Psychosis Questions & Answers

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Not to be confused with Psychopathy. For other uses, see Psychosis (disambiguation)

Psychosis refers to an abnormal condition of the mind, and is a generic psychiatric term for a mental state often described as involving a "loss of contact with reality". People with psychosis are described as *psychotic*. People experiencing psychosis may exhibit some personality changes and thought disorder. Depending on its severity, this may be accompanied by unusual or bizarre behavior, as well as difficulty with social interaction and impairment in carrying out daily life activities.

Psychosis (as a sign of a psychiatric disorder) is a diagnosis of exclusion. That is, a new-onset episode of psychosis is not considered a symptom of a psychiatric disorder until other relevant and known causes of psychosis are properly excluded.[2] Medical and biological laboratory tests should exclude central nervous system diseases and injuries, diseases and injuries of other organs, psychoactive substances, toxins, and prescribed medications as causes of symptoms of psychosis before any psychiatric illness can be diagnosed.[2] In medical training, psychosis as a sign of illness is often compared to fever since both can have multiple causes that are not readily apparent.[2]

The term "psychosis" is very broad and can mean anything from relatively normal aberrant experiences through to the complex and catatonic expressions of schizophrenia and bipolar type 1 disorder.[3][4][5] In properly diagnosed psychiatric disorders (where other causes have been excluded by extensive medical and biological laboratory tests), psychosis is a descriptive term for the hallucinations, delusions, sometimes violence, and impaired insight that may occur.[4][6] Psychosis is generally the term given to noticeable deficits in normal behavior (negative signs) and more commonly to diverse types of hallucinations or delusional beliefs, especially as regards the relation between self and others as in grandiosity and pronoia/paranoia.

An excess in dopaminergic signalling is hypothesized to be linked to the positive symptoms of psychosis, especially those of schizophrenia. However, this hypothesis has not been definitively supported. The dopaminergic mechanism is thought to be causal in an aberrant perception or evaluation of the salience of environmental stimuli.[7] Many antipsychotic drugs accordingly target the dopamine system; however, meta-analyses of placebo-controlled trials of these drugs show either no significant difference in effects between drug and placebo, or a moderate effect size, suggesting that the pathophysiology of psychosis is much more complex than an overactive dopamine system.[8][9]

1 Signs and symptoms

People with psychosis normally have one or more of the following: hallucinations, delusions, catatonia, or a thought disorder. Impairments in social cognition also occur.[10][11]

1.1 Hallucinations

A hallucination is defined as sensory perception in the absence of external stimuli. Hallucinations are different from illusions, or perceptual distortions, which are the misperception of external stimuli.[12] Hallucinations may occur in any of the senses and take on almost any form, which may include simple sensations (such as lights, colors, tastes, and smells) to experiences such as seeing and interacting with fully formed animals and people, hearing voices, and having complex tactile sensations.

Auditory hallucinations, particularly experiences of hearing voices, are the most common and often prominent feature of psychosis. Hallucinated voices may talk about, or to, the person, and may involve several speakers with distinct personalities. Auditory hallucinations tend to be particularly distressing when they are derogatory, commanding or preoccupying. However, the experience of hearing voices need not always be a negative one. One research study has shown that the majority of people who hear voices are not in need of psychiatric help.[13] The Hearing Voices Movement has subsequently been created to support voice hearers, regardless of whether they are considered to have a mental disorder or not.

1.2 Delusions

Psychosis may involve delusional beliefs, some of which are paranoid in nature. Put simply, delusions are false beliefs that a person holds on to, without adequate evidence. It can be difficult to change the belief, even with evidence to the contrary. Common themes of delusions are

persecutory (person believes that others are out to harm him/her), grandiose (person believing that he or she has special powers or skills), etc. Persons with Ekbom syndrome may have delusional beliefs of an imaginary parasite infestation,[14] whereas depressed persons might have delusions consistent with their low mood (e.g., delusions that they have sinned, or have contracted serious illness, etc.). Karl Jaspers has classified psychotic delusions into *primary* and *secondary* types. Primary delusions are defined as arising suddenly and not being comprehensible in terms of normal mental processes, whereas secondary delusions are typically understood as being influenced by the person's background or current situation (e.g., ethnicity; also religious, superstitious, or political beliefs).[15]

1.3 Catatonia

Catatonia describes a profoundly agitated state in which the experience of reality is generally considered impaired. There are two primary manifestations of catatonic behavior. The classic presentation is a person who does not move or interact with the world in any way while awake. This type of catatonia presents with waxy flexibility. Waxy flexibility is when someone physically moves part of a catatonic person's body and the person stays in the position even if it is bizarre and otherwise nonfunctional (such as moving a person's arm straight up in the air and the arm staying there).

