WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 15, 198-223. Review Article ISSN 2277– 7105

TREATMENT OF PSYCHOSIS DISRORDER

Satish D. Pawar*[1], Javed S. Shaikh[1], Dr. Vanita Kanase[2] and Dr. Sudha Rathod[3]

[1]Oriental College of Pharmacy, Sector 2, Behind Sanpada Railway Station, Sanpada West, Navi Mumbai, Maharashtra 400705.

[2]HOD Pharmacology.

[3]Principal Oriental College of Pharmacy.

Article Received on
26 Sept. 2017,

Revised on 16 Oct. 2017,
Accepted on 06 Nov. 2017

DOI: 10.20959/wjpr201715-10067

***Corresponding Author**
Satish D. Pawar
Oriental College of Pharmacy, Sector 2, Behind Sanpada Railway Station, Sanpada West,
Navi Mumbai, Maharashtra 400705.

ASBSTRACT

Psychosis is refers to an abnormal condition of mind in which person loss his contact with reality and the person suffures from psychosis is called as psychotic. Psychosis makes people confuse or misintepret what is going on around him. Psychosis disorder associates mainly with delusion, hallucination and catatonia. In hallucination psychotic may heared a vice and that are not real.delusion means psychotic makes so many false belief and makes confuse himself.

Psychosis is mainly occurring in 80% of people with age between of 18-30. Psychosis may occur due to schizophrenia, due to narcotic substance, Parkinson's disease there are many typical and atypical drugs are available in pharmaceutical market, which are act on various neurotransmitter that is dopamine, serotonin, acetyl choline, etc. A newely approved molecule pemavanserine is used to treat Parkinson induced psychosis. There are many alternative treatments are also avaible now days such as ayurvedic, homeopathic, Chinese traditional medicine, aromatherapy, rTms, MST and many Music therapy may used simultaneously with allopathic therapy and produce grasting improvement in patient health. Psychosis can seriously disrupt life of psychotic patient and his development, so that it is important to get early help.

Defination - Psychosis refers to an abnormal condition of the mind described as involving a "loss of contact with reality".

People with psychosis are described as psychotic. People experiencing psychosis may exhibit some personality changes and thought disorder. Depending on its severity, this may be accompanied by unusual or bizarre behavior, as well as difficulty with social interaction and impairment in carrying out daily life activities.

Psychosis (as a medical sign of a psychiatric disorder) is a diagnosis of exclusion. That is, a new-onset episode of psychosis is not considered a symptom of a psychiatric disorder until other relevant and known causes of psychosis are properly excluded.[1] Medical and biological laboratory tests should exclude central nervous system diseases and injuries, diseases and injuries of other organs, psychoactive substances and toxins as causes of symptoms of psychosis before any psychiatric illness can be diagnosed.[1] In medical training, psychosis as a sign of illness is often compared to fever since both can have multiple causes that are not readily apparent.[1]

The term "psychosis" is very broad and can mean anything from relatively normal aberrant experiences through to the complex and catatonic expressions of schizophrenia and bipolar type 1 disorder.[2][3][4] In properly diagnosed psychiatric disorders (where other causes have been excluded by extensive medical and biological laboratory tests), psychosis is a descriptive term for the hallucinations, delusions and impaired insight that may occur.[3][5] Psychosis is generally the term given to noticeable deficits in normal behavior (negative signs) and more commonly to diverse types of hallucinations or delusional beliefs, particularly with regard to the relation between self and others as in grandiosity and pronoia or paranoia.

Many antipsychotic drugs accordingly target the dopamine system; however, meta-analyses of placebo-controlled trials of these drugs show either no significant difference in effects between drug and placebo, or a moderate effect size, suggesting that the pathophysiology of psychosis is much more complex than an overactive dopamine system.[6][7]

Signs and symptoms

People with psychosis normally have one or more of the following: hallucinations, delusions, catatonia, or a thought disorder. Impairments in social cognition also occur.[8][9]

Hallucinations

A hallucination is defined as sensory perception in the absence of external stimuli. Hallucinations are different from illusions, or perceptual distortions, which are the misperception of external stimuli.[10]

