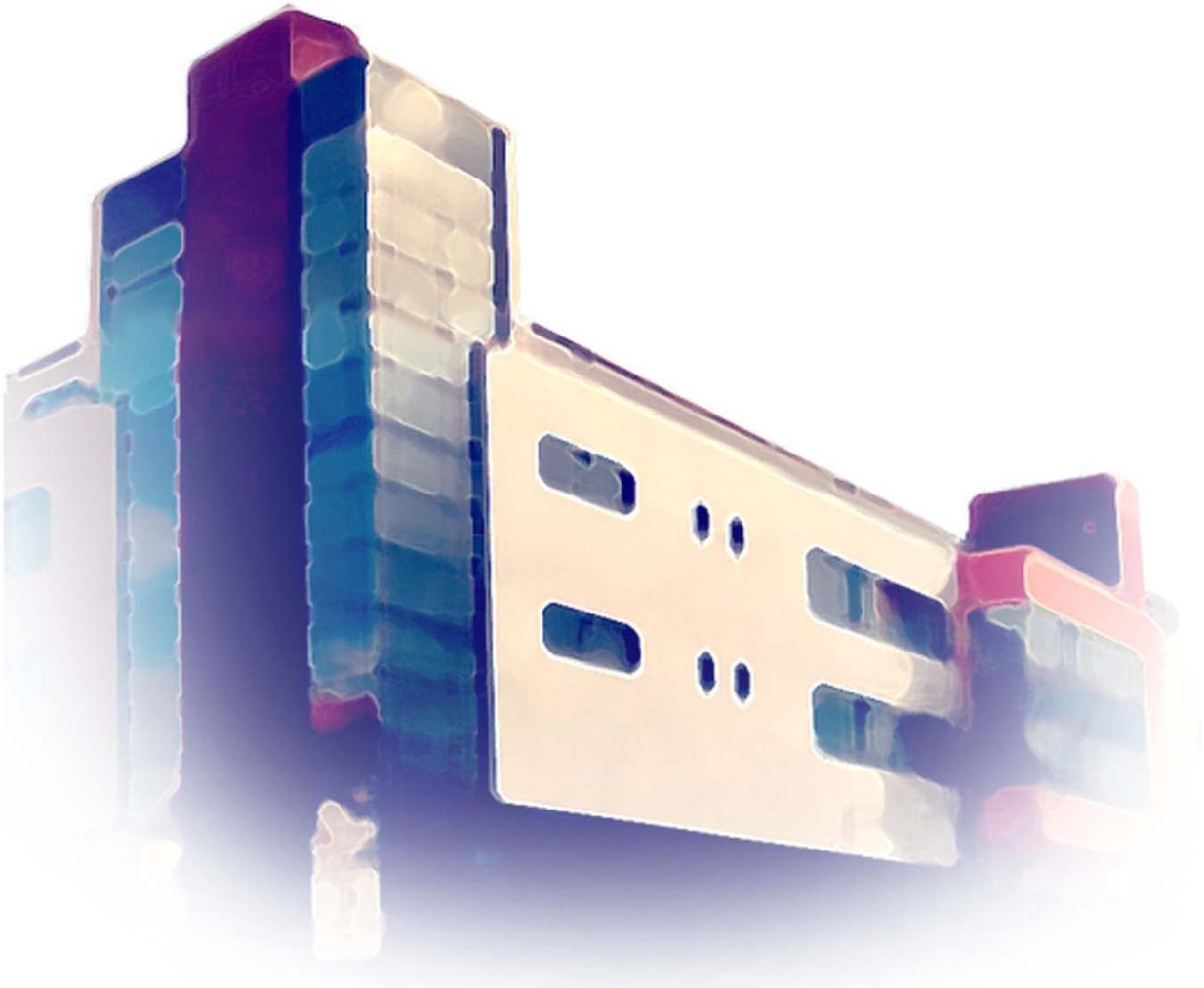
Laura Moisi

The Science of Depression. Sketch of a non-reductive, multi-level approach



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The Science of Depression

Sketch of a non-reductive, multi-level approach

Bachelor Thesis in Cognitive Science

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> *I have studiously tried to avoid ever using the word 'madness' to describe my condition. Now and again, the word slips out, but I hate it. 'Madness' is too glamorous a term to convey what happens to most people who are losing their minds. That word is too exciting, too literary, too interesting in its connotations, to convey the boredom, the slowness, the dreariness, the dampness of depression.*
>
> Elizabeth Wurtzel – Prozac Nation (1994)

1. Introduction

Depression – a condition characterized by a sense of insurmountable hopelessness, loss of significance and interests in life – is the most common mental illness today and its prevalence is steadily increasing. While certain types of stigmatization associated with depressive suffering have declined, other types of overhasty simplification have taken over. One prominent misconception of depression – often made in the attempt to do away with a lingering stigmatization – is to portray it as a mere "disease of the brain, much like asthma is a disease of the lungs."[1] However, in order to realize that depression is a phenomenon too complex and too intricately world-related to be captured by the 'grammar' of the brain alone, one just has to consult the field of neuroscience itself. Today, leading neuroscientists and neuropsychiatrists emphasize the multidimensionality of the illness and the importance of contextual factors in the development of the condition. Another misleading simplification of depression, however, is to try to explain the nature of the illness solely in terms of environmental factors, with complete disregard of biological implications. This is especially counter the fact that antidepressants, which influence certain brain processes, often successfully relieve depressive symptoms. If neuroscientific advancement can determine the specific brain mechanisms involved in depression and accurately explain the actions of antidepressants, it certainly provides a deepened understanding of the illness, which, taken together with environmental aspects, can lead to a more holistic comprehension of depression.

Although many researchers are in principle well aware of the complexity of depression, when it comes to scientific and psychiatric practice, the intricacy of the illness still plays an astonishingly little role. This being said, the motivation underlying this thesis is to reveal the non–reductive and multifactorial nature of depression. The basic aim, in this regard, is to demonstrate the need for an integration of different scientific branches for bringing about a thorough explanation of the illness – in terms of origins, development, experience, diagnosis, and treatment.

1 Quoted from Potash 2007.

On this note, the first part of the paper presents an account of the experience of depression which takes into consideration the many autobiographical narratives on the illness. For this reason, a phenomenological perspective will be incorporated in order to demonstrate in which way depression can be understood as indeed a "different world", as many sufferers relate in staggering terms.[2] For this purpose, particular focus will be laid on the concept of *existential feeling* as proposed by Matthew Ratcliffe[3] and, as will be shown, on related alterations in bodily experience and in the experience of time.

In the second part of the thesis, some of the currently most relevant biological accounts of depression, such as the notorious serotonin imbalance hypothesis, the neuroplasticity perspective, the recently proposed theory about global dysfunctions in neural pathways as well as genetic factors will be carefully considered in terms of their contribution to insights into this illness. As will be elucidated, current neuroscientific accounts have advanced from reductionist views on mental illness and the way the brain functions, which regard human behavior as completely determined by neuronal wirings. Rather, the new conceptions display the brain as an organ with an essentially plastic nature, allowing variable, adaptive and by and large 'free' human behavior. This new commencement in neuroscience, guided by the concept of brain plasticity, will turn out as crucial in providing an understanding of depression that implicates the social dimension of the illness.

In consideration of the sociocultural and economic embeddedness of depression, which will be discussed in the third and last part, I will first address issues on the recent developments in psychiatric diagnosis and classification such as the widespread neglect of a contextual embedding of a person in the diagnosis which results in an insufficient distinction between normal sadness and depression. Afterwards, I will discuss some aspects of an intriguing sociocultural theory of the development of depression recently proposed by Alain Ehrenberg, whose approach underpins the neuroscientific concept of plasticity as the central mechanism guiding brain function. Ehrenberg's theory and the idea of brain plasticity will reveal the way in which depression may be understood as both, a disease of the brain and of our times.

2 Cf. Wolpert 1999, xii.
3 Cf. Ratcliffe 2005, 2008, 2009, 2010.

2. The Experience of Depression

> That's the one thing I want to make clear about depression: It's got nothing at all to do with life. In the course of life, there is sadness and pain and sorrow, all of which, in their right time and season, are normal—unpleasant, but normal. Depression is in an altogether different zone because it involves a complete absence: absence of affect, absence of feeling, absence of response, absence of interest. The pain you feel in the course of a major clinical depression is an attempt on nature's part (…) to fill up the empty space. But for all intents and purposes, the deeply depressed are just the walking, waking dead.[4]

The term depression is habitually employed today, usually denoting a feeling of being "down", of intense sadness or a mood of general reluctance in participating in life. On some occasions, it conveys that someone is having a bad day, on others, it may signal a serious alteration in mood that requires professional help and thus indeed can be called depression. In determining whether the affective changes a person experiences constitute a depressive episode, mental health professionals usually consult one of the two present standard classification system of mental disorders, the Diagnostic and Statistical Manual of Mental Disorders – in its latest edition, the DSM-IV – and the International Classification of Diseases, short, ICD-10. While the DSM is released by the American Psychiatric Association, the ICD-10 is published by the World Health Organization, which revises the handbook about every ten years. Both classification systems categorize depression as an affective disorder, more precisely, a mood disorder. There are numerous different types of depression that the DSM and the ICD-10 have distinguished: Severe depressive episode, dysthymic depressive episode, bipolar disorder, substance-induced mood disorder, seasonal affective disorder and many others. In this paper, however, the term depression will be used rather broadly in order to capture what these specific subcategories have in common. The two classification guidebooks resemble one another, but since the DSM-10 employs a more specific and detailed account of the various mental illnesses it defines, it is also used for research purposes and facilitates interaction between health professionals with different scientific backgrounds.