The other type of catatonia is more of an outward presentation of the profoundly agitated state described above. It involves excessive and purposeless motor behaviour, as well as extreme mental preoccupation that prevents an intact experience of reality. An example is someone walking very fast in circles to the exclusion of anything else with a level of mental preoccupation (meaning not focused on anything relevant to the situation) that was not typical of the person prior to the symptom onset. In both types of catatonia there is generally no reaction to anything that happens outside of them. It is important to distinguish catatonic agitation from severe bipolar mania, although someone could have both.

1.4 Thought disorders

Thought disorder describes an underlying disturbance to conscious thought and is classified largely by its effects on speech and writing. Affected persons show loosening of associations, that is, a disconnection and disorganization of the semantic content of speech and writing. In the severe form speech becomes incomprehensible and it is known as "word salad".

2 Causes

Many causes of schizophrenia are also causes of psychosis.

2.1 Psychiatric disorder

From a diagnostic standpoint, organic disorders were those believed caused by physical illness affecting the brain (that is, psychiatric disorders secondary to other conditions), while functional disorders were considered disorders of the functioning of the mind in the absence of physical disorders (that is, primary psychological or psychiatric disorders). The materialistic view of the mind–body problem holds that mental disorders arise from physical processes; in this view, the distinction between brain and mind, and therefore between organic and functional disease, is an artificial one. Subtle physical abnormalities have been found in illnesses traditionally considered functional, such as schizophrenia. The DSM-IV-TR avoids the functional/organic distinction, and instead lists traditional psychotic illnesses, psychosis due to general medical conditions, and substance-induced psychosis.

Primary psychiatric causes of psychosis include the following:[16][17][18]

- schizophrenia and schizophreniform disorder
- affective (mood) disorders, including severe depression, and severe depression or mania in bipolar disorder (manic depression). People experiencing a psychotic episode in the context of depression may experience persecutory or self-blaming delusions or hallucinations, while people experiencing a psychotic episode in the context of mania may form grandiose delusions.
- schizoaffective disorder, involving symptoms of both schizophrenia and mood disorders
- brief psychotic disorder, or acute/transient psychotic disorder
- delusional disorder (persistent delusional disorder)
- chronic hallucinatory psychosis

Psychotic symptoms may also be seen in[18]

- schizotypal disorder
- certain personality disorders at times of stress (including paranoid personality disorder, schizoid personality disorder, and borderline personality disorder)
- major depressive disorder in its severe form although it is possible and more likely to have severe depression without psychosis

- bipolar disorder in severe mania and/or severe depression although it is possible to have severe mania and/or severe depression without psychosis as well, in fact that is more commonly the case
- post-traumatic stress disorder
- induced delusional disorder
- Sometimes in obsessive-compulsive disorder
- Dissociative disorders, due to many overlapping symptoms, careful differential diagnosis includes especially dissociative identity disorder.[19]

Stress is known to contribute to and trigger psychotic states. A history of psychologically traumatic events, and the recent experience of a stressful event, can both contribute to the development of psychosis. Short-lived psychosis triggered by stress is known as brief reactive psychosis, and patients may spontaneously recover normal functioning within two weeks.[20] In some rare cases, individuals may remain in a state of full-blown psychosis for many years, or perhaps have attenuated psychotic symptoms (such as low intensity hallucinations) present at most times.

2.1.1 Normal states

Brief hallucinations are not uncommon in those without any psychiatric disease. Causes or triggers include:[18]

- Falling asleep and waking: hypnagogic and hypnopompic hallucinations, which are entirely normal[21]
- Bereavement, in which hallucinations of a deceased loved one are common[18]
- Severe sleep deprivation[22][23][24]
- Sensory deprivation and sensory impairment
- Caffeine intoxication
- An extremely stressful event

2.1.2 Subtypes

Subtypes of psychosis include:

- Menstrual psychosis, including circa-mensual (approximately monthly) periodicity, in rhythm with the menstrual cycle.
- Postpartum psychosis, occurring recently after childbirth
- Monothematic delusions
- Myxedematous psychosis
- Occupational psychosis
- Stimulant psychosis
- Tardive psychosis
- Shared psychosis
- Cycloid psychosis

2.1.3 Cycloid psychosis

Cycloid psychosis is psychosis that progresses from normal to full-blown usually within a few hours, not related to drug intake or brain injury.[25] In addition, diagnostic criteria include at least four of the following symptoms:[25]

