

Psychotic depression

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Psychotic depression, also known as **depressive psychosis**, is a major depressive episode that is accompanied by psychotic symptoms.^[1] It can occur in the context of bipolar disorder or major depressive disorder.^[1] It can be difficult to distinguish from schizoaffective disorder; that disorder requires the presence of psychotic symptoms for at least two weeks without any mood symptoms present.^[1] Diagnosis using the DSM-IV involves meeting the criteria for a major depressive episode, along with the criteria for the "psychotic features" specifier.^[2]

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Symptoms

Individuals with psychotic depression experience the symptoms of a major depressive episode, along with one or more psychotic symptoms, including delusions and/or hallucinations.^[1] Delusions can be classified as mood congruent or incongruent, depending on whether or not the nature of the delusions is in keeping with the individual's mood state.^[1] Common themes of mood congruent delusions include guilt, punishment, personal inadequacy, or disease.^[3] Half of patients experience more than one kind of delusion.^[1] Delusions occur without hallucinations in about one-half to two-thirds of patients with psychotic depression.^[1] Hallucinations can be auditory, visual, olfactory (smell), or haptic (touch).^[1] Severe anhedonia, loss of interest, and psychomotor retardation are typically present.^[4]

Cause

Psychotic symptoms tend to develop after an individual has already had several episodes of depression without psychosis.^[1] However, once psychotic symptoms have emerged, they tend to reappear with each future depressive episode.^[1] The prognosis for psychotic depression is not considered to be as poor as for

schizoaffective disorders or primary psychotic disorders.^[1] Still, those who have experienced a depressive episode with psychotic features have an increased risk of relapse and suicide compared to those without psychotic features, and they tend to have more pronounced sleep abnormalities.^{[1][3]}

The families of those who have experienced psychotic depression are at increased risk for both psychotic depression and schizophrenia.^[1]

Most patients with psychotic depression report having an initial episode between the ages of 20 and 40. Over a lifetime, it appears that patients with psychotic depression experience an average of 4 to 9 episodes. As with other depressive episodes, psychotic depression tends to be episodic, with symptoms lasting for a certain amount of time and then subsiding. While psychotic depression can be chronic (lasting more than 2 years), most depressive episodes last less than 24 months. Unlike psychotic disorders such as schizophrenia and schizoaffective disorder, patients with psychotic depression generally function well between episodes, both socially and professionally.

Differential diagnosis

Psychotic symptoms are often missed in psychotic depression, either because patients do not think their symptoms are abnormal or they attempt to conceal their symptoms from others.^[1] On the other hand, psychotic depression may be confused with schizoaffective disorder.^[1] Due to overlapping symptoms, differential diagnosis includes also dissociative disorders.^[5]

Pathophysiology

There are a number of biological features that may distinguish psychotic depression from non-psychotic depression. The most significant difference may be the presence of an abnormality in the hypothalamic pituitary adrenal axis (HPA) axis. The HPA axis appears to be dysregulated in psychotic depression, with dexamethasone suppression tests demonstrating higher levels of cortisol following dexamethasone administration (i.e. lower cortisol suppression).^[1] Those with psychotic depression also have higher ventricular-brain ratios than those with non-psychotic depression.^[1]

Treatment

Several treatment guidelines recommend either the combination of a second-generation antidepressant and atypical antipsychotic or tricyclic antidepressant monotherapy or electroconvulsive therapy (ECT) as the first-line treatment for unipolar psychotic depression.^{[6][7][8][9]}

Pharmaceutical treatments can include tricyclic antidepressants, atypical antipsychotics, or a combination of an antidepressant from the newer, more well tolerated SSRI or SNRI categories and an atypical antipsychotic.^[7] Olanzapine may be an effective monotherapy in psychotic depression,^[10] although there is evidence that it is ineffective for depressive symptoms as a monotherapy;^{[7][11]} and olanzapine/fluoxetine is more effective.^{[7][11]} Quetiapine monotherapy may be particularly helpful in psychotic depression since it has both antidepressant and antipsychotic effects and a reasonable tolerability profile compared to other atypical antipsychotics.^{[12][13][14]} The current drug-based treatments of psychotic depression are reasonably

effective but can cause side effects, such as nausea, headaches, dizziness, and weight gain.^[15] Tricyclic antidepressants are particularly dangerous in overdose due to their potential to cause potentially-fatal cardiac arrhythmias.^[7]

In the context of psychotic depression, the following are the most well-studied antidepressant/antipsychotic combinations

First-generation

- Amitriptyline/perphenazine^[16]
- Amitriptyline/haloperidol^[17]

Second-generation

- Venlafaxine/quetiapine?^[18]
- Olanzapine/fluoxetine^[11]
- Olanzapine/sertraline^[19]

In modern practice of ECT a therapeutic clonic seizure is induced by electrical current via electrodes placed on an anaesthetised, unconscious patient. Despite much research the exact mechanism of action of ECT is still not known.^[20] ECT carries the risk of temporary cognitive deficits (e.g., confusion, memory problems), in addition to the burden of repeated exposures to general anesthesia.^[21]

Research

Among the newer experimental treatments is the study of glucocorticoid antagonists, including mifepristone.^[22] These strategies may treat the underlying pathophysiology of psychotic depression by correcting an overactive HPA axis. By competitively blocking certain neuro-receptors, these medications render cortisol less able to directly act on the brain.

Mifepristone showed initial promise in psychotic major depression, a form of depression that is difficult to treat; however, a Phase III clinical trial was terminated early due to lack of efficacy.^[23]

Transcranial magnetic stimulation (TMS) is being investigated as an alternative to ECT in the treatment of depression. TMS involves the administration of a focused electromagnetic field to the cortex to stimulate specific nerve pathways.

Research has shown that psychotic depression differs from non-psychotic depression in a number of ways:^[24] potential precipitating factors,^{[25][26][27]} underlying biology,^{[28][29][30][31]} symptomatology beyond psychotic symptoms,^{[32][33]} long-term prognosis,^{[34][35]} and responsiveness to psychopharmacological treatment and ECT.^[36]

Prognosis

The long-term outcome for psychotic depression is generally poorer than for non-psychotic depression.^[7]

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