Delusion

Delusions are false beliefs that a person holds on to, without adequate evidence. It can be difficult to change the belief, even with evidence to the contrary. Common themes of delusions are persecutory (person believes that others are out to harm them), grandiose (person believing that they have special powers or skills), etc. Persons with Ekbom syndrome may have delusional beliefs of an imaginary parasite infestation.[11]

Catotonia

Catatonic depression is a type of depression that causes someone to remain speechless and motionless for an extended period.[12] At the other end of the extreme, the individual can demonstrat.e motor activity that is considered "excessive" and "peculiar," such as echolalia (mimicking sounds) or Echopraxia (mimicking movements). This is called catatonic excitement.[13] A disturbance in one's ability to generate a logical sequence of ideas, as indicated by disordered speech and/or writing thought disorder may be a symptom of many different mental disorders, but is most commonly associated with schizophrenia or some related psychotic disorder. A person with a thought disorder is usually someone who is suffering from something that is need of professional mental health help sooner rather than later.[14]

Psychiatric disorder

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

traditional psychotic illnesses, psychosis due to general medical conditions and substance-induced psychosis.

Primary psychiatric causes of psychosis include the following:[15] [16] [17]
Schizophrenia and schizophrenic form disorder
Affective (mood) disorders, including severe depression and severe depression or mania in bipolar disorder (manic depression). People experiencing a psychotic episode in the context of depression may experience persecutory or self-blaming delusions or hallucinations, while people experiencing a psychotic episode in the context of mania may form grandiose delusions.

Schizoaffective disorder, involving symptoms of both schizophrenia and mood disorders
Brief psychotic disorder, or acute/transient psychotic disorder
Delusional disorder (persistent delusional disorder)
Chronic hallucinatory psychosis
Psychotic symptoms may also be seen in.[17]

Schizotypal disorder
Certain personality disorders at times of stress (including paranoid personality disorder, schizoid personality disorder and borderline personality disorder).

Major depressive disorder in its severe form, although it is possible and more likely to have severe depression without psychosis.

Bipolar disorder in 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.[18]

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.[19] 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.

TYPES OF PSYCHOSIS

1) Normal states

Brief hallucinations are not uncommon in those without any psychiatric disease. Causes or triggers include:[17]

Falling asleep and waking: hypnagogic and hypnopompic hallucinations, which are entirely normal.[20]

Bereavement, in which hallucinations of a deceased loved one are common.[17]

Severe sleep deprivation.[21][22][23]

2) Cycloid psychosis

Cycloid psychosis is psychosis that progresses from normal to full-blown, usually within a few hours, not related to drug intake or brain injury.[24] In addition, diagnostic criteriainclude at least four of the following symptoms:[24]

Confusion

Mood-incongruent delusions

Hallucinations

Pan-anxiety, a severe anxiety not bound to particular situations or circumstances

Happiness or ecstasy of high degree.[24]

3) Schizophrenia: a psychiatric disorder characterised by disordered thinking and behaviour, which often includes delusions and hallucinations. Psychotic symptoms are experienced for at least six months, together with significant social or occupational dysfunction.

4) Schizophreniform disorder: symptoms are similar to schizophrenia, but persist for between one and six months.

5) Schizoaffective disorder: occasionally psychotic symptoms are experienced in the absence of mood symptoms.

6) Delusional disorder - Involves holding strong, false beliefs (delusions). Hallucinations are usually not present and psychosocial functioning may not be markedly impaired nor behaviour blatantly strange.

7) Substance-induced psychosis: drug and alcohol use or withdrawal can result in psychotic symptoms. These may disappear once the effects of the substances or withdrawal symptoms wear off and sometimes it is also occur initially due to administration of stimulant drug like methamphetamine.

8) Dementia: psychotic symptoms may appear with memory disturbances in conditions that cause physiological deterioration of the brain, such as a head injury, AIDS, post-encephalitis, Alzheimer's disease or a brain tumour.

9) Bipolar disorder (manic depression): psychosis generally appears as part of a more general severe mood disturbance. Psychotic symptoms tend to match your mood.

10) Postpartum psychosis: psychosis that may develop during the six month period after childbirth. This is usually part of a severe mood disorder.