- Confusion
- Mood-incongruent delusions
- Hallucinations
- Pan-anxiety, a severe anxiety not bound to particular situations or circumstances
- Happiness or ecstasy of high degree
- Motility disturbances of akinetic or hyperkinetic type
- Concern with death
- Mood swings to some degree, but less than what is needed for diagnosis of an affective disorder

Cycloid psychosis occurs in people of generally 15–50 years of age.[25]

2.2 Medical conditions

A very large number of medical conditions can cause psychosis, sometimes called *secondary psychosis*.[18] Examples include:

- disorders causing *delirium* (*toxic psychosis*), in which consciousness is disturbed
- neurodevelopmental disorders and chromosomal abnormalities, including velocardiofacial syndrome
- neurodegenerative disorders, such as Alzheimer's disease,[26] dementia with Lewy bodies,[27] and Parkinson's disease[28]
- focal neurological disease, such as stroke, brain tumors,[29] multiple sclerosis,[30] and some forms of epilepsy
- malignancy (typically via masses in the brain, paraneoplastic syndromes, or drugs used to treat cancer)

- infectious and postinfectious syndromes, including infections causing delirium, viral encephalitis, HIV,[31] malaria,[32] Lyme disease,[33][34][35] syphilis[36][37]
- endocrine disease, such as hypothyroidism, hyperthyroidism, adrenal failure, Cushing's syndrome, hypoparathyroidism and hyperparathyroidism; sex hormones also affect psychotic symptoms and sometimes childbirth can provoke psychosis, termed puerperal psychosis
- inborn errors of metabolism, such as Succinic semialdehyde dehydrogenase deficiency, porphyria and metachromatic leukodystrophy[38][39][40]
- nutritional deficiency, such as vitamin B_{12} deficiency[41][42]
- other acquired metabolic disorders, including electrolyte disturbances such as hypocalcemia,[43] hypernatremia,[44] hyponatremia,[45] hypokalemia,[46] hypomagnesemia,[47] hypermagnesemia,[48] hypercalcemia,[49] and hypophosphatemia,[50] but also hypoglycemia,[51] hypoxia, and failure of the liver or kidneys
- autoimmune and related disorders, such as systemic lupus erythematosus (lupus, SLE),[52] sarcoidosis,[53] Hashimoto's encephalopathy,[54][55][56] and anti-NMDA-receptor encephalitis[57]
- poisoning, by therapeutic drugs (see below), recreational drugs (see below), and a range of plants, fungi, metals, organic compounds, and a few animal toxins[18]
- some sleep disorders, including hallucinations in narcolepsy (in which REM sleep intrudes into wakefulness)[18]

Psychosis can even be caused by familiar ailments such as flu[58][59] or mumps.[60]

2.3 Psychoactive drugs

Main article: Substance-induced psychosis

Various psychoactive substances (both legal and illegal) have been implicated in causing, exacerbating, and/or precipitating psychotic states and/or disorders in users. This may be upon intoxication, for a more prolonged period after use, or upon withdrawal.[18] Individuals who have a substance induced psychosis tend to have a greater awareness of their psychosis and tend to have higher levels of suicidal thinking compared to individuals who have a primary psychotic illness.[61] Drugs that can induce psychotic symptoms include cannabis, cocaine, amphetamines, cathinones, psychedelic drugs (such as LSD and psilocybin), κ-opioid receptor agonists (such as enadoline and salvinorin A) and NMDA receptor antagonists (such as phencyclidine and ketamine).[18] While psychedelic drugs may cause psychosis-like experiences while the user is under the effects of the drugs, clinical studies do not suggest that psychedelics cause long-term mental health problems.[62]

2.3.1 Alcohol

Further information: Long-term effects of alcohol § Mental health effects

Approximately three percent of people who are suffering from alcoholism experience psychosis during acute intoxication or withdrawal. Alcohol related psychosis may manifest itself through a kindling mechanism. The mechanism of alcohol-related psychosis is due to the long-term effects of alcohol resulting in distortions to neuronal membranes, gene expression, as well as thiamin deficiency. It is possible in some cases that alcohol abuse via a kindling mechanism can cause the development of a chronic substance induced psychotic disorder, i.e. schizophrenia. The effects of an alcohol-related psychosis include an increased risk of depression and suicide as well as causing psychosocial impairments.[63]

2.3.2 Cannabis

Further information: Causes of schizophrenia § Cannabis and Long-term effects of cannabis § Schizophrenia

