Ministry of Defence

Synopsis of Causation

Schizophrenia

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Disclaimer

This synopsis has been completed by medical practitioners. It is based on a literature search at the standard of a textbook of medicine and generalist review articles. It is not intended to be a meta-analysis of the literature on the condition specified.

Every effort has been taken to ensure that the information contained in the synopsis is accurate and consistent with current knowledge and practice and to do this the synopsis has been subject to an external validation process by consultants in a relevant specialty nominated by the Royal Society of Medicine.

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1. Definition

1.1. Schizophrenia is a severe and complex mental disorder. It is the most common form of psychosis and is currently regarded by some as a broad syndrome which includes an array of allied disorders rather than as a single disease entity. Although once classified as one of the functional psychiatric disorders, schizophrenia is now widely regarded primarily as an abnormality of brain neurophysiology.

1.2. Schizophrenia is characterised by fundamental and characteristic distortions of thinking and perception, and by inappropriate or blunted affect. Intellectual capacity is usually maintained, but those functions that characterise an individual's individuality and self-direction are disturbed.

1.3. The condition is defined in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM IV), published by the American Psychiatric Association, as follows (in summary)

1.3.1. **A. Characteristic symptoms:** Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated):

(1) delusions

(2) hallucinations

(3) disorganized speech (e.g., frequent 'derailment' or incoherence)

(4) grossly disorganized or catatonic behaviour

(5) negative symptoms, i.e., affective flattening, alogia, or avolition

Note: Only one Criterion A symptom is required if delusions are bizarre or hallucinations consist of a voice keeping up a running commentary on the person's behaviour or thoughts, or two or more voices conversing with each other.

1.3.2. **B. Social/occupational dysfunction:** For a significant portion of the time since the onset of the disturbance, one or more major areas of functioning such as work, interpersonal relations, or self-care are markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement).

1.3.3. **C. Duration:** Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or two or more symptoms listed in Criterion A present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).

1.3.4. **D. Schizoaffective and Mood Disorder exclusion:** Schizoaffective Disorder and Mood Disorder With Psychotic Features have been ruled out because either (1) no Major

Depressive, Manic, or Mixed Episodes have occurred concurrently with the active-phase symptoms; or (2) if mood episodes have occurred during active-phase symptoms, their total duration has been brief relative to the duration of the active and residual periods.

1.3.5. **E. Substance/general medical condition exclusion:** The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

1.3.6. **F. Relationship to a Pervasive Developmental Disorder:** If there is a history of Autistic Disorder or another Pervasive Developmental Disorder, the additional diagnosis of Schizophrenia is made only if prominent delusions or hallucinations are also present for at least a month (or less if successfully treated).

1.4. The condition is often classified into a number of varieties according to the clinical presentation; namely paranoid, catatonic, hebephrenic and simple subtypes. However a large proportion of patients fail to fit clearly into any of these categories and are described as suffering from "undifferentiated" schizophrenia. This classification is discussed further in the next section.

1.5. The disorder affects approximately one person in every 100, a figure which is remarkably stable across racial, cultural, and national lines. Although it can occur in younger children it is rare before puberty and usually manifests itself between the ages of 15 and 35 years. The lifetime risk is equal for both sexes, but the onset is earlier and outcome is poorer in males than in females. Disease onset in individuals over the age of 45 years is uncommon.

2. Clinical features

2.1. **Onset** In about 50% of patients, the onset of the disease is insidious. There may be a prodromal phase in which there is poor school or work performance, lack of attention to personal hygiene and appearance, decreasing emotional responsiveness, and behaviour patterns which are not characteristic of the individual. In other cases, the condition may begin abruptly in a person who previously functioned normally.

2.2. There is accumulating evidence that some aspects of schizophrenia are manifest years before the condition is formally diagnosed. Clarifying the pathological relationship between these early subtle intellectual and behavioural abnormalities and disease could provide markers for the early prediction of future psychosis. These premorbid cognitive and behavioural manifestations may be slight and only detectable by special tests.[1,23]

2.3. **Signs and symptoms** A number of signs and symptoms are characteristic of the condition, including hallucinations, delusions, disorganised speech, catatonia, and bizarre behaviour. These are described briefly below.

2.3.1. **Hallucinations** These are usually auditory, but hallucinations of taste, touch, and smell may also occur. Auditory hallucinations usually take the form of voices, which may be deafening and forceful, or quiet and indistinct. So called "command hallucinations," are voices that tell the patient what to do. They may be faint and suggestive or demanding and imperious. They may instruct the patient to perform innocuous tasks, but at other times they may command the patient to harm themselves or – rarely – to hurt other people.