According to the DSM, which is sometimes referred to as the "bible of psychiatry" due to its undisputed authority in many medical circles, a person experiences a major depressive episode if she feels a "depressed mood or loss of interest or pleasure in nearly all activities for at least two weeks" and at least five of the following symptoms during that time: depressed mood for the most part of the day, diminished interest or pleasure, significant gain or loss of weight, inability to sleep or sleeping too much, reduced control of bodily movements, fatigue, feelings of worthlessness or guilt, inability to think or concentrate, thoughts of death or suicide.[5] For a dysthymic depressive

4 Quote from Elizabeth Wurtzel in Wolpert 1999, 132.
5 Cf. Wolpert 1999, 17.

episode, a milder but longer enduring type of depression, a person must experience a depressed mood in the last two weeks for most part of the day and additionally two of previously listed symptoms.[6] Based on these symptom clusters and the changes in affectivity reported by persons seeking help, psychiatrists determine whether a person endures a depressive episode or not.

However, skimming through some pages of the countless autobiographical accounts offered by authors who have suffered from depression, it becomes evident that the changes in affectivity that make this illness so peculiar are not alterations in specific emotions, but an alteration in their entire world experience – changes in all their dealings with things and people in their surroundings. In this respect, a numeration of the different emotions and thoughts that depressives, compared to healthy persons, have or lack, as presented in the DSM-IV and also in the ICD-10, however helpful it is in terms of a statistical analysis that facilitates diagnosis, is certainly insufficient for a complete understanding of what constitutes the experience of depression. Having said this, a list of symptoms equally fails to convey one substantial aspect of depression at which the author Elizabeth Wurtzel is getting in the above quote when she says that depression "has nothing at all to do with life": that depression itself is an entirely different kind of being in the world, not merely one and the same as in everyday life but with more feelings of fatigue and less interests in activities or pleasure. In this regard, the sadness a depressed person feels, for example, has little to do with the kind of sadness felt in everyday life, in which we still feel intimately connected with others; similarly, the fear or anxiety of a depressed individual is not about some threatening event or situation but rather about one's mere existence itself: "in depression, one day you wake up afraid you are going to live."[7]

Seen in this light, an encompassing account of the experience of depression must incorporate the often reported distinction between feelings experienced in everyday life and depression – a difference that cannot be made intelligible in terms of alterations in certain feelings or perspectives towards the world, since it is not particular emotions that determine the "strangeness" of the experience, but rather a background that shapes the range of emotions and attitudes a person can have towards the world. Thus, incorporating a phenomenological stance in explaining the experience of depression, that is, an analysis that acknowledges changes in the structure of experience, is necessary in order to convey what gives the experience of depression its essential character.

6 Cf. Wolpert 1999, 18.
7 Quote from Wurtzel in Wolpert 1999, 132.

2.1.Existential feelings

The philosopher Matthew Ratcliffe has promoted this kind of background structure of reality as *existential feelings*, i.e. "ways of finding oneself in the world"[8] or the "very sense of being" that attaches to world-experience.[9] Whereas emotions, that is essentially intentional feelings, such as anger, pride, love or hate, are understood as affective states about one's relation to some event, situation, person or object in the world, existential feelings are conceptualized as feelings about one's entire being in the world – in other words, as the "feel of life as such."[10] Accordingly, existential feelings are always presupposed by more specific affective experiences about particular things and to that effect determine the very possibility of there being intentional states such as emotions.[11]

Of course, the boundary between specifically directed emotions and existential feelings may be slippery. The sorrow felt after losing a loved one, for example, may initially be experienced as an intensive feeling about one's relation with that person and eventually turn into an all-encompassing sadness characterized by a sense of estrangement from the entire world. It is difficult to tell at which point the feeling shifts from being about something specific to the way that one's entire existence is enveloped by it. Despite this blurry margin, there is a crucial difference: while the feeling about one's entire being in the world constitutes a background of experience which determines the different way in which things can matter, a specific feeling, such as sorrow, in contrast always presupposes such a background structure of experience, which makes it possible to experience that particular emotion in the first place.[12] For example, in order for somebody to be able to feel sorrow, something has to matter in a certain way.[13]

As becomes apparent from many autobiographical descriptions of depression, what the authors are trying to explain is that central to the experience are alterations of the former kind – in the entire structure of experience – rather than specifically directed feelings. One author, for example, describes his depression in terms of an existential separation from the world: "The world spat me out, I was no longer part of it."[14] Others describe a sense of immutable isolation from other

8 Cf. Ratclfiffe 2009, 236.
9 Cf. Ratclfiffe 2009, 230.
10 Cf. Slaby/Stephan 2008, 509.
11 In this regard, existential feelings might be understood as "pre-intentional" states rather than intentional states per se. See Ratcliffe 2010, 368.
12 Cf. Ratcliffe 2010, 359.
13 Cf. Ratcliffe 2010, 362.
14 Original version: "Die Erde spie mich aus, ich gehörte nicht mehr dazu." Quoted from Kuiper 2007, 68.

things and people in the world by feeling "sheated in india-rubber"[15]. Yet others emphasize having lost a sense of familiarity, of "feeling at home" in the world – "a sense of something gone cockeyed in the domestic universe I'd dwelt in so long, so comfortably."[16]

Given that it is not the particular situations or events that form the core of their affective alterations, it is difficult for depressed persons to express their feelings, because they cannot make them intelligible in terms of specific differences.[17] As can be noticed in the above passages, the descriptions contain strikingly figurative elements. When it comes to explicating the experience, most authors eventually "escape into" metaphorical descriptions, and some even say that the experience is "inexplicable" and "impossible" to describe: "Depression is a disorder of mood, so mysteriously painful and elusive in the way it becomes known to the self (...) as to verge close to being beyond description."[18] One author even claims that "if you can describe your depression you almost certainly have not truly experienced it."[19] In view of depression as essentially involving an alteration in background feelings, it is not surprising that depressives struggle to depict the experience in a precise manner. Not only because of the difficulty to specify the changes in experience in terms of concrete differences, but also because their enormous impact is not familiar from everyday life. This is quite contrary to saying that existential feelings don't play an immensely important role in our everyday engagement with the world. Without them, it is difficult to conceive of anything bearing any significance, because they form a background of experience which determines the ways in which we are able to experience things as mattering in the first place.[20] In normal life, however, we usually encounter a background of experience characterized by a purposive connectedness and practical relatedness to the world, which opens up possibilities of practical engagement and for this reason remains unnoticed, at least for the most part.

Yet given that depressive individuals have lost the practical connectedness with the world and to that effect experience a sudden constraint in terms of possibilities to engage with the world, they perceive this background structure of reality in a painfully salient way. In this respect, depressive patients report feeling a complete absence of affect, of feeling, of interest and of significance, but cannot attribute the vanished meaning to specific things, people or situations in the world. More specifically, however, their felt absence is at bottom not a matter of actual absence of interest and significant relations with people and things, but rather an absence of the mere

15 Cf. Ratcliffe 2009, 229.
16 Styron 2001
17 Cf. Ratcliffe 2009, 239.
18 Quoted from Styron 1990, 7.
19 Quoted from Wolpert 1999, 1.
20 Cf. Ratcliffe 2010.

possibility of conceiving of meaningful connections with the world. In this way, whereas in everyday life existential feelings are taken for granted precisely because they open up a certain space of possibilities for practical engagement with the world, in depression, they enter the foreground of experience because they reveal a *space of impossibilities* to connect with the world.

This fundamental alteration in one's relation to the world accompanied by changes in one's practical possibility space, in turn, is indispensably connected with a change in temporality as experienced by the depressed person. In light of a diminished sense of possibilities, depressives cannot conceive of the possibility of a meaningful change in their situation or their surroundings anymore and as a consequence they are incapable to envision the future (as potentially different from the present state). However, before examining these changes in the experience of time, I will first discuss the alteration in bodily feelings that is inseparably connected with a change in existential feelings.

2.2. Bodily feelings and depression

> What I had begun to discover is that, mysteriously and in ways that are totally remote from normal experience, the gray drizzle of horror induced by depression takes on the quality of physical pain. But it is not an immediately identifiable pain, like that of a broken limb.[21]

Several autobiographical accounts emphasize a "surprisingly physical sensation"[22] of depression and an "almost bodily pain", which is nevertheless distinctly different from actual physical pain. This often reported difficulty to express the experience of depression in terms of a physical feeling that nevertheless differs from a "purely" bodily sensation is directly related to the general view of bodily experiences and world directed experiences as two separate things.[23]

The inability to conceive of the possibility that bodily feelings and world-directed affective states are essentially involved in one and the same experience may be due to the intuition that "something apparently so trivial and self-directed" cannot be "a major constituent of something important and world-directed."[24] In this way, the struggle that depressed persons have with describing the way the body feels and their whole world-experience as two separate things that nevertheless seem inextricable, has its roots in a misconception of bodily feelings.[25] The origin of the misunderstanding is that, usually, bodily feelings are solely associated with bodily sensations

21 Quoted from Styron 1990, 50.
22 Cf. Wolpert 1999, 61.
23 Cf. Ratcliffe 2009, 233f.
24 Quoted from Ratcliffe 2005, 44.
25 Cf. Ratcliffe 2009, 233.

that have only the body as their object of perception, such as a tickling or the pain caused by a broken limb. However, such bodily sensations are by far not the only ways in which the body is involved in experience. For example, when you touch an object with your hand, the primary object of that perception is not your hand but the object that you perceive through your hand.[26] This reasoning also applies to more sophisticated world-experiences, which are "disclosed through diffuse, holistic bodily feelings."[27] In this regard, as many contemporary accounts of affectivity have pointed out, "feeling and conceptual thought cannot be viewed as opposites"[28]. Being genuinely engaged in a situation in contrast to conceiving of the matter in a detached manner always implies a certain bodily involvement, because that is what distinguishes the former from the latter. This shows that only because something is felt *in* the body, this feeling does not have to be *about* the body.[29] After all, "we don't perceive our bodies in complete isolation from how we perceive everything else, and then link the two kinds of perception together by means of some subsequent mental process."[30] Rather, a sense of bodily feelings is already integral to world-experience. In this regard, existential feelings experienced by depressed people are, just like emotions and other intentional states, always also and simultaneously bodily feelings – that is, the affliction of depression is bodily and world-directed at the same time.[31]