According to some studies, the more often cannabis is used the more likely a person is to develop a psychotic illness,[64] with frequent use being correlated with twice the risk of psychosis and schizophrenia.[65][66] While cannabis use is accepted as a contributory cause of schizophrenia by some,[67] it remains controversial, with pre-existing vulnerability to psychosis emerging as the key factor that influences the link between cannabis use and psychosis.[68][69] Some studies indicate that the effects of two active compounds in cannabis, tetrahydrocannabinol (THC) and cannabidiol (CBD), have opposite effects with respect to psychosis. While THC can induce psychotic symptoms in healthy individuals, CBD may reduce the symptoms caused by cannabis.[70]

Cannabis use has increased dramatically over the past few decades whereas the rate of psychosis has not increased. Together, these findings suggest that cannabis use may hasten the onset of psychosis in those who may already be predisposed to psychosis.[71] High-potency cannabis use indeed seems to accelerate the onset of psychosis in predisposed patients.[72] A 2012 study concluded that cannabis plays an important role in the development of

psychosis in vulnerable individuals, and that cannabis use in early adolescence should be discouraged.[73]

2.3.3 Methamphetamine

Main article: Methamphetamine psychosis

Methamphetamine induces a psychosis in 26-46 percent of heavy users. Some of these people develop a long-lasting psychosis that can persist for longer than six months. Those who have had a short-lived psychosis from methamphetamine can have a relapse of the methamphetamine psychosis years later after a stress event such as severe insomnia or a period of heavy alcohol abuse despite not relapsing back to methamphetamine. Individuals who have long history of methamphetamine abuse and who have experienced psychosis in the past from methamphetamine abuse are highly likely to rapidly relapse back into a methamphetamine psychosis within a week or so of going back onto methamphetamine.

2.4 Medication

Administration, or sometimes withdrawal, of a large number of medications may provoke psychotic symptoms.[18] Drugs that can induce psychosis experimentally and/or in a significant proportion of patients include amphetamine and other sympathomimetics, dopamine agonists, ketamine, corticosteroids (often with mood changes in addition), and some anticonvulsants such as vigabatrin.[18][74]

2.5 Other

A 2014 study found no evidence that familial risk accounts for associations between childhood physical abuse and psychotic disorder, or that it substantially increases the odds of psychosis among individuals reporting abuse.[75]

3 Pathophysiology

The first brain image of an individual with psychosis was completed as far back as 1935 using a technique called pneumoencephalography[76] (a painful and now obsolete procedure where cerebrospinal fluid is drained from around the brain and replaced with air to allow the structure of the brain to show up more clearly on an X-ray picture).

The purpose of the brain is to collect information from the body (pain, hunger, etc.), and from the outside world, interpret it to a coherent world view, and produce a meaningful response. The information from the senses enter the brain in the primary sensory areas. They process the information and send it to the secondary areas where the information is interpreted. Spontaneous activity in the primary sensory areas may produce hallucinations, which the secondary areas misinterpret as information from the real world.

For example, a PET or fMRI scan of a person who claims he hears voices may show activation in the primary auditory cortex, or parts of the brain involved in the perception and understanding of speech.[77]

Tertiary brain cortex collects the interpretations from the secondary cortexes and creates a coherent world view of it. A study investigating structural changes in the brains of people with psychosis showed there was significant grey matter reduction in the right medial temporal, lateral temporal, and inferior frontal gyrus, and in the cingulate cortex bilaterally of people before and after they became psychotic.[78] Findings such as these have led to debate about whether psychosis itself causes excitotoxic brain damage and whether potentially damaging changes to the brain are related to the length of psychotic episode. Recent research has suggested that this is not the case[79] although further investigation is still ongoing.

Studies with sensory deprivation have shown that the brain is dependent on signals from the outer world to function properly. If the spontaneous activity in the brain is not counterbalanced with information from the senses, loss from reality and psychosis may occur after some hours. A similar phenomenon is paranoia in the elderly, when poor eyesight, hearing and memory make the person abnormally suspicious of the environment.

On the other hand, loss from reality may also occur if the spontaneous cortical activity is increased so that it is no longer counterbalanced with information from the senses. The 5-HT2A receptor seems to be important for this, since psychedelic drugs that activate them produce hallucinations.

However, the main feature of psychosis is not hallucinations, but the inability to distinguish between internal and external stimuli. Close relatives to psychotic patients may hear voices, but since they are aware that they are unreal they can ignore them, so that the hallucinations do not affect their reality perception. Hence they are not considered psychotic.

