Chapter 13: Mental Illness

# Brain scene investigation: Cautionary tales in psychiatry: The questionable creation of Sheri Storm’s multiple personalities

Under the influence of drugs and the personal whims of a psychiatrist, Sheri Storm was led to believe she had multiple personalities and repressed memories of ritualistic abuse. Evidence-based therapies are needed to ensure that all patients receive treatment that is based on scientific data, rather than opinion.

# The challenge of classifying and treating mental illness

## The meandering search for the roots of mental illness

As early as the 5th century BC, the brain was suggested as the source of many (what we now call) mental illnesses. As time has gone on and technology has progressed, scientists are increasingly focused on biological causes/correlates of the symptoms of mental illnesses, rather than looking for causes in unconscious desires or cosmic events.

## Early biological therapies for mental illnesses

Electroconvulsive therapy was an early treatment for mental illness (e.g., depression), along with sedative barbiturates. Later treatments primarily focused on psychopharmacologicdrugs. Brain surgery for mental illness has ancient roots, but lobotomies were a popular option in the mid-20th century. Moniz received a Nobel Prize related to his frontal lobotomy work, despite a lack of evidence for positive results, and data showing negative effects of frontal lobotomies.

## Contemporary mental health classifications

The ICD encompasses all medical disorders (has a chapter for mental disorders); the DSM is devoted exclusively to mental disorders. The current DSM lists ~400 disorders, although empirical support is lacking for various categories/ subtypes of certain disorders. Lack of biomarkers for many disorders, and the finding that distinct disorders seem to have similar neurobiological underpinnings makes classification difficult even in principle.

# Schizophrenia

Mental fragmentation and conflict. *Positive* symptoms: delusions, hallucinations; *negative* symptoms: diminished emotions/thought processes

## Causes

Neurochemical candidates. Chlorpromazine was accidentally discovered to have some effect in treating schizophrenia. Excess dopamine was initially suggested as a cause, but further data was against this view. Acetylcholine and glutamate have also been implicated.

Neuroanatomical candidates. Smaller: temporal and frontal lobes, thalamus volume; Larger ventricles; loss of gray matter during adolescence.

Genetic and environmental factors. Identical twins don’t necessarily both have schizophrenia (50% concordance), or show the same disorder time course if they both have schizophrenia. Growing up in an urban environment has been linked with schizophrenia, perhaps due to too high or too low levels of social cohesion/support.

## Treatment strategies

Pharmacological approach is most common. First-generation anti-psychotics were about 20% effective; second-generation drugs were effective for some patients that did not respond to first generation drugs, but they too have side effects. Cognitive remediation and compensatory therapies are available for patients that do not respond to pharmacological approaches or don’t want the side effects. These non-pharmacological approaches may take longer to initially take effect, but have fewer side effects and work on neural plasticity principles rather than specifically targeting a neurotransmitter system.

# Depression

About 17% of the US will be diagnosed as depressed at some point in their life.

## Causes

Neurochemical candidates. The monoamine hypothesis of depression suggests that depression symptoms are caused by low levels of serotonin and norepinephrine; evidence is mixed however, though many treatments focus on serotonin. Cortisol may also play a role, linked with chronic stress. Low levels of BDNF have also been implicated, which may be exacerbated by increased stress.

### Neuroanatomical candidates. Anatomical candidates linked with symptoms. Lank of motivation for pleasurable activities: nucleus accumbens. Depressed individuals may not see link between effort and pleasurable outcome. Lack of concentration/cognitive difficulties: PFC. Chronic stress may also affect hippocampal volume/function in depressed individuals.

The network hypothesis. Depression may result from disrupted activity-dependent neuroplasticity. Antidepressants work by facilitating neuroplasticity and encouraging neurogenesis. Difficult to assess this hypothesis because directly measuring changes to neural networks in humans is not usually possible.

## Treatment strategies

ECT. ECT is still used for patients that do not respond to other approaches. Shows some short-term effectiveness, side effects include memory loss. rTMS is a more gentile alternative that does not induce seizures but appears less effective than ECT.

Pharmacotherapy. MAOIs, tricyclics, and SSRIs are the most common options. The difficulty of true double-blind studies (patients/clinicians may now who is taking the drug based on the presence of drug-specific side effects) has rendered the clinical data hard to interpret.

Cognitive and behavioral therapies. The existence of placebo and nocebo effects is *prima facie* evidence for the potential of cognitive interventions on depression. Cognitive therapy typically focuses on ridding the destructive beliefs of the patient. Effects are typically longer lasting that drug therapies; combined approaches are possible. Behavioral therapies focus on how the patient interacts with the external environment. The success of behavioral therapies may be due to the patients learning the contingency between their behavior and positive outcomes (effort-based reward model).

Emerging therapeutic approaches. Deep brain stimulation of the subcallosal cingulate gyrus and lateral habenula have shown promise for depression treatment.

## Bipolar disorder

Patients with bipolar disorder have the lows of depression but also manic periods where they often engage in dangerous/risky behaviors. Lithium is the most common treatment for bipolar disorder, likely affects serotonin. Effective in 70-80% of patients.

# Anxiety Disorders and Other Related Disorders

Anxiety is a feature of life, but out of control anxiety can cause severe disruptions.

## Diagnoses of Anxiety Disorders and Other Related Disorders

*State* anxiety reflects the immediate situation; *trait* anxietyrepresents a person’s more permanent tendencies to experience/express anxiety.

## Common Causes

Anxiety disorders are triggered by excessive levels of anxiety. Amygdala response to an anxiety-provoking stimulus is greater in anxious patients; dysfunction of the GABA system (suppression of inhibition) has been implicated.

Stress response is mediated by glucocorticoid receptors (GR) and mineralocorticoid receptors (MR); these systems may be disrupted by chronic or severe stress, leading to improper responses to future stressors.

Genetic predispositions and stressful life events interact to produce responses that are vulnerable to the emergence of an anxiety disorder.

Environmental contexts can also prompt uncertainty/anxiety and trigger obsessions characteristic of OCD.

## Treatment Strategies

SSRIs are a common treatment, but they are not fast acting. Surgery is an option for extreme cases (bilateral lesions to the lower medial OFC and the anterior cingulate bundle area). Behavioral approaches (e.g., exposure therapy) have also shown success for treating anxiety disorders. fMRI data confirm differences in brain activity in PFC after exposure therapy.

# Context matters: Virtual reality for spider phobias

Virtual reality can create realistic, safe environments for exposure therapy. The environmental is also exactly controlled, allowing the patient to experience the phobic stimulus in a variety of contexts, which has been shown to aid in recovery.

## Evolutionary roots

Compulsive behavior has nonhuman analogs (e.g., excessive grooming) and shows similarities across human cultures, such as obsession about germs. Some obsessions are triggered by specific events as with Howie Mandel and the sand flies.

# Laboratory explorations: Schizophrenia and prepulse inhibition

Individuals with schizophrenia do not show prepulse inhibition to the degree of healthy controls. An animal model for this sensory gating deficit implicates dopamine deficiency as a likely cause. Lesions to several areas (temporal and prefrontal cortices and the ventral tegmental area) also reduce prepulse inhibition, producing behavior analogous to that seen in patients with schizophrenia.