Depression: historical aspects

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Abstract

Depression, a relatively modern term first introduced in 19th century replacing melancholy, was first described as far back as 2000 BCE in ancient Mesopotamia. The understanding of the causes and treatment of depression has evolved over the centuries with Europeans in the Middle Ages regarding it as a condition caused by the spirits that needed exorcisms by priests and in worst cases the death of the sufferer. Whilst more humane understanding and treatments were practiced in the rising Islamic civilisation during the Middle Ages, it was not until the 20th century that knowledge gained from medical science began to be applied to its understanding and treatment, with the latter remaining somewhat limited until the 1960s with the introduction of tricyclic antidepressants. Depression is a complex disorder with biological, psychological and social factors contributing to its development; it is therefore not surprising that multiple methods incorporating biological and psychosocial methods are likely to be needed for an effective treatment. The complexity of depression has not yet allowed full understanding of its causes and pathophysiology, and hence not resulted in totally effective treatment.

In this brief article, I will chart the history of depression, its proposed causes and treatment, from ancient times to the modern era.

Ancient times to the Middle Ages

The term depression was derived from the Latin verb deprimere, "to press down" and it is interesting to note that it only came in to use in the 19th century, replacing the older term melancholia (1). Whilst there is a likelihood of prehistoric human suffering from depression, the earliest written account of depression (then known as melancholia) appeared in 2000 BCE in ancient Mesopotamia. By 500 BCE further documentations of melancholia along with other mental illnesses appeared in Greek, Roman, Babylonian, Chinese, and Egyptian civilizations.

The Greek physician Hippocrates, in 400 BCE, proposed that personality traits and mental illnesses were related to body fluids, called humours, and whether they were in balance. He further classified mental illnesses into mania, melancholia (depression), and phrenitis (brain fever).

Hippocrates attributed melancholia to excessive black bile in the spleen. His ideas of treating melancholia included bloodletting, bathing, exercise, and dieting.

From the early to mid Christian period (400 - 1000 CE) depression along with other mental illnesses were seen as spiritual rather then physical conditions in which afflicted individuals were considered to be possessed by the devil, demons, or witches, having capacity to infect others. Those afflicted would have exorcisms carried out by priests, whilst in extreme cases they were even drowned or burned by the mobs.

A somewhat more humane description and management of depression and other mental illnesses began to be practiced in the rising Islamic civilisation. In 900 CE, Rhazes, and other Islamic physicians, described the brain as the root of mental illness and melancholia. Indeed, the treatments reflected enlightenment and included hydrotherapy and various forms of behaviour therapy. The great Islamic physician Avicenna in the 11th century described melancholia as a depressive type of mood disorder with the sufferer experiencing phobias (2).

In Europe, witch-hunts and executions of the sufferers of mental illnesses (including depression) continued well in to the 17th century. However, a number of enlightened physicians, influenced by Hippocrates, began to believe that mental illnesses were the result of natural causes.

Robert Burton in 1621 published the Anatomy of Melancholy, in which psychological and social causes

of depression were described. The suggested treatments included dietary measures, exercise, distraction, travel, cleanses, bloodletting, herbal remedies, marriage and music therapy.

Late into the 18th century, aggression was suggested as a cause and sufferers were encouraged to exercise, use music, take dietary measures and to talk about their problems with friends, family or a physician.

From the Dark Ages to the Age of Enlightenment

French psychiatrists, Falret and Baillarger (1854) independently described the alternation between melancholia and mania (later known as manic-depressive disorder or by its more modern name bipolar affective disorder) (3). However, it is argued that Falret and Baillarger may not have been the first to describe bipolar affective disorder, since earlier descriptions of this were suggested in the writings of Arateus of Cappadocia (an ancient Greek physician).

During the 1800s, a wide variety of "treatments" were given to depressed individuals, which included, being immersed in water (keeping under water for as long as possible without drowning), early forms of electroshock therapy, special diets, enemas and induced vomiting.

From the Age of Enlightenment to modern times

In 1895, the famous German psychiatrist Emil Krapelin distinguished depression from schizophrenia and suggested medical intervention to treat melancholy. Around the same period, psychodynamic theory and psychoanalysis became popular as treatments for depression.

The Austrian neurologist, Sigmund Freud (1917), classified melancholia into two categories of loss: real or symbolic. He suggested loss weakened the ego, resulting in self-destructive behaviours, and encouraged psychoanalysis (the talking cure) to resolve unconscious conflicts.

