Neurobiology of Depression

Depression can affect every aspect of life. A patient undergoing a major depressive episode who receives treatment with any antidepressant will often experience symptomatic improvement. However, oftentimes treatment does not reach the goal of remission (complete cessation of all symptoms of depression) until several different pharmacotherapies have been utilized, possibly in combination. Understanding the neurobiology underlying depressive symptomatology may allow clinicians the opportunity to treat the symptoms specifically, based upon brain mechanisms and the interplay among genes, circuits and symptoms. This chapter focuses on the neurobiology of depression, and offers a review of the three monoamines hypothetically linked not only to the symptoms of a major depressive episode, but also to the treatment of those symptoms.
FIGURE 1.1. Mood charts illustrate a spectrum of syndromal states upon which a patient’s mood can be charted over time. Mood monitoring can be conducted intermittently in a clinical setting or continuously via patient self-report in the form of a mood diary. Tracking the course of illness can greatly assist in identifying disease states, diagnosing accurately, and assessing treatment response.
Patients with a depressive temperament may be regularly sad or apathetic but do not have a sufficient degree or number of symptoms to qualify for the diagnosis of dysthymia or a major depressive episode. Individuals with depressive temperament may be more at risk for a future mood disorder.

Dysthymia is a less severe form of depression than major depressive disorder (MDD), but is long-lasting and generally unrelenting for two years or more.
**Identifying Mood Disorders:**

**Depression and Double Depression**

**FIGURE 1.4.** Major depressive disorder (MDD) is characterized by single or recurrent major depressive episode(s); most people with MDD will experience recurrent episodes. This is the most common mood disorder.

**FIGURE 1.5.** Double depression is characterized by unremitting dysthymia interrupted by major depressive episode(s). Between episodes there is poor inter-episode recovery.
Although both patients in this mood chart are presenting with identical current symptoms of a major depressive episode over the past several days (A), patient 1 has unipolar depression whereas patient 2 has bipolar depression. So, what is the difference? The pattern of past symptoms (B) is quite different; for example, patient 1 has experienced a prior depressive episode whereas patient 2 has experienced a prior hypomanic episode.

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Are Mood Disorders Progressive?

FIGURE 1.7. Is major depressive disorder (MDD) progressive? Some believe that un(der)treated unipolar depression can develop into a bipolar spectrum condition, eventually to the point of treatment resistance.
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According to this hypothesis, depression caused by deficiency of 5HT, NE and/or DA is theoretically returned to a normal state by antidepressants that increase the synaptic action of monoamines, such as those that block presynaptic monoamine transporters (also called reuptake pumps) as shown here.

**FIGURE 1.10.** According to this hypothesis, depression caused by deficiency of 5HT, NE and/or DA is theoretically returned to a normal state by antidepressants that increase the synaptic action of monoamines, such as those that block presynaptic monoamine transporters (also called reuptake pumps) as shown here.
FIGURE 1.11. The monoamine receptor hypothesis builds on the classic monoamine hypothesis of depression by suggesting that decreased activity of monoamine neurotransmitters (5HT, NE, DA) causes upregulation of postsynaptic monoamine receptors, leading to depression.