2.3.2. **Delusions** are almost invariably present in schizophrenia. They may take many forms, but ideas of persecution are particularly common, and patients often complain that thoughts are being inserted into them by some external person or organisation. Grandiose delusions also are not infrequent, and patients may believe that they occupy an exalted position in society.

2.3.3. **Disorganised speech** may be a feature of the condition. Often described as "loosening of associations" the patient's speech becomes illogical; ideas are juxtaposed that have no possible connection, and the patient expresses purposeless, disjointed concepts.

2.3.4. **Catatonia** may be present. The term refers to a psychomotor disturbance which may involve mutism, negativism, rigidity, purposeless excitement, echolalia, echopraxia, and inappropriate posturing.

2.3.5. **Bizarre behaviour** Patients may exhibit bizarre behaviour of various kinds. They may perform odd caricatures of normal gestures, or their speech may be erratic in modulation or cadence. A bizarre gait may be assumed. In some instances there is a marked disconnection between facial expression and reported emotion; the patient may laugh or cry inappropriately.

2.3.6. **Cognitive impairment** Cognitive deficits are a core feature of schizophrenia. Areas that show particular impairment include sustained attention (vigilance), executive function (the ability to plan and use abstract concepts), language skills, working memory (the ability to recall, process, and manipulate information), and verbal learning and

memory.[4,5,6]

2.4. **Classification of symptoms** Symptoms are sometimes categorised as follows:

2.4.1. **Positive symptoms** which include hallucinations, usually auditory; delusions and disorganised speech and behaviour.

2.4.2. **Negative symptoms** which include a decrease in emotional range, poverty of speech, loss of interest, and inertia.

2.4.3. **Cognitive symptoms** as described in 2.3.6.

2.5. **Subtypes of schizophrenia** As discussed in the previous section, the various subtypes or varieties of schizophrenia are loosely characterised by particular associations of symptoms. This classification may be useful in predicting likely patient behaviour in different situations and in formulating the prognosis, although not infrequently a patient will not fit precisely into any one subtype.

2.5.1. **Paranoid schizophrenia** is mainly characterized by hallucinations and delusions of a paranoid nature. Other features of the condition such as inappropriate affect and bizarre behaviour are either absent or relatively minor. Usually the hallucinations are auditory and hostile in nature, and delusions relate to ideas of persecution by family and colleagues. This may lead to suspiciousness and anger and occasionally, violence.

2.5.2. **Catatonic schizophrenia** This subtype may take the form of stuporous catatonia or excited catatonia.

- **Stuporous catatonia** In this subtype of the condition there is immobility, negativism, mutism and sometimes posturing. The patient may remain silently in one position for long periods and resist attempts to feed or wash them.

- **Excited catatonia** Patients exhibit purposeless, frenzied activity or stereotyped, meaningless activity, and at times act in an impulsive, unpredictable way. Speech is often bizarre, stereotyped and declamatory.

2.5.3. **Hebephrenic schizophrenia** This variety tends to have an earlier onset than the other subtypes. It may develop insidiously and although delusions and hallucinations are present, they are relatively minor. Bizarre behaviour is common, with loosened associations, and bizarre and inappropriate affect. Patients may occupy themselves with purposeless, often childish activities or may be withdrawn and inaccessible. Delusions, if they occur, tend to be hypochondriacal in nature.

2.5.4. **Simple schizophrenia** often begins in childhood and progresses gradually and insidiously over many years. Delusions, hallucinations, and loosening of associations are not a marked feature, if indeed they occur at all. Instead the clinical picture is dominated by the impoverishment of thought, and flattening of affect. As the years pass these patients gradually lose sight of their former ambitions; they lose interest in their former friends and acquaintances and may appear shiftless and idle. They may appear content to lie in bed or sit in their room all day. Sometimes fleeting bizarre behaviour may occur, or a passing delusion. Usually these patients attract little attention; some continue to live with aged parents; others live in hostels for the remainder of their lives.

2.5.5. **Undifferentiated schizophrenia** Not uncommonly the clinical picture fails to conform to any of these subtypes, when the term “atypical schizophrenia” is employed. Occasionally the features of the case may change with time and so the case ceases to fit the original definition.