German psychiatrist Kurt Schneider introduced the terms "endogenous depression" and "reactive depression" (4). However, these terms were later abandoned as the complex nature of depression began to be further understood.

Effective medical treatments for depression, particularly that of the severe type, remained elusive well into the late 19th and early 20th centuries. This, at times, led to some drastic measures such as surgical destruction of the frontal part of the brain (lobotomy), which unfortunately had many negative effects including personality changes, poor decision making and, on occasion, death.

The 1930s witnessed the introduction of electroshock therapy (without anaesthesia), which leads to induction of a seizure lasting from 20 to 90 seconds, whilst in the 1940s lithium was introduced by an Australian psychiatrist, J.F.J. Cade, to treat psychosis and the manic stages of bipolar disorder (5).

From having no available antidepressant medications prior to the 1950s, a major leap into the treatment of depression took place in 1952 when an anti-tuberculosis drug isoniazid (a monoamine oxidase inhibitor (MAOI)) was used to treat depression following the discovery of its mood lifting effects on patients with tuberculosis. Around the same period, whilst searching for antipsychotics, imipramine (the first tricyclic antidepressant) was discovered and later marketed as an antidepressant in the 1960s.

Building upon knowledge gained from tricyclic antidepressants, Russian scientists Izyaslav Laptin and Gregory Oxenkrug noted mood elevation when the brain's serotonergic activity was supplemented by tryptophan. They were the first to propose an association between serotonin and its antidepressant effects (6). In 1982 marketing of the first selective serotonin reuptake inhibitor (SSRI) pheniramine (zimelidine) took place. However, it was withdrawn a few years later due to concerns about the development of Guillain-Barré syndrome in some of the treated patients. It was not long (1988) before the world's most famous antidepressant fluoxetine (Prozac) was launched by Eli Lilly. Subsequently, a number of SSRIs were developed and were marketed as more selective and therefore more effective, safer, and better tolerated than the older tricyclic antidepressants. They were certainly much less toxic in overdose than most tricyclic antidepressants. However, they had their own side effect profile (such as gastric and sexual problems) and unfortunately, as much as 30 - 40% of depressed individuals failed to respond.

The next two decades witnessed the introduction of more antidepressants such as bupropion (an atypical antidepressant), moclobemide (a reversible monoamine oxidase inhibitor (RIMA)), venlafaxine (a seroto-

nin-norepinephrine reuptake inhibitor (SNRI)), mirtazapine (a tetracyclic) and vortioxetine (sometimes described as "multi-modal" because of its effects on several serotonin receptors along with having receptor affinity to dopamine and norepinephrine transporters).

However, unfortunately none of the post-SSRI antidepressants can be considered as a major advance in the treatment of depression with the possible exception of ketamine. Ketamine was originally developed in the 1960s as a dissociative anaesthetic agent. Its antidepressant effects were first reported in 2000 by Berman and colleagues (7). Remarkably, ketamine is not only fast acting (having antidepressant effects within hours) but has also been found to be effective in treatment-resistant cases (8). The antidepressant mode of action of ketamine is still being elucidated. It has been suggested that this might be through its potent NMDA receptor antagonism (9).

It is clear that current antidepressants have limitations with regard to their adverse effects and efficacy. In parallel, further development of various talking therapies (e.g. cognitive behaviour therapy, dialectical behaviour therapy) and their delivery methods (individual, group, family, and internet) continues.

As for the physical treatments, electroconvulsive therapy (ECT) became more humane with the introduction of anaesthesia. However, with stigma being constantly attached to ECT, various forms of neurostimulation began to be developed. These included deep brain stimulation (DBS) in the 1950s, repetitive transcranial stimulation (rTMS) in the 1990s and transcranial direct current stimulation (tDCS) in the 1960s - 70s. Other forms of stimulation include vagus nerve stimulation (VNS) (10).

With some evidence linking dysfunction in the innate immune system with depression, the possible role of anti-inflammatory drugs as antidepressants is increasingly being explored, opening a new chapter in antidepressant medication (11).

In conclusion, our ideas about the description, causes and treatment of depression since the ancient times are continuing to evolve. Whilst, our understanding of the causes and pathophysiological basis of depression and its treatment have come a long way in the light of modern medicine, we still do not have a full understanding of depression or how to treat it fully. The quest for a complete understanding and totally effective treatment for depression continue.

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