Psychosis has been traditionally linked to the neurotransmitter dopamine. In particular, the dopamine hypothesis of psychosis has been influential and states that psychosis results from an overactivity of dopamine function in the brain, particularly in the mesolimbic pathway. The two major sources of evidence given to support this theory are that dopamine receptor D2 blocking drugs (i.e., antipsychotics) tend to reduce the intensity of psychotic symptoms, and that drugs that boost dopamine activity (such as amphetamines and cocaine) can trigger psychosis in some people (see amphetamine psychosis).[7] However, increasing evidence in recent times has pointed to a possible

dysfunction of the excitory neurotransmitter glutamate, in particular, with the activity of the NMDA receptor.

This theory is reinforced by the fact that dissociative NMDA receptor antagonists such as ketamine, PCP and dextromethorphan (at large overdoses) induce a psychotic state more readily than dopaminergic stimulants, even at "normal" recreational doses. The symptoms of dissociative intoxication are also considered to mirror the symptoms of schizophrenia, including negative psychotic symptoms, more closely than amphetamine psychosis. Dissociative induced psychosis happens on a more reliable and predictable basis than amphetamine psychosis, which usually only occurs in cases of overdose, prolonged use or with sleep deprivation, which can independently produce psychosis. New antipsychotic drugs that act on glutamate and its receptors are currently undergoing clinical trials.

The connection between dopamine and psychosis is generally believed complex. While dopamine receptor D2 suppresses adenylate cyclase activity, the D1 receptor increases it. If D2-blocking drugs are administered the blocked dopamine spills over to the D1 receptors. The increased adenylate cyclase activity affects genetic expression in the nerve cell, which takes time. Hence antipsychotic drugs take a week or two to reduce the symptoms of psychosis. Moreover, newer and equally effective antipsychotic drugs actually block slightly less dopamine in the brain than older drugs whilst also blocking 5-HT2A receptors, suggesting the 'dopamine hypothesis' may be oversimplified.[80] Soyka and colleagues found no evidence of dopaminergic dysfunction in people with alcohol-induced psychosis[81] and Zoldan et al. reported moderately successful use of ondansetron, a 5-HT_3 receptor antagonist, in the treatment of levodopa psychosis in Parkinson's disease patients.[82]

Psychiatrist David Healy has criticised pharmaceutical companies for promoting simplified biological theories of mental illness that seem to imply the primacy of pharmaceutical treatments while ignoring social and developmental factors that are known important influences in the aetiology of psychosis.[83]

Some theories believe many psychotic symptoms are a problem with the perception of ownership of internally generated thoughts and experiences.[84] For example, the hallucination of hearing voices may arise from internally generated speech that is mislabeled by the psychotic person as coming from an external source.

It has been suggested that persons with bipolar disorder may have increased activity of the left hemisphere compared to the right hemisphere of the brain, while persons with schizophrenia have increased activity in the right hemisphere.[85]

Increased level of right hemisphere activation has also been found in people who have high levels of paranormal beliefs[86] and in people who report mystical experiences.[87] It also seems that people who are more creative are also more likely to show a similar pattern of brain activation.[88] Some researchers have been quick to point out that this in no way suggests that paranormal, mystical or creative experiences are in any way *by themselves* a symptom of mental illness, as it is still not clear what makes some such experiences beneficial and others distressing.

3.1 Neurobiology

In otherwise normal individuals, exogenous ligands can produce psychotic symptoms. NMDA receptor antagonists, such as ketamine, can produce a similar psychosis to that experienced in schizophrenia.[89]

Prolonged or high dose use of psychostimulants can alter normal functioning, making it similar to the manic phase of bipolar disorder.[90] NMDA antagonists replicate some of the so-called "negative" symptoms like thought disorder in subanesthetic doses (doses insufficient to induce anesthesia), and catatonia in high doses. Psychostimulants, especially in one already prone to psychotic thinking, can cause some "positive" symptoms, such as delusional beliefs, particularly those persecutory in nature.

4 Diagnosis

Psychosis is first and foremost a diagnosis of exclusion.[2] So a new-onset episode of psychosis *cannot* be considered a symptom of a psychiatric disorder until other relevant and known causes of psychosis are properly excluded, or ruled out.[2] Many clinicians improperly perform, or entirely miss this step, introducing avoidable diagnostic error and misdiagnosis.[2]

An initial assessment includes a comprehensive history and physical examination by a physician, psychiatrist, psychiatric nurse practitioner or psychiatric physician assistant. Biological tests should be performed to exclude psychosis associated with or caused by substance use, medication, toxins, surgical complications, or other medical illnesses.