2.6. **Post-psychotic depression** During episodes of partial remission of the “positive” symptoms of schizophrenia, some patients may develop a prolonged and pervasive depressed mood along with typical vegetative symptoms. This condition is often referred to as a “post-psychotic depression,” and increases the risk of suicide. It should not be confused with the frequent, transient, and isolated depressive symptoms seen during an exacerbation of the other components of the illness.

2.7. **Clinical course** Schizophrenia is a chronic disease, which can exhibit one of two patterns. In the so-called type I case, the condition waxes and wanes; there is no regular pattern and the alternating cycle of exacerbations and partial remissions ranges from weeks to months, or even years. In the other, type II, there is a more or less stable chronic state.

3. Aetiology

Pathophysiological considerations

3.1. The search for the anatomical site of the abnormal processes that underlie the clinical manifestations of schizophrenia has been assisted by significant advances in *in vivo* brain imaging and post-mortem techniques. Attention has focused on abnormalities of:

- Ventricles
- Limbic system
- Prefrontal cortex
- Temporal lobe
- Other neocortical regions

3.1.1. **Ventricles** Enlarged ventricles are one of the most consistently reported features suggesting a neuroanatomical abnormality in schizophrenia. Some workers also report the finding in first degree relatives with the condition, but not all agree with this observation and it is generally thought that the phenomenon may merely represent a secondary manifestation of brain atrophy, or reflect a consequence of antipsychotic medication.

3.1.2. **Limbic system** Abnormalities of certain limbic structures, particularly the hippocampus, have been implicated in schizophrenia. These structures have an important role in attention, memory, emotional expression and social relationships and are leading candidates for the neuroanatomical site of the condition.

3.1.3. **Prefrontal cortex** This area of the brain is responsible for the most sophisticated functions, and integrates information from all other cortical areas. The specific functions of the structure include the working memory, which is used to temporarily store and manipulate information. Other parts of the prefrontal cortex are involved with emotional expression, and the genetics of the prefrontal neurons, the circuits which link them and the underlying neurochemistry are currently being intensively investigated.

3.1.4. **Temporal lobe** The superior temporal gyrus and allied structures are known to undergo changes in patients with schizophrenia.

3.1.5. **Other brain structures** have been implicated in the condition, including the corpus striatum and the thalamus.

Aetiology

3.2. The cause of schizophrenia is at present unknown, although twin and adoption studies clearly demonstrate that it aggregates in families, with this clustering largely attributable to genetic factors. However it is clear that both neurodevelopmental deviance and environmental influences both play a role in the causation of the condition.

3.3. **Genetic factors** It is unlikely that schizophrenia is a single gene disorder. It is also unlikely that just a small number of genes exerting large effects may result in vulnerability to the condition. The focus of investigation is now on multiple genes of small to moderate effect, which may interact with each other and with other, non-genetic risk factors.[7,8] A large number of studies in the past 30 years have attempted to identify a clear genetically-determined susceptibility to schizophrenia.

3.3.1. **Family prevalence studies** The chance of developing schizophrenia is approximately ten times greater among first-degree family members of individuals with the condition.[9] There is a six times- and two times greater chance of developing schizophrenia respectively in second and third degree relatives of patients with the disease.[10]

3.3.2. **Adoption studies** Adopted children with schizophrenia have significantly higher rates of the disorder in biological first degree relatives (4.1%) than do control adoptees (0.5%).[11] Some workers have concluded that significantly more adopted children who were born to mothers with schizophrenia themselves developed the condition (9.1%) than did control offspring.[12]

3.3.3. **Twin studies** indicate that concordance of schizophrenia is 50% among monozygotic twins and 8-12% among dizygotic twins, compared with 1% among the general population.[9] While these results are impressive, they suggest that other, non-genetic factors must play a role in the aetiology.

3.3.4. **Linkage and association studies** Research continues to try to identify genes which may be responsible for schizophrenia but so far no definite associations have been identified. However a number of new genomic avenues are currently being explored. Recent improvements in technology have resulted in the implication of genes at several chromosomal loci.[13]

3.4. **Neurodevelopmental abnormalities** A number of studies have reported a higher rate of prenatal and birth complications in infants who subsequently developed schizophrenia. These include pre-eclampsia, prematurity, and low birth weight. One of the explanations proposed is that hypoxia resulting from these complications adversely affects the hippocampus and certain neurocortical areas which are particularly sensitive to a deficiency of oxygen. However, meta-analyses suggest that in general, obstetric complications only increase the risk of schizophrenia from 1.3- to twofold. Therefore these factors could only account for only a small number of cases and much further research will be required in order to elucidate the mechanisms underlying this association.