This inextricability of bodily feelings and one's fundamental sense of being becomes especially salient in depression, where the world becomes a place that no longer offers the possibilities that it used to offer. Hence, the body is felt in a peculiar way because it is no longer experienced as something *through which* those possibilities can be actualized; the body becomes "object-like", strange, inanimate, conspicuous.[32] The philosopher and psychiatrist Thomas Fuchs describes this change of the body from being a medium for experiencing things outside the body to the object of one's whole experience, as a "corporealization" of the body as opposed to "the lived body".[33] Many authors on depression illustrate feeling their body as heavy and more salient than usual. It seems that in depression, the body's implicit role in everyday life has been traded in against experiencing one's body in a peculiarly conspicuous way. The body has lost its "lightness, fluidity, and mobility of a medium" and has turned into "a heavy, solid body" felt as an obstacle with regard

26 Cf. Ratcliffe 2009, 233.
27 Cf. Slaby 2008, 437.
28 Cf. Slaby/Stephan 2008, 513.
29 Cf. Ratcliffe 2005, 48.
30 Cf. Ratcliffe 2010, 363.
31 Cf. Ratcliffe 2009, 233.
32 Cf. Ratcliffe 2009, 231.
33 Cf. Fuchs 2003, 224.

to connecting with the world."[34]

The role played by the body as a hindrance to accomplish things in the world rather than a medium of one's activities, is reflected, among other things, by the fact that the most trivial things seem impossible to do for many depressive individuals. In normal life, we wake up, get out of bed, walk to the bathroom, step into the shower, proceed with our daily routines and all these bodily movements are accomplished in an effortless manner, because we feel a purposive connection with the world and with our everyday projects. In depression, in contrast, these things take an enormous amount of effort precisely because an essential part of the existential changes in depression, characterized by feelings of alienation, disconnectedness and sense of insignificance, is a feeling of the body as heavy, useless and dysfunctional.

A striking example is given by the author Andrew Solomon, writing in the *New York Times* about the struggle he had with taking a shower while he was depressed. Even though he could mentally go through the steps involved in taking a shower, they seemed "like 14 steps as painful and difficult as the stations of the cross."[35] Now that he experienced severe depression, it seemed to him that it had been easier to "make his way toward the tip of a plane's wing against a powerful wind at 6.000 feet" while he was skydiving than it was now to get out of bed and take a shower.[36]

In terms of pure physical effort, it seems that skydiving should clearly take more effort than getting into the shower. However, what Solomon tries to convey by this comparison is the painful, seemingly unbearable amount of effort that one little move of his body required – a kind of exertion that is unknown in normal life, in which the body is experienced as that through which one can actualize possibilities, purposes, goals in the world. Without this space of possibilities, without a practical engagement, however, the depressed person feels like she has to accomplish each little move not through the body, but almost against it. As it were, because not one of these 14 little steps seems to have a purpose. After all, what has been lost is a purposive embedding, a meaningful connection with the world, an orienting goal that is required to make the little steps in one's daily routine so effortless.

The alteration in existential feelings and the space of possibilities experienced by depressives are not only inseparably related to a change in bodily feelings, but also to a drastic change in the experience of time.

34 Cf. Fuchs 2005, 99.
35 Andrew Solomon in Wolpert 1999, 3.
36 Cf. Wolpert 1999, 3.

2.3. Alterations in the possibility space and the experience of time

In order to grasp the often reported inescapability of depression, it is necessary to emphasize once more that the absence felt in depression is not crucially about *actual* connections with people and things in the world (which are lost), but rather about the absence of the *mere possibility* of experiencing them.[37] Thus, the problem is not that specific things seem inaccessible, but that meaningful connections with anything in the world are perceived solely in terms of impossibilities.

This change in experiencing possibilities is directly linked to an altered experience of time in depression – an essential aspect of human experience, because persons are not only beings that are purposively entangled with the world, but they are also "temporal beings, beings who interact (…) with their worlds over time."[38] In this regard, the concept of "lived time" must be distinguished from an objective account of temporality, referring to the amount of time that has actually passed. Lived time denotes the present awareness one has about the change from one experience to the next and provides the "situational sensing of experienced time".[39] For example, 30 minutes seem to pass very slowly when we are doing something very boring like waiting for the bus, or it can seem like a very short time, for example when we engage in a pleasant conversation with a friend.

As concerns the experience of temporality in depression, many patients report that time passes by very slowly, some even say that "time, in its entirety, has gone by".[40] What is meant is that the structure of temporality has undergone a drastic change in which the term "future" does not bear any meaning any more. The psychiatrist Erwin Strauss explained this altered temporality by noting that, "the depressed person no longer lives time as his own; instead it comes upon him from in front and overrides him."[41] One way to conceive of this change in temporality is in terms of the existential changes implicated in depression which involve an alteration in the sense of what is possible. Due to the fact that the world no longer offers possibilities of significant change, depressives experience an inconceivability of things being otherwise and a sense of inescapability.[42] In this regard, it is not surprising that the transitory nature of the present is lost and with that the future is not perceived as "an open absence in the present" any longer but turns into something impossible, into a "static presence in the present."[43]

37 Cf. Ratcliffe 2010, 360.
38 Quoted from Wyllie 2005, 174.
39 Cf. Wyllie 2005, 174.
40 Quoted from Kuiper 2007, 85. Original version: "Die Zeit, sie ist vergangen."
41 Cf. Fuchs 2001, 180.
42 Cf. Ratcliffe 2009, 231.
43 Cf. Wyllie 2005, 180.

> That's the thing about depression: A human being can survive almost anything, as long as she sees the end in sight. But depression is so insidious, and it compounds daily, that it's impossible to ever see the end. The fog is like a cage without a key.[44]

Given the impossibility of a future, the present no longer incorporates the possibility of modification. This is crucial, because in normal life, any situation contains the possibility of change. The loss of hope, of possibilities and with that of futurity, in turn, augments the despair of depressive individuals, because they cannot conceive of the possibility of recovering from depression, since for depressives, the future is experienced as a mere repetition of the present.

This change in the experience of time, characterized by the inability to conceive of a future, also makes the escape from the past impossible, which in a way explains the – sometimes quite irrational – feelings of guilt prominent in depression. After all, to be guilty implies that something is unresolved and irreparable, which is stuck in an unfinished state. "Guilt means the real insight into the irreversibility of lived time, a fact that manifests itself in the strongest of all human perspectives, namely on one's death."[45] Due to the fact that the depressed person cannot conceive of the possibility of significant change to resolve the things she feels guilty about, the guilt feelings sometimes become very disproportionate. For example, one author writes about his depression:

> What has happened can never be undone again.(...) If one does not accomplish something in time, it is never done anymore. (...)[46] The real essence of time is indelible guilt.[47] The deepest abyss I fall into is the thought that even God cannot help me, for He cannot undo anything."[48]

In summary, the aim of this chapter was to give an understanding of the experience of depression by incorporating a phenomenological view of the matter. Needless to note, an encompassing phenomenological account of the experience of depression would require a lot more than this paper can offer.

In the end, the main point to be conveyed is that the alterations at the heart of depression are not in terms of feelings about specific matters in the world, but in terms of a background structure of experience that shapes the range of specific emotions, perceptions and thoughts the depressed person can have in the first place. In this regard, a phenomenological approach that takes the structure of experience into consideration is indispensable when it come to interpreting and comprehending the condition. An exhaustive understanding of the experience, in turn, is relevant

44 Cf. Wurtzel 1994.
45 Buber 1960, 110f. See also Fuchs 2003, 231.
46 Kuiper 2007:17. See also Fuchs 2001, 180.
47 Kuiper 2007, 58.
48 Kuiper 2007,162.

for neuroscientific accounts of depression, because it is important to have a thorough understanding of an experience in order to study its neural correlates.[49]

The draft of a phenomenological account presented here also firmly establishes the crucial difference between the experience of depression and the "normal" feelings encountered in everyday life. This is a clear advance over the mere listing of the specific diverging feelings, perceptions and thoughts of depressives compared to normal persons, as it takes place in the current DSM. In a phenomenological view, the feelings we experience in normal life are embedded in specific background feeling reflecting one's entire being in the world, usually characterized by a practical connectedness with the world, whereas depression in contrast is itself an alteration in such background feelings of reality. On this view, phenomenological approaches may also contribute to diagnostic matters in a science of depression by revealing a drastic distinction, particularly between normal sadness and depression – a difference that is not always acknowledged in psychiatric practice today, as will be argued later in the paper.

3. Neurobiological accounts of Depression

The assumption that depression can be located in the brain has begun to shape the personal and public understanding of mental illnesses in terms of responsibility and identity, particularly, the self-understanding of depressive individuals today. It allows patients to separate themselves from the disease, to conceive of the illness as somehow external, even though it is residing "on the inside", to say that "there is something wrong with my brain" rather than "there is something wrong with me"[50]. In regard of today's general fascination with neuroscientific explanations of mental illness and the impact on patients, this chapter will be entirely devoted to the perspective and insights into depression that neuroscience offers. The aim is to present as much as possible of an accurate glimpse into the current research and portrayal of depression in neuroscience. Hopefully, this might lay the grounds for a perspective on the brain which does not exclude or downplay the relevance of the various external factors that play such an important role in depression.

One consensus among scientists with regard to the biological basis of depression is that the illness involves a disruption in some or several processes in the brain and that a recovery from the illness involves a re-establishment in the processes that went awry. The opinions diverge as to

49 Cf. Ratcliffe 2009, 240.
50 Quoted from Thompson 1995, 189f.

which biological processes are involved, in which way and also as to how the effects observed from antidepressant treatment can be explained. I will start by discussing the development of pharmacological antidepressants and the presumably most straightforward and popular explanation of antidepressant effects, namely the hypothesis that the drugs restore a chemical imbalance in the brain of the depressives.