Delirium should be ruled out, which can be distinguished by visual hallucinations, acute onset and fluctuating level of consciousness, indicating other underlying factors, including medical illnesses.[91] Excluding medical illnesses associated with psychosis is performed by using blood tests to measure:

- Thyroid-stimulating hormone to exclude hypo- or hyperthyroidism,
- Basic electrolytes and serum calcium to rule out a metabolic disturbance,
- Full blood count including ESR to rule out a systemic infection or chronic disease, and

- Serology to exclude syphilis or HIV infection.

Other investigations include:

- EEG to exclude epilepsy, and an
- MRI or CT scan of the head to exclude brain lesions.

Because psychosis may be precipitated or exacerbated by common classes of medications, medication-induced psychosis should be ruled out, particularly for first-episode psychosis. Both substance- and medication-induced psychosis can be excluded to a high level of certainty, using a

- Urinalysis and a
- Full serum toxicology screening.

Because some dietary supplements may also induce psychosis or mania, but cannot be ruled out with laboratory tests, a psychotic individual's family, partner, or friends should be asked whether the patient is currently taking any dietary supplements.[92]

Common mistakes made when diagnosing people who are psychotic include:[2]

- Not properly excluding delirium,
- Not appreciating medical abnormalities (e.g., vital signs),
- Not obtaining a medical history and family history,
- Indiscriminate screening without an organizing framework,
- Missing a toxic psychosis by not screening for substances *and* medications
- Not asking family or others about dietary supplements,
- Premature diagnostic closure, and
- Not revisiting or questioning the initial diagnostic impression of primary psychiatric disorder.

Only after relevant and known causes of psychosis are excluded, a mental health clinician may make a psychiatric differential diagnosis using a person's family history, incorporating information from the person with psychosis, and information from family, friends, or significant others.

Types of psychosis in psychiatric disorders may be established by formal rating scales. The Brief Psychiatric Rating Scale (BPRS)[93] assesses the level of 18 symptom constructs of psychosis such as hostility, suspicion, hallucination, and grandiosity. It is based on the clinician's interview with the patient and observations of the patient's behavior over the previous 2–3 days. The patient's family can also answer questions on the behavior report. During the initial assessment and the follow-up, both positive and negative symptoms of psychosis can be assessed using the 30 item Positive and Negative Symptom Scale (PANSS).[94]

5 Prevention

The evidence for the effectiveness of early interventions to prevent psychosis appeared inconclusive.[95] Whilst early intervention in those with a psychotic episode might improve short term outcomes, little benefit was seen from these measures after five years.[96] However, there is evidence that cognitive behavioral therapy (CBT) may reduce the risk of becoming psychotic in those at high risk,[97] and in 2014 the UK National Institute for Health and Care Excellence (NICE) recommended preventive CBT for people at risk of psychosis.[98][99]

6 Treatment

The treatment of psychosis depends on the specific diagnosis (such as schizophrenia, bipolar disorder or substance intoxication). The first-line psychiatric treatment for many psychotic disorders is antipsychotic medication,[100] which can reduce the positive symptoms of psychosis in about 7 to 14 days.

The choice of which antipsychotic to use is based on benefits, risks, and costs.[96] It is debatable whether, as a class, typical or atypical antipsychotics are better,[101][102] though there is evidence of amisulpride, olanzapine, risperidone and clozapine being the most effective medications.[103] Typical antipsychotics have equal drop-out and symptom relapse rates to atypicals when used at low to moderate dosages.[104] There is a good response in 40–50%, a partial response in 30–40%, and treatment resistance (failure of symptoms to respond satisfactorily after six weeks to two or three different antipsychotics) in 20% of people.[105] Clozapine is an effective treatment for those who respond poorly to other drugs ("treatment-resistant" or "refractory" schizophrenia),[106] but it has the potentially serious side effect of agranulocytosis (lowered white blood cell count) in less than 4% of people.[96][107][108]

Most people on antipsychotics get side effects. People on typical antipsychotics tend to have a higher rate of extrapyramidal side effects while some atypicals are associated with considerable weight gain, diabetes and risk of metabolic syndrome; this is most pronounced with olanzapine, while risperidone and quetiapine are also associated with weight gain.[103] Risperidone has a similar rate of extrapyramidal symptoms to haloperidol.[103]

6.1 Early intervention

Main article: Early intervention in psychosis

Early intervention in psychosis is on the observation that identifying and treating someone in the early stages of a psychosis can improve their longer term outcome.[109] This approach advocates the use of an intensive multidisciplinary approach during what is known as the critical period, where intervention is the most effective, and prevents the long term morbidity associated with chronic psychotic illness.

