, I cannot account for all of these but simply conclude that mismatches interacting with psychological mechanisms of low mood with inputs related to defeat or loss, commonly social, arguably explain some variance in vulnerability to clinical depression.

Moreover, support for the mismatches leading to depression comes from evolutionary genetics and psychiatric epidemiology. There is evidence of cultural and historical differences in the prevalence of depressive disorders. It is plausible that some of its variance can be explained by mismatches, which would imply ancestral neutrality and large genotype-environment interactions (Keller & Miller, 2006). If the alleles that cause susceptibility to depression in modern environments were neutral, or near neutral, under ancestral social environments, there should be large genotype-environment interactions between variance in depressive symptoms and the environmental factors responsible for the mismatches (Keller & Miller, 2006).

Finally, the mismatch scenario is compatible with polygenic mutation-selection balance, also explaining variance in depression (Keller & Miller, 2006).

Low mood becomes clinical depression through dysregulations

If depression becomes a disorder when mechanisms of low mood dysfunction, the question becomes how this dysfunction happens. The dysregulation theories of depression can help answer this question.

According to dysregulation theories of depression, clinical levels of depression are not adaptive in themselves. Maladaptive forms happen when mechanisms of low mood become a pervasive, self-maintaining failure of sensory attenuation, thus causing rumination, false inferences, and an inability to test these beliefs by acting on the world (Badcock et al. 2017, p. 191). As for how this happens, several causes of dysregulation have been proposed in the literature.

Chronic and consistent stress and stress sensitivity have been proposed to disrupt affective systems by several evolutionary psychologists (Allen & Badcock, 2006; Badcock et al. 2017; Luyten & Fonagy, 2018). Hence, it seems reasonable to argue that the mutations loads underlying the genetics of individual differences in affect reactivity, might lead individuals at the high end of the normal distribution to become clinical depression more quickly due to higher stress sensitivity and thus a higher probability of ending up with dysregulated affective systems (Keller & Miller, 2006; Nettle, 2004). Also, the detrimental effects of stress on the nervous systems, such as the hippocampal atrophy seen in clinical depressives (Sheline et al. 1996), and hyperactivation of the HPA-axis, might further dysregulate affective neurobiology and make individuals more likely to become clinically depressed (Carr & McNulty, 2016).

Following this logic, even prolonged adaptive depression might increase the probability of dysregulating neuro-affective systems and increase the chances of clinical depression. This process could arguably happen through kindling of the neurobiology underlying affective mechanisms (Nettle, 2004). This also explains why the biggest risk factor for depression is having been depressed before and why clinical depression tends to be chronic and recurrent (Nettle, 2004). Finally, it has been proposed that excessive stress in childhood and

adolescence is especially likely to dysregulate affective mechanisms and underlying neurobiology (Luyten & Fonagy, 2018; Badcock et al. 2017). This is probably caused by brain maturation, increasing sensitivity to social threats (Badcock et al. 2017). Also, from an evolutionary biological perspective, differential susceptibility to environmental effects may have been selected for. Having children with different susceptibility to parental influence would have been beneficial in terms of fitness. The less susceptible children would be less affected by maladaptive parental practices that would have reduced the fitness of more susceptible children. In contrast, the more susceptible children would benefit more from good parental practices that would improve the fitness of these children. Inclusive fitness theory predicts that the children's relatives benefit from this differential susceptibility since they share a certain percentage of their genes (Belsky & Pluess, 2009). Hence, individual differences in plasticity during this sensitive period might explain the increased vulnerability to dysregulation.

I have argued for how mismatches might lead to inappropriate activation of low mood mechanisms, and excessive stress, mutation load, and kindling could lead to clinical depression by dysregulating neuro-affective systems. I will end the paper by discussing the limitations of my arguments and exemplify how the eclectic approach between BG and EG could be carried out in research.

Limitations and research possibilities

Since no empirical studies have researched the conceptualization of depression I have argued for here, I have had to rely on research examining predictions associated with the conceptualization, which is a limitation of my arguments. As mentioned previously, the theory to data ratio in EP is already high, which makes this more problematic.
Moreover, I have not explicitly accounted for the large sex-differences for clinical depression (Kessler & Bromet, 2013), which lowers the explanatory value of my arguments.

Additionally, if research demonstrates bipolar disorder to be a more severe version of clinical depression, my arguments will need to be adjusted to include dysregulations of "good mood mechanisms".

Finally, the lack of non-shared environmental factors identified for vulnerability to depression makes the environmental variance explained by low mood mechanisms vague. I will proceed by illustrating how a study could mitigate the weaknesses of the lack of sex-difference explanations and non-shared environmental factors.

As I have argued, individual difference models can be integrated with adaptationist models, so it follows that this is so for integration with models of sex-differences. As an example, I will use Martel's (2013) argument that high levels of estradiol in females during puberty due to sexual selection effects lead to effects on the serotonin-system, making females more sensitive to interpersonal stressors than males. This argument predicts that significant non-shared environmental factors for vulnerability to depression will be especially impactful for females if they are due to interpersonal stressors. To test this, a longitudinal twin study could be done testing the effects of the number of close friends during puberty for males and females. Controlling for levels of neuroticism and parental neuroticism and baseline depressive symptoms for both twins and their parents would be necessary. The twins would then ideally be followed for the rest of their lives and be tested for depressive symptoms e.g., every year. Based on Wakefield's (1992) arguments, evaluation of dysfunction, and harm of the depressive symptoms should be made to identify plausible underlying dysregulations of neuro-affective systems responsible for low mood. This study could arguably test whether some variance in sex differences in clinical depression is due to differential sensitivity to interpersonal stress. Although this hypothetical study is far from perfectly designed, and I cannot discuss possible psychometric tools to employ, I argue it does illustrate how one could mitigate the limitations of my arguments. For further descriptions on twin-study designs and statistical methods for handling data in behavioral genetics see Knopik et al. (2017)

Conclusion

In this thesis, I have accounted for different evolutionary theories of the etiology of depression, namely adaptationist theories, dysregulation theories, and theories of individual differences. I have argued for the benefit of integrating theories from evolutionary psychopathology with behavioral genetic findings. I have done this due to the theory-data ratio of evolutionary psychopathology and to avoid "just-so stories" of adaptationism. This is both a possibility from a theoretical point of view and concerning the philosophy of science between EP and BG since there are no incommensurable differences between them. Finally, concerning the question of the evolutionary etiology of clinical depression I have argued that depression is likely not an adaption in itself, but rather a result of mutation-selection balance leading to a polygenic continuum of affect reactivity interacting with adaptive time-lags, and other genotype-environment interactions, to produce dysregulations in the adaptive capacity for low mood. The normal distribution of affect reactivity around an adaptive peak, leads to several implications: 1) depression becomes a disorder when it is both harmful and dysfunctional. 2) depression can be a disorder throughout the continuum, and it is thus essential to take the environment of the depressed individual into account before evaluating whether the depression is a clinical one.

A strength of this conceptualization of depression is that it explains that depression is continuous with the adaptive low mood while still maintaining differentiation between clinical and non-clinical depression by proposing a distinction between function and dysfunction arguably caused by dysregulation of neuro-affective systems. Thus, by using this eclectic approach, I have been able to account for both individual commonalities- and differences, explain the etiology of the symptoms of depression, the comorbidity between depression and other internalizing disorders, and the chronicity and recurrence of clinical depression.

Limitations of this conceptualization include the need for more empirical evidence, lack of sex-difference explanations, and finally, vague proposals about the non-shared environmental variance underlying the vulnerability for depression.

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