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# PSYCHOSIS AND SCHIZOPHRENIA

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**Psychosis, including schizophrenia, is often seen as a very serious group of conditions that may not be as accessible to psychotherapy. However, this seems to be incorrect. A communication focused approach can help to better understand it and to conceive better treatment modalities.**

Keywords: panic attack, anxiety, psychotherapy, medication, psychiatry

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## Introduction

Psychosis is an abnormal condition of the mind that results in difficulties determining what is real and what is not. Symptoms may include false beliefs (delusions) and seeing or hearing things that others do not see or hear (hallucinations). Other symptoms may include incoherent speech and behavior that is inappropriate for the situation. There may also be sleep problems, social withdrawal, lack of motivation, and difficulties carrying out daily activities. In the United States about 3% of people develop psychosis at some point in their lives. Symptoms resembling those of schizophrenia have been described in the Ebers papyrus, an Egyptian medical papyrus of herbal knowledge dating to circa 1550 BC.

The core problem in psychosis is that the source of communicated information can no longer be identified correctly. For example, one hears a thought in the outside world or feels that outside events begin to influence the thoughts in one's mind. This leads to situations where the imaginary and the real become confused, and the separation between the outside and the inside world become less clear.

## Psychosis

From a diagnostic standpoint, organic disorders were believed to be 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). 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:

- schizophrenia and schizophreniform disorder
- affective (mood) disorders, including major 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:

- schizotypal personality 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 the manic and mixed episodes of bipolar I disorder and depressive episodes of both bipolar I and bipolar II; however, it is possible to experience such states without psychotic symptoms.
- 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.

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.[30] 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.

## Schizophrenia

The symptoms of schizophrenia usually begin in early adulthood and come on gradually. People with schizophrenia may experience hallucinations (most reported are hearing voices), delusions (often bizarre or persecutory in nature), and disorganized thinking and speech. The last may range from loss of train of thought, to sentences only loosely connected in meaning, to speech that is not understandable known as word salad. Social withdrawal, sloppiness of dress and hygiene, and loss of motivation and judgment are all common in schizophrenia. Distortions of self-experience such as feeling as if one's thoughts or feelings are not really one's own to believing thoughts are being inserted into one's mind, sometimes termed passivity phenomena, are also common. There is often an observable pattern of emotional difficulty, for example lack of responsiveness. Impairment in social cognition is associated with

schizophrenia, as are symptoms of paranoia. Social isolation commonly occurs. Difficulties in working and long-term memory, attention, executive functioning, and speed of processing also commonly occur. John Nash, an American mathematician and joint recipient of the 1994 Nobel Prize for Economics, who had schizophrenia. His life was the subject of the 2001 Academy Award-winning film *A Beautiful Mind*.

Schizophrenia affects around 0.3–0.7% of people at some point in their life, or 24 million people worldwide as of 2011. It occurs 1.4 times more frequently in males than females and typically appears earlier in men—the peak ages of onset are 25 years for males and 27 years for females. Onset in childhood is much rarer, as is onset in middle or old age. This is also diagnostically important because an onset of psychotic symptoms later in life is even more likely to be caused by non-psychiatric medical conditions.

## Diagnosis

Schizophrenia is diagnosed based on criteria in either the American Psychiatric Association's (APA) fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM 5)*, or the World Health Organization's *International Statistical Classification of Diseases and Related Health Problems (ICD-10)*. These criteria use the experiences reported by the patient and the observations of behavior and communication made by family, friends and the therapist.

## Criteria

The ICD-10 criteria put more emphasis on Schneiderian first-rank symptoms<sup>1</sup> than the DSM-5. The current proposal for the ICD-11 criteria for schizophrenia recommends adding self-disorder as a symptom. Symptoms associated with schizophrenia occur along a continuum in the population and must reach a certain severity and level of impairment, before a diagnosis is made.

The ICD-10 lists the following subgroups of schizophrenia:

- F20.0 Paranoid schizophrenia
- F20.1 Disorganized schizophrenia
- F20.2 Catatonic schizophrenia
- F20.3 Undifferentiated schizophrenia
- F20.5 Residual schizophrenia

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<sup>1</sup> In the early 20th century, the psychiatrist Kurt Schneider listed the forms of psychotic symptoms that he thought distinguished schizophrenia from other psychotic disorders. These are called first-rank symptoms or Schneider's first-rank symptoms. They include delusions of being controlled by an external force, the belief that thoughts are being inserted into or withdrawn from one's conscious mind, the belief that one's thoughts are being broadcast to other people and hearing hallucinatory voices that comment on one's thoughts or actions or that have a conversation with other hallucinated voices.

- F20.8 Other schizophrenia
- F20.9 Schizophrenia, unspecified

If signs of disturbance are present for more than a month but less than six months, the diagnosis of schizophreniform disorder is applied. Psychotic symptoms lasting less than a month may be diagnosed as brief psychotic disorder, and various conditions may be classed as psychotic disorder not otherwise specified. If the psychotic symptoms are the direct physiological result of a general medical condition or a substance, then the diagnosis is one of a psychosis secondary to that condition. Schizophrenia is not diagnosed if symptoms of pervasive developmental disorder are present unless prominent delusions or hallucinations are also present.

According to the DSM-5, to be diagnosed with schizophrenia, two diagnostic criteria have to be met over much of the time of a period of at least one month, with a significant impact on social or occupational functioning for at least six months. The person had to be suffering from

- Delusions
- hallucinations, or
- disorganized speech.

A second symptom could be negative symptoms, or severely disorganized or catatonic behavior.

## Schizoaffective Disorder

Schizoaffective disorder is diagnosed if symptoms of mood disorder are substantially present alongside psychotic symptoms. Schizoaffective disorder may have etiologies which are different from schizophrenia, but to what extent is still unknown.

## Differential diagnosis

- Individual symptoms by themselves or in varying combinations can also be present in other conditions. Some common examples are:
- Psychotic symptoms may be present in several other mental disorders, including bipolar disorder, borderline personality disorder, drug intoxication, and drug-induced psychosis.
- Delusions are also present in delusional disorder, and social withdrawal in social anxiety disorder, avoidant personality disorder and schizotypal personality disorder.
- Schizotypal personality disorder has symptoms that are similar but less severe than those of schizophrenia.
- Schizophrenia occurs along with obsessive-compulsive disorder (OCD) considerably more often than could be explained by chance, although it can be difficult to distinguish obsessions that occur in OCD from the delusions of schizophrenia.

- Benzodiazepine withdrawal can induce psychotic symptoms, which may mimic schizophrenia.
- In childhood various childhood fantasies can be experienced as very real. They are occasionally mistaken for psychotic symptoms.

## Medical and Neurological Examination

Several conditions can cause psychotic or psychotic-like symptoms. These include the following:

- metabolic disturbance
- systemic infection
- syphilis
- AIDS dementia complex
- Epilepsy
- limbic encephalitis
- brain lesions

Stroke, multiple sclerosis, hyperthyroidism, hypothyroidism, and dementias such as Alzheimer's disease, Huntington's disease, frontotemporal dementia, and the Lewy body dementias may also be associated with schizophrenia-like psychotic symptoms.

It may be necessary to rule out a delirium, which is usually caused by an underlying medical condition and often manifests with

- acute onset and fluctuating level of consciousness, and
- visual hallucinations

## Signs and symptoms

The symptoms of psychosis are the result of changes in how information is processed. Common is that the source of information is no longer interpreted correctly. For example, a thought turns into a voice which is heard from the outside. In this instance, the source is no longer identified correctly. It is not entirely clear why this happens. However, if one knows how this works, it is possible to integrate it and thereby reduce the fear of it and the extent to which hearing voices can interfere with everyday life. It also makes it possible to subject what one hears as voice to the same psychotherapeutic processes that would, for example, apply to ruminations or fearful content. Reality is subjective and awareness of a mental process can help to work with its outcomes. Communication-focused therapy (CFT) aims at awareness for internal and external communication patterns, which clinically also seems helpful in psychosis.(Haverkamp, 2012, 2017b)

## Symptom organization

Schizophrenia is often described in terms of positive and negative (or deficit) symptoms. Positive symptoms are those that most people do not normally experience but are present in people with schizophrenia. They can include delusions, disordered thoughts and speech, and tactile, auditory, visual, olfactory and gustatory hallucinations, typically regarded as manifestations of psychosis. Hallucinations are also typically related to the content of the delusional theme. Positive symptoms generally respond well to medication.

Negative symptoms are deficits of normal emotional responses or of other thought processes and are less responsive to medication. They commonly include flat expressions or little emotion, poverty of speech, inability to experience pleasure, lack of desire to form relationships, and lack of motivation. Negative symptoms appear to contribute more to poor quality of life, functional ability, and the burden on others than positive symptoms do. People with greater negative symptoms often have a history of poor adjustment before the onset of illness, and response to medication is often limited.

The validity of the positive and negative construct has been challenged by factor analysis studies. A cluster of symptoms around hallucination and a separate cluster for disorganization may be a more helpful categorization of the symptoms than combining them in the category of positive symptoms.

Some non-psychiatric symptoms, such as an increased need to drink fluids (polydipsia), can often be observed, while there is also an increased co-morbidity for irritable bowel syndrome, for example. Some of these non-psychiatric symptoms may be overlooked if not specifically asked for.

## Cognitive Dysfunction

Deficits in cognitive abilities are widely recognized as a core feature of schizophrenia. The extent of the cognitive deficits someone experiences is a predictor of how functional they will be, the quality of occupational performance, and how successful they will be in maintaining treatment. The presence and degree of cognitive dysfunction in people with schizophrenia has been reported to be a better indicator of functionality than the presentation of positive or negative symptoms. The deficits impacting the cognitive function are found in a large number of areas, including

- working memory
- long-term memory
- verbal declarative memory
- semantic processing
- episodic memory
- attention
- learning (particularly verbal learning).

Self-instructional training can help patients with schizophrenia to alter their thinking, attention, and language behaviors by verbalizing tasks, engaging in cognitive rehearsal, giving self-instructions, giving coping statements to the self to handle failure, and providing self-reinforcement for success. This led to improvements in recall tasks, less nonsensical verbalizations, and greater satisfaction and quality of life, which in itself probably has a protective effect against psychotic symptoms by lowering fears and anxiety and allowing a better connection with the sense of self.

## Verbal Memory

Deficits in verbal memory are common in schizophrenia. Verbal memory impairment in schizophrenia has been linked to a decreased ability to semantically encode. Healthy individuals usually remember words with positive connotations better than words with negative connotations. However, in those suffering from schizophrenia, both categories of words are remembered more or less equally. It could either be argued that the positive or negative value of the words is not recognized adequately or that the value no longer has as much an effect on the storage or access of the information. Thus, the impairment of memory can be linked to an impairment in the extraction of meaning or in how this information then affects the processing and storage of other information. If anhedonia is a state in which emotional signals are not processed and used as effectively, or differently from other people, it could be connected with alterations in storing and retrieving certain types of information, such as verbal messages or constructs.

## Onset

The onset of the disorder is usually between ages 18 and 25 for men and between 25 and 35 for women, and in 40% of men and 23% of women diagnosed with schizophrenia, the condition manifested itself before the age of 19. A prodromal state can often be seen two to three years before the onset of the full set of symptoms.

## Prodrome

The DSM-III-R published by the American Psychiatric Association in 1987 focuses mainly on observable behavioral changes in its description of the prodromal features of schizophrenia. It provides operationalized criteria of nine symptoms for the schizophrenic prodrome:

- Marked social isolation or withdrawal
- Marked impairment in role functioning
- Markedly peculiar behavior
- Marked impairment in personal hygiene and grooming
- Blunted or inappropriate affect

- Digressive, vague, overelaborate or circumstantial speech, or poverty of speech, or poverty of content of speech
- Odd beliefs or magical thinking
- Unusual perceptual experiences
- Marked lack of initiative, interests, or energy

This list of criteria has been dropped from the DSM-IV published in 1994. The ICD-10 published in the same year by the WHO acknowledges a prodrome as part of the schizophrenic syndrome, while prodromal symptoms are not included in its description of schizophrenia (Keith and Matthews 1991)

## Hallucinations

As mentioned, a hallucination is an internal communication event which is perceived as an external one. 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. In an illusion an individual correctly identifies a communication event as external, however, it is distorted by internal communication events.

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. Hallucinations are generally characterized as being vivid, and uncontrollable.

Auditory hallucinations, particularly experiences of hearing voices, are the most common and often prominent feature of psychosis. They are a classical symptom of schizophrenia, although not everyone suffering from schizophrenia also has them. However, they may be underreported in schizophrenia, as rapping or knocking sounds at night or noise from installations are frequently auditory hallucinations that need to be actively asked for. In any case, it is important to remember that visual hallucinations, which are often popularly associated with schizophrenia, only occur in up to half of schizophrenic patients and are less common than auditory hallucinations, which studies give a prevalence in schizophrenia of significantly more than 50% and often over 90% and which can be overlooked if not asked for.

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

- Falling asleep (hypnagogic hallucination) and waking (hypnopompic hallucination)
- Bereavement, in which hallucinations of a deceased loved one are common
- Severe sleep deprivation
- Trauma

## Voices

Auditory hallucinations are most commonly intelligible voices. They make be conversing or commenting about the patient. If they are imperative or commanding, they can elevate the risk that the patient may do something which he or she would not have done otherwise. This is another reason why it is important to educate patients on their condition and help them identify the type of communication patterns they are using and the source where the perceived information is coming from.

Since the sense of wholeness and connectedness of one's body can suffer in psychosis, hallucinations may also come from body parts. Auditory (extracampine) hallucinations may also originate from a particular body part, such as a tooth, which is not so rare. It may extend to a person hearing a whole symphony or a pop song coming from the body part, for example.

## Delusions

Delusions are an interpretation of reality in a way which does not agree with the interpretations held by other people. Thus, delusions depend to a degree on the beliefs and views held in the community one lives in. The underlying process is again the interpretation of incoming information in a way which does not agree with the conclusions others draw from similar information. Since the sensory inputs, for example, are largely similar to those of others, the delusion must be a result of how the information is processed.

One explanation could be how existing information is weighed, making it possible that something highly unlikely is seen as the most likely interpretation of reality. At the same time, it seems to require that the focus is increased on an aspect of reality to the exclusion of others. Delusions are a heightened feeling of certainty about something which is most often not entirely unlikely, but very highly so.

Often, below the delusion are emotional signals which are, as in hallucinations, seen as happening in the outside world rather than on the inside. An emotional signal of anger may in this way lead to feeling persecuted by secret agents. While the secret agents themselves may not be angry, persecution is a close enough metaphorical expression for anger. As in the case of hallucinations, the information can thus not lead to the necessary changes that help the individual adapt better to the environment and have success in it. Rather than figuring out why one is angry and making changes in one's life, such as putting boundaries in place or changing jobs, one feels persecuted by secret agents, which only leads to further withdrawal.

The distinguishing feature between delusional thinking and full-blown delusions is the degree with which they impact functioning. Other delusions than the one mentioned include delusions of reference (beliefs that a particular stimulus has a special meaning that is directed at the holder of belief), grandiose delusions (delusions that a person has a special power or importance), thought broadcasting (the belief that one's thoughts are audible) and thought insertion (the belief that one's thoughts are not one's own). The DSM-5 characterizes certain delusions as 'bizarre' if they are clearly implausible or are incompatible within the cultural

context, while it is unlikely that any insight can be gained from the question whether one should label a delusion as 'bizarre' or not.

Historically, 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. However, in doing so he seemed to focus more on the external situation of a person, including the culture, rather than the internal signals, whether emotional or otherwise, that could also make a delusion 'comprehensible'.

## Disorganization

While it is customary to talk about 'disorganized thinking' and 'disorganized speech' interchangeably, they are not the same. It is perfectly conceivable that a person has an internal world which seems quite clear and internally consistent to that person, but that the large differences between the internal world and the world of others makes meaningful communication near or fully impossible. When talking to someone who barely speaks one's language, the loss in understanding can cause significant stress and seemingly disorganized speech behavior. However, internally all along the world may be quite organized. Mistaking someone for an angry monster does not necessarily attest to a disorganized world, but it makes speaking to the angry drooling one eye monster quite a challenge, and the interaction is bound to be disorganized. The psychotic aspect is the existence of the monster, which causes any interaction to appear disorganized. This author thus believes there should be a clearer delineation between disorganized thinking, disorganized speech and cognitive impairment.

### Disorganized speech

Disorganized speech is a common externally observable symptom in psychosis. Characteristics of disorganized speech include rapidly switching topics, called derailment or loose association; switching to topics that are unrelated, called tangential thinking; incomprehensible speech, called word salad or incoherence.

### Disorganized motor behavior

Disorganized motor behavior includes repetitive, odd, or sometimes purposeless movement. One may add catatonia to disorganized motor behaviors, but it will be mentioned separately.

### Self-Distortion

Distortions of self-experience such as feeling as if one's thoughts or feelings are not really one's own to believing thoughts are being inserted into one's mind, sometimes termed passivity phenomena, are also common. There is often an observable pattern of emotional

difficulty, for example lack of responsiveness. Impairment in social cognition is associated with schizophrenia, as are symptoms of paranoia. Social isolation commonly occurs. Difficulties in working and long-term memory, attention, executive functioning, and speed of processing also commonly occur. In one uncommon subtype, the person may be largely mute, remain motionless in bizarre postures, or exhibit purposeless agitation, all signs of catatonia. People with schizophrenia often find facial emotion perception to be difficult. It is unclear if the phenomenon called "thought blocking", where a talking person suddenly becomes silent for a few seconds to minutes, occurs in schizophrenia.

## Catatonia

Catatonia describes a profoundly agitated state in which the experience of reality is generally considered impaired. There are two presentations of catatonia, one without movements and one with a lot of movement. Both, however, have in common that the individual is to an outside observer no longer interacting with the environment. That is, the information from the outside is no longer decoded or processed in a way which seem adaptive and helpful in getting the own needs met in the patient's outside reality.

- Stupor 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. Patients may also switch their position suddenly and then remain in their new position for a length of time.
- Catatonic excitement is a state of constant purposeless agitation and excitation. Individuals in this state are extremely hyperactive, but without any discernible purpose within the outside world.
- Malignant catatonia is an acute onset of excitement, fever, autonomic instability, delirium and may be fatal.

The presence of hallucinations and delusions may be more obvious in catatonic excitement because the patient seems to react to an internal script of a different version of the world. In other words, some information about the internal representation of the world is still discernible by an outside observer. In the case of stupor, the patient has largely cut off any communication with the outside world, which makes it difficult in this situation to gage what he or she may be experiencing on the inside.

Catatonia is interesting from a communication viewpoint because it represents often a point at which the divergence between the internal representation of the outside world and the outside world as experienced by others is particularly great, and a disconnect may also partially serve to protect the patient from an experience of complete chaos.

## Negative symptoms

While abnormal variations in the processing of information in psychosis can lead to positive symptoms in the form of hallucinations or delusions, they can also lead to negative symptoms, which mainly affect the use of emotional signals and a patient's communication with the world. Since the negative symptoms signify a lost function, there can be theoretically a large number of potential negative symptoms.

The ICD-10 provides the following areas of negative symptoms:

- marked apathy
- paucity of speech
- blunting or incongruity of emotional responses

The DSM-5 includes the following list:

- affective flattening
- alogia (poverty of speech)
- avolition (an inability to initiate and persist in goal-directed activities)

Anhedonia, the inability to find or derive pleasure from activities or relationships, and other symptoms have been described as associated symptoms in DSM-5.