11) Delirium: psychotic symptoms may be part of an acute confusional state that results from another severe medical disorder, such as meningitis, septicaemia or after an epileptic convulsion.[25]

Complications

People with a history of psychosis are much more likely to have drug and/or alcohol misuse problems. This may be because such substances can provide short-term symptom relief, although they usually make symptoms worse in the long term. People with psychosis also have a higher than average risk of suicide. It's estimated that 1 in 5 people with psychosis will attempt to commit suicide at some point in their life and 1 in 25 people with psychosis will kill themselves.[26]

TREATMENT OF PSYCHOSIS

Classification of Drugs[27]

Phenothiazine: Aliphatic side chain – Chlorpromazine, Triflupromazine

Piperidine side chain - Thioridazine

Piperazine side chain – Trifluperazine, Fluphenazine

Butyrophenones: Haloperidol, Trifluperidole, Penfluridole

Thioxanthenes: Flupenthixol

Other heterocyclics: Pimozide, Loxapine

Atypical antipsychotic: Risperidone, Olanzapine, Aripiprazole

Chlorpromazine

The prototypical phenothiazine antipsychotic drug. Like the other drugs in this class, chlorpromazine's antipsychotic actions are thought to be due to long-term adaptation by the brain to blocking dopamine receptors. Chlorpromazine has several other actions and therapeutic uses, including as an antiemetic and in the treatment of intractable hiccup.[28] Chlorpromazine have several adverse effects such as weight gain, sedation, Acute moment disorder. One of the main adverse effect is parkinsonism.[29]

Pharmacokinetic parameter – 1) Administration – i/m, i/v, oral

2) t1/2 – 18 to 30hrs

3) It is metabolized by CYP 2D6 and drug gets cumulate on chronic administration.[27]

Contraindication - Absolute contraindications include:[30]

Circulatory

CNS depression

Coma

Drug intoxication

Bone marrow suppression

Phaeochromocytoma

Hepatic failure

Active liver disease

Haloperidole

It has effectssimilar to the phenothiazines.[34] The drug binds preferentially to D2 and α1 receptors at low dose (ED50 = 0.13 and 0.42 mg/kg, respectively) and 5-HT2 receptors at a higher dose (ED50 = 2.6 mg/kg). Given that antagonism of D2 receptors is more beneficial on the positive symptoms of schizophrenia and antagonism of 5-HT2 receptors on the negative symptoms, this characteristic underlies haloperidol's greater effect on delusions, hallucinations and other manifestations of psychosis.[31] Common side effects of haloperidole

are Constipation; diarrhea; dizziness; drowsiness; dry mouth; headache; loss of appetite; nausea; restlessness; stomach upset; trouble sleeping. yellowing of the skin or eyes.[32]

Flupenthixole

Flupenthixol is a thioxanthene antipsychotic. The mechanism of action of Flupenthixol is not completely understood. Flupenthixol is a powerful antagonist of both D1 and D2 dopamine receptors and an alpha-adrenergic receptor antagonist. It's antipsychotic activity is thought to be related to blocks postsynaptic dopamine receptors in the CNS.[33] It is used to treat the symptom such as hearing, seeing, or sensing things that are not real, having mistaken beliefs, and feeling unusually suspicious. Hypokinesia, Hyperkinesia, Parkinsonism, Blood dyscrasias. Some uncommon adverse effects are Fainting, Palpitations.[35]

Pimozide - Pimozide acts as an antagonist of the D2, D3 and D4 receptors and the 5-HT7 receptor. It is also a hERG blocker.

Similarly to other typical antipsychotics pimozide has a high affinity for the Dopamine D2 receptor and this likely results in its sexual (due to prolactin hypersecretion) and extrapyramidal side effects as well as its therapeutic efficacy against the positive symptoms of schizophrenia.[36]

Risperidone

Risperidone was synthesized based on attempts to replicate clozapine effectiveness without its side effects profile. The goal was to develop a drug with low risk of extrapyramidal symptoms (EPS) based on the assumption that a high 5-HT2A/D2 ratio could confer this property.[37] However, when prescribed at higher doses, risperidone produces EPS consistently[38] risperidone occupies 75-80% of striatal D2 receptors when administered to patients suffering from schizophrenia at a dose of 6 mg/day.[39]

Olanzepin

Olanzapine has a higher affinity for 5-HT2A serotonin receptors than D2 dopamine receptors, which is a common property of all atypical antipsychotics, aside from the benzamide antipsychotics such as amisulpride. Olanzapine also had the highest affinity of any second-generation antipsychotic towards the P-glycoprotein in one in vitro study.[40] Side effects of olanzepin are Drowsiness, dizziness, lightheadedness, stomach upset, dry mouth, constipation, increased appetite, or weight gain may occur.[41]

Famous Atypical antipsychotic drug.