7 History

The word *psychosis* was introduced to the psychiatric literature in 1841 by Karl Friedrich Canstatt in his work *Handbuch der Medizinischen Klinik*. He used it as a shorthand for 'psychic neurosis'. At that time neurosis meant any disease of the nervous system, and Canstatt was thus referring to what was considered a psychological manifestation of brain disease.[110] Ernst von Feuchtersleben is also widely credited as introducing the term in 1845,[111] as an alternative to insanity and mania.

The term stems from Modern Latin *psychosis*, "a giving soul or life to, animating, quickening" and that from Ancient Greek ψυχή (*psyche*), "soul" and the suffix -ωσις (*-osis*), in this case "abnormal condition".[112][113]

The word was also used to distinguish a condition considered a disorder of the mind, as opposed to *neurosis*, which was considered a disorder of the nervous system.[114] The psychoses thus became the modern equivalent of the old notion of madness, and hence there was much debate on whether there was only one (unitary) or many forms of the new disease.[115] One type of broad usage would later be narrowed down by Koch in 1891 to the 'psychopathic inferiorities' - later renamed abnormal personalities by Schneider.[110]

The division of the major psychoses into manic depressive illness (now called bipolar disorder) and dementia praecox (now called schizophrenia) was made by Emil Kraepelin, who attempted to create a synthesis of the various mental disorders identified by 19th century psychiatrists, by grouping diseases together based on classification of common symptoms. Kraepelin used the term 'manic depressive insanity' to describe the whole spectrum of mood disorders, in a far wider sense than it is usually used today.

In Kraepelin's classification this would include 'unipolar' clinical depression, as well as bipolar disorder and other mood disorders such as cyclothymia. These are characterised by problems with mood control and the psychotic episodes appear associated with disturbances in mood, and patients often have periods of normal functioning between psychotic episodes even without medication. Schizophrenia is characterized by psychotic episodes that appear unrelated to disturbances in mood, and most non-medicated patients show signs of disturbance between psychotic episodes.

7.1 Treatment

Early civilizations considered madness a supernaturally inflicted phenomenon. Archaeologists have unearthed skulls with clearly visible drillings, some datable back to 5000 BC suggesting that trepanning was a common treatment for psychosis in ancient times.[116] Written record of supernatural causes and resultant treatments can be traced back to the New Testament. Mark 5:8-13 describes a man displaying what would today be described as psychotic symptoms. Christ cured this "demonic madness" by casting out the demons and hurling them into a herd of swine. Exorcism, is still utilized in some religious circles as a treatment for psychosis presumed to be demonic possession.[117] A research study of out-patients in psychiatric clinics found that 30 per cent of religious patients attributed the cause of their psychotic symptoms to evil spirits. Many of these patients underwent exorcistic healing rituals that, though largely regarded as positive experiences by the patients, had no effect on symptomology. Results did, however, show a significant worsening of psychotic symptoms associated with exclusion of medical treatment for coercive forms of exorcism.[118]

The medical teachings of the fourth-century philosopher and physician, Hippocrates of Cos, proposed a natural, rather than supernatural, cause of human illness. In Hippocrates' work, the Hippocratic corpus, a holistic explanation for health and disease was developed to include madness and other "diseases of the mind." Hippocrates writes:

> Men ought to know that from the brain, and from the brain only, arise our pleasures, joys, laughter, and jests, as well as our sorrows, pains, griefs and tears. Through it, in particular, we think, see, hear, and distinguish the ugly from the beautiful, the bad from the good, the pleasant from the unpleasant…. It is the same thing which makes us mad or delirious, inspires us with dread and fear, whether by night or by day, brings sleeplessness, inopportune mistakes, aimless anxieties, absentmindedness, and acts that are contrary to habit.
> —Hippocrates of Cos, the Hippocratic corpus

Hippocrates espoused a theory of humoralism wherein disease is resultant of a shifting balance in bodily fluids including blood, phlegm, black bile, and yellow bile.[119] According to humoralism, each fluid or "humour" has temperamental or behavioral correlates. In the case of

psychosis, symptoms are thought to be caused by an excess of both blood and yellow bile. Thus, the proposed surgical intervention for psychotic or manic behavior was bloodletting.[120]

18th century physician, educator, and widely considered "Founder of American Psychiatry," Benjamin Rush, also prescribed bloodletting as a first-line treatment for psychosis. Although not a proponent of humoralism, Rush believed that active purging and bloodletting were efficacious corrections for disruptions in the circulatory system, a complication he believed was the primary cause of "insanity." [121] Although Rush's treatment modalities are now considered antiquated and brutish, his contributions to psychiatry, namely the biological underpinnings of psychiatric phenomenon including psychosis, have been invaluable to the field. In honor of such contributions, Benjamin Rush's image is in the official seal of The American Psychiatric Association.