From a communication perspective, it is important to note that our description of positive symptoms often entails a patient's perception of the world, or the consequences of that perception, while negative symptoms

## Causes

Psychosis has many different causes. These include mental illness, such as schizophrenia or bipolar disorder, sleep deprivation, some medical conditions, certain medications, and drugs such as alcohol or cannabis. One type, known as postpartum psychosis, can occur after giving birth. The neurotransmitter dopamine is believed to play a role. Acute psychosis is considered primary if it results from a psychiatric condition and secondary if it is caused by a medical condition. The diagnosis of a mental illness requires excluding other potential causes. Testing may be done to check for central nervous system diseases, toxins, or other health problems as a cause.

Stressful events or anything that interferes significantly with the normal workings of the central nervous system can potentially lead to psychotic or quasi-psychotic symptoms. Psychotic symptoms are thus not specific to a condition but can arise from several abnormalities in the information processing of the brain. As most psychiatric symptoms are a result of more global alterations in the information processing of the brain, psychotic symptoms are not an exception.

Genetic and environmental factors play a role in the development of schizophrenia. People with a family history of schizophrenia who have a transient psychosis have a 20–40% chance of being diagnosed with schizophrenia one year later.

## The Dopamine Hypothesis

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.

## Pathophysiology

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 accentuate dopamine release, or inhibit its reuptake (such as amphetamines and cocaine) can trigger psychosis in some people (see stimulant psychosis).

## NMDA Receptors

An abnormally low levels of glutamate receptors found in the postmortem brains of those diagnosed with schizophrenia. Post-mortem studies demonstrate decreased expression of GAD67, GAT-1 and GABAA receptor subunits in the prefrontal cortex, although this appears to be restricted to certain neurons. In vivo imaging of GABAergic signaling appears to be moderately reduced, this may be dependent upon treatment and disease stage.

NMDA receptor dysfunction has been proposed as a mechanism in psychosis. 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. The symptoms of dissociative intoxication are also considered to mirror the symptoms of schizophrenia, including negative psychotic symptoms.

Reduced glutamate function is linked to poor performance on tests requiring frontal lobe and hippocampal function, and glutamate can affect dopamine function, both of which have been

implicated in schizophrenia. However, positive symptoms fail to respond to glutamatergic medication.

## Dopamine

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.

Particular attention has been paid to the function of dopamine in the mesolimbic pathway of the brain. This focus largely resulted from the accidental finding that phenothiazine drugs, which block dopamine function, could reduce psychotic symptoms. It is also supported by the fact that amphetamines, which trigger the release of dopamine, may exacerbate the psychotic symptoms in schizophrenia. The influential dopamine hypothesis of schizophrenia proposed that excessive activation of D2 receptors was the cause of (the positive symptoms of) schizophrenia. Although postulated for about 20 years based on the D2 blockade effect common to all antipsychotics, it was not until the mid-1990s that PET and SPET imaging studies provided supporting evidence. Dopamine D2/D3 receptors are elevated in schizophrenia, but the effect size is small, and only evident in medication naive schizophrenics. On the other hand, presynaptic dopamine metabolism and release is elevated despite no difference in dopamine transporter. The altered synthesis of dopamine in the nigrostriatal system have been confirmed in several human studies. Hypoactivity of dopamine D1 receptor activation in the prefrontal cortex has also been observed. The hyperactivity of D2 receptor stimulation and relative hypoactivity of D1 receptor stimulation is thought to contribute to cognitive dysfunction by disrupting signal to noise ratio in cortical microcircuits. The dopamine hypothesis is now thought to be simplistic, partly because newer antipsychotic medication (atypical antipsychotic medication) can be just as effective as older medication (typical antipsychotic medication), but also affects serotonin function and may have slightly less of a dopamine blocking effect.

## Serotonin

Moreover, newer and equally effective antipsychotic drugs actually block slightly less dopamine in the brain than older drugs whilst also blocking 5-HT<sub>2A</sub> receptors, suggesting the 'dopamine hypothesis' may be oversimplified. Soyka and colleagues found no evidence of dopaminergic dysfunction in people with alcohol-induced psychosis and Zoldan et al reported moderately successful use of ondansetron, a 5-HT<sub>3</sub> receptor antagonist, in the treatment of levodopa psychosis in Parkinson's disease patients.

## Reduced Grey Matter Volume

The anatomical level may be too coarse to get additional insight into the pathogenesis of psychosis. However, the selective variations in morphology and activity in certain areas of the brain may be able to point at underlying processes that could be affected in psychosis.

Schizophrenia is associated with subtle differences in brain structures, found in forty to fifty percent of cases, and in brain chemistry during acute psychotic states. Studies using neuropsychological tests and brain imaging technologies such as fMRI and PET to examine functional differences in brain activity have shown that differences seem to occur most commonly in the frontal lobes, hippocampus, and temporal lobes. Reductions in brain volume are most pronounced in grey matter structures, and correlate with duration of illness, although white matter abnormalities have also been found. A progressive increase in ventricular volume as well as a progressive reduction in grey matter in the frontal, parietal, and temporal lobes has also been observed. These differences have been linked to the neurocognitive deficits often associated with schizophrenia. Because neural circuits are altered, it has alternatively been suggested that schizophrenia could be thought of as a neurodevelopmental disorder with psychosis occurring as a possibly preventable late stage. There has been debate on whether treatment with antipsychotics can itself cause reduction of brain volume.

Both first episode psychosis, and high-risk status is associated with reductions in grey matter volume. Reductions in

- right middle temporal gyrus
- right superior temporal gyrus
- right parahippocampus
- right hippocampus
- right middle frontal gyrus
- left anterior cingulate cortex

have been observed in high risk populations. People with schizophrenia who are medication compliant have an association with enlarged lateral ventricles in the brain.

## Hypoactivation

During attentional tasks, first episode psychosis is associated with hypoactivation in the right middle frontal gyrus, a region generally described as encompassing the dorsolateral prefrontal cortex (dlPFC). In congruence with studies on grey matter volume, hypoactivity in the right insula, and right inferior parietal lobe is also reported. With the exceptions of reduced deactivation of the inferior frontal gyrus during cognitive tasks (i.e. hyperactivation), highly consistent and replicable hypoactivity in the right insula, dorsal anterior cingulate cortex, and precuneus, as well as hyperactivity in the right basal ganglia and thalamus is observed.

Decreased grey matter volume in conjunction with hypoactivity is observed in the dorsal ACC, right anterior/middle insula, and left middle insula. Decreased grey matter volume and hyperactivity is reported in the ventral anterior cingulate cortex, and more posterior regions of the insula.

### *Hallucinations*

Studies during acute experience of hallucinations demonstrate increased activity in primary or secondary sensory cortices. As auditory hallucinations are most common in psychosis, most robust evidence exists for increased activity in the left middle temporal gyrus, left superior temporal gyrus, and left inferior frontal gyrus (i.e. Broca's area). Activity in the ventral striatum, hippocampus, and ACC are related to the lucidity of hallucinations, and indicate that activation or involvement of emotional circuitry are key to the impact of abnormal activity in sensory cortices. Together, these findings indicate abnormal processing of internally generated sensory experiences, coupled with abnormal emotional processing, results in hallucinations. One proposed model involves a failure of feedforward networks from sensory cortices to the inferior frontal cortex, which normally cancel out sensory cortex activity during internally generated speech. The resulting disruption in expected and perceived speech is thought to produce lucid hallucinatory experiences.

### *Delusions*

The two-factor model of delusions posits that dysfunction in both belief formation systems and belief evaluation systems are necessary for delusions. Dysfunction in evaluations systems localized to the right lateral prefrontal cortex, regardless of delusion content, is supported by neuroimaging studies and is congruent with its role in conflict monitoring in healthy persons. Abnormal activation and reduced volume is seen in people with delusions, as well as in disorders associated with delusions such as frontotemporal dementia, psychosis and Lewy body dementia. Furthermore, lesions to this region are associated with "jumping to conclusions", damage to this region is associated with post-stroke delusions, and hypometabolism this region associated with caudate strokes presenting with delusions.

The aberrant salience model suggests that delusions are a result of people assigning excessive importance to irrelevant stimuli. In support of this hypothesis, regions normally associated with the salience network demonstrate reduced grey matter in people with delusions, and the neurotransmitter dopamine, which is widely implicated in salience processing, is also widely implicated in psychotic disorders.

Specific regions have been associated with specific types of delusions. The volume of the hippocampus and parahippocampus is related to paranoid delusions in Alzheimer's disease, and has been reported to be abnormal post mortem in one person with delusions. Capragas delusions have been associated with occipito-temporal damage and may be related to failure to elicit normal emotions or memories in response to faces.

## Negative symptoms

Psychosis is associated with ventral striatal hypoactivity during reward anticipation and feedback. Hypoactivity in the left ventral striatum is correlated with the severity of negative symptoms.

While anhedonia is a commonly reported symptom in psychosis, hedonic experiences are actually intact in most people with schizophrenia. The impairment that may present itself as anhedonia probably actually lies in the inability to identify goals, and to identify and engage in the behaviors necessary to achieve goals.

Studies support a deficiency in the neural representation of goals and goal directed behavior by demonstrating that receipt (not anticipation) of reward is associated with robust response in the ventral striatum.

- Reinforcement learning is intact when contingencies are implicit, but not when they require explicit processing.
- Reward prediction errors (during functional neuroimaging studies), particularly positive ones are abnormal.
- Anterior cingulate cortex (ACC) response, taken as an indicator of effort allocation, does not increase with reward or reward probability increase, and is associated with negative symptoms. The ACC is involved in certain higher-level functions, such as attention allocation, reward anticipation, decision-making, ethics and morality, impulse control (e.g. performance monitoring and error detection), and emotion. It probably also plays a role in autonomic functions.
- Deficits in dorsolateral prefrontal cortex (DLPFC) activity and failure to improve performance on cognitive tasks when offered monetary incentives are present. An important function of the DLPFC is the executive functions, such as working memory, cognitive flexibility, planning, inhibition, and abstract reasoning. The DLPFC is also the highest cortical area that is involved in motor planning, organization and regulation.
- Dopamine mediated functions are abnormal.

## Genetics

Estimates of the heritability are that 80% of the individual differences in risk to schizophrenia is associated with genetics. The greatest single risk factor for developing schizophrenia is having a first-degree relative with the disease (risk is 6.5%), while more than 40% of monozygotic twins of those with schizophrenia are also affected. If one parent is affected the risk is about 13% and if both are affected the risk is nearly 50%.

Many genes are known to be involved in schizophrenia, each of small effect and unknown transmission and expression. The summation of these effect sizes into a polygenic risk score can explain at least 7% of the variability in liability for schizophrenia. Around 5% of cases of schizophrenia are understood to be at least partially attributable to rare copy number variants (CNVs), including 22q11, 1q21 and 16p11. These rare CNVs increase the risk of someone

developing the disorder by up to a factor of twenty and are frequently comorbid with autism and intellectual disabilities. There is a genetic relation between the common variants which cause schizophrenia and bipolar disorder, an inverse genetic correlation with intelligence and no genetic correlation with immune disorders.

## Environment

Environmental factors associated with the development of schizophrenia include the living environment, drug use, and prenatal stressors.

Maternal stress has been associated with an increased risk of schizophrenia, possibly in association with reelin. Maternal Stress has been observed to lead to hypermethylation and therefore under-expression of reelin, which in animal models leads to reduction in GABAergic neurons, a common finding in schizophrenia. Maternal nutritional deficiencies, such as those observed during a famine, as well as maternal obesity have also been identified as possible risk factors for schizophrenia. Both maternal stress and infection have been demonstrated to alter fetal neurodevelopment through pro-inflammatory proteins such as IL-8 and TNF.

Parenting style seems to have no major effect, although people with supportive parents do better than those with critical or hostile parents. Childhood trauma, death of a parent, and being bullied or abused increase the risk of psychosis. Living in an urban environment during childhood or as an adult has consistently been found to increase the risk of schizophrenia by a factor of two, even after taking into account drug use, ethnic group, and size of social group. Other factors that play an important role include social isolation and immigration related to social adversity, racial discrimination, family dysfunction, unemployment, and poor housing conditions.

It has been hypothesized that in some people, development of schizophrenia is related to intestinal tract dysfunction such as seen with non-celiac gluten sensitivity or abnormalities in the intestinal flora. A subgroup of persons with schizophrenia present an immune response to gluten different from that found in people with celiac, with elevated levels of certain serum biomarkers of gluten sensitivity such as anti-gliadin IgG or anti-gliadin IgA antibodies.

## Developmental factors

Factors such as hypoxia and infection, or stress and malnutrition in the mother during fetal development, may result in a slight increase in the risk of schizophrenia later in life. People diagnosed with schizophrenia are more likely to have been born in winter or spring (at least in the northern hemisphere), which may be a result of increased rates of viral exposures in utero. The increased risk is about five to eight percent. Other infections during pregnancy or around the time of birth including *Toxoplasma gondii* and *Chlamydia*, and some pathogens seropositivity are linked to an increase in risk. Viral infections of the brain during childhood are also linked to a risk of psychosis during adulthood.

## Trauma

Traumatic life events have been linked with elevated risk in developing psychotic symptoms. Childhood trauma has specifically been shown to be a predictor of adolescent and adult psychosis. Approximately 65% of individuals with psychotic symptoms have experienced childhood trauma, such as physical or sexual abuse and physical or emotional neglect.

Increased individual vulnerability toward psychosis may interact with traumatic experiences promoting onset of future psychotic symptoms, particularly during sensitive developmental periods. Importantly, the relationship between traumatic life events and psychotic symptoms appears to be dose-dependent in which multiple traumatic life events accumulate, compounding symptom expression and severity. This suggests trauma prevention and early intervention may be an important target for decreasing the incidence of psychotic disorders and ameliorating its effects.

## Medical conditions

It is important to identify whether a patient with psychotic symptoms may be suffering from a medical condition which requires urgent attention. But even if a patient is not in an acute state, it is important to know to which extent medical factors may play a causative role in the psychotic condition. If a psychosis is largely medically founded, a psychotherapy can still be useful in dealing with the traumatization and other psychological consequences of the psychosis, but it should then be less focused on trying to gain insight into what might trigger or maintain it.

Medical conditions that are known to cause psychotic symptoms include the following:

- conditions causing delirium as a toxic psychosis, in which consciousness is disturbed
- neurodevelopmental disorders and chromosomal abnormalities
- neurodegenerative disorders
  - Alzheimer's disease
  - dementia with Lewy bodies
  - Parkinson's disease
- focal neurological disease, such as stroke, brain tumors, multiple sclerosis, and some forms of epilepsy
- malignancy (typically via masses in the brain, paraneoplastic syndromes)
- infectious and postinfectious syndromes, including infections causing delirium, viral encephalitis, HIV/AIDS, malaria, syphilis
- endocrine disorders, such as
  - hypothyroidism
  - hyperthyroidism
  - Cushing's syndrome
  - hypoparathyroidism and hyperparathyroidism

- significant alterations in sex hormones
- giving birth can provoke psychosis (postpartum psychosis)
- genetic metabolic disorders
  - succinic semialdehyde dehydrogenase deficiency
  - porphyria
  - metachromatic leukodystrophy
- nutritional deficiency, such as vitamin B12 deficiency
- other acquired metabolic disorders, including
  - electrolyte disturbances such as hypocalcemia, hypernatremia, hyponatremia, hypokalemia, hypomagnesemia, hypermagnesemia, hypercalcemia, and hypophosphatemia
  - hypoglycemia
  - hypoxia
- failure of the liver or kidneys
- autoimmune and related disorders
  - systemic lupus erythematosus (lupus, SLE)
  - sarcoidosis
  - Hashimoto's encephalopathy
  - anti-NMDA-receptor encephalitis
  - non-celiac gluten sensitivity
- poisoning, by therapeutic drugs, recreational drugs, and a range of plants, fungi, metals, organic compounds, and a few animal toxins
- sleep disorders
  - narcolepsy (in which REM sleep intrudes into wakefulness)
- parasitic diseases
  - neurocysticercosis

## Psychoactive drugs

Various psychoactive substances (both legal and illegal) have been implicated in causing, exacerbating, or precipitating psychotic states or disorders in users, with varying levels of evidence. The psychosis can occur either when being intoxicated or during withdrawal.

About half of those with schizophrenia use drugs or alcohol excessively. Amphetamine, cocaine, and to a lesser extent alcohol, can result in a transient stimulant psychosis or alcohol-related psychosis that presents very similarly to schizophrenia. Although it is not generally believed to be a cause of the illness, people with schizophrenia use nicotine at much higher rates than the general population.

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.

Substances that have been linked to psychotic symptoms include

- alcohol
- cannabis
- cocaine
- amphetamines
- cathinone
- psychedelic drugs (such as LSD and psilocybin)
- $\kappa$ -opioid receptor agonists
- NMDA receptor antagonists, including phencyclidine and ketamine

Caffeine may worsen symptoms in those with schizophrenia and cause psychosis at very high doses in people without the condition.

## Alcohol

Alcohol abuse can occasionally cause the development of a chronic, substance-induced psychotic disorder via a kindling mechanism. Alcohol use is not associated with an earlier onset of psychosis.

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.

## Cannabis

Cannabis can be a contributory factor in schizophrenia, potentially causing the disease in those who are already at risk. The increased risk may require the presence of certain genes within an individual or may be related to preexisting psychopathology. Early exposure is strongly associated with an increased risk. The size of the increased risk is not clear, but appears to be in the range of two to three times greater for psychosis. Higher dosage and greater frequency of use are indicators of increased risk of chronic psychoses.

There have been debates, sometimes quite heated, about the type of link between cannabis use and psychosis for a long time. The problem with most studies in this area is that constellations of diverse individual factors, including the environment, play such an important role that conventional statistical tools and approaches cannot provide the answers one looks for, and particularly not with the desired confidence.

According to some studies, the more often cannabis is used the more likely a person is to develop a psychotic illness, with frequent use being correlated with twice the risk of psychosis and schizophrenia. However, it is difficult to distinguish this from a use of cannabis as self-medication in patients who experience early and incomplete symptoms of psychosis. As the progression of psychosis can vary among individuals, and in some cases linger for many years, or even indefinitely, in a partial clinical picture, there is no way of saying for sure what would have happened if the patient would not have used cannabis.

While cannabis use is accepted as a contributory cause of schizophrenia by some, it remains controversial, with pre-existing vulnerability to psychosis emerging as the key factor that influences the link between cannabis use and psychosis. 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.

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. High-potency cannabis use indeed seems to accelerate the onset of psychosis in predisposed patients. 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. However, it is quite possible in theory at least that CBD by itself could even lower the experienced stress that could trigger a psychosis. The main risk of CBD may be that it could lead to the use of THC and CBD, but this would need to be explored further.

## Methamphetamine

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.[citation needed] 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.[citation needed]

## Medication

Administration, or sometimes withdrawal, of a large number of medications may provoke psychotic symptoms. Drugs that can induce psychosis experimentally or in a significant proportion of people include amphetamine and other sympathomimetics, dopamine agonists,

ketamine, corticosteroids (often with mood changes in addition), and some anticonvulsants such as vigabatrin. Stimulants that may cause this include lisdexamfetamine.

Meditation may induce psychological side effects, including depersonalization, derealization and psychotic symptoms like hallucinations as well as mood disturbances.

## Other drugs

Other drugs may be used only as coping mechanisms by people who have schizophrenia, to deal with depression, anxiety, boredom, and loneliness.

## Diagnosis

To make a diagnosis of a mental illness in someone with psychosis other potential causes must be excluded. An initial assessment includes a comprehensive history and physical examination by a health care provider. Tests may be done to exclude substance use, medication, toxins, surgical complications, or other medical illnesses. A person with psychosis is referred to as psychotic.

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. 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 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.

Common mistakes made when diagnosing people who are psychotic include:

- 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.