Clozapine

Clozapine is classified as an atypical antipsychotic drug because it binds to serotonin as well as dopamine receptors.[42] Clozapine is a partial agonist[43] at the 5-HT1A subunit of the serotonin receptor, putatively improving depression, anxiety and the negative cognitive symptoms associated with schizophrenia.[44] clozapine also act on GABAB receptor and increases dopamine level.[45][46] Clozapine also causes release of glutamate and D-serine by acting as an agonist at glycine site of NMDA receptor.[47] The elimination half-life of clozapine is about 14 hours at steady state conditions (varying with daily dose). Clozapine is extensively metabolized in the liver, via the cytochrome P450 system, to polar metabolites suitable for elimination in the urine and feces. The major metabolite, norclozapine (desmethyl-clozapine), is pharmacologically active.[48] Side effect of clozapine are Agranulocytosis, Hypersalivation, Cardiac toxicity, Urinary incontinence, Weight gain and diabetes, Gastrointestinal hypomotility

NEW DRUGS

Pimavanserine - Pimavanserin (INN), or pimavanserin tartate (USAN), marketed under the trade name Nuplazid, is a non-dopaminergic atypical antipsychotic[49] developed by Acadia Pharmaceuticals for the treatment of Parkinson's disease psychosis and schizophrenia. Pimavanserin has a unique mechanism of action relative to other antipsychotics, behaving as a selective inverse agonist of the serotonin 5-HT2A receptor, with 40-fold selectivity for this site over the 5-HT2C receptor and no significant affinity or activity at the 5-HT2B receptor or dopamine receptors.[50] The drug has met expectations for a Phase III clinical trial for the treatment of Parkinson's disease psychosis,[51] and has completed Phase II trials for adjunctive treatment of schizophrenia alongside an antipsychotic medication.[52] On September 2, 2014, the United States Food and Drug Administration granted Breakthrough Therapy status to Acadia's New Drug Application for pimavanserin.[53] Side effects of pimavanserine are nausea, constipation, swelling of the extremities, walking abnormally and hallucination.[54]

DRUGS UNDER CLINICAL TRIAL

BL-1020

BL-1020 (perphenazine gamma-aminobutyrate) - It has been introduced by BioLineRx[55], It is an investigational orally-active antipsychotic for the possible treatment of schizophrenia,

it's an ester of GABA and perphenazine and pharmacologically it acts as a D2 antagonist and GABA agonist.[56] In March 2013, it went into the II/III trial phase.[57]

Lumateperone (ITI-007) is an investigational atypical antipsychotic which is currently under development by Intra-Cellular Therapies, licensed from Bristol-Myers Squibb, for the treatment bipolar disorder, depression and sleep and behavioral disturbance in dementia, autism and other neuropsychiatric disorders.[58]

It acts as a 5-HT2A receptor antagonist, a partial agonist of presynaptic D2 receptors and an antagonist of postsynaptic D2 receptors and a SERT blocker.[59][60] It also possesses affinity for the D1 receptor and weak affinity for the α1A- and α1B-adrenergic receptors and D4 receptor. Lumateperone does not significantly bind to the 5-HT2B, 5-HT2C, H1, or mACh receptors.[58]

Clinical studies - IT improves social function, as well as in allevates depressive symptoms in schizophrenia patients with comorbid depression, whereas risperidone had no effect and less weight gain, did not increse prolactin level, did not show akathesia There was no evidence of extrapyramidal symptoms or increase in suicidal ideation or behavior.[61][62]