3.1. Antidepressants and the Chemical Imbalance Hypothesis

‘Behind every crooked thought . . . lies a crooked molecule’[51]

The first pharmacological antidepressants have been developed as early as in the middle of the 20th century and they are still the most widely applied treatment for depression today. Interestingly, however, the initial development of antidepressants has “rarely, if ever, been based on rational design – that is the application of rigorous basic science leading to the synthesis of a particular compound.”[52] Rather, progress relied on the (more or less accidental) observation that certain drugs that were used to target other illnesses were often also improving depressive symptoms. During the 1940s, drugs with a tricyclic chemical structure, today called Tricyclic Antidepressants (abbreviation TCAs) were tried out for the treatment of Parkinson's disease. One of these substances, imipramine, was found to have an antidepressant effect. Around the same time, another type of drug has been developed, which inhibits the enzym momoamine oxidase, thus called Monoamine-Oxidase inhibitor, short MAOI. One of these drugs, inproniazid, was used for treating tuberculosis and by chance was found to have an antidepressive effect on the patients, enhancing the patients' vitality and restoring their sense of well-being.[53]

In different ways, all antidepressants are assumed to work by increasing the influence of neurotransmitters in the brain, which are essential for communication between cells, ensuring that they are available for longer periods of time at their sites of action. The early antidepressants, tricyclics (TCAs) and monoamino-oxidase inhibitiors (MAOI), however, had a pitfall in that they targeted many neurotransmitter systems at once, and hence had a vast range of sometimes serious side effects. The development of a new kind of antidepressants during the 1980s turned out to be a case *sui generis* not only regarding their widespread application in treating depression, but also in terms of the “hype” they created. These new kind of antidepressants had the great advantage over

51 Slater 1999, 108. See also Frazer 2001, 61.
52 Quoted from Wolpert 1999, 133.
53 Cf. Wolpert 1999, 134f.

the earlier ones in that they selectively targeted the serotonin system, preventing nerve cells from taking up too much of the neurotransmitter serotonin. Accordingly, they were called SSRIs – selective serotonin reuptake inhibitors. These turned out to have comparatively few and "harmless" side effects in comparison with MAOs and TCAs.[54]

The "family of SSRIs" contains the substances paroxetine, sertraline, fluvoxamine, citalopram and the by far most commonly prescribed SSRI until today, fluoxetine hydrochloride – better known as Prozac. All SSRIs have similar side effects. However, the advantage of Fluoxetine was that it demonstrated the least need for dose titration.[55] Since the drug Prozac has been introduced into clinical use for the treatment of patients with depression in 1988, it has become the most widely prescribed antidepressant drug in the world. By the year of 1994, Prozac was "the second most commonly prescribed drug in the United States, after Zantac, an ulcer remedy".[56] At that time, six million people were taking the drug in the USA, and 11 million people worldwide. Within the next 5 years, the use of Prozac had risen to 38 million.[57] As these numbers show, the application of Prozac has explosively increased since it was introduced. Perhaps more significantly, this "green and creamy pulvule"[58] has contributed to the emergence of the brain as an organ of public fascination.[59]

During the 1990s, the fascination with antidepressants has extended from psychiatrists' offices to the public, as is vividly documented by the flurry of very optimistic autobiographies from sufferers. Soon, the story of this wonder drug made the covers of many national periodicals. The Rolling Stone deemed Prozac the "hot yuppie upper, and all the major network newsmagazines and day-time talk shows began to do their Prozac-saved-my-life segments."[60] In the book "Listening to Prozac" by Peter Kramer, one among many insightful accounts of the "popular" effects of antidepressants, depressive individuals revealed late-breaking statements about the effects of the drug on their personality that stood in contrast to the traditional, old-fashioned view that antidepressants change or harm one's mind and character. According to some of these persons, who in part had suffered from depression for their entire life, on Prozac, for the first time in their life, they felt like themselves.[61]

Such and other general observations that Prozac *works* eventually led to the notorious

54 Cf. Frazer 2001, 60.
55 Cf. Rossi 2004.
56 Quoted from Wurtzel 1998, 296.
57 Cf. Frazer 2001, 57.
58 Cf. Frazer 2001, 58.
59 Cf. Frazer 2001, 58.
60 Quoted from Wurtzel 1994, 297.
61 Cf. Kramer 1993.

"Serotonin Hypothesis" according to which depression is basically a chemical imbalance in the neurotransmitter serotonin in the brain. Kramer, for example, explains such an amine hypothesis through an analogy between depression and other diseases : "A person who has too little insulin suffers from diabetes; an excess of insulin causes low blood sugar (...). An excess of amines was thought to cause mania . . . and a deficiency, depression"[62]. The action of antidepressants has not only had a vast impact on the way people conceived of depression, but also on the way scientists oriented their research on depression – from now on, their main focus was on the neurotransmitters serotonin and noradrenalin in the brain.

Today, however, the chemical imbalance theory about the brain and the nature of depression has become the cause of numerous controversial debates. The suspicion began with a meta study on every placebo-controlled clinical trial submitted for initial approval to the FDA of the six most widely used antidepressant drugs approved between 1987 and 1999: Prozac, Paxil, Zoloft, Celexa, Serzone, and Effexor.[63] They found that, in many cases, placebos were 80 percent as effective as the drugs.[64] The distrust in antidepressants started to increase and in parallel, the "chemical imbalance hypothesis" became known as "pseudo scientific".[65]

And yet, in contrast to these findings stand the numerous accounts of depression in which people report their recovery from depression as a result of treatment with antidepressants. Could it be that all these people were just fooling themselves and others? Probably not. But what the new controversial studies revealed was that treatment with antidepressants is rather unspecific and by far not optimal. In this regard, the appealing equation of depression with a chemical imbalance in the brain was most likely too easy of an explanation. Suddenly, waves of insights were spread in news shows and articles, realizing that even if antidepressants do work, concluding from that observation that depression is caused by a chemical imbalance in the brain amounts simply to a logical mistake. Only because something works to stabilize a condition, it does not have to cause the illness in the first place. Jeff Lacasse, a participant in a study that points out the invalidity of the chemical imbalance hypothesis[66], made a keen analogy in a news show: Concluding from the effects of Prozac that depression is caused by a chemical imbalance in the brain is like drinking a few bears at the end of a bad day and concluding from the fact that you feel relaxed afterwards that you must have suffered from a lack of alcohol in your brain.[67]

62 Quoted from Kramer 1993, 53.
63 Cf. Kirsch et al. 2002.
64 Cf. Kirsch et al. 2002.
65 Cf. See Lacasse/Leo 2005.
66 Cf. Lacasse/Leo 2005.
67 See Fountain, K. (Host) 2006.

Altogether, even though the serotonin hypothesis is a very popular way of advertising antidepressants – the pharma company Pfizer still states on their German website that "there is a lack of serotonin in case of depression"[68]– there is not a single peer-reviewed article supporting claims of serotonin deficiency in depression, while there are many articles that present counter evidence.[69] Dr. Wayne Goodman, Chair of the US Food and Drug Administration's (FDA) Psychopharmacologic Drugs Advisory Committee states that "biological psychiatrists have looked very closely for a serotonin imbalance or dysfunction in patients with depression or obsessive compulsive disorder and, to date, it has been elusive".[70] In similar line of thought, Ireland's drug regulator prohibited the statement on a patient information leaflet in psychiatry offices which states that paroxetine, an SSRI, "works by bringing serotonin levels back to normal."[71]

Of course, the fact that the claims about the connection between levels of serotonin in the brain and the nature of depression have been formulated in such an exaggerated manner does not mean that the neurotransmitters serotonin and noradrenalin don't play *any* role in depression. However, what the debates reveal is that treatment with SSRI is by far not optimal, and that depression is too complex an illness for it to reduced to a chemical imbalance in the brain. In fact, in spite of different approaches to explain the observed effects on depressives due to antidepressants, the exact way in which they work is still very little understood. One major curiosity in terms of the serotonin explanation of the drug effects that made scientists skeptical is why they take so long to produce the effects, about 6 weeks, when they bring about an immediate increase of serotonin levels.[72] If nothing else, it is also this observed time lag until antidepressants "kick in" that has led researchers to devote their research to other aspects of brain functions.

3.2. Brain Plasticity and Adult Neurogenesis

Today, scientific research on depression has moved away from focusing on the assumption that a lack of particular neurotransmitters causes an imbalance in the brain – a hypothesis that was inspired, in the first place, by the treatment effects of antidepressants. Rather, many scientists are currently adopting an understanding of depression in which antidepressants work in a much more complex and indirect way in bringing about the observed effects. They now draw a picture in which

68 Original: "Bei einer Depression besteht ein Mangel an Serotonin." See Pfizer Pharma GmbH 2009.
69 Cf. Lacasse/Leo 2005, 1213.
70 Wayne Goodman quoted in Meek 2006.
71 See Meek 2006.
72 Cf. Lehrer 2006.

the respective neurotransmitters play supportive roles, at best.

The new emerging outlook on depression involves different lines of research, and one remarkable focus of recent studies that has been in the spotlight lately involves the link between depression and *brain plasticity*. Neuroplasticity – a fundamental adaptive process of brain cells – allows the connection between neurons to vary in strength, a phenomena that is thought to be required, among other things, for adaptation to stress.[73] Chronic stress, however, a well investigated cause of depression, has been shown to disrupt the mechanisms of neuroplasiticity.[74] Stress produces stress hormones, so called adrenal steroids, which lead to an increase in body function such as blood pressure and heart rate. When these hormones stay active for long periods of time, they can alter neuronal signaling in multiple ways. For example, they can change the signaling pathways implicated in synaptic plasticity.