## Prevention

Prevention of schizophrenia is difficult as there are no reliable markers for the later development of the disorder. There is tentative evidence for the effectiveness of early interventions to prevent schizophrenia. There is some evidence that early intervention in those with a psychotic episode may improve short-term outcomes, but there is little benefit from these measures after five years. Attempting to prevent schizophrenia in the prodrome phase is of uncertain benefit and therefore as of 2009 is not recommended. Cognitive behavioral therapy may reduce the risk of psychosis in those at high risk after a year and is recommended in this group, by the National Institute for Health and Care Excellence (NICE). Another preventative measure is to avoid drugs that have been associated with development of the disorder, including cannabis, cocaine, and amphetamines.

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

Early intervention in psychosis is based on the observation that identifying and treating someone in the early stages of a psychosis can improve their longer term outcome. This approach advocates the use of an intensive multi-disciplinary 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.

## Treatment

The primary treatment of schizophrenia is antipsychotic medications, often in combination with psychological and social supports. Hospitalization may occur for severe episodes either voluntarily or (if mental health legislation allows it) involuntarily. Long-term hospitalization is uncommon since deinstitutionalization beginning in the 1950s, although it still occurs. Community support services including drop-in centers, visits by members of a community mental health team, supported employment and support groups are common. Some evidence indicates that regular exercise has a positive effect on the physical and mental health of those with schizophrenia. As of 2015 it is unclear if transcranial magnetic stimulation (TMS) is useful for schizophrenia. Early treatment is crucial. With every relapse there seems to be a larger risk that some symptoms may become chronic and irreversible, particularly cognitive impairments, anhedonia, indifference, apathy and other negative symptoms.

Medication is often cited as the first treatment instrument, followed by psychotherapy and social support. While medication can indeed often lead to a rapid decrease in symptoms, psychotherapy is frequently underutilized, probably due to a lack in resources, but also due to a lack in understanding what psychotherapy can accomplish.

Fortunately, the crude biological treatments of the past have been left behind in most of the world. Treatments like the insulin shock therapy or surgical approaches may have helped some patients, but they came at a tremendous cost in severe and often irreversible side effects, including a partial or substantial loss in personality, and not seldomly even death. In the late 1930s, Egas Moniz conceived the leucotomy, the prefrontal lobotomy, in which the fibers connecting the frontal lobes to the rest of the brain were severed. Fortunately, from the 1970s onward, this practice was largely discontinued as antipsychotic medication which has its origins in the 1950s became better tolerated and more effective and found wide-spread use.

On the psychotherapeutic side, early work with psychotic and schizophrenic patients showed that it could have an effect on symptoms, at a time when most medical quarters were openly thinking of and practicing psychosurgery. Freud's former student Wilhelm Reich explored independent insights into the physical effects of neurotic and traumatic upbringing and published his holistic psychoanalytic treatment with a schizophrenic. With his incorporation of breathwork and insight with the patient, a young woman, she achieved adequate self-management skills to end the therapy.

## Medication

The first-line psychiatric treatment for schizophrenia is antipsychotic medication, which can reduce the positive symptoms often within days in an acute episode. Treatment was revolutionized in the mid-1950s with the development and introduction of chlorpromazine.

Haloperidol has become a mainstay in the pharmacological treatment of acute episodes of schizophrenia. For the longer-term treatment, mainly atypical or second-generation antipsychotics are used, such as olanzapine, quetiapine, aripiprazole, risperidone, amisulpride and others. Medication has made most cases of schizophrenia quite manageable, allowing patients to pursue their everyday jobs and raise a family. In about half of patients there is a good response and in another third a partial response. Their effect on negative symptoms and cognitive impairments is, however, generally smaller than on the positive (productive) symptoms of psychosis. Clozapine is an effective treatment for those who respond poorly to other drugs ("treatment-resistant" or "refractory" schizophrenia), but it has the potentially serious, and even lethal, side effect of agranulocytosis (lowered white blood cell count) in a small fraction of the patients.

Patients on typical antipsychotics tend to have a higher rate of extrapyramidal side effects while some atypical antipsychotics are associated with considerable weight gain, diabetes and risk of metabolic syndrome. Olanzapine probably carries the highest risk, while risperidone and quetiapine are also associated with weight gain. Risperidone has a similar rate of extrapyramidal symptoms to haloperidol, although probably mostly in a higher dose range. Olanzapine, and to some degree quetiapine and possibly risperidone, have the added benefit of being sleep inducing.

Potential side effects of all antipsychotics, possibly with the exception of clozapine and arguably to a lesser degree in the second-generation antipsychotics, include irreversible Parkinsonian symptoms such as tardive dyskinesia.

## Typical vs Atypical Antipsychotics

Second generation, or atypical, antipsychotics are usually considered to lead to less, and particularly less severe side effects. While older antipsychotics, like haloperidol, are often used in acute psychotic states, over time they may be more prone to lead to such irreversible side effects as tardive dyskinesia, which belongs to the group of extrapyramidal side effects. This is probably the reason one sees less involuntary facial movements, including the movements of the tongue, in a younger population suffering from psychosis, while it is unclear whether atypical antipsychotics truly lead to lower rates of tardive dyskinesia. All the newer antipsychotics, maybe excepting clozapine, can also lead to extrapyramidal side effects, albeit probably less frequently.

The frequent main problem with second generation antipsychotics is the greater risk of a metabolic syndrome. This is probably related to the greater affinity for serotonin receptors, which at the same time, together with the different affinities for dopamine receptor subclasses, may also lead to the lower rates of extrapyramidal side effects. Atypical antipsychotics, particularly olanzapine, are associated with considerable weight gain, diabetes and risk of metabolic syndrome. Risperidone and quetiapine can also lead to weight gain, aripiprazole due to its different pattern of receptor affinities probably considerably less so.

For people who are unwilling or unable to take medication regularly, long-acting depot preparations of antipsychotics may be used to achieve control. They reduce the risk of relapse to a greater degree than oral medications. However, they should only be used if the patient has been on the oral preparation for a sufficient length of time and without side effects that could be a reason for concern, because once the depot has been administered it stays in the body and gives off medication for weeks or months.

## Discontinuing Medication

Antipsychotic medication should be reduced carefully, and then only gradually, unless side effects require an immediate stop or switch to another medication. Aside from a metabolic syndrome and other changes of blood parameters, one always has to keep in mind the risk from a relapse to the individual and his or her environment. It is generally understood a higher the number of psychotic episodes can lead to greater chronicity with more permanent and potentially irreversible negative side effects, such as cognitive impairments, lack of motivation and emotional flattening.(Haverkamp, 2013) The American Psychiatric Association thus suggests considering stopping antipsychotics in some people if there are no symptoms for more than a year.

## Psychosocial Therapies

A number of psychosocial interventions may be useful in the treatment of schizophrenia including:

- family therapy
- assertive community treatment
- supported employment
- cognitive remediation
- skills training
- token economic interventions
- psychosocial interventions for substance use and weight management

## Psychotherapy

There are many approaches for schizophrenia from a psychotherapeutic perspective. Unfortunately, due to lack of resources this important long-term treatment is often relegated to a lesser importance, if it is initiated at all.

Psychological treatments such as acceptance and commitment therapy (ACT) are possibly useful in the treatment of psychosis, helping people to focus more on what they can do in terms of valued life directions despite challenging symptomology.

In psychosis, standardized treatment guidelines recommend psychotherapy (National Institute for Clinical Excellence [NICE], 2014). Meta-analyses show positive effects both on symptoms and recovery (Lysaker et al., 2010; Jones et al., 2012; Okuzawa et al., 2014), especially for therapies >20 sessions (Sarin et al., 2011).

Many psychological mechanisms have been implicated in the development and maintenance of schizophrenia. Cognitive biases have been identified in those with the diagnosis or those at risk, especially when under stress or in confusing situations. Some cognitive features may reflect global neurocognitive deficits such as memory loss; others may be related to particular issues and experiences.

Despite a demonstrated appearance of blunted affect, recent findings indicate that many people diagnosed with schizophrenia are emotionally responsive, particularly to stressful or negative stimuli, and that such sensitivity may cause vulnerability to symptoms or to the disorder. Some evidence suggests that the content of delusional beliefs and psychotic experiences can reflect emotional causes of the disorder, and that how a person interprets such experiences can influence symptomatology. The use of "safety behaviors" (acts such as gestures or the use of words in specific contexts) to avoid or neutralize imagined threats may actually contribute to the chronicity of delusions. Further evidence for the role of psychological mechanisms comes from the effects of psychotherapies on symptoms of schizophrenia.

## CBT and Psychodynamic Psychotherapy

Even with adequate medication management and adherence, at least half of patients continue to suffer from distressing psychotic symptoms (Robinson, Woerner, McMeniman, Mendelowitz, & Bilder, 2004). This points to the importance of psychotherapy, which can be a highly selective way to bring about change, both psychological and neurobiological. (Haverkamp, 2017a, 2018b) The majority of research is on cognitive behavioral therapy (CBT) (Burns et al., 2014; Hutton and Taylor, 2014). However, meta-analyses have found no clear evidence that CBT is superior to other psychotherapeutic approaches (Tolin, 2010; Jones et al., 2012). Since the techniques among the studied therapeutic approaches varied significantly, it may be what all the communication-oriented therapies have in common, communication, which helps achieve results. Communication-Focused Therapy (CFT) as a psychotherapeutic model which works directly with communication mechanisms (Haverkamp, 2010, 2018a) will be outlined below. It must be added, however, that even with the obvious benefit millions of patients derive from psychotherapy every year, the factors driving psychotherapeutic change in psychosis remain understudied (Stafford et al., 2013).

Mentalization-based psychodynamic psychotherapy is another psychotherapeutic approach, which targets disturbances of awareness of the self and others in patients with psychotic-

spectrum disorders. Mentalization-based psychotherapy may offer a useful adjunct to antipsychotic medication and psychosocial evidence-based treatments in the care of individuals in the early phase of psychotic disorders.

The findings from the Danish schizophrenia project (DNS) support the use of psychodynamic psychotherapy for psychosis in patients with a first-episode schizophrenia spectrum disorder. The study was designed as a prospective, comparative, longitudinal multi-site investigation of consecutively referred patients who were included during two years. The patients in the treatment group underwent manualized individual supportive psychodynamic psychotherapy (SPP) in addition to treatment as usual. The intervention group improved significantly on measures of both PANSS and GAF scores, with large effect sizes at two years follow-up after inclusion. Further, improvement on GAF function ( $p = 0.000$ ) and GAF symptom ( $p = 0.010$ ) significantly favored SPP in combination with treatment as usual over treatment as usual alone.

## Communication-Focused Therapy® (CFT)

Communication-Focused Therapy (CFT) was developed by the author to focus more specifically on the communication process between patient and therapist and use it to help the patient acquire more insight and better skills in it. The central piece is that the sending and receiving of meaningful messages is at the heart of any process leading to changes in thoughts or external situations. CBT, psychodynamic psychotherapy and IPT help because they define a format in which communication processes take place that can bring about change without focusing on them. CFT tries to be more efficient in a therapeutic sense by focusing on them more directly.

At the start when treating psychosis, it may appear difficult to engage in a constructive communication process. However, organisms in general tend to react to information if it reaches them somehow. Even in states which seem very closed off, the brain still receives and processes information streaming in from the external world. Persistence, and in many cases antipsychotic medication as a supportive tool, often help to get the patient to a point where they get used to the constant messages, fears decline, and it becomes easier to initiate a response. It is important to remember that it is almost impossible under normal circumstances not to interact with someone who repeatedly sends messages at oneself.

Psychosis means losing touch with reality in one's perception of what is real. It is thus a failure in meaningful communication. Medication is often the first-line treatment, and many psychotherapy schools are reluctant to work with people suffering from psychotic symptoms. However, underlying most psychotherapies is the belief in the effectiveness of interpersonal communication, the 'talk therapy'. Since in psychosis there are patterns of communication with oneself and others that are causing symptoms and are not helpful to the individual, using therapy to change them can be very helpful in the treatment and management of psychosis.

## Reality

When people speak of reality, they really often mean shared reality. Shared reality is the perceptions the majority of people have. It does not necessarily mean that this is the 'true' reality, but it is how the majority of people see the world.

The shared reality may not necessarily be the 'best' reality. Someone could be happy interpreting the world in a different way. Part of the shared reality is due to a shared anatomy and physiology; another part is due to the exchange of information between people. Psychosis affects how information is processed. Besides medication, helping people to have a different perspective on the flows of information and process them differently is an important way to treat psychosis. By helping patients to receive more information and be more perceptive to reality, they can also 'build' a reality which causes less suffering and is better suited to have their needs and wants met.

An important feature of reality is where one perceives that information is coming from. If one hears voices, internal thoughts are misinterpreted as external voices, or if one feels pursued by a secret agent, an aggressive emotion, for example, leads to an aggressive person in the outside world. Better insight into communication and learning communication skills can also help the patient to better localize sources of messages and build a more stable view and sense of reality.

## Learning through Communication

Learning to identify better the sources of information, inside one's own body and in the outside world, can help to attach the correct meaning to a sensation or a voice one hears. This can be trained in the communication space of a psychotherapeutic setting. Practicing communication and reflecting on it helps the patient to develop greater insight and sharpen his or her communication skills.

Learning about communication usually includes a theoretical psychoeducational component and a practical component. Engaging in communication can be important to increase one's confidence and skills in the process. At the same time, better proficiency in communication also makes any other learning processes easier.

## Resources

Patients suffering from psychosis often lose a sense of their own resources because the self becomes fleeting and less accessible. In the therapeutic interaction, through the communication process a more stable distinction between the inside and outside worlds can be established, which strengthens the sense of self, and thus makes the own resources more accessible.

Using communication more optimally can, for example, compensate for various cognitive impairments which are often a part of psychosis. Certain strengths can be used better if the communication with oneself and the world around improves. Resources can also be easier felt and relied upon if one communicates better with oneself, which may include being better at identifying where information comes from, especially if it represents an emotion, what it means, and how one can react to it.

## Psychosis

Psychosis is an abnormal condition of the mind that involves a loss of contact with reality. People experiencing psychosis may exhibit 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. Generally, psychosis involves noticeable deficits in normal behavior and thought (negative symptoms) and often various types of hallucinations or delusional beliefs, particularly with regard to the relation between self and others as in grandiosity or paranoia (positive symptoms).

Unfortunately, psychosis as a diagnostic term is often used after other reasons have been excluded. It may therefore be more illuminating to think of psychosis as a mental process involving changes in how information flows and how these flows are interpreted, which can occur in various psychiatric conditions.

## Misinterpretation of Sources of Information

As the information can no longer be correctly attributed to an outside or an inside source, the individual experiences own thoughts coming from outside in the form of voices or people on the outside as part of internal mental processes and might experience this as people having influence on the own thoughts. From the differently perceived localization of perceptions and messages a different reality is constructed. Since the pieces often do not integrate as well into it as in the shared reality, gaps can result, which then lead to fears, often of an intense and existential nature.

## Misinterpretation of Messages

A misinterpretation of messages is different from a misinterpretation of the sources of information, but they often seem to go hand in hand in psychosis. The conviction that someone is pursued by a neighbor, who is a spy, can be a misinterpretation of an emotion towards this neighbor as a (real) outside event, while a smile from the neighbor in the hallway can be interpreted as her satisfaction about having made a plan to harm the patient, which would be a misinterpretation of her original message of saying 'Hi'.

A misinterpretation of messages usually occurs with respect to the universe of the patient, emotionally and perceptually. When focusing on the communication in therapy, it is therefore important to first get a sense for the universe the patient finds himself or herself in, both perceptually and emotionally. This information allows the therapist to build a better rapport with the patient, since the messages from the therapist will be interpreted by the patient within the context of this universe.

## A Diversity of Symptoms

A host of symptoms can be deduced from the underlying mechanism. Psychosis is often used descriptive term for the hallucinations, delusions and impaired insight that may occur as part of a psychiatric disorder. More correct would be to use it to describe the alterations in information recognition and processing. Some symptoms can be due to a misinterpretation in the source of the information, or as a misinterpretation of one's own position relative to the source of information, while others are clearly due to a misinterpretation of the messages.

## Communication is Life

We engage constantly in communication. The cells in our bodies do so with each other using electrical current, molecules, vibrations or even electromagnetic waves. People communicate with each other also through a multitude of channels, which may on several technologies and intermediaries. It does not have to be an email. Spoken communication requires multiple signal translations from electrical and chemical transmission in the nervous system to mechanical transmission as the muscles and the air stream determine the motions of the vocal chords and then as sound waves travelling through the air, followed by various translations on the receiving end. At each end, in the sender and in the receiver, there is also a processing of information which relies on the highly complex networks of the nervous system. Communication, in short, happens everywhere all the time. It is an integral part of life. Certain communication patterns can, however, also contribute to experiencing anxiety and panic attacks.

## Autoregulation

Communication is an autoregulatory mechanism. It ensures that living organisms, including people, can adapt to their environment and live a life according to their interests, desires, values, and aspirations. This does not only require communicating with a salesperson, writing an exam paper or watching a movie, but also finding out more about oneself, psychologically and physically. Whether measuring one's strength at the gym or engaging in self-talk, this self-exploration requires flows of relevant and meaningful information. Communication allows us to have a sense of self and a grasp of who we are and what we need and want in the world, but it has to be learned similar to our communication with other people.

## Understanding Psychosis

In psychosis the internal and external worlds cannot be distinguished as accurately anymore. They seem to blend into each other. This can cause various symptoms that are then summarized as 'psychotic'. However, each symptom should make sense in the context of the patient's communication patterns as well as the life experiences and emotions the patient faces, which influence the content of the psychosis. Having an understanding for what is happening, is important because it also helps make the patient feel more secure.

Another feature of psychosis is a more or less strong divergence from the patient's perceived world from the shared reality, maybe one aspect which allows artists with intermittent moderate psychosis to paint stunning works of art. This divergence is largely driven by emotions or thoughts which become disassociated from the fabric of the patient's self and personality.

## External vs Internal Reward

It has been shown that rewarding behavior could actually lead to decreases in that behavior in schizophrenic patients, while training and instructing the patient lead to improvements. One might speculate that training and instruction can lead to internal reward which is more motivating than external reward. Thus, even in patients suffering from psychosis, and probably especially here, motivation can be fostered and increased by using the same approaches as in people not suffering from psychosis.

## Meaningful Communication

When an individual suffers from psychosis, a first important step is to help the patient see meaning in the communication process, particularly a relevance to own needs and interests. This helps to build and maintain the motivation which is necessary for a communication oriented therapeutic process. It also helps the patient build a greater sense of efficacy when interacting with his or her environment.

Since the communication process is usually significantly affected in psychosis, it may seem even more difficult to identify and interpret meaning in the messages. This is, however, not necessarily the case. To the contrary, patients suffering from psychosis often see meaning in the world in places where others do not. The drive to see meaning and meaningful connections in information from oneself and the world has not decreased, but the supply of information has.

## Learning about Communication

The first step is to learn about communication, to see how it works, what its constituents are and the purposes it can serve. Often it helps to go through examples that may be of special relevance to the patient. Analyzing them and looking at different options and different outcomes help to illustrate to the patient the importance of the process.

For the learning process, it is important that the therapist has a sense of the patient's perceptual and emotional world. This enables the therapist to use communication styles and messages which are interpreted by the patient not as hostile, deferential or lacking in empathy. Early in the therapeutic process the interaction should help to build a strong and stable therapeutic relationship. This is already part of the learning process and should come first.

## Observing Communication

Splitting up communication and being able to identify its components helps to observe the process and the variations, large and small, in it. Observing is not only a learning experience, but also helps to develop interest for it and see the possibilities in influencing and shaping interactions with others. An interaction can exist in many shapes and forms, while the underlying communication processes adhere to common rules and laws. It helps the patient to appreciate the common underlying mechanisms, which can increase trust in the process and a sense of stability in the world, and, at the same time, to see an interaction as a dynamic group of interacting communication events.