RP-5063

RP-5063, also known as RP-5000, is an investigational atypical antipsychotic which is under development of Reviva Pharmaceuticals for the treatment of schizophrenia and schizoaffective disorder. Reviva Pharmaceuticals also intends to investigate RP-5063 for the treatment of psychosis/agitation associated with Alzheimer's diseasepsychosis, attention deficit hyperactivity disorder (ADD/ADHD) and autism. RP5063 is a multimodal neuromodulator which has successfully completed the global Phase 2 clinical trial.[63]

F-15063

It is orally active atypical antipsychotic drug. It is an antagonist at the D2/D3receptors, partial agonist at the D4 receptor and agonist at the 5-HT1A receptor. it has greater affinity towards the 5-HT1A receptor as compared to clozapine, aripiprazole.[64]

ALTERNATIVE THERAPY

Glycine therapy[65]

Glycine is known to act as an agonist for NMDA. That is it mimics NMDA. Glycine is an amino acid that is found in the protein of all living things. The normal human diet results in

an intake of about 2 grams of glycine daily. It is believed that supplementing with glycine may not only have antispastic activity but it may also have antipsychotic activity along with anti-oxidant and anti-inflammatory properties. It was found that glycine was well tolerated by the patients and that there was a significant reduction in negative symptoms. The size of the sample, however, was small and the length of the study was short but the researchers did conclude that the efficacy of risperidone and olanzapine might be augmented using high dose adjuvant glycine treatment. The researchers found that there were significant improvements in negative, positive, cognitive and depression symptoms. While gylycine and D-serine both act as NMDA agonists, there are differences between them. Glycine passes the blood brain barrier with greater difficulty and thus more of it must be taken in order for it to reach the brain than D-serine. However, D-serine has been found to cause kidney damage in rats and, until its safety has been determined, it is not approved for clinical use in the U.S. sometimes glycine antagonist is also used which increase the synaptic availability of glycine by inhibiting its reuptake through a compound called the glycine transporter – 1 or GlyT-1. Sacrasine is a natural amino acid that appears to have those properties.

Ampakines

This is the research direction that Dr. Donald C Goff of Harvard is taking and he told that AMPA receptor activity modulated with AMPAKINE drugs may provide a new and highly affective approach to treating a number of central nervous system disorders such as Alzheimer's disease and schizophrenia. Ampakines are able to open the gated NMDA channels in the brain by depolarization. That is, changing the membrane cells electrically to become more positive. This has the effect of removing the magnesium blockade, opens the channel and allows more NMDA to be present.

It is highly recommended that it only be done in consultation with the doctor and that the glycine used is made to either prescription or pharmaceutical grade standards. Clinical trials have begun with 15 gm per day and the dose is then increased by 15 gm per day every 3 days until a total dose of 60 gm/day has been achieved. This dose is based upon an average weight for the individual of about 150 pounds.It is not recommended to try this if you are on clozapine therapy because clozapine also act as agonist at the glycine site of the NMDA receptor, from astrocytes,[66] and reduces the expression of astrocytic glutamate transporters These are direct effects that are also present in astrocyte cell cultures not

containing neurons. Clozapine prevents impaired NMDA receptor expressioncaused by NMDA receptor antagonists.[67]

AYURVEDIC TREATMENT

In Ayurveda Psychic disorder is called as MANOVIKARA.[68]

RAJATBHASM

Rajat bhasma contains silver calcinated silver particle. It is also called as rajatha or Tara patra. The fine powdern silver is processed with lime juice and then dried and heated under high temperature. The fine powder of silver is processed with lime juice then dried and heated under high temperature.[69]

Panax ginseng

It is considered good for improving memory, thinking and concentration. In a 2008 study, Canadian researchers found that Panax ginseng helped reduce the some of the negative symptoms of schizophrenia, including flat affect (lack of emotional expression) in the patients. It is believed to hit the same brain receptors as antipsychotic drugs. Dose of panax ginseng is 200mg daily for several weeks after consultation with physician.[70]

Ginkgo biloba

It may help enhance the effectiveness of antipsychotics. It is also believed to protect against neural damage caused by antipsychotics. Dose of biloba is 360 mg of a standardized extract of Ginkgo biloba daily in divided doses for up to 16 weeks.[70]

Brahmi

Brahmi, also called bacopa, is popularly used in Ayurvedic medicine to enhance cognitive ability. Animal studies indicate that it can also help improve schizophrenia. Dose of brahmi is 500 mg of brahmi extract daily, at least for 1 month.Although the exact mechanism as to how it works is not known, it is believed to help stabilize certain chemicals in the brain. It also exhibits neuroprotective properties.[70]