Early 20th century treatments for severe and persisting psychosis were characterized by an emphasis on shocking the nervous system. Such therapies include insulin shock therapy, cardiazol shock therapy, and electroconvulsive therapy.[122] Despite considerable risk, shock therapy was considered highly efficacious in the treatment of psychosis including schizophrenia. The acceptance of high-risk treatments led to more invasive medical interventions including psychosurgery.[123]

In 1888, Swiss psychiatrist, Gottlieb Burckhardt, performed the first medically sanctioned psychosurgery in which the cerebral cortex was excised. Although some patients showed improvement of symptoms and became more subdued, one patient died and several developed aphasia and/or seizure disorders. Burckhardt would go on to publish his clinical outcomes in a scholarly paper. This procedure was met with criticism from the medical community and his academic and surgical endeavors were largely ignored.[124] In the late 1930s, Egas Moniz conceived the leucotomy (AKA prefrontal lobotomy) in which the fibers connecting the frontal lobes to the rest of the brain were severed. Moniz's primary inspiration stemmed from a demonstration by neuroscientists, John Fulton and Carlyle's 1935 experiment in which two chimpanzees were given leucotomies and pre and post surgical behavior was compared. Prior to the leucotomy, the chimps engaged in typical behavior including throwing feces and fighting. After the procedure, both chimps were pacified and less violent. During the Q&A, Moniz asked if such a procedure could be extended to human subjects, a question that Fulton admitted was quite startling.[125] Moniz would go on to extend the controversial practice to humans suffering from various psychotic disorders, an endeavor for which he received a Nobel Prize in 1949.[126] Between the late 1930s and early 1970s, the leucotomy was a widely accepted practice, often performed in non-sterile environments such as small outpatient clinics and patient homes.[125] Psychosurgery remained standard practice until the discovery of antipsychotic pharmacology in the 1950s.[127]

The first clinical trial of antipsychotics (also commonly known as neuroleptics) for the treatment of psychosis took place in 1952. Chlorpromazine (brand name: Thorazine) passed clinical trials and became the first antipsychotic medication approved for the treatment of both acute and chronic psychosis. Although the mechanism of action was not discovered until 1963, the administration of chlorpromazine marked the advent of the dopamine antagonist, or first generation antipsychotic.[128] While clinical trials showed a high response rate for both acute psychosis and disorders with psychotic features, the side-effects were particularly harsh, which included high rates of often irreversible Parkinsonian symptoms such as tardive dyskinesia. With the advent of atypical antipsychotics (also known as second generation antipsychotics) came a dopamine antagonist with a comparable response rate but a far different, though still extensive, side-effect profile that included a lower risk of Parkinsonian symptoms but a higher risk of cardiovascular disease.[129] Atypical antipsychotics remain the first-line treatment for psychosis associated with various psychiatric and neurological disorders including schizophrenia, bipolar disorder, major depressive disorder, anxiety disorders, dementia, and some autism spectrum disorders.[130]

It is now known that dopamine is the primary neurotransmitter implicated in psychotic symptomology. Thus, blocking dopamine receptors (namely, the dopamine D2 receptors) and decreasing dopaminergic activity continues to be an effective but highly unrefined pharmacologic goal of antipsychotics. Recent pharmacological research suggests that the decrease in dopaminergic activity does not eradicate psychotic delusions or hallucinations, but rather attenuates the reward mechanisms involved in the development of delusional thinking; that is, connecting or finding meaningful relationships between unrelated stimuli or ideas.[7] The author of this research paper acknowledges the importance of future investigation:

> The model presented here is based on incomplete knowledge related to dopamine, schizophrenia, and antipsychotics—and as such will need to evolve as more is known about these.
> —Shitij Kapur, From dopamine to salience to psychosis—linking biology, pharmacology and phenomenology of psychosis

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10 External links

- psychosis-bipolar.com - For persons afflicted, relatives and professionals: information, trialog, interactive therapy portal
- Understanding psychotic experiences from mental health charity Mind

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