Important is that the patient learns to be able to look at the bigger picture, to observe communication as it takes place, whether it involves the patient or not. This essentially requires being able to take a step out and away from oneself to observe the dynamic without engaging in it at the same time. Over time, this becomes automatic enough that observation and engagement can alternate in one's awareness so quickly that they seem to be simultaneous.

A patient can learn about communication if the therapist reflects and comments on what happens in the communication space between the patient and the therapist. This teaches the patient patterns and skills through the expertise and experience of the therapist. However, it requires that the therapist has this expertise and experience. Especially for a psychotic patient, it is important to show this not just in theory, but also in practice through trying out new communication experiences which then translate into new perspective of the world and oneself.

## Experimenting

Experimenting with communication in its different flavors can give the patient a greater sense of effectiveness with respect to the environment as well as oneself. It gives patients a greater sense of being in control, which is helpful because patients with psychosis often experience helpless and hopelessness, which can also cause some of the sudden emotional outbursts seen in severe cases of psychosis, such as schizophrenia.

A gradual increase in the scope or difficulty in the scope of experimentation probably works best. It can start with little everyday encounters and end with dating. People generally feel more vulnerable the more they feel they expose about themselves. For patients suffering from psychosis this anxiety is much greater, because they sense that their perceived world and the shared reality diverge. Own emotions may also feel real, which makes their visibility to others even more risky. The fear of getting hurt at the core of one's mental structure is universal, the hurt, however, seems more devastating in a patient suffering from psychosis because the structure is already under considerable stress.

## Reflecting

The newly gained knowledge and skills around communication needs to be processed, which can help increase the confidence and sense of effectiveness in the world. This should not be solely about control, but more about seeing oneself as a part of something bigger which is not something to be afraid of, but helps individuals to address and meet their needs and wants.

## The Communication Space

Depending on the environment we move through different communication spaces in everyday life. The communication space is the space in which messages are being sent and received. If one is talking to someone over the phone who lives on a different continent, the communication space extends to this person, while not including the neighbor in the apartment next door, unless the walls are really thin.

To a patient suffering from psychosis the communication space can be extremely large or extremely small, but it usually diverges considerably from that of other people. Thoughts, for example, can be influenced from a large distance, or, at the other extreme, a patient could fully disconnect from the environment. To someone suffering from psychosis the internal world largely determines the communication space, while other people's communication space is determined through an interaction with the environment.

In therapy, it is important to make the patient aware of the communication space he or she builds and what influences it. This is an important component of learning about communication and bringing about change through it.

## Experiencing the World

Psychosis often leads to a vicious cycle which leads to less rather than more communication. Anxieties and a changed perception of reality can lead to a disengagement from it, which reduces the ability to distinguish internal from external reality even more. Practicing and discussing with the patient new ways to communicate, including new communication patterns and better reflection on them, increases the patient's ability to experience and bring about change in the world.

Next to improving interactions with others, a better identification and understanding of meaning helps to anchor the patient better in the shared reality, which makes everyday life and planning for the future easier.

## Identifying Meaning in the World

Fears brought about by the divergence of the perceived reality from the shared reality lead to social isolation and withdrawal, which in turn reinforce feelings of fear and loneliness or frustrations. To break this cycle, it is helpful to help the patient to find more relevance in aspects of the shared reality. This is usually not a process which happens from one day to the next, but over time leads to a closer alignment of the patient's perceptions and intentions with the shared reality

Communication helps in identifying and finding meaning, either communication with oneself or with others. The exchange of messages is like a learning process in which meaning can be identified, found and accumulated. Through meaningful interactions one accumulates more meaning, more connectedness with oneself and the world and reduces the need for thoughts and behaviors which are triggered by fears, guilt, self-blame and other negative emotions. This also helps against depression and anxiety.

There are essentially two techniques to help the patient with identifying and interpreting relevance and meaning in the world. One is by directly discussing with the patient what he or she needs and wants and how this can be met in the world, the second is by helping the patient to have better interactions with the environment which make it easier to see relevance and meaning in the environment. Usually, a combination of both leads to a good outcome.

## Increasing Interactions

Perceiving more meaning also makes interacting with others and oneself more meaningful. This has a positive effect on one's interaction patterns, how and in which one way one relates to one's environment and exchanges messages with it. As the anxiety about interactions with

others decreases, it should become easier to become more socially involved with others, at least to the extent which would feel comfortable to the individual also without the illness.

In the beginning this often requires reducing fears associated with situations or people that are a result of the psychotic experience. Different interpretations of information and the sources of information lead to the perception of a world which is not only less stable but seems to contain real threats, even if the latter ones are just own emotions or thoughts which have manifested as real to the patient. Meaningful interactions with the world can reduce the divergence of realities and also the fear, because they stabilize the patient's experience in the world. To be meaningful the interactions should be an exchange of messages that are relevant to the patient's interests, values or aspirations. This is one reason why it is important to discuss with the patient and get a sense for the patient's needs, wants and values. The next step is then to help the patient find and make interactions that are helpful and meaningful to him or her. With the additional focus on communication, whether in a therapeutic session, internal thoughts or between the patient and others, interactions should become easier and the fears of them lower.

## Values, Needs and Aspirations

Often, individuals suffering from psychosis become uncertain about what is really important to them and the fit between these values and interests and their current life situation. In all areas of life, having one's needs, wants and values met, leads to a higher quality of life. If one values helping others in a specific way, it is important to find ways to engage in this activity, because it will result in a positive feeling. Harm to oneself and others is usually a consequence of some disconnect with one's own feelings, needs, wants and values. Burnout or verbal abuse of another person may be examples.

The change in one's relation with oneself and the environment, as well as the resulting change in the sense of self, make it usually harder for an individual suffering from psychosis to identify correctly the own needs, wants, values, and aspirations, partly out of fear that they could disturb a fragile feeling reality even more. In this situation, it is helpful to help the patient understand that connecting with them actually adds stability, rather than taking away from it. One way to reduce the fear of getting closer to and identifying key parameters about oneself is to help the patient emotionally reconnect. The emotions are the sum of vast amounts of information, such as a feeling of happiness as the product of perceptions of a situation and associated thoughts, and can, if they are owned by the patient, lead to a greater feeling of stability. Helping the patient to notice and identify them more accurately can lower fears and make the inner world, and thus also the outer world in psychosis, seem more predictable. It is important to add in this context, that emotional instability is not so much due to too much of emotions, but a consequence of impairments in a patient's internal communication with the own emotions. The inability to read the emotions accurately leads to the sense of instability, or even the emotional and existential 'void' which is so prevalent in a patient with borderline personality disorder.

## Meaningful Messages as the Instrument of Change

Communication is the vehicle of change. The instruments are meaningful messages which are generated and received by the people who take part in these interactions. In a therapeutic setting, keeping the mutual flow of information relevant and meaningful brings change in both people who take part in this process. The learning curve for the patient may be steeper in certain respects because he or she spends less time in this interaction style than a therapist.

The main objective is that patients can make communication work for themselves on their own. Looking at communication patterns and how meaning is generated in a therapeutic session should not only help with a concrete situation or problem in the moment but provide the tools to work with a multitude of situations or problems in the future. The key to build motivation and use communication processes, is to understand that meaning, information about information which is relevant to and resonates with the recipient of the message, is very much at the heart of it. Becoming better at sending and receiving, interpreting and working with meaning can make the world for an individual suffering from psychosis more stable and broadens the scope of change that can be affected on the world and oneself. Better insight and skills around communication and meaning take some time but can have a lasting beneficial effect for and individual suffering from psychosis.

## Knowing Where Information Comes From

In the end, the patient should also have a better sense of communicating and knowing where information comes from. Not only does this help this reduce the divergence between the experienced world and the shared world, but it also helps to use information and communication better. Being able to identify a source of information can make it easier to identify meaning and respond to it. This helps build a stronger sense of self, better relationships and imparts greater confidence in dealing with everyday life as well towards fulfilling own aspirations. Greater insight and skills into communication can accomplish this.

## Prognosis

If not treated, schizophrenia has an unfavorable long-term prognosis. When it becomes chronic, changes to the personality and some symptoms of the condition may become largely irreversible. This often also leads to loss of relationships and livelihood, and some schizophrenia sufferers begin to self-medicate with illegal drugs.

Schizophrenia has great human and economic costs. It results in a decreased life expectancy by 10–25 years. This is primarily because of its association with obesity, poor diet, sedentary lifestyles, and smoking, with an increased rate of suicide playing a lesser role. Antipsychotic medications may also increase the risk. These differences in life expectancy increased between the 1970s and 1990s.

Schizophrenia is a major cause of disability, with active psychosis ranked as the third-most-disabling condition after quadriplegia and dementia and ahead of paraplegia and blindness. Approximately three-fourths of people with schizophrenia have ongoing disability with relapses and 16.7 million people globally are deemed to have moderate or severe disability from the condition. Some people do recover completely and others function well in society. Most people with schizophrenia live independently with community support. About 85% are unemployed. Some evidence suggests that paranoid schizophrenia may have a better prospect than other types of schizophrenia for independent living and occupational functioning. In people with a first episode of psychosis a good long-term outcome occurs in 42%, an intermediate outcome in 35% and a poor outcome in 27%. Outcomes for schizophrenia appear better in the developing than the developed world. These conclusions have been questioned.

There is a higher than average suicide rate associated with schizophrenia. This has been cited at 10%, but a more recent analysis revises the estimate to 4.9%, most often occurring in the period following onset or first hospital admission. Several times more (20 to 40%) attempt suicide at least once. There are a variety of risk factors, including male gender, depression, and a high intelligence quotient.

Schizophrenia and smoking have shown a strong association in studies worldwide. Use of cigarettes is especially high in those diagnosed with schizophrenia, with estimates ranging from 80 to 90% being regular smokers, as compared to 20% of the general population. Those who smoke tend to smoke heavily, and additionally smoke cigarettes with high nicotine content. Some propose that this is in an effort to improve symptoms. Among people with schizophrenia use of cannabis is also common.

## Into the Future

From the discussion it should be obvious that there is still much to be done in improving the treatment of psychosis and schizophrenia. However, particularly on the side of psychotherapy, there is a widespread lack in using the tools we already have available. This is non-excusable, and the argument of a lack of resources does not make it better.

A greater focus on communication, internal and external, can help to move the treatment of schizophrenia forward in ways that may not even be fathomed yet.



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## References

- American Psychiatric Association (2013). *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.). Arlington: American Psychiatric Publishing. pp. 101–05. ISBN 978-0-89042-555-8.
- Ferri FF (2010). *Ferri's differential diagnosis : a practical guide to the differential diagnosis of symptoms, signs, and clinical disorders* (2nd ed.). Philadelphia, PA: Elsevier/Mosby. p. Chapter S. ISBN 978-0-323-07699-9.
- Jones D (2003) [1917]. Roach P, Hartmann J, Setter J, eds. *English Pronouncing Dictionary*. Cambridge: Cambridge University Press. ISBN 978-3-12-539683-8.
- "Schizophrenia". National Institute of Mental Health. January 2016. Archived from the original on 25 November 2016. Retrieved 3 February 2016.
- Owen MJ, Sawa A, Mortensen PB (July 2016). "Schizophrenia". *Lancet*. 388 (10039): 86–97. doi:10.1016/S0140-6736(15)01121-6. PMC 4940219. PMID 26777917.
- Laursen TM, Munk-Olsen T, Vestergaard M (March 2012). "Life expectancy and cardiovascular mortality in persons with schizophrenia". *Current Opinion in Psychiatry*. 25 (2): 83–8. doi:10.1097/YCO.0b013e32835035ca. PMID 22249081.
- GBD 2015 Mortality and Causes of Death Collaborators (October 2016). "Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015". *Lancet*. 388 (10053): 1459–1544. doi:10.1016/s0140-6736(16)31012-1. PMC 5388903. PMID 27733281.
- Buckley PF, Miller BJ, Lehrer DS, Castle DJ (March 2009). "Psychiatric comorbidities and schizophrenia". *Schizophrenia Bulletin*. 35 (2): 383–402. doi:10.1093/schbul/sbn135. PMC 2659306. PMID 19011234.
- Chadwick B, Miller ML, Hurd YL (October 2013). "Cannabis Use during Adolescent Development: Susceptibility to Psychiatric Illness". *Frontiers in Psychiatry (Review)*. 4: 129. doi:10.3389/fpsy.2013.00129. PMC 3796318. PMID 24133461.
- Haverkamp, C. J. (2010). *Communication and Therapy* (3rd ed.). Dublin: Psychiatry Psychotherapy Communication Publishing Ltd.
- Haverkamp, C. J. (2012). A Case of Psychosis. *J Psychiatry Psychotherapy Communication*, 1(3), 61–67.
- Haverkamp, C. J. (2013). Antipsychotics: Emotional Flattening vs Apathy. *J Psychiatry Psychotherapy Communication*, 2(2), 31–32.
- Haverkamp, C. J. (2017a). *Change a Life*.
- Haverkamp, C. J. (2017b). Communication-Focused Therapy (CFT) for Psychosis. *J Psychiatry Psychotherapy Communication*, 6(4), 116–119.

- Haverkamp, C. J. (2018a). Atypical Depressions. *J Psychiatry Psychotherapy Communication*, 9(4), 91–97.
- Haverkamp, C. J. (2018b). *Psychiatric Conditions, Psychotherapy and Medication* (1st ed.). Dublin: Psychiatry Psychotherapy Communication Publishing Ltd.
- Kavanagh DH, Tansey KE, O'Donovan MC, Owen MJ (February 2015). "Schizophrenia genetics: emerging themes for a complex disorder". *Molecular Psychiatry*. 20 (1): 72–6. doi:10.1038/mp.2014.148. PMID 25385368.
- Picchioni MM, Murray RM (July 2007). "Schizophrenia". *BMJ*. 335 (7610): 91–5. doi:10.1136/bmj.39227.616447.BE. PMC 1914490. PMID 17626963.
- Kane JM, Correll CU (2010). "Pharmacologic treatment of schizophrenia". *Dialogues in Clinical Neuroscience*. 12 (3): 345–57. PMC 3085113. PMID 20954430.
- Becker T, Kilian R (2006). "Psychiatric services for people with severe mental illness across western Europe: what can be generalized from current knowledge about differences in provision, costs and outcomes of mental health care?". *Acta Psychiatrica Scandinavica. Supplementum*. 113 (429): 9–16. doi:10.1111/j.1600-0447.2005.00711.x. PMID 16445476.
- Global Burden of Disease Study 2013 Collaborators (August 2015). "Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013". *Lancet*. 386 (9995): 743–800. doi:10.1016/S0140-6736(15)60692-4. PMC 4561509. PMID 26063472.
- Lawrence RE, First MB, Lieberman JA (2015). "Chapter 48: Schizophrenia and Other Psychoses". In Tasman A, Kay J, Lieberman JA, First MB, Riba MB. *Psychiatry* (fourth ed.). John Wiley & Sons, Ltd. pp. 798, 816, 819. doi:10.1002/9781118753378.ch48. ISBN 978-1-118-84547-9.
- Foster A, Gable J, Buckley J (September 2012). "Homelessness in schizophrenia". *The Psychiatric Clinics of North America*. 35 (3): 717–34. doi:10.1016/j.psc.2012.06.010. PMID 22929875.
- Hor K, Taylor M (November 2010). "Suicide and schizophrenia: a systematic review of rates and risk factors". *Journal of Psychopharmacology*. 24 (4 Suppl): 81–90. doi:10.1177/1359786810385490. PMC 2951591. PMID 20923923.
- Heinz A, Voss M, Lawrie SM, Mishara A, Bauer M, Gallinat J, et al. (September 2016). "Shall we really say goodbye to first rank symptoms?". *European Psychiatry*. 37: 8–13. doi:10.1016/j.eurpsy.2016.04.010. PMID 27429167.
- Brunet-Gouet E, Decety J (December 2006). "Social brain dysfunctions in schizophrenia: a review of neuroimaging studies". *Psychiatry Research*. 148 (2–3): 75–92. doi:10.1016/j.pscychresns.2006.05.001. PMID 17088049.
- Hirsch SR, Weinberger DR (2003). *Schizophrenia*. Wiley-Blackwell. p. 481. ISBN 978-0-632-06388-8.
- Ungvari GS, Caroff SN, Gerevich J (March 2010). "The catatonia conundrum: evidence of psychomotor phenomena as a symptom dimension in psychotic disorders".

- Schizophrenia Bulletin. 36 (2): 231–8. doi:10.1093/schbul/sbp105. PMC 2833122. PMID 19776208.
- Kohler CG, Walker JB, Martin EA, Healey KM, Moberg PJ (September 2010). "Facial emotion perception in schizophrenia: a meta-analytic review". *Schizophrenia Bulletin*. 36 (5): 1009–19. doi:10.1093/schbul/sbn192. PMC 2930336. PMID 19329561. Archived from the original on 25 July 2015.
- Current diagnosis & treatment psychiatry (2nd ed.). New York: McGraw-Hill Medical. 2008. p. 48. ISBN 978-0-07-142292-5.
- Oyebode F (2014). *Sims' Symptoms in the Mind E-Book: Textbook of Descriptive Psychopathology*. Elsevier Health Sciences. p. 152. ISBN 978-0-7020-5555-3.
- Baier M (August 2010). "Insight in schizophrenia: a review". *Current Psychiatry Reports*. 12 (4): 356–61. doi:10.1007/s11920-010-0125-7. PMID 20526897.
- Pijnenborg GH, van Donkersgoed RJ, David AS, Aleman A (March 2013). "Changes in insight during treatment for psychotic disorders: a meta-analysis". *Schizophrenia Research*. 144 (1–3): 109–17. doi:10.1016/j.schres.2012.11.018. PMID 23305612.
- Fadgyas-Stanculete M, Buga AM, Popa-Wagner A, Dumitrascu DL (2014). "The relationship between irritable bowel syndrome and psychiatric disorders: from molecular changes to clinical manifestations". *Journal of Molecular Psychiatry*. 2 (1): 4. doi:10.1186/2049-9256-2-4. PMC 4223878. PMID 25408914.
- Goroll AH, Mulley AG (2011). *Primary Care Medicine: Office Evaluation and Management of The Adult Patient: Sixth Edition*. Lippincott Williams & Wilkins. ISBN 978-1-4511-2159-9.
- Sims A (2002). *Symptoms in the mind: an introduction to descriptive psychopathology*. Philadelphia: W. B. Saunders. ISBN 978-0-7020-2627-0.
- Kneisl C, Trigoboff E (2009). *Contemporary Psychiatric-Mental Health Nursing (2nd ed.)*. London: Pearson Prentice Ltd.
- American Psychiatric Association. Task Force on DSM-IV. (2000). *Diagnostic and statistical manual of mental disorders: DSM-IV-TR*. American Psychiatric Pub. p. 299. ISBN 978-0-89042-025-6.
- Velligan DI, Alphas LD (1 March 2008). "Negative Symptoms in Schizophrenia: The Importance of Identification and Treatment". *Psychiatric Times*. 25 (3). Archived from the original on 6 October 2009.
- Smith T, Weston C, Lieberman J (August 2010). "Schizophrenia (maintenance treatment)". *American Family Physician*. 82 (4): 338–9. PMID 20704164.
- Buxbaum J, Sklar P, Nestler E, Charney D (2013). "17". *Neurobiology of Mental Illness (4th ed.)*. Oxford University Press. ISBN 978-0-19-993495-9.
- Bozikas VP, Andreou C (February 2011). "Longitudinal studies of cognition in first episode psychosis: a systematic review of the literature". *The Australian and New Zealand Journal of Psychiatry*. 45 (2): 93–108. doi:10.3109/00048674.2010.541418. PMID 21320033. Archived from the original on 30 November 2016.
- Dauvermann MR, Whalley HC, Schmidt A, Lee GL, Romaniuk L, Roberts N, Johnstone EC,