Ashwagandha

Ashwagandha is another calming herb useful for depression, anxiety and other psychiatric disorders due to its anxiolytic and antidepressant effect. According a 2013 study published in the Indian Journal of Pharmacology, this herb can offer blood glucose and cholesterol lowering effects to combat the side effects of antipsychotics associated with higher incidence

of metabolic syndrome. Dose of ashwagandha is 500 mg capsules, 4 times a day for at least 1 month.[71] Some of mechanism of action of ashwagandha is, it blocks the activity of ACETYL-CHOLINESTEARASE (AChE) thus PREVENTING or SLOWING the breakdown of the endogenous neurotransmitter ACETYLCHOLINE; by doing so, nerve cell transmission is enhanced and synaptic strength is increased - increasing acetylcholine may also improve anxiety disorders by reducing excessive sympathetic nervous system activity and also it act as a GABA mimetic.[72]

Chamomile

Chamomile has soothing and calming properties. It also promotes restful sleep and thus is useful for those suffering from psychic disorder.[73] Chemical compounds present within chamomile bind to GABA receptors, modulate monoamine neurotransmission and have neuroendocrine effects.[73]

BASIL

Basil leaves have excellent antioxidant properties and also promote brain functionality to improve the symptoms of schizophrenia.[74]

RAUWOLFIA

The pharmacological activity of Rauwolfia is due to the presence of several alkaloids of which reserpine is the most important, it is a powerful sedative substance, hence Rauwolfia has been employed for centuries for the relief of various central nervous system disorders, both psychic and motor, including anxiety states, excitement, maniacal behavior associated with psychosis, schizophrenia, insanity, insomnia and epilepsy. It is also used as a fever relieving medicine.[75]

HOMEOPATHIC TREATMENT[76]

There are a lot of remedies may use in homeopathy to cure a schizophrenic patient because in homeopathy we do not look at a disease but we analyzing the whole patient and all medicines are prescribed according to his symptoms, but we always give preference to mental symptom.

DRUG	USED TO TREAT SYMPTOM
Cocculus Indicus	Disposition to take everything in bad part and to be angry.
Platinum Metallicum	Thinks she stands alone in the world. The delusion of the senses, feeling as of being too large and on the contrary, all other things and persons seem to be too small and too low.
Veratrum Album	Tired of life, but fear of dying. Strong tendency to be frightened and

	timidity. Insanity with singing, whistling, laughing, the inclination to run from places to place.
Aconite Napellus	Fearful anticipation of approaching death; predicts the day he is to die. Fear of specters and dark.
Cannabis Indica	Delirium tremendous, trembling, hallucinations, tendency to become furious, nausea. Thinks himself to be Christ or emperor.
Hyoscyamus	Delirium without consciousness does not know anybody. Delirium tremendous sees ghosts, demons, etc
Stramonium	Furious loquacious delirium. The boy seems to see black people, black clouds and grasps at air. Saw people coming out all corners, feel that he is in his own grave.
Thuja	As if a strange person were at his side as if the soul were separated from the body; as if the body especially the limbs were of glass and would break easily, as if a living animal were in the abdomen. Getting orders from dead souls, think someone controlling his mind.

CHINESE TRADITIONAL MEDICINE[77]

Chinese medicine has traditionally placed schizophrenic patients into the categories of dian kuang (withdrawal and mania), kuang zheng(manic condition) or chi dai(feeblemindedness).

Liver qi stagnation and phlegm accumulation –

Main Symptoms - Emotional depression, insomnia, a dull-flat affect, incoherent-illogical speech, visual or auditory hallucinations, when stagnation of qi is predominant: the tongue is dark, purple or pale with a slimy or thin white coating; the pulse is wiry and slippery. When accumulation of phlegm is predominant: the tongue is swollen with a thick and sticky coating Treatment principle: Soothe the Liver, resolve phlegm, open the Heart orifices, strengthen the Spleen and calm the spirit.