Given that stress is thought to cause depression, researchers started to conceive of the possibility that depression may be the result of a reduction in neuroplasticity which leads to a failure in making appropriate adaptive responses to the environment. Ronald Duman, a professor of psychiatry and pharmacology at Yale, notes that "while the precise nature of the relationship between the pathophysiology of major depression and possible dysfunction of neuroplasticity remains poorly understood, it is likely that an intimate relationship exists."[75]

In this regard, scientists began to explore the possibility that if depression entails a deficit in neuroplasticity, the effects observed from antidepressant treatment may be due to an enhancement in neuroplasticity and a reversal of the deficits produced during the depressive episode.[76] Evidence in this direction comes from studies showing that antidepressants increase synaptic plasticity in animal models. Recent reports suggest that a chronic administration of an SSRI increases long term potentiation (LTP),which is a mechanism responsible for synaptic plasticity, and acts against the stress-induced impairment of LTP in specific cell populations in the hippocampus that are well known for their ability of synaptic plasticity.[77] Furthermore, chronic SSRI administration has been reported to have reversed a stress-induced impairment of LTP.[78] Taken together, these studies indicate that chronic antidepressant treatment increases cellular plasticity, as well as blocks the effects of stress on particular cell populations of hippocampal neurons.[79]

73 Cf. Pittenger/Duman 2008, 95.
74 Cf. Pittenger/Duman 2008, 95.
75 Cf. Pittenger/Duman 2008, 88.
76 Cf. Pittenger/Duman 2008, 96.
77 Cf. Vouimba et al. (2006) and Holderbach et al. (2007) in Pittenger/Duman 2008, 97.
78 Cf. Rocher et al (2004) in Pittenger/Duman 2008, 97.
79 Cf. Pittenger/Duman 2008, 97.

Another line of evidence supporting the hypothesis that antidepressant treatment leads to alterations in neuroplasticity is the regulation of neurogenesis – the brain's capability of producing new neurons – by antidepressants. Contrary to a "long-standing dogma" in neuroscience, "clear evidence now demonstrates that new neurons are generated in the adult mammalian brain"[80] – a mechanism which is prominent in the dentate gyrus region of the hippocampal formation.[81] Given that neurogenesis has been finally accepted as a mechanism that occurs in the adult brain, scientists investigated whether the chronic stress underlying depression may not simply lead to a reduction of cells, or slow down the growth of cells, but even prevent new cells from being born.[82] Numerous studies show that chronic stress damages the brain by suppressing the release of neurotrophic factors, types of protein which help neurons grow, survive and contribute to supporting neuroplasticity, such as Brain-derived neurotrophic factor (BDNF).[83] Studies with animal models show that rats with induced daily unpredictable stressors reduced the generation of new neurons in the rat dentate gyrus, while control rats had an unchanged amount of neurons in that brain region.[84]

Given that, in chronic stress, there is a reduction in cell production due to the decreased action of trophic factors, scientists investigated the manifest question whether the action of antidepressants would result in an increase of neurogenesis. In this regard, the effects of antidepressants may be to act against these adverse cellular effects, which may be regarded as a loss of neural plasticity, by blocking or reversing the atrophy of neurons and by increasing cell survival and function. And in fact, some studies have found that chronic antidepressant administration increases the expression of neurotrophic factors in the hippocampus.[85]

Interestingly, an increase in Neurogenesis is thought to be caused not only by antidepressant treatments, but also by "other kinds of plasticity-inducing stimuli, such as environmental enrichment, exercise, and electrical stimulation."[86] In this way, the neurogenesis hypothesis of depression serves to explain why at least in mild cases of depression, exercise is said to improve symptoms. In general, the hypothesis suggests how different approaches in treatment in depression may all invoke a mechanism for cell production and thereby allowing the system to adapt much better to stress or adverse circumstances.

However, in order to ensure that the observed neurogenesis is not merely a side effect of the

80 Cf. Pittenger/Duman 2008, 94.
81 Cf. Pittenger/Duman 2008, 94.
82 Cf. Lehrer 2006.
83 see Pittenger/Duman 2008, 98.
84 Cf. Pittenger/Duman 2008, 90.
85 Cf. Pittenger/Duman 2008, 98.
86 Cf. Pittenger/Duman 2008, 102.

antidepressant drugs, but actually causes the relief provided by antidepressants, researches conducted additional investigations with mice deprived of the capability of neurogenesis. The basic assumption was that if the effects of antidepressants were due to the increase of serotonin, then the inability of neurogenesis should have no effect on their functioning.[87] This hypothesis was tested at the University of Columbia by the research team of Rene Hen and a postdoctoral researcher, Luca Santarelli, who gave antidepressants to mice that had lost the ability to produce new hippocampal neurons. They then measured two behaviors believed to be related to depression: interest in food and interest in grooming. In normal mice, antidepressants increase food consumption and coat care, while mice under stress lose interest in both. After four weeks on the antidepressants, however, the behavior of the neurogenesis-impaired mice did not change with either of the two drugs tested: Prozac and imipramine, a tricyclic. The results, Hen says, "show there is a need for neurogenesis to cause antidepressant-like effects in mice" and that new neurons are necessary for the drugs' mood-altering effects in people.[88] With regard to the speculation whether an inability to produce new neurons causes depression in the first place, Hen advises to be careful with hasty interpretations: "It could be a decrease in neurogenesis, or a change in some other hippocampal property. Lack of neurogenesis is probably not the only, or even the main, cause."[89] What the finding clearly suggests, says Hen, is the necessity to re-think "the role of the hippocampus, which is usually only associated with learning and memory, not mood."[90]

In any case, caution is recommended with hasty interpretations, because the precise relation between changes in plasticity and the action of antidepressants in the brain is not readily straightforward and clear. Although these studies suggest a common underlying mechanism between the action of antidepressants and cell growth, there is not enough evidence yet for assuming a causal relationship. Scientists hope that as their understanding of the complex relationships between stress, depression, and neuroplasticity grows, the functional interrelationship of one to the other will become more clear.[91] In the end, the upshot of the discussed research results is that impaired mechanisms of neuroplasticity may be a core pathophysiological feature of depression – "that chronic stress is an important causal factor in the development of this impairment, and that antidepressant treatments act, at least in part, through mitigation of impaired mechanisms of plasticity."[92]

87 Cf. Lehrer 2006.
88 Cf. Conova 2003.
89 Cf. Conova 2003.
90 Quoted from Conova 2003.
91 Cf. Pittenger/Duman 2008, 102.
92 Quoted from Pittenger/Duman 2008, 102.

3.3. Brain patterns and the Neurocircuitry of depression

Current research and current debates concerning "hot topics" relating to the neurobiological basis of depression and treatment optimization are not restricted to the molecular level. One of the leading neuroscientists working on depression today, Helen Mayberg, who is based at Emory University's School of Medicine, has focused her research for a long time on the neural pathways in the brain that go awry during depression. She does this mainly by measuring the activity in and connectivity between certain brain regions.

In order to determine the dysfunctional neural pathways in depression, scientists are looking for common regional abnormalities among depressives and contrasting them with normal control subjects. In this regard, Mayberg, as thousands of other scientists, relies on two recently developed techniques for recognizing activity in specific brain areas, namely functional Magnetic Resonance Imaging techniques, short fMRI and positron emission tomography Positron emission tomography, or PET. Whereas the older of the two techniques, PET, measures the glucose – a source of energy for the cell – and the oxygen metabolism within the brain, the newer developed and today most commonly applied imaging technique, fMRI, measures changes in blood flow in the brain. The difference between the two is that PET reflects the areas of the brain which are active at a given time and those which are inactive – it shows the "movement" of brain activity; fMRI on the other hand, represents the metabolic activity of the brain.

Most brain imaging studies, both with fMRI and PET, have found decreased activity in the frontal cortex of depressive patients compared to healthy controls. However, even though the most common and consistent finding is decreased frontal lobe function, some studies also show normal frontal as well as increased frontal lobe activity. The fact that these brain regions differ in activity among the same study group indicates that there is not one specific brain area involved in all patients who are depressed. Therefore, these and other inconsistencies among depressives' brain activity point to the fact that depression will probably not be the result of *a single* dysfunctional brain region or *one specific* biological process, but rather stemming from changes in a complex multidimensional network of different mechanisms.[93]

In order to establish an appropriate understanding of the neurobiological basis of depression, which can account for the reported discrepancies in brain activity, Mayberg proposes a neural

93 Cf. Mayberg 2003, 194.

network model which basically assumes that depression is caused not merely by a dysfunctional single biological process or brain area but rather by the failure in the coordination of the interaction of different brain circuits, foremost the limbic-cortical pathways. Because it doesn't correlate depression with one specific brain area, this model can also explain the well recognized heterogeneity of depressive symptoms, that is in mood, motor, cognitive or sleep pattern changes that vary from patient to patient."[94] In line with this view, Mayberg has suggested that frontal hyperactivity is conceived as an "exaggerated or maladaptive compensatory process resulting in psychomotor agitation" that serves to "over-ride a persistent negative mood generated by abnormal chronic activity of limbic-subcortical structures."[95] In contrast, decreased frontal lobe activity may be "the failure to initiate or maintain such a compensatory state, with resulting apathy, psychomotor slowness and impaired executive functioning.[96] In this regard, Mayberg hopes that further research could improve treatment by adjusting the respective ineffective compensatory states as measured by the pattern of regional abnormalities.

Even though the model proposed by Mayberg focuses mainly on direct measures of brain functioning in the development of new clinical diagnosis and treatment methods, the approach does not attempt to overlook the contributions of genetics, early-life loss, or exogenous factors, but rather to include these variables within the disease construct at the brain level.

