

Causes of Treatment-Resistant Depression

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Depression is one of the most common mental disorders, with an estimated 5% of the global population being affected. It's also one of the leading causes of disability in the world. Treatments for depression include therapy, medication, and may also include electroconvulsive therapy or transcranial magnetic stimulation.

However, these treatments alone aren't sufficient to improve depressive symptoms in certain individuals. When this occurs, it's known as treatment-resistant depression. Definitions for treatment-resistant depression vary, but it usually occurs when at least two treatment attempts do not bring about effective symptom relief.

The causes behind treatment-resistant depression aren't clear but current studies have shown potential risk factors. These include brain and body risk factors, family history and genetics, and lifestyle factors.

Brain & Body Risk Factors

Let's take a look at some of the factors that may precede treatment-resistant depression.

Other Underlying Health Issues

Depression can be comorbid with certain physical conditions. These include heart disease, gastrointestinal problems, and hypertension. Treatment-resistant depression has also been strongly associated with chronic non-cancer pain conditions.

Chronic health issues and treatment-resistant depression can lead to a chicken-and-egg problem, in that it's unclear how much one affects the other.

Mental health conditions such as eating disorders, substance abuse, post-traumatic stress disorder, and personality disorders can also occur alongside depression.

Some studies have even found treatment-resistant depression to be a risk factor for developing other mental health conditions. Researchers in Sweden examined 121,699 patients between the ages of 18 and 69 with a diagnosis of major depressive disorder.

Of these individuals, 13% had treatment-resistant depression and these patients were found to be at a greater risk for developing substance use disorders than those without treatment-resistant major depressive disorder.

Metabolic Abnormalities

Clinical investigations have also determined that nutritional deficiencies and metabolic disorders can play a role in treatment-resistant depression. One study examined the blood, urine, and cerebrospinal fluid of 33 participants with treatment-resistant depression. It found that 21 of the participants had metabolic abnormalities, with cerebral folate (vitamin B9) deficiency being the most common.

There have also been studies that link major depressive disorder to vitamin D deficiency. However, a clear association between vitamin D deficiency and treatment-resistant depression has not been identified.

Family History & Genetics

It is well established that individuals with a family history of depression have a higher likelihood of developing clinical depression themselves over the course of their lifetime. Studies have made this connection for clinical depression as a whole, but there has not been much examination of the family history risk factors for treatment-resistant depression specifically.

Research studying the link between genetic predisposition and treatment-resistant depression is still in its infancy. However, findings have identified certain biomarkers that put individuals at a higher risk of treatment-resistant depression. Further empirical data is required to determine which treatments are appropriate for those with these biomarkers.

Lifestyle Risk Factors

Some lifestyle factors can put you at risk for treatment-resistant depression.

Misdiagnosis

Unfortunately, misdiagnosis is a common occurrence with mental health conditions. This can be due to symptoms overlapping with several possible diagnoses, which occurs frequently with mental disorders.

One study of 309 patients with severe psychiatric disorders found that nearly 40% were misdiagnosed.

Furthermore, individuals with bipolar disorder are often misdiagnosed with a depressive disorder. In a study of 466 patients in psychiatric units diagnosed with major depressive disorder, 57% reported hypomanic symptoms when screened, suggestive of a bipolar diagnosis.

Problems With Medication

Antidepressants can take up to six weeks to work. Individuals often stop taking a drug too early, before the medication has time to take full effect. Some people may also skip doses or stop medications prematurely due to unpleasant side effects.

Furthermore, antidepressants may interact with drugs taken for other physical or mental health conditions. One study that examined over 14,000 inpatient participants found that drug interactions occurred frequently, with higher chances of adverse reactions with each additional drug taken.

Antidepressants can also have different effects from person to person. What provides significant relief for one may be insufficient for another, so it's important to try different medications and different doses until you figure out what works best.

Diagnosis

Treatment-resistant depression is not included in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). However, many mental health professionals consider this diagnosis when there have been at least two failed treatment attempts.

It's important to speak to your physician or psychiatrist if current treatment methods are not providing you relief. Your doctor can perform a more thorough evaluation to rule out other physical or mental health conditions, and re-evaluate your treatment regimen.

Treatment

Approximately 20% to 40% of individuals with major depression do not exhibit an adequate clinical improvement with antidepressants.

How Your Doctor Determines If Treatment Has Failed

Your doctor will consider several factors before considering a medication-based treatment method a failure. These include:

- the level of compliance with the current treatment regimen
- the amount of time you took the medication
- the dosage

Your Doctor May Recommend a Different Medication

If your doctor feels a particular medication is not adequately helping your depression, they may doctor may prescribe a different antidepressant or add an additional type of medication to augment your current regimen.

Cognitive-Behavioral Therapy

Your doctor may also refer you to a psychotherapist if you aren't already seeing one. Cognitive-behavioral therapy has been shown to be beneficial to add to medication for treatment-resistant depression.

Other Treatment Types

Additional treatments for treatment-resistant depression include vagus nerve stimulation (VNS), electroconvulsive therapy (ECT), and ketamine.

Spravato Nasal Spray (FDA-approved)

The FDA has also approved Spravato (esketamine), a nasal spray that can help treatment-resistant depression. Each treatment approach comes with its own risks and benefits, so it's important to speak to your healthcare team to see which is best for you.

How to Cope With Treatment-Resistant Depression

Dealing with treatment-resistant depression can be challenging. If you are dealing with treatment-resistant depression, here's what you can do to cope:

- **Prioritize self-care.** Do your best to eat healthily, get enough sleep, and exercise regularly. Each of these actions can help reduce some of your depressive symptoms.
- **Manage your stress.** Life will inevitably have ongoing pressures, but it's essential to engage in stress reduction techniques to help manage your stress. These can include journaling, meditation, or yoga.
- **Ditch drugs and alcohol.** These substances can make your symptoms worse, more difficult to treat and may interact with the current medications you are taking.
- **Adhere to your treatment plan.** Both therapy and medications can take time before you notice improvements. It's important to stick your treatment plan so it has the chance to take full effect.

15 Sources

Verywell Mind uses only high-quality sources, including peer-reviewed studies, to support the facts within our articles. Read our editorial process to learn more about how we fact-check and keep our content accurate, reliable, and trustworthy.

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