Main acupuncture points: Taichong LIV-3, Hegu L.I.-4, Neiguan P-6, Laogong P-8, Renzhong DU-26, Dazhui DU-14, Juque REN-14, Xingjian LIV-2, Yongquan KID-1, Shaoshang LU-11, Fenglong ST-40 and Fengfu DU-16. Use reducing method on all points for 30 minutes.

Deficiency of the Heart and Spleen - Main symptoms: Excessive thinking and difficulty thinking, anxiety, insomnia, palpitations, confusion, fatigue, poor appetite, dull pale complexion.

Treatment principle: Strengthen the Spleen, nourish the Heart and calm the spirit.

Main acupuncture points: Xinshu BL-15, Weishu BL-21, Neiguan P-6, Shenmen HE-7, Zusanli ST-36 and Dazhong KID-4. Use reinforcing method on all points for 30 minutes.

Yang deficiency of the Spleen and Kidney.

Main symptoms: Advanced age, no desire to speak, bodily weakness and fatigue, poor appetite, fear of cold, cold extremities, dull pale complexion, a pale tongue with a thin white coating and a weak, deep and fine pulse.

Treatment principle: Strengthen and warm the Spleen and Kidney, transform phlegm and open the Heart's orifices.

Main acupuncture points: Shenshu BL-23, Weishu BL-21, Weishu BL-21, Shenmen HE-7, Zusanli ST-36, Guanyuan REN-4 and Baihui DU-20. Use reinforcing method and moxa for 30 minutes.

Yin deficiency of the Heart and Kidney due to excessive fire.

Main symptoms: Long-term mania, fatigue, insomnia, restlessness, irritability, confusion, emaciation, flushed face, low-grade fever in the afternoon, heat in the five centres, scanty dark urine.

Treatment principle: Nourish the Heart and Kidney yin, clear fire from the Heart and calm the spirit. Main acupuncture points: Xinshu BL-15, Shenshu BL-23, Houxi SI-3, ShenmenHE-7, ZusanliST-36, Yongquan KID-1 and Sanyinjiao SP-6 with reinforcing method for 30 minutes. Laogong P-8, Daling P-7, Danshu BL-19 and Taichong LIV-3 with reducing method for 30 minute.

AROMATHERAPY

Aromatherapy is the treatment or prevention of disease by use of essential oils. Other stated uses include pain and anxiety reduction, enhancement of energy and short-term memory, relaxation, hair loss prevention and reduction of eczema-induced itching.[78][79] Two basic mechanisms are offered to explain the purported effects. One is the influence of aroma on the brain, especially the limbic system through the olfactory system.[80] The other is the direct pharmacological effects of the essential oils.[81]

Modes of application

The modes of application of aromatherapy include:

Aerial diffusion: for environmental fragrancing or aerial disinfection.

Direct inhalation: For respiratory disinfection, decongestant, expectoration as well as psychological effects.

Topical applications: For general massage, baths, compresses, therapeutic skin care.[82]

ENERGY MEDICINES

Bioelectromagnetic-based therapies use verifiable electromagnetic fields, such as pulsed fields, alternating-current, or direct-current fields in an unconventional manner.[7] Magnetic healing does not claim existence of supernatural energies, but asserts that magnets can be used to defy the laws of physics to influence health and disease.[83]

MUSIC THERAPY

Musical therapy is a sub-type of psychotherapy that involves an individual listening to music as a means of improving both communication and interpersonal skills. Most types of music therapy are based loosely around traditional cognitive-behavioral therapy. Music therapy involves both listening as well as expression. It was noted that "active participation" among individuals with mental illness showed better results than individuals that remained passive. The majority of music therapy treatments occur over a three month period.[84]

ELECTROCONVULSIVE THERAPY

It is particularly useful for people who suffer from psychotic depressions orintractable mania, people who cannot take antidepressants due to problems of health or lack of response & pregnant women who suffer from depression ormania. A patient who is very intent on suicide, & who would not wait 3 weeksfor an antidepressant to work, would be a good candidate for ECT because itworks more rapidly. In fact, suicide attempts are relatively rare after ECT. The patient is put to sleep with a very short-acting barbiturate, & then thedrug succinycholine is administered to temporarily paralyze the muscles so they do not contract during the treatment & cause fractures. An electrode is placed above the temple of the nondominant side of the brain, & a second in the middle of the forehead (this is called unilateral ECT); or one electrode is placed above each temple (this is called bilateral ECT). A very small current is passed through the brain, activating it & producing a seizure. Because the patient is anesthetized & his body is totally relaxed by the succinycholine, he sleeps peacefully while an electroencephalogram (EEG) monitors the seizure activity & an electrocardiogram (EKG) monitors the heart. The current is applied for one second or less, & the patientbreathes pure oxygen through a mask. The duration of a clincally effective siezure