> "[Depression] can be conceptualized as a multidimensional, systems-level disorder affecting discrete, but functionally integrated, pathways. Moreover, depression is not simply the result of dysfunction in one or more of these elements, but also involves failure of the remaining system to maintain homeostatic emotional control in times of increased cognitive or somatic stress. While mechanisms mediating this 'failure' are not yet characterized, they are thought likely to be multifactorial, with genetic vulnerability, affective temperament, developmental insults and environmental stressors all considered important contributors."[97]

The crucial assumption in this evolving depression model is that particular dysfunctions in some level of the network in depression do not exclude other factors, but assume a general collapse in maintenance or adaptation of certain neural pathway circuitries."[98]

Given that depression may be the result of a failure to maintain a certain brain circuitry, Mayberg assumes that a coordinated modulation of these pathways is required for illness recovery. The pathways involved in depression treatment have been investigated for a long time by Mayberg

94 Cf. Mayberg 2003, 194.
95 Cf. Mayberg 2003, 194.
96 Cf. Mayberg 2003, 194.
97 Quoted from Mayberg 2003, 194.
98 Cf. Mayberg 2003, 194.

in a series of treatment studies, in which the scientist and her colleagues compared the brain activity of patients during the depressive episode with activity in the same brain regions after the patients had recovered from the condition. The studies identified a complex interaction of a distributed set of both limbic and cortical brain regions. However, there does not appear to be one common pathway for recovery. "You do not get the same brain changes when people recover from medication as when they recover from cognitive therapy," Mayberg reports.[99] This fits the model of depression suggested by Mayberg: "If we think of depression as a neural systems disorder, we can envision that different forms of treatment (…) are actually targeting different components of this network in different ways, and that should resonate with everyone who takes care of patients."[100]

However, one commonality that the researchers have found among these different studies is that a modulation of the circuitry between subcortical parts, such as the brain stem, and cortical regions as the amygdala are in any case important for illness remission, regardless of treatment modality – be it pharmacological or cognitive therapy or surgical interventions. The important issue in optimizing treatment is to develop methods for distinguishing disease-specific and response-specific interactions among the regions involved in this depression network.[101] In this way, scientists hope to eventually come up with "clinical algorithms that will discriminate patient subgroups, optimize treatment selection, predict relapse risk, and provide markers of disease vulnerability."[102]

This is especially important given that many patients do not respond to any of the commonly used treatment methods for depression. In case of depressive patients who did not respond to other types of treatment (such as pharmacology or cognitive therapy), Mayberg and colleagues applied a recently developed new treatment, so called Deep Brain Stimulation (DBS). DBS involves the implantation of a device, called "brain pacemaker", which sends electrical impulses to specific parts of the brain and thereby has the potential to alter the neural connections in the patient's brain. The researchers found that chronic DBS of a brain region referred to as the subgenual cingulate or Brodman area 25 resulted in "a striking and sustained remission of depression" in four of six patients with very resistant depression.[103] One post-study finding from this research group is particularly intriguing in that Mayberg's patients describe that after DBS treatment they were able to experience the complete range of emotions, particularly normal sadness and that their emotional reactivity was "quite different from the emotional "blunting" many of them experienced while

99 Cf. Balzac 2004.
100 Cf. Balzac 2004.
101 Cf. Mayberg 2003, 194.
102 Quoted from Mayberg 2003, 194.
103 Cf. Mayberg et al. 2005.

taking conventional serotonergic antidepressants or atypical antipsychotics."[104]

The fact that depressives remained in a state of recovery and were able to feel normal sadness after treatment with DBS, but not with antidepressants, might suggest that DBS targets in a more direct manner the implicated neuronal pathways than antidepressants, whose action in the brain might be more or less "blind". However, the reason why antidepressants, despite their imprecision, seem to work, Mayberg suggests, is because of the compensatory ability of the overall neuronal circuit in depression. A functional integrity of these pathways might in this regard also explain the comparable clinical efficacy of pharmacological and cognitive treatments.

Based on the assumption that there is sustained compensatory capacity in the overall depression circuit, one might hypothesize that different interventions with diverse major mechanisms of action should be just as effective. However, given that, nowadays, the determining of the right treatment for each patient involves a series of trial-and error-methods, it would be a great advantage to know what type of treatment is indicated by a specific brain pattern and thereby employ the adequate method for each patient right from the start. In this regard, the approach taken by Mayberg has the potential to revolutionize medical treatment by saving patients "years of unsuccessful treatment."[105]

Despite the advances in her approach, Mayberg acknowledges that the research has a long way to go: "We can't be so arrogant that we think we know exactly what a pattern of activity in the brain means," says Mayberg. "When I see Area 25 light up because the person is sad, I still don't know if that's generating the sadness, or if that's the signal trying to turn off the sadness." She hopes that in the future, scientists will find out more precise information about the neural pathways that go awry in depression and that prospective treatment methods will target more specific brain areas compared to the quite unspecific action of antidepressants: "We need to move away from a one-size-fits-all approach to mental illness."[106]

3.4. Genetic factors and life events

While scientists focus on different kinds of biological processes that contribute to the development of depression, when it comes to identifying what causes these mechanisms to go awry, most scientists emphasize one and the same cause, namely acute or chronic stress. However, one curiosity in this regard is that not everybody who experiences stressful life events becomes

104 H. Mayberg in Pies 2008, 17.
105 Cf. Mayberg in Suttie 2007.
106 Cf. Mayberg in Suttie 2007.

depressed. Hence, one important question that scientists have kept asking for some time now is what constitutes the specific *vulnerability* some people seem to have towards becoming depressed and that others lack. In trying to understand the origin of such individual diverging of reactions to similar circumstances, researchers have began to conduct studies on the statistical relation between depression and genetic makeup.

The classic studies in this regard have been conducted with twins. Studies with identical twins show that if one twin has a severe depression there is a 50 percent chance that the other will also become depressed. In case of non-identical twins, the chance is smaller, yet still higher than average, lying at 25 percent. In this regard, it was clear that genetic makeup plays an important role in depression. However, the exact genes involved in forming a susceptibility for depression were unknown. If the respective genes could be identified, scientists thought, "we would know which proteins were at fault in depressives, and this could tell us which cellular processes were involved, and could therefore suggest new treatments."[107]

In this respect, a recent study by Caspi et al. is of immense importance in terms of an increased understanding of the genes involved in depression. Although for a long time scientists assumed that the 5-HTT gene, which is the transporter gene involved in serotonin reuptake mechanisms, is involved in depression, no direct connection between this gene and depression had been shown. At least until the studies conducted by Caspi et al., which for the first time evidently demonstrated that mutations in the 5-HTT gene, which comes in the form of short or long alleles, moderate a person's likelihood to suffering from depression after stressful events.[108] However, the study is equally important also in another aspect, namely in that it emphasizes that the observed influences of genes on depression can only be understood in terms of an interaction model between genes and environment.

The study was conducted over a long period of time with a group of individuals born around the same time (birth cohort) who had different genotypes for the 5-HTT gene. When the subjects were 26 years old, the researchers evaluated whether or not the subjects had experienced one or multiple stressful events and whether or not they developed a depression. The researchers focused on stressful events occurring after age 21 and depression diagnosed after age 21. Depression after stress was then related to the subjects' genotypes. The results indicate that persons who carried a short version of the 5-HHT gene were significantly more likely to show a depressive behavior than

107 Quoted from Wolpert 1999, 44.
108 Cf. Caspi, et. al. 2003.

the ones with a long version of the gene.[109] This indicates that a particular gene can have a strong influence on the way that an individual reacts to difficult life events and thus provides a predisposition to become depressed.

As already remarked, the scientists employed a gene-environment interaction model that predicted depression as a result of environmental stress and interaction with the 5-HHT gene. However, in order to ensure the unambiguity of the gene-environmental interaction model, the researchers conducted additional measures to rule out the possibility that what has been interpreted as environmental factors are actually genetic factors influencing the person's tendency to experience adverse life events.[110] The results clearly demonstrate that the observed interaction is a true gene-environment interaction.

In this regard, the researchers emphasize that the study illustrates that genetic factors may not directly "cause" the disease, but only moderate responses to environmental factors.[111] In general, research on genetic makeup and depression has moved away from the earlier assumption that a mental illness can be traced down to the action of specific genes, and towards a model which puts most emphasis on the interaction between genes and environment. In this regard, even though researchers hope to be able to develop new treatment methods for depression based on these new insights, at the same time, most are hopeful in a rather cautious way, aware of the fact that no direct paths will be found from a single gene to such a complex psychiatric disorder. This attitude is especially adequate in view of the multifactoriality of depression and the fact that it is far from clear how the serotonin pathway imposes its precise effect on the illness.

Summing up, one can say that neuroscience has opened up many fascinating ways to understand the mechanisms underlying depression. However, a clear and simple picture of the condition has not been revealed so far and is not likely to be revealed in the future. Instead, various complicated mechanisms and influences need to be taken into account. From a phenomenological perspective, which is grounded in the experience of "real life depression", this is not very surprising, as the illness of depression has long been seen to be multi-faceted and complexly entwined with all the processes that make up a person's being in the world. One next step in the interdisciplinary research of depression should be a more thorough integration of phenomenological and narrative approaches with state-of-the-art neuroscience, in order to explore possible ways to

109 Cf. Caspi, et. al. 2003, 286.
110 Cf. Caspi et al. 2003, 287.
111 Cf. Caspi, et. al. 2003, 288.

better match reported experience with neuronal mechanisms. But the complexity does not stop there. Like probably no other illness, depression is influenced by socio-cultural circumstances. These factors need again a different kind of analysis. In the end, only if the experience, the underlying neurobiology and the social dynamics that embed the illness in various ways are taken together, we have a chance of reaching a sufficiently balanced and inclusive account of the many faces of depressive illness.

4. Sociocultural aspects of depression

The prevalence of people diagnosed with depression has vastly increased in the past decades. The increase of depression today has been explained in different ways – some argue that it is due to a neglect of normal suffering in the diagnostic field itself, others see it as a consequence of changes in Western societies. I will start by discussing the first hypothesis, and then proceed to present some elements of an intriguing sociocultural theory of modern depression.