- Lawrie SM, Moorhead TW (1 January 2014). "Computational neuropsychiatry - schizophrenia as a cognitive brain network disorder". *Frontiers in Psychiatry*. 5: 30. doi:10.3389/fpsy.2014.00030. PMC 3971172. PMID 24723894.
- Shah JN, Qureshi SU, Jawaid A, Schulz PE (June 2012). "Is there evidence for late cognitive decline in chronic schizophrenia?". *The Psychiatric Quarterly*. 83 (2): 127–44. doi:10.1007/s11126-011-9189-8. PMID 21863346.
- Goldberg TE, Keefe RS, Goldman RS, Robinson DG, Harvey PD (April 2010). "Circumstances under which practice does not make perfect: a review of the practice effect literature in schizophrenia and its relevance to clinical treatment studies". *Neuropsychopharmacology*. 35 (5): 1053–62. doi:10.1038/npp.2009.211. PMC 3055399. PMID 20090669.
- Kurtz MM, Moberg PJ, Gur RC, Gur RE (December 2001). "Approaches to cognitive remediation of neuropsychological deficits in schizophrenia: a review and meta-analysis". *Neuropsychology Review*. 11 (4): 197–210. doi:10.1023/A:1012953108158. PMID 11883669.
- Tan BL (August 2009). "Profile of cognitive problems in schizophrenia and implications for vocational functioning". *Australian Occupational Therapy Journal*. 56 (4): 220–8. doi:10.1111/j.1440-1630.2008.00759.x. PMID 20854522.
- Cirillo MA, Seidman LJ (June 2003). "Verbal declarative memory dysfunction in schizophrenia: from clinical assessment to genetics and brain mechanisms". *Neuropsychology Review*. 13 (2): 43–77. doi:10.1023/A:1023870821631. PMID 12887039.
- Pomarol-Clotet E, Oh TM, Laws KR, McKenna PJ (February 2008). "Semantic priming in schizophrenia: systematic review and meta-analysis". *The British Journal of Psychiatry*. 192 (2): 92–7. doi:10.1192/bjp.bp.106.032102. PMID 18245021.
- Addington J, Cadenhead KS, Cannon TD, Cornblatt B, McGlashan TH, Perkins DO, Seidman LJ, Tsuang M, Walker EF, Woods SW, Heinssen R (May 2007). "North American Prodrome Longitudinal Study: a collaborative multisite approach to prodromal schizophrenia research". *Schizophrenia Bulletin*. 33 (3): 665–72. doi:10.1093/schbul/sbl075. PMC 2526151. PMID 17255119.
- Ochoa S, Usall J, Cobo J, Labad X, Kulkarni J (2012). "Gender differences in schizophrenia and first-episode psychosis: a comprehensive literature review". *Schizophrenia Research and Treatment (Review)*. 2012: 1–9. doi:10.1155/2012/916198. PMC 3420456. PMID 22966451.
- Amminger GP, Leicester S, Yung AR, Phillips LJ, Berger GE, Francey SM, Yuen HP, McGorry PD (May 2006). "Early-onset of symptoms predicts conversion to non-affective psychosis in ultra-high risk individuals". *Schizophrenia Research*. 84 (1): 67–76. doi:10.1016/j.schres.2006.02.018. PMID 16677803.
- Parnas J, Jorgensen A (November 1989). "Pre-morbid psychopathology in schizophrenia spectrum". *The British Journal of Psychiatry*. 155 (5): 623–7. doi:10.1192/s0007125000018109. PMID 2611591.

- Coyle J (2006). "Chapter 54: The Neurochemistry of Schizophrenia". In Siegal GJ, et al. *Basic Neurochemistry: Molecular, Cellular and Medical Aspects* (7th ed.). Burlington, MA: Elsevier Academic Press. pp. 876–78. ISBN 978-0-12-088397-4.
- Khandaker GM, Barnett JH, White IR, Jones PB (November 2011). "A quantitative meta-analysis of population-based studies of premorbid intelligence and schizophrenia". *Schizophrenia Research*. 132 (2–3): 220–7. doi:10.1016/j.schres.2011.06.017. PMC 3485562. PMID 21764562.
- Welham J, Isohanni M, Jones P, McGrath J (May 2009). "The antecedents of schizophrenia: a review of birth cohort studies". *Schizophrenia Bulletin*. 35 (3): 603–23. doi:10.1093/schbul/sbn084. PMC 2669575. PMID 18658128.
- Drake RJ, Lewis SW (March 2005). "Early detection of schizophrenia". *Current Opinion in Psychiatry*. 18 (2): 147–50. doi:10.1097/00001504-200503000-00007. PMID 16639167.
- Combs DR, Mueser KT, Gutierrez MM (2011). "Chapter 8: Schizophrenia: Etiological considerations". In Hersen M, Beidel DC. *Adult psychopathology and diagnosis* (6th ed.). John Wiley & Sons. ISBN 978-1-118-13884-7.
- O'Donovan MC, Williams NM, Owen MJ (October 2003). "Recent advances in the genetics of schizophrenia". *Human Molecular Genetics*. 12 Spec No 2: R125–33. doi:10.1093/hmg/ddg302. PMID 12952866.
- Farrell MS, Werge T, Sklar P, Owen MJ, Ophoff RA, O'Donovan MC, Corvin A, Cichon S, Sullivan PF (May 2015). "Evaluating historical candidate genes for schizophrenia". *Molecular Psychiatry*. 20 (5): 555–62. doi:10.1038/mp.2015.16. PMC 4414705. PMID 25754081.
- Schork AJ, Wang Y, Thompson WK, Dale AM, Andreassen OA (February 2016). "New statistical approaches exploit the polygenic architecture of schizophrenia--implications for the underlying neurobiology". *Current Opinion in Neurobiology*. 36: 89–98. doi:10.1016/j.conb.2015.10.008. PMC 5380793. PMID 26555806.
- Kendler KS (March 2016). "The Schizophrenia Polygenic Risk Score: To What Does It Predispose in Adolescence?". *JAMA Psychiatry*. 73 (3): 193–4. doi:10.1001/jamapsychiatry.2015.2964. PMID 26817666.
- Lowther C, Costain G, Baribeau DA, Bassett AS (September 2017). "Genomic Disorders in Psychiatry-What Does the Clinician Need to Know?". *Current Psychiatry Reports*. 19 (11): 82. doi:10.1007/s11920-017-0831-5. PMID 28929285.
- Craddock N, Owen MJ (February 2010). "The Kraepelinian dichotomy - going, going... but still not gone". *The British Journal of Psychiatry*. 196 (2): 92–5. doi:10.1192/bjp.bp.109.073429. PMC 2815936. PMID 20118450.
- Negrón-Oyarzo I, Lara-Vásquez A, Palacios-García I, Fuentealba P, Aboitiz F (March 2016). "Schizophrenia and reelin: a model based on prenatal stress to study epigenetics, brain development and behavior". *Biological Research*. 49: 16. doi:10.1186/s40659-016-0076-5. PMC 4787713. PMID 26968981.
- Brown AS (January 2011). "The environment and susceptibility to schizophrenia". *Progress in Neurobiology*. 93 (1): 23–58. doi:10.1016/j.pneurobio.2010.09.003. PMC 3521525.

PMID 20955757.

- le Charpentier Y, Hoang C, Mokni M, Finet JF, Biaggi A, Saguin M, Plantier F (2005). "[Histopathology and ultrastructure of opportunistic infections of the digestive tract in acquired immunodeficiency syndrome]". *Archives d'Anatomie et de Cytologie Pathologiques*. 40 (2–3): 138–49. doi:10.1289/ehp.7572. PMC 1280409. PMID 16140635.
- Dvir Y, Denietolis B, Frazier JA (October 2013). "Childhood trauma and psychosis". *Child and Adolescent Psychiatric Clinics of North America*. 22 (4): 629–41. doi:10.1016/j.chc.2013.04.006. PMID 24012077.
- Misiak B, Krefft M, Bielawski T, Moustafa AA, Sasiadek MM, Frydecka D (April 2017). "Toward a unified theory of childhood trauma and psychosis: A comprehensive review of epidemiological, clinical, neuropsychological and biological findings". *Neuroscience and Biobehavioral Reviews*. 75: 393–406. doi:10.1016/j.neubiorev.2017.02.015. PMID 28216171.
- van Os J (April 2004). "Does the urban environment cause psychosis?". *The British Journal of Psychiatry*. 184 (4): 287–8. doi:10.1192/bjp.184.4.287. PMID 15056569.
- Selten JP, Cantor-Graae E, Kahn RS (March 2007). "Migration and schizophrenia". *Current Opinion in Psychiatry*. 20 (2): 111–5. doi:10.1097/YCO.0b013e328017f68e. PMID 17278906.
- Nemani K, Hosseini Ghomi R, McCormick B, Fan X (January 2015). "Schizophrenia and the gut-brain axis". *Progress in Neuro-Psychopharmacology & Biological Psychiatry*. 56: 155–60. doi:10.1016/j.pnpbp.2014.08.018. PMID 25240858.
- Lachance LR, McKenzie K (February 2014). "Biomarkers of gluten sensitivity in patients with non-affective psychosis: a meta-analysis". *Schizophrenia Research (Review)*. 152 (2–3): 521–7. doi:10.1016/j.schres.2013.12.001. PMID 24368154.
- Gregg L, Barrowclough C, Haddock G (May 2007). "Reasons for increased substance use in psychosis". *Clinical Psychology Review*. 27 (4): 494–510. doi:10.1016/j.cpr.2006.09.004. PMID 17240501.
- Sagud M, Mihaljević-Peles A, Mück-Seler D, Pivac N, Vuksan-Cusa B, Brataljenović T, Jakovljević M (September 2009). "Smoking and schizophrenia" (PDF). *Psychiatria Danubina*. 21 (3): 371–5. PMID 19794359.
- Large M, Sharma S, Compton MT, Slade T, Nielssen O (June 2011). "Cannabis use and earlier onset of psychosis: a systematic meta-analysis". *Archives of General Psychiatry*. 68 (6): 555–61. doi:10.1001/archgenpsychiatry.2011.5. PMID 21300939.
- Niesink RJ, van Laar MW (October 2013). "Does Cannabidiol Protect Against Adverse Psychological Effects of THC?". *Frontiers in Psychiatry (Review)*. 4: 130. doi:10.3389/fpsy.2013.00130. PMC 3797438. PMID 24137134.
- Parakh P, Basu D (August 2013). "Cannabis and psychosis: have we found the missing links?". *Asian Journal of Psychiatry (Review)*. 6 (4): 281–7. doi:10.1016/j.ajp.2013.03.012. PMID 23810133. Cannabis acts as a component cause of psychosis, that is, it increases the risk of psychosis in people with certain genetic or

environmental vulnerabilities, though by itself, it is neither a sufficient nor a necessary cause of psychosis.

- Gage SH, Hickman M, Zammit S (April 2016). "Association Between Cannabis and Psychosis: Epidemiologic Evidence". *Biological Psychiatry*. 79 (7): 549–56. doi:10.1016/j.biopsych.2015.08.001. PMID 26386480.
- Leweke FM, Koethe D (June 2008). "Cannabis and psychiatric disorders: it is not only addiction". *Addiction Biology*. 13 (2): 264–75. doi:10.1111/j.1369-1600.2008.00106.x. PMID 18482435.
- Volken R (June 2004). "Viruses and schizophrenia: a focus on herpes simplex virus". *Herpes*. 11 Suppl 2 (Suppl 2): 83A–88A. PMID 15319094.
- Arias I, Sorlozano A, Villegas E, de Dios Luna J, McKenney K, Cervilla J, Gutierrez B, Gutierrez J (April 2012). "Infectious agents associated with schizophrenia: a meta-analysis". *Schizophrenia Research*. 136 (1–3): 128–36. doi:10.1016/j.schres.2011.10.026. PMID 22104141.
- Khandaker GM (August 2012). "Childhood infection and adult schizophrenia: a meta-analysis of population-based studies". *Schizophr. Res.* 139 (1–3): 161–8. doi:10.1016/j.schres.2012.05.023. PMC 3485564. PMID 22704639.
- Broome MR, Woolley JB, Tabraham P, Johns LC, Bramon E, Murray GK, Pariante C, McGuire PK, Murray RM (November 2005). "What causes the onset of psychosis?". *Schizophrenia Research*. 79 (1): 23–34. CiteSeerX 10.1.1.117.9835. doi:10.1016/j.schres.2005.02.007. PMID 16198238.
- Bentall RP, Fernyhough C, Morrison AP, Lewis S, Corcoran R (June 2007). "Prospects for a cognitive-developmental account of psychotic experiences". *The British Journal of Clinical Psychology*. 46 (Pt 2): 155–73. doi:10.1348/014466506X123011. PMID 17524210.
- Kurtz MM (April 2005). "Neurocognitive impairment across the lifespan in schizophrenia: an update". *Schizophrenia Research*. 74 (1): 15–26. doi:10.1016/j.schres.2004.07.005. PMID 15694750.
- Cohen AS, Docherty NM (July 2004). "Affective reactivity of speech and emotional experience in patients with schizophrenia". *Schizophrenia Research*. 69 (1): 7–14. doi:10.1016/S0920-9964(03)00069-0. PMID 15145465.
- Horan WP, Blanchard JJ (April 2003). "Emotional responses to psychosocial stress in schizophrenia: the role of individual differences in affective traits and coping". *Schizophrenia Research*. 60 (2–3): 271–83. doi:10.1016/S0920-9964(02)00227-X. PMID 12591589.
- Smith B, Fowler DG, Freeman D, Bebbington P, Bashforth H, Garety P, Dunn G, Kuipers E (September 2006). "Emotion and psychosis: links between depression, self-esteem, negative schematic beliefs and delusions and hallucinations". *Schizophrenia Research*. 86 (1–3): 181–8. doi:10.1016/j.schres.2006.06.018. PMID 16857346.
- Beck, AT (2004). "A Cognitive Model of Schizophrenia". *Journal of Cognitive Psychotherapy*. 18 (3): 281–88. doi:10.1891/jcop.18.3.281.65649.

- Bell V, Halligan PW, Ellis HD (May 2006). "Explaining delusions: a cognitive perspective". *Trends in Cognitive Sciences*. 10 (5): 219–26. doi:10.1016/j.tics.2006.03.004. PMID 16600666.
- Freeman D, Garety PA, Kuipers E, Fowler D, Bebbington PE, Dunn G (January 2007). "Acting on persecutory delusions: the importance of safety seeking". *Behaviour Research and Therapy*. 45 (1): 89–99. doi:10.1016/j.brat.2006.01.014. PMID 16530161.
- Kuipers E, Garety P, Fowler D, Freeman D, Dunn G, Bebbington P (October 2006). "Cognitive, emotional, and social processes in psychosis: refining cognitive behavioral therapy for persistent positive symptoms". *Schizophrenia Bulletin*. 32 Suppl 1: S24–31. doi:10.1093/schbul/sbl014. PMC 2632539. PMID 16885206.
- Torres US, Portela-Oliveira E, Borgwardt S, Busatto GF (December 2013). "Structural brain changes associated with antipsychotic treatment in schizophrenia as revealed by voxel-based morphometric MRI: an activation likelihood estimation meta-analysis". *BMC Psychiatry*. 13: 342. doi:10.1186/1471-244x-13-342. PMC 3878502. PMID 24359128.
- Kircher T, Thienel R (2006). "Functional brain imaging of symptoms and cognition in schizophrenia". *The Boundaries of Consciousness*. Amsterdam: Elsevier. p. 302. ISBN 978-0-444-52876-6.
- Olabi B, Ellison-Wright I, McIntosh AM, Wood SJ, Bullmore E, Lawrie SM (July 2011). "Are there progressive brain changes in schizophrenia? A meta-analysis of structural magnetic resonance imaging studies". *Biological Psychiatry*. 70 (1): 88–96. doi:10.1016/j.biopsych.2011.01.032. PMID 21457946.
- Haijma SV, Van Haren N, Cahn W, Koolschijn PC, Hulshoff Pol HE, Kahn RS (September 2013). "Brain volumes in schizophrenia: a meta-analysis in over 18 000 subjects". *Schizophrenia Bulletin*. 39 (5): 1129–38. doi:10.1093/schbul/sbs118. PMC 3756785. PMID 23042112.
- Green MF (2006). "Cognitive impairment and functional outcome in schizophrenia and bipolar disorder". *The Journal of Clinical Psychiatry*. 67 Suppl 9 (Suppl 9): 3–8, discussion 36–42. doi:10.4088/jcp.1006e12. PMID 16965182.
- Insel TR (November 2010). "Rethinking schizophrenia". *Nature*. 468 (7321): 187–93. Bibcode:2010Natur.468..187I. doi:10.1038/nature09552. PMID 21068826.
- Moncrieff J, Leo J (September 2010). "A systematic review of the effects of antipsychotic drugs on brain volume". *Psychological Medicine (Systematic Review)*. 40 (9): 1409–22. doi:10.1017/S0033291709992297. PMID 20085668.
- Van Haren NE, Cahn W, Hulshoff Pol HE, Kahn RS (December 2013). "Confounders of excessive brain volume loss in schizophrenia". *Neuroscience and Biobehavioral Reviews (Review)*. 37 (10 Pt 1): 2418–23. doi:10.1016/j.neubiorev.2012.09.006. PMID 23000300.
- Laruelle M, Abi-Dargham A, van Dyck CH, Gil R, D'Souza CD, Erdos J, McCance E, Rosenblatt W, Fingado C, Zoghbi SS, Baldwin RM, Seibyl JP, Krystal JH, Charney DS, Innis RB (August 1996). "Single photon emission computerized tomography imaging of amphetamine-induced dopamine release in drug-free schizophrenic subjects". *Proceedings of the National Academy of Sciences of the United States of America*. 93 (17): 9235–40.

Bibcode:1996PNAS...93.9235L. doi:10.1073/pnas.93.17.9235. PMC 38625. PMID 8799184.

- Howes OD, Kambeitz J, Kim E, Stahl D, Slifstein M, Abi-Dargham A, Kapur S (August 2012). "The nature of dopamine dysfunction in schizophrenia and what this means for treatment". *Archives of General Psychiatry*. 69 (8): 776–86. doi:10.1001/archgenpsychiatry.2012.169. PMC 3730746. PMID 22474070.
- Fusar-Poli P, Meyer-Lindenberg A (January 2013). "Striatal presynaptic dopamine in schizophrenia, part II: meta-analysis of [(18)F]/[(11)C]-DOPA PET studies". *Schizophrenia Bulletin*. 39 (1): 33–42. doi:10.1093/schbul/sbr180. PMC 3523905. PMID 22282454.
- Weinstein JJ, Chohan MO, Slifstein M, Kegeles LS, Moore H, Abi-Dargham A (January 2017). "Pathway-Specific Dopamine Abnormalities in Schizophrenia". *Biological Psychiatry*. 81 (1): 31–42. doi:10.1016/j.biopsych.2016.03.2104. PMC 5177794. PMID 27206569.
- Salavati B, Rajji TK, Price R, Sun Y, Graff-Guerrero A, Daskalakis ZJ (January 2015). "Imaging-based neurochemistry in schizophrenia: a systematic review and implications for dysfunctional long-term potentiation". *Schizophrenia Bulletin*. 41 (1): 44–56. doi:10.1093/schbul/sbu132. PMC 4266301. PMID 25249654.
- Winterer G, Weinberger DR (November 2004). "Genes, dopamine and cortical signal-to-noise ratio in schizophrenia". *Trends in Neurosciences*. 27 (11): 683–90. doi:10.1016/j.tins.2004.08.002. PMID 15474169.
- Jones HM, Pilowsky LS (October 2002). "Dopamine and antipsychotic drug action revisited". *The British Journal of Psychiatry*. 181 (4): 271–5. doi:10.1192/bjp.181.4.271. PMID 12356650.
- Konradi C, Heckers S (February 2003). "Molecular aspects of glutamate dysregulation: implications for schizophrenia and its treatment". *Pharmacology & Therapeutics*. 97 (2): 153–79. doi:10.1016/S0163-7258(02)00328-5. PMC 4203361. PMID 12559388.
- Lahti AC, Weiler MA, Tamara Michaelidis BA, Parwani A, Tamminga CA (October 2001). "Effects of ketamine in normal and schizophrenic volunteers". *Neuropsychopharmacology*. 25 (4): 455–67. doi:10.1016/S0893-133X(01)00243-3. PMID 11557159.
- Coyle JT, Tsai G, Goff D (November 2003). "Converging evidence of NMDA receptor hypofunction in the pathophysiology of schizophrenia". *Annals of the New York Academy of Sciences*. 1003 (1): 318–27. Bibcode:2003NYASA1003..318C. doi:10.1196/annals.1300.020. PMID 14684455.
- Tuominen HJ, Tiihonen J, Wahlbeck K (January 2005). "Glutamatergic drugs for schizophrenia: a systematic review and meta-analysis". *Schizophrenia Research*. 72 (2–3): 225–34. doi:10.1016/j.schres.2004.05.005. PMID 15560967.
- de Jonge JC, Vinkers CH, Hulshoff Pol HE, Marsman A (2017). "GABAergic Mechanisms in Schizophrenia: Linking Postmortem and In Vivo Studies". *Frontiers in Psychiatry*. 8: 118. doi:10.3389/fpsy.2017.00118. PMC 5554536. PMID 28848455.
- American Psychiatric Association (2013). *Diagnostic and Statistical Manual of Mental Disorders (5th ed.)*. Arlington: American Psychiatric Publishing. ISBN 978-0-89042-555-

8.