3.5. **Immune dysfunction** Several workers have proposed that schizophrenia may be associated with impaired immune function, including the possibility of an autoimmune process.[14] Results are conflicting, but research continues.

3.6. **Neurochemical abnormalities** A number of neurochemical changes have been implicated in schizophrenia.

3.6.1. **The role of dopamine** The current view proposes that schizophrenia may be associated with a dopaminergic imbalance. On the one hand, an excess of subcortical dopamine function may cause hyperstimulation of D_2 receptors with resultant positive symptoms, while on the other, a deficit in cortical dopamine function may cause hypostimulation of D_1 receptors, resulting in negative symptoms and cognitive impairment.[15] Despite considerable efforts to obtain experimental data to support this hypothesis, clear

identification of abnormalities in dopamine function in schizophrenia has remained elusive.

3.6.2. **The role of serotonin** The effects of the drug lysergic acid diethylamide (LSD) mimic the manifestations of schizophrenia in many respects. Further interest has been aroused by the observation that LSD affects serotonin neurotransmission. However in LSD psychosis, visual hallucinations are commonest and auditory hallucinations are rare, while in schizophrenia the opposite is true. Further research into the role of serotonin in schizophrenia is awaited.[16]

3.6.3. **Other neurochemical systems** Other research has implicated the norepinephrine, cholinergic, glutamatergic, GABAergic, and neuropeptide systems.

3.7. **Hypothalamic-pituitary-adrenal axis dysregulation** Abnormalities in the regulation of the hypothalamic-pituitary-adrenal axis have been identified by some researchers in subjects with schizophrenia.[17] However, findings have been less than consistent.[18]

Environmental risk factors

3.8. Although liability to schizophrenia appears to a significant degree to be controlled by genetic influences, a number of environmental risk factors have been identified.

3.9. **Viral infection** It has been observed that a higher than expected number of children born during influenza epidemics subsequently develop schizophrenia. Furthermore, a greater proportion of patients with schizophrenia are born in the winter months, when there is a higher rate of viral infections of all kinds. Based on these observations it has been proposed that exposure to viral infection *in utero* may represent a neurodevelopmental risk factor for schizophrenia.[19,20,21] As yet however direct evidence for an aetiological link with viral infection is lacking.

3.10. **Sociodemographic factors** A number of sociodemographic factors have been associated with an increased risk of schizophrenia. These include immigrant status, poverty and social deprivation, and an urban environment.

3.10.1. **Immigrant status** A clear association between migration and schizophrenia has been noted in a number of European and US settings. However the high incidence among African-Caribbean population of the United Kingdom has attracted most attention. A 6- to 18-fold higher incidence over the non-immigrant white population has been found by various workers, and a number of explanations have been put forward to explain this. Some of the increase has been perceived as a result of poor housing, high rates of unemployment and social isolation, racial harassment and low self-esteem.[22,23,24]

3.10.2. **Poverty and social deprivation** Poverty and lower socioeconomic status have long been linked to higher rates of schizophrenia.[25,26] The reasons for this association are unknown.

3.10.3. **Urban birth and rearing** A statistical association between urban birth and rearing and the subsequent development of schizophrenia has been noted since the 1930s.[27,28,29] The mechanisms of this association are unclear.

3.11. **Drug and substance abuse** It has long been considered that there is a correlation between drug and substance abuse and vulnerability to psychosis.[30,31,32,33] A review of the

literature has estimated that the risk of psychosis is twice as likely in cannabis users compared to non-users.[34,35] A large German study following 2,437 individuals aged 14-24 for four years concluded that young cannabis users are more likely than non-users to develop psychosis, particularly if they also have other risk factors.[36] Furthermore the researchers found a dose-response relation between frequency of cannabis use and risk of psychosis. Notably, the effect of cannabis use was much stronger in those with a genetic predisposition for psychosis than in those without (difference in risk 23.8% and 5.6%, respectively). A systematic review of cannabis use and psychosis[37] concluded that early use of cannabis appeared to increase the risk of schizophrenia, and these authors too identified a dose-response relationship. While the reason for the association between drug abuse and schizophrenia is unknown, one possible mechanism relates to traumatic early life experiences, which have been shown to predispose individuals to both psychosis and substance abuse. Recent research has provided evidence that a functional polymorphism of the gene cathecol-O-methyltransferase (COMT), which is involved in dopamine metabolism, interacts with adolescent cannabis use to increase vulnerability to psychosis.[38] It is suggested that this interaction may be limited to cannabis use during a sensitive period of brain development in adolescence.