4.1. The promotion of psychiatric illness and the "loss of sadness"

> It seemed that suddenly, some time in 1990, I ceased to be this freakishly depressed person who had scared the hell out of people…, and I instead became downright trendy. This private world of loony bins and weird people that I had always felt I occupied and hid in had suddenly been turned inside out so that it seemed like this was one big Prozac Nation, one big mess of malaise.[112]

According to statistic estimations, 10 to 15 percent of the German population is diagnosed at least once during their lifetime with depression.[113] In the last decade, the amount of antidepressants that were prescribed has increased more than twice from 150 million per day doses in 1987, to 327 million day doses in 1996. [114] More than 31 million prescriptions were written for antidepressants last year in the UK – a six percent rise since 2005.[115] In the USA, an estimated 26.2 percent, that is about one in four adults, is diagnosed with a mental disorder in a given year[116] – a figure that translates into altogether 57.7 million people.[117]

How does it come that so many people are so miserable? Are we really more mentally disturbed nowadays than we were 30 years ago? Or are psychiatrists merely confusing ranges of

112 Quoted from Wurtzel 1994, 297.
113 See DAK-Pressestelle 2001.
114 Cf. DAK-Pressestelle 2001.
115 Cf. Wighton 2007.
116 Cf. National Institute of Mental Health, U.S. 2008.
117 Cf. National Institute of Mental Health, U.S. 2008.

normal behaviors with mental illnesses? Confronted with such issues, mental health professionals usually argue that this development is wholly intelligible simply because mental illnesses get recognized better today and because more people are willing to see a doctor when they have mental problems.[118]

However, many journalists and popular writers propose a different explanation.[119] According to some critical authors, the vast increase in people diagnosed with mental illnesses originates in a confusion of normal behaviors with mental disorders in psychiatry. The confusion is thought to be especially present in "Prozac nation"[120] America, among other reasons because U.S. pharma companies are allowed to directly advertise their drugs to consumers. Not only do these advertisements employ equations of mental illness with chemical imbalances in the brain that are scientifically unsubstantiated,[121] but they also promote drugs for ill-defined chronic conditions that essentially affect normal people that simply go about their life's daily business. Given that many people feel sad at times, stressed out, tired and exhausted, many of those watching the advertisements may be intrigued to consider whether their incomplete well-being is not simply a lack of serotonin in the brain, for example. Within a culture that is highly medicalized and hyper-concerned about health issues, some authors argue, the expansion of the market is guaranteed if one just finds more and more new market niches. Thus, what gets promoted even more than the new fancy drugs are new illnesses.[122] In this regard, a review of the book "Shyness: How normal behavior became a sickness" by Christopher Lane, claims that the new selling strategy of pharmaceutical companies, together with doctors, is trying to convince us that "there are only two kinds of people: those with medical conditions that require drug treatment and those who don't know it yet."[123]

These developments in classifying ever more human problems and mood changes as mental illness can also be witnessed in other Western societies. After all, four out of five of the currently classified mental illnesses, in the DSM-IV as well as in the European version, the ICD 10, were conceived as normal mood variations until around 30 years ago.[124] Astonishingly, the currently 943-page incarnation"[125] of the DSM has started out as only a "small, spiral-bound handbook (DSM-I)" in 1952. Back then, it only listed 106 disorders. 16 years later, the second version contained 182

118 Cf. Schnurr 2008, 16.
119 For example Schnurr (2008), Angell (2009), Horwitz/Wakefield (2007), Lane (2008).
120 Cf. Wurtzel 1994, 297.
121 Cf. Lacasse/Leo 2005.
122 Cf. Schnurr 2008, 18.
123 Quoted from Angell 2009.
124 Cf. Schnurr 2008, 12.
125 Cf. Angell 2009.

disorders, the third edition from 1980 suddenly included 265 and the current, 1994 edition, lists altogether 297 mental illnesses. Thus, in less than 50 years, the number of mental disorders has tripled.[126]

According to a book called "The Loss of Sadness" by the sociologist Allan Horwitz and the philosopher and mental health expert Jerome Wakefield, the vast increase in conditions regarded as mental illnesses results from a neglect, in today's psychiatry, of the distinction between normal life problems and mental disorders. This tendency, according to the authors, originates from the major transformation that the DSM went through during the 1970s. The goal was to move away from Freud and psychoanalysis to more rigorously scientific methods by means of objective, comparable, countable and measurable criteria for diagnosis ("evidence-based medicine"). Thus, a certain number of symptoms displayed over a particular period of time were established as criterial for each mental illness. However, the problem with the new allegedly scientific accounts of the disorders was that the context in which the sufferers lived and became ill had been completely left out. This is why, when people today are classified as depressive, the diagnosis solely depends on the number and period of symptoms, independently of the particular existential and social situations that they are embedded in.[127]

This kind of decontextualization is a serious problem, because the lack of an objective measurement and the heterogeneity of symptoms makes the diagnosis of depression anything but a straightforward enterprise. It permits the psychiatrist to assign his categories and interpretations to the problems independent of the situation in which they occur.[128] Not surprisingly, this increases the risk of misdiagnosing normal reactions to a difficult environment as mental disorders, since it ignores the relationship of symptoms to the context in which they emerge.[129]

This neglect of the context in which individual suffering is embedded correlates with the general tendency today to situate human problems exclusively inside an individual's brain or mind. For example, the theatre play "The death of a Salesman" by Arthur Miller is a play produced in the 1950s as a drama about the downfall of man due to difficult social circumstances. Ever since the play's debut in 1949, critics have discussed the symbolism of the salesman, some said that he is "a stand-in for the long-suffering common man" others saw him as "a suicidal victim of the capitalist machine", yet others deemed him as just a man "undone by his own ignorance and womanizing".[130]

126 Cf. Schnurr 2008, 12.
127 Cf. Schnurr 2008, 12.
128 Cf. Marsella 2003.
129 Cf. Horwitz/Wakefield 2007, vii.
130 Cf. McKinley 1999.

Performed 50 years later, however, this play yielded the following headline on a review by the New York Times: "Get that man some Prozac."[131] It turned out that when, out of curiosity, the Broadway directors sent the script to two psychiatrists, both responded that Willy was manic-depressive. Hence, what 50 years ago indicated a social problem, now indicates a psychiatric illness.

Daniel Hell, a professor of psychiatry from Switzerland, explains such changes in what is taken to be a mental disorder as the result of the cultural background that psychiatry finds itself in. After all, mental disorder is, to a significant extent at least, "a matter of definition."[132] The best example for the arbitrariness of what constitutes a mental disorder is particularly revealed by the fact that homosexuality has been conceived of as a mental disorder and has only been banned from the diagnostic manual in 1987 after protest from the gay lobby.[133] It is amazing how fast what has been a mental illness on one day can become normal the next.

Recently, psychiatrists have even discussed to include in the DSM a disorder named "chronic whine disorder" with the major symptom being constant complaining.[134] As a parody of the current medicalization and the exaggerated conditions proposed by mental health experts, the Australian artist Julianne Cooper has promoted a fake advertisement campaign for a fictitious drug in the internet. The drug's name was "havidol", which sounds similar to "have it all" and was supposed to cure the equally fictitious mental disorder Dysphoric Social Attention Consumption Deficit Anxiety Disorder. The symptoms of this fictitious condition: despite all achievements, one still feels like something is missing in life. The campaign motto: "When more is not enough".[135]

And yet, proclaiming that the large number of mentally ill people, particularly depressed people, is simply the result of a collective exaggeration of mental health experts would be another inadequate simplification of the problem. Psychiatrists and Drug Companies may invent new mental disorders and trivialize human problems, but they most certainly do not invent the sufferings themselves – what they do is simplify them, cheer them on and give the impression of an easy way out.

In the end, the increase in people with depression can also be explained by acknowledging that certain types of behaviors and mood changes that were normal 30 years ago pose an impairment in life today. Bad moods, bad days and signs of rigidity in character cannot be afforded as easily as in an earlier day. Thus, the explosion in the numbers of depression may best be

131 Cf. McKinley 1999.
132 Cf. Daniel Hell in Schnurr 2008,12.
133 Cf. Schnurr 2008, 12.
134 Cf. Schnurr 2008, 12.
135 Cf. Schnurr 2008, 22.

understood not only in terms of a hype in medicalization, but on a more wide-ranging conception, as a result of more general shifts in today's societies' rules and norms.

4.2. "The Fatigue of Being oneself"

"In effect, anyone who is not flexible deserves to disappear."[136]

It is assumed that those born after 1955 are three times as likely to become depressed as their grandparents' generation. While only one percent of Americans born before 1905 had gone through a depressive episode by the age of seventy-five, six percent of those born after 1955 suffered from depression by the age of twenty-four.[137] Even though much of this increase is probably owed to the fact that depression is recognized at higher rates today than in the past, it is at least plausible that a change in the social structure has also contributed to a great extent to this development.

If our grandparents did not lead the lives they wanted to, this was usually due to external constraints imposed on them by a hierarchical, rigid structure of society. Today, however, a time in which individuals face a vast range of possibilities and freedoms to turn their lives into whatever they want, to be authentic selves, the responsibility for actually leading a life ones wants lies solely on each individual himself. In the "The Fatigue of being oneself", the French Sociologist Alain Ehrenberg develops such an idea about depression – in brief, that depression may be the side effect of the tiresome demand to be oneself – thus at bottom, as he puts it, an "illness of freedom".

According to Ehrenberg, depression is the downside of having overcome the strict norms and rules prevalent during the 19th and early 20th century.[138] It is the price we pay for the transition from a society in which one had to subordinate to authorities to our modern society which expects individuality and creative, proactive behavior, constant initiative and self-sustained motivation.

These cultural changes have given rise to a new kind of suffering, which is not characterized by external constraints but to the contrary, by the vast range of possibilities for achieving self fulfillment and an authentic way of life. Whereas the nervous disorder in the beginning of the 20th century was the pathological side of a repressive capitalism, depression is the negative side-effect of a new capitalist society that turns the authentic self into a means of productivity and keeps

136 Quoted from Malabou 2004, 46.
137 Cf. Wurtzel 1994, 299.
138 Cf. Ehrenberg 1994,19.

challenging it until the individual is exhausted. [139]

In this way, the absence of centrality and hierarchy, the absence of clear and localized conflict, and the necessity of being mobile and adaptable constitute new causes of anxiety, and ultimately new causes of psychiatric illness.[140] For example, in the contemporary work environment,

> disciplinary models of human resource management are on the decline, in favor of norms that encourage autonomous behavior, even for personnel on the bottom of the hierarchy…Modes of regulation and domination of the workforce are now based less on mechanical obedience than on initiative: responsibility, the capacity to evolve, to form projects, motivations, flexibility, etc. (…). The model imposed on the worker is no longer that of the man-machine of repetitive labor, but that of the entrepreneur of flexible labor.[141]

On this score, the depressed person becomes sick because she "cannot stand this conception of a careerist whose very existence is conceived as a business or a series of projects."[142] Put in the harsh terms of present-day capitalism, this turns the depressed individual into a person who suffers from a lack of "adaptability" and thus, ultimately, "employability". [143]

However, as Ehrenberg explicates, these structural changes in society extend to every domain of our world: in school, work place, in the family and in friendships, the new rules that guide us are "no longer obedience, discipline, and conformity to morals, but flexibility, change, reaction time, etc.".[144] The traditional political consciousness of the individuals that resulted from their conflicts with society has vanished. It has been replaced by the psychologization of social relations. What has been perceived as an external constraint, i.e. authorities and their strict demands, now has shifted inwards.