Tandon R, Gaebel W, Barch DM, Bustillo J, Gur RE, Heckers S, Malaspina D, Owen MJ, Schultz S, Tsuang M, Van Os J, Carpenter W (October 2013). "Definition and description of schizophrenia in the DSM-5". *Schizophrenia Research*. 150 (1): 3–10. doi:10.1016/j.schres.2013.05.028. PMID 23800613.

As referenced from PMID 23800613, Heckers S, Tandon R, Bustillo J (March 2010). "Catatonia in the DSM--shall we move or not?". *Schizophrenia Bulletin* (Editorial). 36 (2): 205–7. doi:10.1093/schbul/sbp136. PMC 2833126. PMID 19933711.

Barch DM, Bustillo J, Gaebel W, Gur R, Heckers S, Malaspina D, Owen MJ, Schultz S, Tandon R, Tsuang M, Van Os J, Carpenter W (October 2013). "Logic and justification for dimensional assessment of symptoms and related clinical phenomena in psychosis: relevance to DSM-5". *Schizophrenia Research*. 150 (1): 15–20. doi:10.1016/j.schres.2013.04.027. PMID 23706415.

Jakobsen KD, Frederiksen JN, Hansen T, Jansson LB, Parnas J, Werge T (2005). "Reliability of clinical ICD-10 schizophrenia diagnoses". *Nordic Journal of Psychiatry*. 59 (3): 209–12. doi:10.1080/08039480510027698. PMID 16195122..

Pope HG (April 1983). "Distinguishing bipolar disorder from schizophrenia in clinical practice: guidelines and case reports". *Hospital & Community Psychiatry*. 34 (4): 322–8. doi:10.1176/ps.34.4.322. PMID 6840720.

McGlashan TH (February 1987). "Testing DSM-III symptom criteria for schizotypal and borderline personality disorders". *Archives of General Psychiatry*. 44 (2): 143–8. doi:10.1001/archpsyc.1987.01800140045007. PMID 3813809.

Gabbard GO (15 May 2007). *Gabbard's Treatments of Psychiatric Disorders, Fourth Edition (Treatments of Psychiatric Disorders)*. American Psychiatric Publishing. pp. 209–11. ISBN 978-1-58562-216-0.

Murray ED, Buttner N, Price BH (2012). "Depression and Psychosis in Neurological Practice". In Bradley WG, Daroff RB, Fenichel GM, Jankovic J. *Bradley's neurology in clinical practice*. 1 (6th ed.). Philadelphia, PA: Elsevier/Saunders. pp. 92–111. ISBN 978-1-4377-0434-1.

Cannon TD, Cornblatt B, McGorry P (May 2007). "The empirical status of the ultra high-risk (prodromal) research paradigm". *Schizophrenia Bulletin*. 33 (3): 661–4. doi:10.1093/schbul/sbm031. PMC 2526144. PMID 17470445.

Marshall M, Rathbone J (June 2011). "Early intervention for psychosis". *The Cochrane Database of Systematic Reviews* (6): CD004718. doi:10.1002/14651858.CD004718.pub3. PMC 4163966. PMID 21678345.

de Koning MB, Bloemen OJ, van Amelsvoort TA, Becker HE, Nieman DH, van der Gaag M, Linszen DH (June 2009). "Early intervention in patients at ultra high risk of psychosis: benefits and risks". *Acta Psychiatrica Scandinavica*. 119 (6): 426–42. doi:10.1111/j.1600-0447.2009.01372.x. hdl:1871/17133. PMID 19392813.

Stafford MR, Jackson H, Mayo-Wilson E, Morrison AP, Kendall T (January 2013). "Early interventions to prevent psychosis: systematic review and meta-analysis". *BMJ*. 346:

- f185. doi:10.1136/bmj.f185. PMC 3548617. PMID 23335473.
- McGurk SR, Mueser KT, Feldman K, Wolfe R, Pascaris A (March 2007). "Cognitive training for supported employment: 2-3 year outcomes of a randomized controlled trial". *The American Journal of Psychiatry*. 164 (3): 437–41. doi:10.1176/appi.ajp.164.3.437. PMID 17329468.
- Gorczynski P, Faulkner G (May 2010). "Exercise therapy for schizophrenia". *The Cochrane Database of Systematic Reviews* (5): CD004412. doi:10.1002/14651858.CD004412.pub2. PMC 4164954. PMID 20464730.
- Dougall N, Maayan N, Soares-Weiser K, McDermott LM, McIntosh A (August 2015). "Transcranial magnetic stimulation (TMS) for schizophrenia". *The Cochrane Database of Systematic Reviews* (8): CD006081. doi:10.1002/14651858.CD006081.pub2. PMID 26289586.
- Tandon R, Keshavan MS, Nasrallah HA (March 2008). "Schizophrenia, "Just the Facts": what we know in 2008 part 1: overview". *Schizophrenia Research*. 100 (1–3): 4–19. doi:10.1016/j.schres.2008.01.022. PMID 18291627.
- Leucht S, Tardy M, Komossa K, Heres S, Kissling W, Salanti G, Davis JM (June 2012). "Antipsychotic drugs versus placebo for relapse prevention in schizophrenia: a systematic review and meta-analysis". *Lancet*. 379 (9831): 2063–71. doi:10.1016/S0140-6736(12)60239-6. PMID 22560607.
- Harrow M, Jobe TH (September 2013). "Does long-term treatment of schizophrenia with antipsychotic medications facilitate recovery?". *Schizophrenia Bulletin*. 39 (5): 962–5. doi:10.1093/schbul/sbt034. PMC 3756791. PMID 23512950.
- Seeman MV, Seeman P (January 2014). "Is schizophrenia a dopamine supersensitivity psychotic reaction?". *Progress in Neuro-Psychopharmacology & Biological Psychiatry*. 48: 155–60. doi:10.1016/j.pnpbp.2013.10.003. PMC 3858317. PMID 24128684.
- Hartling L, Abou-Setta AM, Dursun S, Mousavi SS, Pasichnyk D, Newton AS (October 2012). "Antipsychotics in adults with schizophrenia: comparative effectiveness of first-generation versus second-generation medications: a systematic review and meta-analysis". *Annals of Internal Medicine*. 157 (7): 498–511. doi:10.7326/0003-4819-157-7-201210020-00525. PMID 22893011.
- Barry SJ, Gaughan TM, Hunter R (June 2012). "Schizophrenia". *BMJ Clinical Evidence*. 2012. PMC 3385413. PMID 23870705. Archived from the original on 11 September 2014.
- Schultz SH, North SW, Shields CG (June 2007). "Schizophrenia: a review". *American Family Physician*. 75 (12): 1821–9. PMID 17619525.
- Taylor DM, Duncan-McConnell D (2000). "Refractory schizophrenia and atypical antipsychotics". *Journal of Psychopharmacology*. 14 (4): 409–18. doi:10.1177/026988110001400411. PMID 11198061.
- Essali A, Al-Haj Haasan N, Li C, Rathbone J (January 2009). "Clozapine versus typical neuroleptic medication for schizophrenia". *The Cochrane Database of Systematic Reviews* (1): CD000059. doi:10.1002/14651858.CD000059.pub2. PMID 19160174.
- Ananth J, Parameswaran S, Gunatilake S, Burgoyne K, Sidhom T (April 2004). "Neuroleptic

- malignant syndrome and atypical antipsychotic drugs". *The Journal of Clinical Psychiatry*. 65 (4): 464–70. doi:10.4088/JCP.v65n0403. PMID 15119907.
- McEvoy JP (2006). "Risks versus benefits of different types of long-acting injectable antipsychotics". *The Journal of Clinical Psychiatry*. 67 Suppl 5: 15–8. PMID 16822092.
- Pharoah F, Mari J, Rathbone J, Wong W (December 2010). "Family intervention for schizophrenia". *The Cochrane Database of Systematic Reviews*. 12 (12): CD000088. doi:10.1002/14651858.CD000088.pub2. PMC 4204509. PMID 21154340.
- Dixon LB, Dickerson F, Bellack AS, Bennett M, Dickinson D, Goldberg RW, Lehman A, Tenhula WN, Calmes C, Pasillas RM, Peer J, Kreyenbuhl J (January 2010). "The 2009 schizophrenia PORT psychosocial treatment recommendations and summary statements". *Schizophrenia Bulletin*. 36 (1): 48–70. doi:10.1093/schbul/sbp115. PMC 2800143. PMID 19955389.
- Jauhar S, McKenna PJ, Radua J, Fung E, Salvador R, Laws KR (January 2014). "Cognitive-behavioural therapy for the symptoms of schizophrenia: systematic review and meta-analysis with examination of potential bias". *The British Journal of Psychiatry (Review)*. 204 (1): 20–9. doi:10.1192/bjp.bp.112.116285. PMID 24385461.
- Jones C, Hacker D, Meaden A, Cormac I, Irving CB, Xia J, Zhao S, Shi C, Chen J (November 2018). "Cognitive behavioural therapy plus standard care versus standard care plus other psychosocial treatments for people with schizophrenia". *The Cochrane Database of Systematic Reviews*. 11: CD008712. doi:10.1002/14651858.CD008712.pub3. PMID 30480760.
- Eichner C, Berna F (July 2016). "Acceptance and Efficacy of Metacognitive Training (MCT) on Positive Symptoms and Delusions in Patients With Schizophrenia: A Meta-analysis Taking Into Account Important Moderators". *Schizophrenia Bulletin*. 42 (4): 952–62. doi:10.1093/schbul/sbv225. PMC 4903058. PMID 26748396.
- van Oosterhout B, Smit F, Krabbendam L, Castelein S, Staring AB, van der Gaag M (January 2016). "Metacognitive training for schizophrenia spectrum patients: a meta-analysis on outcome studies". *Psychological Medicine*. 46 (1): 47–57. doi:10.1017/s0033291715001105. PMID 26190517.
- Liu YC, Tang CC, Hung TT, Tsai PC, Lin MF (April 2018). "The Efficacy of Metacognitive Training for Delusions in Patients With Schizophrenia: A Meta-Analysis of Randomized Controlled Trials Informs Evidence-Based Practice". *Worldviews on Evidence-Based Nursing*. 15 (2): 130–139. doi:10.1111/wvn.12282. PMID 29489070.
- Ruddy R, Milnes D (October 2005). "Art therapy for schizophrenia or schizophrenia-like illnesses". *The Cochrane Database of Systematic Reviews* (4): CD003728. doi:10.1002/14651858.CD003728.pub2. PMID 16235338. Archived from the original on 27 October 2011.
- Ruddy RA, Dent-Brown K (January 2007). "Drama therapy for schizophrenia or schizophrenia-like illnesses". *The Cochrane Database of Systematic Reviews* (1): CD005378. doi:10.1002/14651858.CD005378.pub2. PMID 17253555. Archived from the original on 25 August 2011.

- Erlangsen A, Eaton WW, Mortensen PB, Conwell Y (February 2012). "Schizophrenia--a predictor of suicide during the second half of life?". *Schizophrenia Research*. 134 (2–3): 111–7. doi:10.1016/j.schres.2011.09.032. PMC 3266451. PMID 22018943.
- Saha S, Chant D, McGrath J (October 2007). "A systematic review of mortality in schizophrenia: is the differential mortality gap worsening over time?". *Archives of General Psychiatry*. 64 (10): 1123–31. doi:10.1001/archpsyc.64.10.1123. PMID 17909124.
- Ustün TB, Rehm J, Chatterji S, Saxena S, Trotter R, Room R, Bickenbach J (July 1999). "Multiple-informant ranking of the disabling effects of different health conditions in 14 countries. WHO/NIH Joint Project CAR Study Group". *Lancet*. 354 (9173): 111–5. doi:10.1016/S0140-6736(98)07507-2. PMID 10408486.
- World Health Organization (2008). *The global burden of disease : 2004 update* ([Online-Ausg.] ed.). Geneva, Switzerland: World Health Organization. p. 35. ISBN 9789241563710.
- Warner R (July 2009). "Recovery from schizophrenia and the recovery model". *Current Opinion in Psychiatry*. 22 (4): 374–80. doi:10.1097/YCO.0b013e32832c920b. PMID 19417668.
- American Psychiatric Association. Task Force on DSM-IV. (2000). *Diagnostic and statistical manual of mental disorders: DSM-IV-TR*. American Psychiatric Pub. ISBN 978-0-89042-025-6. p. 314
- Menezes NM, Arenovich T, Zipursky RB (October 2006). "A systematic review of longitudinal outcome studies of first-episode psychosis". *Psychological Medicine*. 36 (10): 1349–62. doi:10.1017/S0033291706007951. PMID 16756689.
- Isaac M, Chand P, Murthy P (August 2007). "Schizophrenia outcome measures in the wider international community". *The British Journal of Psychiatry*. Supplement. 50: s71–7. doi:10.1192/bjp.191.50.s71. PMID 18019048.
- Cohen A, Patel V, Thara R, Gureje O (March 2008). "Questioning an axiom: better prognosis for schizophrenia in the developing world?". *Schizophrenia Bulletin*. 34 (2): 229–44. doi:10.1093/schbul/sbm105. PMC 2632419. PMID 17905787.
- Burns J (August 2009). "Dispelling a myth: developing world poverty, inequality, violence and social fragmentation are not good for outcome in schizophrenia". *African Journal of Psychiatry*. 12 (3): 200–5. doi:10.4314/ajpsy.v12i3.48494. PMID 19894340.
- Palmer BA, Pankratz VS, Bostwick JM (March 2005). "The lifetime risk of suicide in schizophrenia: a reexamination". *Archives of General Psychiatry*. 62 (3): 247–53. doi:10.1001/archpsyc.62.3.247. PMID 15753237.
- Carlborg A, Winnerbäck K, Jönsson EG, Jokinen J, Nordström P (July 2010). "Suicide in schizophrenia". *Expert Review of Neurotherapeutics*. 10 (7): 1153–64. doi:10.1586/ern.10.82. PMID 20586695.
- de Leon J, Diaz FJ (July 2005). "A meta-analysis of worldwide studies demonstrates an association between schizophrenia and tobacco smoking behaviors". *Schizophrenia Research*. 76 (2–3): 135–57. doi:10.1016/j.schres.2005.02.010. PMID 15949648.

- Keltner NL, Grant JS (November 2006). "Smoke, smoke, smoke that cigarette". *Perspectives in Psychiatric Care*. 42 (4): 256–61. doi:10.1111/j.1744-6163.2006.00085.x. PMID 17107571.
- Diagnostic and statistical manual of mental disorders : DSM-IV-TR (4 ed.). American Psychiatric Association. 2000. p. 304. ISBN 978-0-89042-025-6.
- Kumari, Veena; Postma, Peggy (January 2005). "Nicotine use in schizophrenia: The self medication hypotheses". *Neuroscience & Biobehavioral Reviews*. 29 (6): 1021–1034. doi:10.1016/j.neubiorev.2005.02.006. PMID 15964073.
- Cascio MT, Cella M, Preti A, Meneghelli A, Cocchi A (May 2012). "Gender and duration of untreated psychosis: a systematic review and meta-analysis". *Early Intervention in Psychiatry (Review)*. 6 (2): 115–27. doi:10.1111/j.1751-7893.2012.00351.x. PMID 22380467.
- Kumra S, Shaw M, Merka P, Nakayama E, Augustin R (December 2001). "Childhood-onset schizophrenia: research update". *Canadian Journal of Psychiatry*. 46 (10): 923–30. doi:10.1177/070674370104601004. PMID 11816313.
- Hassett A, Ames D, Chiu E, eds. (2005). *Psychosis in the Elderly*. London: Taylor and Francis. p. 6. ISBN 978-1-84184-394-0.
- Jablensky A, Sartorius N, Ernberg G, Anker M, Korten A, Cooper JE, Day R, Bertelsen A (1992). "Schizophrenia: manifestations, incidence and course in different cultures. A World Health Organization ten-country study". *Psychological Medicine. Monograph Supplement*. 20: 1–97. doi:10.1017/S0264180100000904. PMID 1565705.
- Kirkbride JB, Fearon P, Morgan C, Dazzan P, Morgan K, Tarrant J, Lloyd T, Holloway J, Hutchinson G, Leff JP, Mallett RM, Harrison GL, Murray RM, Jones PB (March 2006). "Heterogeneity in incidence rates of schizophrenia and other psychotic syndromes: findings from the 3-center AeSOP study". *Archives of General Psychiatry*. 63 (3): 250–8. doi:10.1001/archpsyc.63.3.250. PMID 16520429.
- Kirkbride JB, Fearon P, Morgan C, Dazzan P, Morgan K, Murray RM, Jones PB (June 2007). "Neighbourhood variation in the incidence of psychotic disorders in Southeast London". *Social Psychiatry and Psychiatric Epidemiology*. 42 (6): 438–45. doi:10.1007/s00127-007-0193-0. PMID 17473901.
- Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. (December 2012). "Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010". *Lancet*. 380 (9859): 2095–128. doi:10.1016/S0140-6736(12)61728-0. hdl:10536/DRO/DU:30050819. PMID 23245604.
- Schneider K (1959). *Clinical Psychopathology* (5 ed.). New York: Grune & Stratton.
- Nordgaard J, Arnfred SM, Handest P, Parnas J (January 2008). "The diagnostic status of first-rank symptoms". *Schizophrenia Bulletin*. 34 (1): 137–54. doi:10.1093/schbul/sbm044. PMC 2632385. PMID 17562695.
- Yuhas D. "Throughout History, Defining Schizophrenia Has Remained a Challenge". *Scientific American Mind* (March/April 2013). Archived from the original on 5 November 2013.

Retrieved 3 March 2013.