3.12. **Other drugs** A number of other agents, such as cocaine and the amphetamines may cause transient psychotic symptoms. However some researchers in the UK have concluded that patients with psychosis do not consume more alcohol or drugs in general than the rest of the population, but they are twice as likely to abuse cannabis.

3.13. **Psychosocial and other stressors** Psychosocial stressors are included in most aetiological models of schizophrenia, usually as precipitating factors in vulnerable individuals, although some studies have reported an increased rate of life events over a longer period prior to the onset of psychosis.[39] However the hypothesis which proposes a direct causative link between life events and the onset of schizophrenia is widely regarded as over-simplistic, and it is generally accepted that exposure to psychosocial stressors alone does not constitute a primary aetiological factor.[40]

3.13.1. **Emotional reactivity to daily life stressors** A number of workers have concluded that higher risk for psychosis is associated with greater levels of emotional reactivity to daily life stressors, in a dose-response fashion. Subtle abnormalities in the way individuals interact with their environment may constitute part of the susceptibility to schizophrenia in those who are genetically vulnerable to it.[41]

3.13.2. **Social adversity in childhood** has been linked to an increased risk of developing psychosis,[42] and increased age- and sex-adjusted hazard ratios for schizophrenia and other psychoses were found for all childhood socioeconomic indicators, ranking from lowest to highest hazard ratio: rented apartments, low socioeconomic status, single-parent households, unemployment, and households receiving social welfare benefits (see 3.10.2.)

3.14. **Post-traumatic Stress Disorder** Approximately 30% of patients with post-traumatic stress disorder (PTSD) show a lifetime prevalence of psychosis.[43] There are at least two theoretical explanations for this observation. Firstly, patients with PTSD and a comorbid schizophrenia may have a primary psychotic disorder then develop PTSD after the onset of psychosis. Alternatively it may be that the psychotic symptoms are secondary to PTSD, and that this association is a subtype of PTSD. Problems with measurement and definition have however caused difficulties in the design and interpretation of research in this area. However, PTSD is defined by a close relationship between the content of the patient's symptoms and

the experience of very traumatic events, and even in veterans exposed to extreme combat stress the distinction between flashbacks and true psychotic symptoms can easily be made.[44]

3.15. **Trauma** For many decades injury to the brain after birth has been suggested as a risk factor for psychosis. In a number of studies the long term follow-up analysis of head-injured cohorts generally seem to suggest a higher cumulative incidence of schizophrenia, but these have prominent methodological shortcomings. The hypothesis has so far attracted little research, but a recent systematic review[45] concluded that given the available published data it is unlikely that head injury causes schizophrenia.

3.16. The consensus view is that schizophrenia arises as a result of interaction between genetic vulnerability and environment. There is evidence that genetic influences increase the risk for schizophrenia by rendering individuals more sensitive to factors such as a dysfunctional early family rearing environment, cannabis, viral infections, complications of birth and pregnancy, and certain environmental risk factors including urban birth or residence, socioeconomic deprivation, and membership of certain ethnic groups.[25]

4. Prognosis

4.1. During the last few years, increasing evidence has suggested that early intervention in schizophrenia improves its long-term outcome. For this reason, there is considerable interest in the observation that some aspects of schizophrenia are manifest years before the condition is formally diagnosed (see section 2.2). These subtle intellectual and behavioural abnormalities might provide markers for the early prediction of future psychosis.

4.2. Conventional antipsychotic drugs such as chlorpromazine and haloperidol have been used for many years, and long-term depot injections of these drugs are effective. However, serious side-effects are common, and include parkinsonism and hyperprolactinaemia. New generation, so-called 'atypical' antipsychotic agents such as clozapine, olanzapine and risperidone are used increasingly, but long-term effectiveness and safety are yet to be established, and weight-gain and diabetes may be troublesome side-effects.

4.3. As described earlier, the disease pursues a fluctuating course in some patients and this pattern may continue for their entire lives. Exacerbations may appear in some cases to be precipitated by psychosocial factors or environmental stressors, but usually they occur without any obvious cause. In many cases after 5 to 20 years, this pattern gives way to a stable chronic state. There is a 10% lifetime risk of suicide in patients with the condition.