These changes in the ways by which society functions, which no longer provide a sense of security and order, might explain why depression is not restricted to people who do not have a promising life ahead of them, who suffer from poverty or endure harsh life events, but also entirely "normal" people with a promising future. For example, Elizabeth Wurtzel recounts how a college writing teacher once reported her astonishment about the pessimistic and harrowing nature of her students' stories. Reading their work, the teachers says, "you'd think they were a generation that was starved, beaten, raped, arrested, addicted, and wartorn (...). The figures in their fictions are victims of hideous violence by accident; they commit crimes, but only for the hell of it; they hate,

139 Cf. Ehrenberg 1994, 20.
140 Cf. Malabou 2004, 49.
141 Ehrenberg (2004) in Malabou 2004, 49.
142 Quoted from Malabou 2004, 49.
143 Cf. Malabou 2004, 49.
144 Ehrenberg (2004) in Malabou 2004, 49.

not understanding why they hate; they are loved or abused or depressed, and don't know why (…). Randomness rules"[145]. The absence of clear order, stability and external boundaries together with expectations of limitless authenticity and flexibility seems to evoke a certain sense of insecurity. In this way, the paradigm shifts from a subordinate to a modern society result in a new situation that "creates a certain vulnerability, a new precariousness, a new fragility."[146]

In these terms, depression might be understood as endowing the individual with a kind of shelter. A form of guardedness that depression embodies seems to become necessary, considering that everyone is required to fulfill a constant demand "of self-mastery, affective and psychical suppleness" and "to adapt to an "unstable, provisional world in flux."[147] Mood Medications, in turn, have the purpose of reducing a precariousness by "targeting the neuronal networks involved in initiative, stimulation, dynamism, and well-being. Medications should give back the appetite for mobility, the capacity to rid oneself of rigidity and of fixity in one's identity."[148] In this way, "to heal means to reintegrate, to restore flexibility."[149]

Overall, it becomes clear that depression amounts to an impairment in terms of a lack of flexibility, a failure to adapt – also in terms of a decrease in neuronal plasticity as has been argued in the previous section. In this regard, it can be understood how both, the sociocultural environment as well as the individual and his physical constitution, play equally important roles in the development of depression: the context which challenges the individual's ability to adapt more and more, and the individual's neuronal flexibility which decreases as a result of the environmental exhaustion, which in turn leads to the failure to adapt. In effect, a vicious circle.[150]

That depression indeed comes down to a reduction in flexibility is also supported by the differences in prevalence between younger and older people. It is well known in neuroscience that the plasticity of the brain decreases with age. Statistic measurements show that while 4,3 percent of 15- 19-years old women suffered from depression in 2006, 18,4 percent of the 55- 60-year old women were afflicted with the illness. Even in men, who suffer much less from depression than women, the increase in prevalence with age is conspicuous, from 1,4 percent in 15-19 year olds to 7,5 percent in 55-60 year olds.[151]

The connection between the individual becoming depressed because he lacks the flexibility

145 Fanny Howe „The Plot sickens" (1961) in Wurtzel 1994, 301.
146 Cf. Malabou 2004, 50.
147 Ehrenberg (2004) in Malabou 2004, 50.
148 Cf. Malabou 2004, 52.
149 Cf. Malabou 2004, 51.
150 Cf. Malabou 2004, 47.
151 See Gesundheitsreport der TK 2008, 25. (Health report released by the TK Germany).

required in the current social and economic organization and a reduction in neuronal plasticity, that is, the cells' ability to be shaped or formed in new ways – is no coincidence. The French philosopher Catherine Malabou makes the interesting observation that the new model of the brain "co-occurs with a radical modification of the economic and social environment."[152] The similarities between the way in which the brain's workings are described by current neuroscience and the norms of neoliberal societies meet also on a more general level in terms of flexibility, adaptability, non-hierarchical structural organization, "mutual support (reparation), freedom of choice (one somehow constructs one's brain), a crossing point between the public and the private (the interaction of the outside and the inside), belonging to many spheres, mobility, openness, availability, autonomy, absence of hierarchy between the network elements, and equality of function."[153]

Is this surprisingly "neo-liberal" brain imposing its model on our social and economic organization or is it that the social and economic changes of the last years affect the way that the brain is viewed?[154] What one can say at the very least is that the recent scientific discourse on brain plasticity contributes to the creation of a new conception of government and socioeconomic structures by attributing an exaggeratedly important role to the absence of a center, to a de-centralized conception of control, "a too rigid prominence to flexibility".[155] In this way, neuroscience not only reflects the way that the society in which it is embedded currently functions, but also implicitly creates the impression that it is normal to be flexible. In effect, what Malabou here detects is the danger of neuroscience becoming ideological: by uncritically reflecting current sociopolitical discourse and by employing the very terms in which the new capitalism defines its model subject.

However, as Malabou nicely demonstrates, flexibility is not the same as plasticity. "To be flexible is to receive form, to be able to fold oneself to take the fold, not to give it." In this regard, "what flexibility lacks is the resource of giving form, the power to create, … the power to style. Flexibility is plasticity minus its genius."[156] Thus, for Malabou, plasticity does not at all mean what flexibility has come to mean in neoliberal contexts, i.e., to adapt to everything, to endure everything. Rather, plasticity, if taken in its full meaning, refers to the potential one has, the possibilities one can realize in one's life. Viewed in this way, the insistence on the full meaning of plasticity against its narrow interpretations in much of the current debate might even unleash some

152 See Jeannerod, M. foreword in Malabou 2004, xii.
153 Cf. Malabou 2004, 53.
154 C.f. Jeannerod, M.foreword in Malabou 2004, xii.
155 Cf. Malabou 2004, 53.
156 Quoted from Malabou 2004, 12.

kind of revolutionary potential: "Securing a true plasticity of the brain means insisting on knowing what it can do and not simply on what it can tolerate."[157]

The reason for this excursion to Malabou's account of the political deep structure of the discourse surrounding brain plasticity is the need to illustrate how depression, which could well be, as we have seen, an illness of neural plasticity, today is partly created, sustained and molded by the demands placed upon the contemporary individual, particularly in the present-day work environment (but not only there). This means that depression research has to include a sociological or cultural studies perspective in order to get at these often diffuse influences. In addition, Malabou has demonstrated that this also offers the chance to subject the discourse of neuroscience to a kind of meta-critique that is, in part, politically inspired. Could it be that, implicitly, neuroscience is simply emulating some of the socio-political mainstream discourses of our time with the result of thereby stabilizing a certain conception of the individual (by declaring it to be "natural")? Unfortunately, this interesting perspective cannot be pursued further in this thesis.[158]

The message here has been that depression can in part be caused by certain social pressures and sustained by a broad mentality surrounding them, in particular when there are strong commercial interests in having many people believe in the pathological nature of their feeling unwell and seeking for quick medical fixes for their conditions. But again, it is extremely hard, maybe even impossible, to pin down precise causal relations. Much more analysis is needed.

5. Conclusion

Altogether, depression must be understood as a multifactorial, complex mental illness that cannot be reduced to one factor, be it genetic make-up, a devastating life event or a chemical imbalance in the brain – not even to changes in social and economic conditions. This poses the challenge of bringing about a science of depression that integrates different levels of explanation. Such an endeavor may start with incorporating a phenomenological perspective into neuroscientific enterprises and into diagnostic matters in order to reveal what is at the core of the experience of depression. Furthermore, a thorough account of depression should begin to consider formulating more

157 Quoted from Malabou 2004, 13.

158 This is a theme in the recently created initiative called "Critical Neuroscience" (see Choudhury, Nagel, Slaby 2009 and www.critical-neuroscience.org)

distinctions between normal reactions to environmental stressors and depression, something that requires acknowledging the situational contexts in which the person is embedded. Moreover, a new personalized treatment, which neuroscientists envision on the brain-level, needs also to be developed on a more general level, incorporating the person's situatedness by means of providing different forms of therapy suited for specific cases.

However, another task in developing a new perspective on depression is to acknowledge that depression has developed from a personal into a social problem. The high increase of depression rates is particularly due to milder forms of the illness, with a suffering characterized mostly as feeling of inadequateness, absence of meaning, loss of excitement. However, in contrast to clinical depression, many people with mild depression still have the hope that they can overcome these tempers – for example, by means of a daily dose fluoxetine. However, these collective low spirits and bad moods that lurk around in many societies today cannot be treated by drugs, because they are, crucially, also a result of the new sociocultural and economic structures which demand limitless flexibility, adaptation to ever new surroundings, high spirits and energy at all times.

As has been shown, some antidepressants are able to restore a lack of plasticity in the brain that reduces the depressed person's ability to adapt to environmental stressors, but what the medications cannot do is solve or remove the problems that caused the depression in the first place. In this regard, the fact that a lack of plasticity in a depressive's brain results in a failure to adapt to the demanded flexibility today must not be understood as a justification for expecting people to submit to the current world order in order to function properly or to avoid social exclusion. Rather, considering the concept of plasticity in a careful way, which implies the capability of evolvement and not merely submission, of creativity in addition to assimilation, it should be understood as a potential means of protest against the current sociocultural and economic situation and as capable of bringing about relevant changes. At the same time, a change in the current social and economic structure that contributes to depression should not be confused for a demand to step back. After all, even if modern depression is often the unpleasant by-product of our newly gained freedom, we are certainly not for that reason wishing to return to the sociocultural conditions of earlier pre-individualist times.

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