- Heinrichs RW (2003). "Historical origins of schizophrenia: two early madmen and their illness". *Journal of the History of the Behavioral Sciences*. 39 (4): 349–63. doi:10.1002/jhbs.10152. PMID 14601041.
- Noll R (2011). *American madness: the rise and fall of dementia praecox*. Cambridge, MA: Harvard University Press. ISBN 978-0-674-04739-6.
- Noll R (2012). "Whole body madness". *Psychiatric Times*. 29 (12): 13–14. Archived from the original on 11 January 2013.
- Hansen RA, Atchison B (2000). *Conditions in occupational therapy: effect on occupational performance*. Hagerstown, MD: Lippincott Williams & Wilkins. ISBN 978-0-683-30417-6.
- Berrios GE, Luque R, Villagran J (2003). "Schizophrenia: a conceptual history" (PDF). *International Journal of Psychology and Psychological Therapy*. 3 (2): 111–140.
- Kuhn R, Cahn CH (September 2004). "Eugen Bleuler's concepts of psychopathology". *History of Psychiatry*. 15 (59 Pt 3): 361–6. doi:10.1177/0957154X04044603. PMID 15386868.
- Stotz-Ingenlath G (2000). "Epistemological aspects of Eugen Bleuler's conception of schizophrenia in 1911" (PDF). *Medicine, Health Care, and Philosophy*. 3 (2): 153–9. doi:10.1023/A:1009919309015. PMID 11079343.
- McNally K (May 2009). "Eugene Bleuler's four As". *History of Psychology*. 12 (2): 43–59. doi:10.1037/a0015934. PMID 19831234.
- Turner T (January 2007). "Chlorpromazine: unlocking psychosis". *BMJ*. 334 Suppl 1 (suppl): s7. doi:10.1136/bmj.39034.609074.94. PMID 17204765.
- Wing JK (January 1971). "International comparisons in the study of the functional psychoses". *British Medical Bulletin*. 27 (1): 77–81. doi:10.1093/oxfordjournals.bmb.a070819. PMID 4926366.
- Rosenhan DL (January 1973). "On being sane in insane places". *Science*. 179 (4070): 250–8. Bibcode:1973Sci...179..250R. doi:10.1126/science.179.4070.250. PMID 4683124.
- Wilson M (March 1993). "DSM-III and the transformation of American psychiatry: a history". *The American Journal of Psychiatry*. 150 (3): 399–410. doi:10.1176/ajp.150.3.399. PMID 8434655.
- Stotz-Ingenlath G (2000). "Epistemological aspects of Eugen Bleuler's conception of schizophrenia in 1911". *Medicine, Health Care, and Philosophy*. 3 (2): 153–9. doi:10.1023/A:1009919309015. PMID 11079343.
- Hayes JA, Mitchell JC (1994). "Mental health professionals' skepticism about multiple personality disorder". *Professional Psychology: Research and Practice*. 25 (4): 410–415. doi:10.1037/0735-7028.25.4.410.
- Putnam FW (1989). *Diagnosis and Treatment of Multiple Personality Disorder*. New York: The Guilford Press. p. 351. ISBN 978-0-89862-177-8.
- Berrios GE, Porter R (1995). *A history of clinical psychiatry: the origin and history of psychiatric disorders*. London: Athlone Press. ISBN 978-0-485-24211-9.

- McNally K (Winter 2007). "Schizophrenia as split personality/Jekyll and Hyde: the origins of the informal usage in the English language". *Journal of the History of the Behavioral Sciences*. 43 (1): 69–79. doi:10.1002/jhbs.20209. PMID 17205539.
- Kim Y, Berrios GE (2001). "Impact of the term schizophrenia on the culture of ideograph: the Japanese experience". *Schizophrenia Bulletin*. 27 (2): 181–5. doi:10.1093/oxfordjournals.schbul.a006864. PMID 11354585.
- Sato M (February 2006). "Renaming schizophrenia: a Japanese perspective". *World Psychiatry*. 5 (1): 53–5. PMC 1472254. PMID 16757998.
- Lee YS, Kim JJ, Kwon JS (August 2013). "Renaming schizophrenia in South Korea". *Lancet*. 382 (9893): 683–4. doi:10.1016/S0140-6736(13)61776-6. PMID 23972810.
- van Os J (February 2016). ""Schizophrenia" does not exist". *BMJ*. 352: i375. doi:10.1136/bmj.i375. PMID 26837945.
- Wu EQ, Birnbaum HG, Shi L, Ball DE, Kessler RC, Moulis M, Aggarwal J (September 2005). "The economic burden of schizophrenia in the United States in 2002". *The Journal of Clinical Psychiatry*. 66 (9): 1122–9. doi:10.4088/jcp.v66n0906. PMID 16187769.
- Maniglio R (March 2009). "Severe mental illness and criminal victimization: a systematic review". *Acta Psychiatrica Scandinavica*. 119 (3): 180–91. doi:10.1111/j.1600-0447.2008.01300.x. PMID 19016668.
- Fazel S, Gulati G, Linsell L, Geddes JR, Grann M (August 2009). "Schizophrenia and violence: systematic review and meta-analysis". *PLoS Medicine*. 6 (8): e1000120. doi:10.1371/journal.pmed.1000120. PMC 2718581. PMID 19668362.
- Large M, Smith G, Nielssen O (July 2009). "The relationship between the rate of homicide by those with schizophrenia and the overall homicide rate: a systematic review and meta-analysis". *Schizophrenia Research*. 112 (1–3): 123–9. doi:10.1016/j.schres.2009.04.004. PMID 19457644.
- Bo S, Abu-Akel A, Kongerslev M, Haahr UH, Simonsen E (July 2011). "Risk factors for violence among patients with schizophrenia". *Clinical Psychology Review*. 31 (5): 711–26. doi:10.1016/j.cpr.2011.03.002. PMID 21497585.
- Valença AM, de Moraes TM (October 2006). "[Relationship between homicide and mental disorders]". *Revista Brasileira de Psiquiatria*. 28 Suppl 2: S62–8. doi:10.1590/s1516-44462006000600003. PMID 17143446.
- Pescosolido BA, Monahan J, Link BG, Stueve A, Kikuzawa S (September 1999). "The public's view of the competence, dangerousness, and need for legal coercion of persons with mental health problems". *American Journal of Public Health*. 89 (9): 1339–45. doi:10.2105/AJPH.89.9.1339. PMC 1508769. PMID 10474550.
- Phelan JC, Link BG, Stueve A, Pescosolido BA (June 2000). "Public Conceptions of Mental Illness in 1950 and 1996: What Is Mental Illness and Is It to be Feared?". *Journal of Health and Social Behavior*. 41 (2): 188–207. doi:10.2307/2676305. JSTOR 2676305.
- Dean OM, Data-Franco J, Giorlando F, Berk M (May 2012). "Minocycline: therapeutic potential in psychiatry". *CNS Drugs*. 26 (5): 391–401. doi:10.2165/11632000-000000000-00000. PMID 22486246.

- Chamberlain IJ, Sampson S (March 2013). Chamberlain IJ, ed. "Nidotherapy for people with schizophrenia". *The Cochrane Database of Systematic Reviews*. 3 (3): CD009929. doi:10.1002/14651858.CD009929.pub2. PMID 23543583.
- Chue P, Lalonde JK (2014). "Addressing the unmet needs of patients with persistent negative symptoms of schizophrenia: emerging pharmacological treatment options". *Neuropsychiatric Disease and Treatment*. 10: 777–89. doi:10.2147/ndt.s43404. PMC 4020880. PMID 24855363.
- Keller WR, Kum LM, Wehring HJ, Koola MM, Buchanan RW, Kelly DL (April 2013). "A review of anti-inflammatory agents for symptoms of schizophrenia". *Journal of Psychopharmacology*. 27 (4): 337–42. doi:10.1177/0269881112467089. PMC 3641824. PMID 23151612.
- Kelly, Evelyn B. (2001). *Coping with schizophrenia* (1st ed.). New York: Rosen Pub. p. 25. ISBN 978-0-8239-2853-8.
- Maio DV, Franscell R (2016). *Morgue: A Life in Death*. St. Martin's Press. p. 236. ISBN 978-1-4668-7506-7.
- Bogousslavsky J, Boller F (2005). *Neurological Disorders in Famous Artists*. Karger Medical and Scientific Publishers. p. 125. ISBN 978-3-8055-7914-8.
- Griswold KS, Del Regno PA, Berger RC (June 2015). "Recognition and Differential Diagnosis of Psychosis in Primary Care". *American Family Physician*. 91 (12): 856–63. PMID 26131945.
- Cardinal RN, Bullmore ET (2011). *The Diagnosis of Psychosis*. Cambridge University Press. p. 279. ISBN 978-1-139-49790-9.
- Foster, Norman L. (2011). *The American Psychiatric Publishing Textbook of Geriatric Neuropsychiatry*. American Psychiatric Pub. p. 523. ISBN 978-1-58562-952-7.
- Leucht S, Arbter D, Engel RR, Kissling W, Davis JM (April 2009). "How effective are second-generation antipsychotic drugs? A meta-analysis of placebo-controlled trials" (PDF). *Molecular Psychiatry*. 14 (4): 429–47. doi:10.1038/sj.mp.4002136. PMID 18180760.
- Ratthalli RD, Jayaram MB, Smith M (May 2010). "Risperidone versus placebo for schizophrenia". *Schizophrenia Bulletin*. 36 (3): 448–9. doi:10.1093/schbul/sbq030. PMC 2879694. PMID 20368309.
- Gibbs, Ronald S. (2008). *Danforth's Obstetrics and Gynecology*. Lippincott Williams & Wilkins. p. 508. ISBN 978-0-7817-6937-2.
- Giddens, Jean Foret (2015). *Concepts for Nursing Practice - E-Book*. Elsevier Health Sciences. p. 348. ISBN 978-0-323-38946-4.
- Association, American Psychiatric (2013). *Diagnostic and statistical manual of mental disorders : DSM-5* (5th ed.). Washington, D.C.: American Psychiatric Association. p. 125. ISBN 978-0-89042-554-1.
- Lewis S, Escalona R, Keith S. "Phenomenology of Schizophrenia". In Sadock V, Sadock B, Ruiz P. Kaplan and Sadock's *Comprehensive Textbook of Psychiatry*. Wolters Kluwer.
- Jaspers K (1997-11-27) [1963]. *Allgemeine Psychopathologie* (General Psychopathology).

Translated by J. Hoenig and M.W. Hamilton from German (Reprint ed.). Baltimore, Maryland: Johns Hopkins University Press. ISBN 978-0-8018-5775-1.

- Cardinal RN, Bullmore, ET (2011). *The Diagnosis of Psychosis*. Cambridge University Press. ISBN 978-0-521-16484-9.
- Ohayon MM, Priest RG, Caulet M, Guilleminault C (October 1996). "Hypnagogic and hypnopompic hallucinations: pathological phenomena?". *The British Journal of Psychiatry*. 169 (4): 459–67. doi:10.1192/bjp.169.4.459. PMID 8894197.
- Sharma V, Mazmanian D (April 2003). "Sleep loss and postpartum psychosis". *Bipolar Disorders*. 5 (2): 98–105. doi:10.1034/j.1399-5618.2003.00015.x. PMID 12680898.
- Chan-Ob T, Boonyanaruthee V (September 1999). "Meditation in association with psychosis". *Journal of the Medical Association of Thailand = Chotmaihet Thangphaet*. 82 (9): 925–30. PMID 10561951.
- Devillieres P, Opitz M, Clervoy P, Stephany J (May–June 1996). "Delusion and sleep deprivation". *L'Encéphale*. 22 (3): 229–31. PMID 8767052.
- Gibson LE, Alloy LB, Ellman LM (November 2016). "Trauma and the psychosis spectrum: A review of symptom specificity and explanatory mechanisms". *Clinical Psychology Review*. 49: 92–105. doi:10.1016/j.cpr.2016.08.003. PMC 5157832. PMID 27632064.
- Misiak B, Krefft M, Bielawski T, Moustafa AA, Sąsiadek MM, Frydecka D (April 2017). "Toward a unified theory of childhood trauma and psychosis: A comprehensive review of epidemiological, clinical, neuropsychological and biological findings". *Neuroscience and Biobehavioral Reviews*. 75: 393–406. doi:10.1016/j.neubiorev.2017.02.015. PMID 28216171.
- Read J, van Os J, Morrison AP, Ross CA (November 2005). "Childhood trauma, psychosis and schizophrenia: a literature review with theoretical and clinical implications". *Acta Psychiatrica Scandinavica*. 112 (5): 330–50. doi:10.1111/j.1600-0447.2005.00634.x. PMID 16223421.
- World Health Organization, *The ICD-10 Classification of Mental and Behavioural Disorders: Clinical descriptions and diagnostic guidelines (CDDG)*, 1992.
- American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR)*, American Psychiatric Association, 2000.
- Shibayama M (2011). "[Differential diagnosis between dissociative disorders and schizophrenia]". *Seishin Shinkeigaku Zasshi = Psychiatria Et Neurologia Japonica*. 113 (9): 906–11. PMID 22117396.
- Jauch DA, Carpenter WT (February 1988). "Reactive psychosis. I. Does the pre-DSM-III concept define a third psychosis?". *The Journal of Nervous and Mental Disease*. 176 (2): 72–81. doi:10.1097/00005053-198802000-00002. PMID 3276813.
- Jeronimus BF, Kotov R, Riese H, Ormel J (October 2016). "Neuroticism's prospective association with mental disorders halves after adjustment for baseline symptoms and psychiatric history, but the adjusted association hardly decays with time: a meta-analysis on 59 longitudinal/prospective studies with 443 313 participants". *Psychological Medicine*. 46 (14): 2883–2906. doi:10.1017/S0033291716001653. PMID

27523506.

- Pillmann F, Marneros A (2004). *Acute and transient psychoses*. Cambridge, UK: Cambridge University Press. p. 188. ISBN 978-0-521-83518-3. OCLC 144618418.
- Lesser JM, Hughes S (December 2006). "Psychosis-related disturbances. Psychosis, agitation, and disinhibition in Alzheimer's disease: definitions and treatment options". *Geriatrics*. 61 (12): 14–20. PMID 17184138.
- McKeith IG (February 2002). "Dementia with Lewy bodies". *The British Journal of Psychiatry*. 180 (2): 144–7. doi:10.1192/bjp.180.2.144. PMID 11823325.
- Wedekind S (June 2005). "[Depressive syndrome, psychoses, dementia: frequent manifestations in Parkinson disease]". *MMW Fortschritte Der Medizin (in German)*. 147 (22): 11. PMID 15977623.
- Arciniegas DB (June 2015). "Psychosis". *Continuum*. 21 (3 Behavioral Neurology and Neuropsychiatry): 715–36. doi:10.1212/01.CON.0000466662.89908.e7. PMC 4455840. PMID 26039850.
- Lisanby SH, Kohler C, Swanson CL, Gur RE (January 1998). "Psychosis Secondary to Brain Tumor". *Seminars in Clinical Neuropsychiatry*. 3 (1): 12–22. PMID 10085187.
- Evans DL, Mason KI, Leserman J, Bauer R, Petitto J (2002-02-01). "Chapter 90: Neuropsychiatric Manifestations of HIV-1 Infection and AIDS". In Davis KL, Charney D, Coyle JT, Nemeroff C. *Neuropsychopharmacology: The Fifth Generation of Progress* (5th ed.). Philadelphia: Lippincott Williams & Wilkins. pp. 1281–1301. ISBN 978-0-7817-2837-9. Archived from the original on 2006-10-19. Retrieved 2006-10-16.
- Nevin RL, Croft AM (June 2016). "Psychiatric effects of malaria and anti-malarial drugs: historical and modern perspectives". *Malaria Journal*. 15: 332. doi:10.1186/s12936-016-1391-6. PMC 4918116. PMID 27335053.
- Friedrich F, Aigner M, Fearn N, Friedrich ME, Frey R, Geusau A (2014). "Psychosis in neurosyphilis -- clinical aspects and implications". *Psychopathology*. 47 (1): 3–9. doi:10.1159/000350059. PMID 23711816.
- Keshavan MS, Kaneko Y (February 2013). "Secondary psychoses: an update". *World Psychiatry*. 12 (1): 4–15. doi:10.1002/wps.20001. PMC 3619167. PMID 23471787.
- Sit D, Rothschild AJ, Wisner KL (May 2006). "A review of postpartum psychosis". *Journal of Women's Health*. 15 (4): 352–68. doi:10.1089/jwh.2006.15.352. PMC 3109493. PMID 16724884.
- Foucher JR, Luck D (2006). "Psychosis related to neurological conditions: pro and cons of the dis- / mis-connectivity models of schizophrenia". *Dialogues in Clinical Neuroscience*. 8 (1): 17–27. PMC 3181754. PMID 16640110.
- Bonnot O, Klünemann HH, Sedel F, Tordjman S, Cohen D, Walterfang M (April 2014). "Diagnostic and treatment implications of psychosis secondary to treatable metabolic disorders in adults: a systematic review". *Orphanet Journal of Rare Diseases*. 9: 65. doi:10.1186/1750-1172-9-65. PMC 4043981. PMID 24775716.
- Sedel F, Baumann N, Turpin JC, Lyon-Caen O, Saudubray JM, Cohen D (October 2007).

- "Psychiatric manifestations revealing inborn errors of metabolism in adolescents and adults". *Journal of Inherited Metabolic Disease*. 30 (5): 631–41. doi:10.1007/s10545-007-0661-4. PMID 17694356.
- Bonnot O, Herrera PM, Tordjman S, Walterfang M (2015). "Secondary psychosis induced by metabolic disorders". *Frontiers in Neuroscience*. 9: 177. doi:10.3389/fnins.2015.00177. PMC 4436816. PMID 26074754.
- Jana DK, Romano-Jana L (October 1973). "Hypernatremic psychosis in the elderly: case reports". *Journal of the American Geriatrics Society*. 21 (10): 473–7. doi:10.1111/j.1532-5415.1973.tb01212.x. PMID 4729012.
- Haensch CA, Hennen G, Jörg J (April 1996). "[Reversible exogenous psychosis in thiazide-induced hyponatremia of 97 mmol/l]". *Der Nervenarzt*. 67 (4): 319–22. PMID 8684511.
- Hafez H, Strauss JS, Aronson MD, Holt C (June 1984). "Hypokalemia-induced psychosis in a chronic schizophrenic patient". *The Journal of Clinical Psychiatry*. 45 (6): 277–9. PMID 6725222.
- Velasco PJ, Manshadi M, Breen K, Lippmann S (1 December 1999). "Psychiatric aspects of parathyroid disease". *Psychosomatics*. 40 (6): 486–90. doi:10.1016/S0033-3182(99)71186-2. PMID 10581976.
- Rosenthal M, Gil I, Habet B (1997). "Primary hyperparathyroidism: neuropsychiatric manifestations and case report". *The Israel Journal of Psychiatry and Related Sciences*. 34 (2): 122–5. PMID 9231574.
- Nanji AA (November 1984). "The psychiatric aspect of hypophosphatemia". *Canadian Journal of Psychiatry*. 29 (7): 599–600. PMID 6391648.
- Losurdo G, Principi M, Iannone A, Amoroso A, Ierardi E, Di Leo A, Barone M (April 2018). "Extra-intestinal manifestations of non-celiac gluten sensitivity: An expanding paradigm". *World Journal of Gastroenterology (Review)*. 24 (14): 1521–1530. doi:10.3748/wjg.v24.i14.1521. PMC 5897856. PMID 29662290.
- Grant KM, LeVan TD, Wells SM, Li M, Stoltenberg SF, Gendelman HE, Carlo G, Bevins RA (March 2012). "Methamphetamine-associated psychosis". *Journal of Neuroimmune Pharmacology*. 7 (1): 113–39. doi:10.1007/s11481-011-9288-1. PMC 3280383. PMID 21728034.
- Krebs TS, Johansen PØ (August 2013). "Psychedelics and mental health: a population study". *PLOS One*. 8 (8): e63972. doi:10.1371/journal.pone.0063972. PMC 3747247. PMID 23976938.
- Broderick P, Benjamin AB (December 2004). "Caffeine and psychiatric symptoms: a review". *The Journal of the Oklahoma State Medical Association*. 97 (12): 538–42. PMID 15732884.
- Cardinal RN, Bullmore ET (2011). *The Diagnosis of Psychosis*. Cambridge University Press. p. 126. ISBN 978-1-139-49790-9.
- Moore TH, Zammit S, Lingford-Hughes A, Barnes TR, Jones PB, Burke M, Lewis G (July 2007). "Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review". *Lancet*. 370 (9584): 319–28. doi:10.1016/S0140-6736(07)61162-3. PMID

17662880.