4.4. By the nature of the condition, some 80% of patients relapse within two years of a treated first episode, usually because of non-adherence to continuing medication. Only one in six patients remains relapse-free and not requiring medication 10-15 years after onset.[46]

4.5. The traditional subtype classification may be helpful in formulating a prognosis. The condition tends to pursue a fluctuating course in patients with **paranoid** or **catatonic** schizophrenia, and the eventual outcome appears to be worse for the latter. The **hebephrenic** and **simple** subtypes tend to pursue either a stable or progressively deteriorating course, and of the two the simple subtype seems to often undergo the most marked deterioration.

4.6. It is doubtful whether in the natural course of events, even in the presence of modern treatment, the condition ever undergoes full resolution. Cases in which prolonged and apparently complete remission occurred have been documented; indeed, in a number of cases patients may appear at first glance to have recovered completely. However, lingering residual symptoms inevitably occur in these individuals, such as fleeting hallucinations, odd ideas and mannerisms, or a certain poverty of thought. Therefore, although it is possible for some patients to function in the community with minimal support, it is very unlikely that, in the natural course of the disease, there is ever a return to complete normality.

5. Summary

5.1. Schizophrenia is a severe and complex mental disorder. It is the most common form of psychosis and is now widely regarded primarily as an abnormality of brain neurophysiology. It is characterised by fundamental and characteristic distortions of thinking and perception, and by inappropriate or blunted affect.

5.2. The cause is unknown, but family, twin, and adoption studies support the role of genetic factors in the aetiology of the condition. Neurodevelopmental disruption may be the result of genetic and/or environmental stressors early in development, leading to subtle alterations in the brain. In addition, in some cases environmental stressors in later life can initiate or exacerbate expression of these genetic or neurodevelopmental defects.

5.3. The prognosis is somewhat unpredictable, but very often after pursuing a fluctuating course of exacerbations and remissions this pattern gives way to a stable chronic state after 5 to 20 years. A high proportion of patients require long-term medication.

6. Related Synopses

Depressive Disorder

Stress (Mental and Physical) and Mental Disease

7. Glossary

affect	The conscious subjective aspect of feeling or emotion.
cognitive	Relating to conscious intellectual activity (as thinking, reasoning, remembering, imagining, or learning).
concordance studies	Research to identify agreement in the types of data that occur in natural pairs. For example, in a trait like schizophrenia, a pair of identical twins is *concordant* if both are affected or both are unaffected, but *discordant* if one of them only is affected.
corpus striatum	Part of the brain located in front of and lateral to the thalamus (*q.v.)* in each cerebral hemisphere.
delusion	A false belief regarding the self or persons or objects outside the self that persists despite the facts.
dizygotic twins	Twins derived from two separate eggs.
dopamine	A monoamine that occurs as a neurotransmitter in the brain.
echolalia	Repetition of what is said by other people as if echoing them.
echopraxia	Pathological repetition of the actions of other people.
hallucination	A perception of something (e.g. a visual image or a sound) with no external cause, usually arising from a disorder of the nervous system.
hippocampus	An area of the brain which is important for long term memory storage.
hyperprolactinaemia	A condition characterised by an increased level of prolactin, a hormone produced by the anterior pituitary gland which prepares the pregnant female's breasts for milk production.

hypoxia	Reduced oxygen supply to tissues.
hypothalamic-pituitary-adrenal axis	The humoral component of an integrated neural and endocrine system that responds to challenges to homeostasis (stressors).
limbic system	A group of subcortical structures of the brain that are concerned especially with emotion and motivation.
monozygotic twins	Twins that are derived from a single egg.
negativism	A tendency to refuse to do, to do the opposite of, or to do something at variance with what is asked.
parkinsonism	A group of neurological disorders characterised by paucity of movement, tremor and muscular rigidity.
pre-eclampsia	A condition developing in late pregnancy that is characterized by a rise in blood pressure, excessive weight gain, generalised oedema, and protein in the urine.
psychosis	A general term denoting a serious mental disorder in which abnormal mental functioning impairs the capacity of the patient to meet the ordinary demands of life.
serotonin	A neurotransmitter; i.e. a substance that transmits nerve impulses across a synapse (a place at which a nervous impulse passes from one neuron to another).
thalamus	Part of the brain that relays impulses and especially sensory impulses to and from the cerebral cortex.
ventricle	One of the system of communicating cavities in the brain.

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