- Leweke FM, Koethe D (June 2008). "Cannabis and psychiatric disorders: it is not only addiction". *Addiction Biology*. 13 (2): 264–75. doi:10.1111/j.1369-1600.2008.00106.x. PMID 18482435.
- Sewell RA, Ranganathan M, D'Souza DC (April 2009). "Cannabinoids and psychosis". *International Review of Psychiatry*. 21 (2): 152–62. doi:10.1080/09540260902782802. PMID 19367509.
- Henquet C, Di Forti M, Morrison P, Kuepper R, Murray RM (November 2008). "Gene-environment interplay between cannabis and psychosis". *Schizophrenia Bulletin*. 34 (6): 1111–21. doi:10.1093/schbul/sbn108. PMC 2632498. PMID 18723841.
- McLaren JA, Silins E, Hutchinson D, Mattick RP, Hall W (January 2010). "Assessing evidence for a causal link between cannabis and psychosis: a review of cohort studies". *The International Journal on Drug Policy*. 21 (1): 10–9. doi:10.1016/j.drugpo.2009.09.001. PMID 19783132.
- Ben Amar M, Potvin S (June 2007). "Cannabis and psychosis: what is the link?". *Journal of Psychoactive Drugs*. 39 (2): 131–42. doi:10.1080/02791072.2007.10399871. PMID 17703707.
- Bhattacharyya S, Morrison PD, Fusar-Poli P, Martin-Santos R, Borgwardt S, Winton-Brown T, Nosarti C, O' Carroll CM, Seal M, Allen P, Mehta MA, Stone JM, Tunstall N, Giampietro V, Kapur S, Murray RM, Zuardi AW, Crippa JA, Atakan Z, McGuire PK (February 2010). "Opposite effects of delta-9-tetrahydrocannabinol and cannabidiol on human brain function and psychopathology". *Neuropsychopharmacology*. 35 (3): 764–74. doi:10.1038/npp.2009.184. PMC 3055598. PMID 19924114.
- Di Forti M, Sallis H, Allegri F, Trotta A, Ferraro L, Stilo SA, et al. (November 2014). "Daily use, especially of high-potency cannabis, drives the earlier onset of psychosis in cannabis users". *Schizophrenia Bulletin*. 40 (6): 1509–17. doi:10.1093/schbul/sbt181. PMID 24345517.
- Dragt S, Nieman DH, Schultze-Lutter F, van der Meer F, Becker H, de Haan L, et al. (January 2012). "Cannabis use and age at onset of symptoms in subjects at clinical high risk for psychosis". *Acta Psychiatrica Scandinavica*. 125 (1): 45–53. doi:10.1111/j.1600-0447.2011.01763.x. PMID 21883099.
- Sander JW, Hart YM, Trimble MR, Shorvon SD (May 1991). "Vigabatrin and psychosis". *Journal of Neurology, Neurosurgery, and Psychiatry*. 54 (5): 435–9. doi:10.1136/jnnp.54.5.435. PMC 488544. PMID 1865207.
- "Adderall XR Prescribing Information" (PDF). United States Food and Drug Administration. December 2013. pp. 4–6. Retrieved 30 December 2013.
- Kuijpers HJ, van der Heijden FM, Tuinier S, Verhoeven WM (2007). "Meditation-induced psychosis". *Psychopathology*. 40 (6): 461–4. doi:10.1159/000108125. PMID 17848828.
- Moore MT, Nathan D, Elliott AR, Laubach C (1935). "Encephalographic studies in mental disease". *American Journal of Psychiatry*. 92 (1): 43–67. doi:10.1176/ajp.92.1.43.
- Fusar-Poli P, Radua J, McGuire P, Borgwardt S (November 2012). "Neuroanatomical maps of

- psychosis onset: voxel-wise meta-analysis of antipsychotic-naive VBM studies". *Schizophrenia Bulletin*. 38 (6): 1297–307. doi:10.1093/schbul/sbr134. PMC 3494061. PMID 22080494.
- Palaniyappan L, Balain V, Liddle PF (October 2012). "The neuroanatomy of psychotic diathesis: a meta-analytic review". *Journal of Psychiatric Research*. 46 (10): 1249–56. doi:10.1016/j.jpsychires.2012.06.007. PMID 22790253.
- Radua J, Borgwardt S, Crescini A, Mataix-Cols D, Meyer-Lindenberg A, McGuire PK, Fusar-Poli P (November 2012). "Multimodal meta-analysis of structural and functional brain changes in first episode psychosis and the effects of antipsychotic medication". *Neuroscience and Biobehavioral Reviews*. 36 (10): 2325–33. doi:10.1016/j.neubiorev.2012.07.012. PMID 22910680.
- Bora E, Fornito A, Yücel M, Pantelis C (February 2012). "The effects of gender on grey matter abnormalities in major psychoses: a comparative voxelwise meta-analysis of schizophrenia and bipolar disorder". *Psychological Medicine*. 42 (2): 295–307. doi:10.1017/S0033291711001450. PMID 21835091.
- Del Casale A, Kotzolidis GD, Rapinesi C, Sorice S, Girardi N, Ferracuti S, Girardi P (2016). "Functional Magnetic Resonance Imaging Correlates of First-Episode Psychoses during Attentional and Memory Task Performance". *Neuropsychobiology*. 74 (1): 22–31. doi:10.1159/000448620. PMID 27698323.
- Brown G, Thompson W. "Functional Brain Imaging in Schizophrenia: Selected Results and Methods". In Swerdlow N. *Behavioral Neurobiology of Schizophrenia and its Treatment*. Springer. pp. 185–189.
- Naasan G. "The Anatomy of Delusions". In Lehner T, Miller B, State M. *Genomics, Circuits, and Pathways in Clinical Neuropsychiatry*. Elsevier Science. pp. 366–369.
- Radua J, Schmidt A, Borgwardt S, Heinz A, Schlagenhauf F, McGuire P, Fusar-Poli P (December 2015). "Ventral Striatal Activation During Reward Processing in Psychosis: A Neurofunctional Meta-Analysis". *JAMA Psychiatry*. 72 (12): 1243–51. doi:10.1001/jamapsychiatry.2015.2196. PMID 26558708.
- Young J, Anticevic A, Barch D. "Cognitive and Motivational Neuroscience of Psychotic Disorders". In Charney D, Sklar P, Nestler E, Buxbaum J. *Neurobiology of Mental Illness* (5th ed.). Oxford University Press.
- Kapur S, Mizrahi R, Li M (November 2005). "From dopamine to salience to psychosis--linking biology, pharmacology and phenomenology of psychosis". *Schizophrenia Research*. 79 (1): 59–68. doi:10.1016/j.schres.2005.01.003. PMID 16005191.
- Egerton A, Fusar-Poli P, Stone JM (2012). "Glutamate and psychosis risk". *Current Pharmaceutical Design*. 18 (4): 466–78. doi:10.2174/138161212799316244. PMID 22239577.
- Bergeron R, Coyle JT (2012). "NAAG, NMDA receptor and psychosis". *Current Medicinal Chemistry*. 19 (9): 1360–4. doi:10.2174/092986712799462685. PMC 3424071. PMID 22304714.
- Adams RA, Stephan KE, Brown HR, Frith CD, Friston KJ (2013). "The computational anatomy

- of psychosis". *Frontiers in Psychiatry*. 4: 47. doi:10.3389/fpsy.2013.00047. PMC 3667557. PMID 23750138.
- Corlett PR, Frith CD, Fletcher PC (November 2009). "From drugs to deprivation: a Bayesian framework for understanding models of psychosis". *Psychopharmacology*. 206 (4): 515–30. doi:10.1007/s00213-009-1561-0. PMC 2755113. PMID 19475401.
- Corlett PR, Honey GD, Krystal JH, Fletcher PC (January 2011). "Glutamatergic model psychoses: prediction error, learning, and inference". *Neuropsychopharmacology*. 36 (1): 294–315. doi:10.1038/npp.2010.163. PMC 3055519. PMID 20861831.
- Corlett PR, Taylor JR, Wang XJ, Fletcher PC, Krystal JH (November 2010). "Toward a neurobiology of delusions". *Progress in Neurobiology*. 92 (3): 345–69. doi:10.1016/j.pneurobio.2010.06.007. PMC 3676875. PMID 20558235.
- Kalkman HO, Loetscher E (July 2003). "GAD(67): the link between the GABA-deficit hypothesis and the dopaminergic- and glutamatergic theories of psychosis". *Journal of Neural Transmission*. 110 (7): 803–12. doi:10.1007/s00702-003-0826-8. PMID 12811640.
- Akbarian S, Huang HS (September 2006). "Molecular and cellular mechanisms of altered GAD1/GAD67 expression in schizophrenia and related disorders". *Brain Research Reviews*. 52 (2): 293–304. doi:10.1016/j.brainresrev.2006.04.001. PMID 16759710.
- Jones HM, Pilowsky LS (October 2002). "Dopamine and antipsychotic drug action revisited". *The British Journal of Psychiatry*. 181 (4): 271–5. doi:10.1192/bjp.181.4.271. PMID 12356650.
- Soyka M, Zetsche T, Dresel S, Tatsch K (May 2000). "FDG-PET and IBZM-SPECT suggest reduced thalamic activity but no dopaminergic dysfunction in chronic alcohol hallucinosis". *The Journal of Neuropsychiatry and Clinical Neurosciences*. 12 (2): 287–8. doi:10.1176/appi.neuropsych.12.2.287. PMID 11001615.
- Zoldan J, Friedberg G, Livneh M, Melamed E (July 1995). "Psychosis in advanced Parkinson's disease: treatment with ondansetron, a 5-HT<sub>3</sub> receptor antagonist". *Neurology*. 45 (7): 1305–8. doi:10.1212/WNL.45.7.1305. PMID 7617188.
- Perry BI, McIntosh G, Weich S, Singh S, Rees K (November 2016). "The association between first-episode psychosis and abnormal glycaemic control: systematic review and meta-analysis". *The Lancet. Psychiatry*. 3 (11): 1049–1058. doi:10.1016/S2215-0366(16)30262-0. PMID 27720402.
- Curran C, Byrappa N, McBride A (September 2004). "Stimulant psychosis: systematic review". *The British Journal of Psychiatry*. 185 (3): 196–204. doi:10.1192/bjp.185.3.196. PMID 15339823.
- "Final rule declaring dietary supplements containing ephedrine alkaloids adulterated because they present an unreasonable risk. Final rule". *Federal Register*. 69 (28): 6787–854. February 2004. PMID 14968803. (69 FR 6814 and 69 FR 6818)
- Overall JE, Gorham DR. The Brief Psychiatric Rating Scale. *Psychol Rep*. 1962;10:799–812
- Kay SR, Fiszbein A, Opler LA (1987). "The positive and negative syndrome scale (PANSS) for schizophrenia". *Schizophrenia Bulletin*. 13 (2): 261–76. doi:10.1093/schbul/13.2.261.

PMID 3616518.

Gaebel W, Zielasek J (March 2015). "Focus on psychosis". *Dialogues in Clinical Neuroscience*. 17 (1): 9–18. PMC 4421906. PMID 25987859.

Marshall M, Rathbone J (June 2011). "Early intervention for psychosis". *The Cochrane Database of Systematic Reviews* (6): CD004718.

doi:10.1002/14651858.CD004718.pub3. PMC 4163966. PMID 21678345.

van Os J, Kapur S (August 2009). "Schizophrenia". *Lancet*. 374 (9690): 635–45.

doi:10.1016/S0140-6736(09)60995-8. PMID 19700006.

Stafford MR, Jackson H, Mayo-Wilson E, Morrison AP, Kendall T (January 2013). "Early interventions to prevent psychosis: systematic review and meta-analysis". *BMJ*. 346: f185. doi:10.1136/bmj.f185. PMC 3548617. PMID 23335473.

National Collaborating Centre for Mental Health (25 March 2009). "Schizophrenia: Full national clinical guideline on core interventions in primary and secondary care" (PDF). Retrieved 25 November 2009.

Kane JM, Correll CU (2010). "Pharmacologic treatment of schizophrenia". *Dialogues in Clinical Neuroscience*. 12 (3): 345–57. PMC 3085113. PMID 20954430.

Hartling L, Abou-Setta AM, Dursun S, Mousavi SS, Pasichnyk D, Newton AS (October 2012).

"Antipsychotics in adults with schizophrenia: comparative effectiveness of first-generation versus second-generation medications: a systematic review and meta-analysis". *Annals of Internal Medicine*. 157 (7): 498–511. doi:10.7326/0003-4819-157-7-201210020-00525. PMID 22893011.

Schultz SH, North SW, Shields CG (June 2007). "Schizophrenia: a review". *American Family Physician*. 75 (12): 1821–9. PMID 17619525.

Smith T, Weston C, Lieberman J (August 2010). "Schizophrenia (maintenance treatment)". *American Family Physician*. 82 (4): 338–9. PMID 20704164.

Taylor DM, Duncan-McConnell D (2000). "Refractory schizophrenia and atypical antipsychotics". *Journal of Psychopharmacology*. 14 (4): 409–18.

doi:10.1177/026988110001400411. PMID 11198061.

Picchioni MM, Murray RM (July 2007). "Schizophrenia". *BMJ*. 335 (7610): 91–5.

doi:10.1136/bmj.39227.616447.BE. PMC 1914490. PMID 17626963.

Essali A, Al-Haj Haasan N, Li C, Rathbone J (January 2009). "Clozapine versus typical neuroleptic medication for schizophrenia". *The Cochrane Database of Systematic Reviews* (1): CD000059. doi:10.1002/14651858.CD000059.pub2. PMID 19160174.

Ost LG (October 2014). "The efficacy of Acceptance and Commitment Therapy: an updated systematic review and meta-analysis". *Behaviour Research and Therapy*. 61: 105–21.

doi:10.1016/j.brat.2014.07.018. PMID 25193001.

Birchwood M, Todd P, Jackson C (1998). "Early intervention in psychosis. The critical period hypothesis". *The British Journal of Psychiatry*. Supplement. 172 (33): 53–9. PMID 9764127.

Bürgy M (November 2008). "The concept of psychosis: historical and phenomenological

- aspects". *Schizophrenia Bulletin*. 34 (6): 1200–10. doi:10.1093/schbul/sbm136. PMC 2632489. PMID 18174608.
- Beer MD (June 1995). "Psychosis: from mental disorder to disease concept". *History of Psychiatry*. 6 (22 Pt 2): 177–200. doi:10.1177/0957154X9500602204. PMID 11639691.
- Berrios GE (July 1987). "Historical aspects of psychoses: 19th century issues". *British Medical Bulletin*. 43 (3): 484–98. PMID 3322481.
- Berrios GE, Beer D (March 1994). "The notion of a unitary psychosis: a conceptual history". *History of Psychiatry*. 5 (17 Pt 1): 13–36. doi:10.1177/0957154X9400501702. PMID 11639278.
- Porter R (2003). *Madness: A Brief History*. US: Oxford University Press. p. 10. ISBN 978-0-19-280267-5.
- Vlachos IO, Beratis S, Hartocollis P (1997). "Magico-religious beliefs and psychosis". *Psychopathology*. 30 (2): 93–9. doi:10.1159/000285035. PMID 9168565.
- Pfeifer S (September 1994). "Belief in demons and exorcism in psychiatric patients in Switzerland". *The British Journal of Medical Psychology*. 67 (3): 247–58. doi:10.1111/j.2044-8341.1994.tb01794.x. PMID 7803317.
- Bennet S (2008). "Mind and madness in classical antiquity". *History of Psychiatry and Medical Psychology*: 175–197. doi:10.1007/978-0-387-34708-0\_3. ISBN 978-0-387-34707-3.
- Spring B, Weinstein L, Lemon M, Haskell A (1991). "Schizophrenia from Hippocrates to Kraepelin". *Clinical Psychology*: 259–277. doi:10.1007/978-1-4757-9715-2\_10. ISBN 978-1-4757-9717-6.
- Rush B (1830). *Medical Inquiries and Observations upon Diseases of the Mind*. Philadelphia. pp. 98–190. ISBN 978-0-559-92167-4.
- Shorter, Edward (1998). *A History of Psychiatry: From the Era of the Asylum to the Age of Prozac*. Hoboken, New Jersey: John Wiley & Sons. ISBN 978-0-471-24531-5.
- Stone JL (March 2001). "Dr. Gottlieb Burckhardt--the pioneer of psychosurgery". *Journal of the History of the Neurosciences*. 10 (1): 79–92. doi:10.1076/jhin.10.1.79.5634. PMID 11446267.
- Gross D, Schäfer G (February 2011). "Egas Moniz (1874-1955) and the "invention" of modern psychosurgery: a historical and ethical reanalysis under special consideration of Portuguese original sources". *Neurosurgical Focus*. 30 (2): E8. doi:10.3171/2011.3.FOCUS10214a. PMID 21284454.
- Pressman JD (1998). *Last Resort: Psychosurgery and the Limits of Medicine*. Cambridge Studies in the History of Medicine. Cambridge, UK: Cambridge University Press. pp. 18–40. ISBN 978-0-521-35371-7. OCLC 36729044.
- Berrios GE (March 1997). "The origins of psychosurgery: Shaw, Burckhardt and Moniz". *History of Psychiatry*. 8 (29 pt 1): 61–81. doi:10.1177/0957154X9700802905. PMID 11619209.
- Mashour GA, Walker EE, Martuza RL (June 2005). "Psychosurgery: past, present, and

- future". *Brain Research. Brain Research Reviews*. 48 (3): 409–19. doi:10.1016/j.brainresrev.2004.09.002. PMID 15914249.
- Stip E (May 2002). "Happy birthday neuroleptics! 50 years later: la folie du doute". *European Psychiatry*. 17 (3): 115–9. doi:10.1016/S0924-9338(02)00639-9. PMID 12052571.
- Crossley NA, Constante M, McGuire P, Power P (June 2010). "Efficacy of atypical v. typical antipsychotics in the treatment of early psychosis: meta-analysis". *The British Journal of Psychiatry*. 196 (6): 434–9. doi:10.1192/bjp.bp.109.066217. PMC 2878818. PMID 20513851.
- Maher AR, Maglione M, Bagley S, Suttorp M, Hu JH, Ewing B, Wang Z, Timmer M, Sultzer D, Shekelle PG (September 2011). "Efficacy and comparative effectiveness of atypical antipsychotic medications for off-label uses in adults: a systematic review and meta-analysis". *JAMA*. 306 (12): 1359–69. doi:10.1001/jama.2011.1360. PMID 21954480.
- Healy D (2002). *The Creation of Psychopharmacology*. Cambridge: Harvard University Press. ISBN 978-0-674-00619-5.
- Sims A (2002). *Symptoms in the mind: An introduction to descriptive psychopathology* (3rd ed.). Edinburgh: Elsevier Science Ltd. ISBN 978-0-7020-2627-0.
- Murray ED, Buttner N, Price BH (April 2012). "Depression and Psychosis in Neurological Practice". In Bradley WG, Daroff RB, Fenichel GM, Jankovic J. *Neurology in Clinical Practice* (6th ed.). Butterworth Heinemann. ISBN 978-1-4377-0434-1.
- Williams P (2012). *Rethinking Madness: Towards a Paradigm Shift In Our Understanding and Treatment of Psychosis*. Sky's Edge Publishing. ISBN 978-0-9849867-0-5.

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