ranges from 30 seconds to sometimes longer than a minute, & the patient wakes up 10 to 15 minutes later.[85] Side effect of electroconvulsive therapy is short-term memoryloss, increase in heart rate and blood pressure.[86]

DEEP BRAIN STIMULATION THERAPY

At present, the procedure is used only for patients whose symptoms cannot be adequately controlled with medications, or whose medications have severe side-effects.[87]

There are a variety of classes of hypotheses to explain the mechanisms of DBS:[88][89]

Depolarization blockade: Electrical currents block the neuronal output at or near the electrode site.

Synaptic inhibition: This causes an indirect regulation of the neuronal output by activating axon terminals with synaptic connections to neurons near the stimulating electrode.

De-synchronization of abnormal oscillatory activity of neurons.

Antidromic activation either activating/blockading distant neurons or blockading slow axons.[90]

How DBS Work?[91]

DBS requires brain surgery. The head is shaved and then attached with screws to a sturdy frame that prevents the head from moving during the surgery. Scans of the head and brain using MRI are taken. The surgeon uses these images as guides during the surgery. Patients are awake during the procedure to provide the surgeon with feedback, but they feel no pain because the head is numbed with a local anesthetic and the brain itself does not register pain.Once ready for surgery, two holes are drilled into the head. From there, the surgeon threads a slender tube down into the brain to place electrodes on each side of a specific area of the brain. In the case of depression, the first area of the brain targeted by DBS is called Area 25, or the subgenual cingulate cortex. This area has been found to be overactive in depression and other mood disorders. But later research targeted several other areas of the brain affected by depression. So DBS is now targeting several areas of the brain for treating depression. In the case of OCD, the electrodes are placed in an area of the brain (the ventral capsule/ventral striatum) believed to be associated with the disorder.After the electrodes are implanted and the patient provides feedback about their placement, the patient is put under general anesthesia. The electrodes are then attached to wires that are run inside the body from

the head down to the chest, where a pair of battery-operated generators are implanted. From here, electrical pulses are continuously delivered over the wires to the electrodes in the brain.

Side effects of DBS - Bleeding in the brain or stroke, Disorientation or confusion, Unwanted mood changes, Movement disorders, Lightheadedness, Trouble sleeping

Transcranial magnetic stimulation (TMS) therapy

Transcranial magnetic stimulation (TMS) is a noninvasive method of delivering electrical stimulation to the brain. A magnetic field is delivered through the skull where it induces electric currents that affect neuronal function. Repetitive TMS (rTMS) is being evaluated as a treatment of depression and otherpsychiatric/neurologic brain disorders.[92] FDA has yet not approved TMS for any psychiatric treatment at the present time.[93]

Magnetic seizure therapy

Magnetic seizure therapy (MST) borrows certain aspects from both ECT and rTMS. Like rTMS, MST uses magnetic pulses instead of electricity to stimulate a precise target in the brain. However, unlike rTMS, MST aims to induce a seizure like ECT. So the pulses are given at a higher frequency than that used in rTMS. Therefore, like ECT, the patient must be anesthetized and given a muscle relaxant to prevent movement. The goal of MST is to retain the effectiveness of ECT while reducing its cognitive side effects.[90]

LOBOTOMY[94]

The first lobotomies were performed in 1935 by Portuguese neurologists Dr. Antonio Egas Moniz and Dr. Almeida Lima. Initially, they drilled holes in the skull on either side of the prefrontal cortex and injected the connecting fibers with alcohol to destroy them. Later on Dr. Moniz used a tool called a LEUCOTOME, after drilling holes in the skull, the doctor pressed on the back of the tool, which extended a wire or metal loop inside. By extending and then retracting the leucotome, he could remove cores of white matter. Ten years later Dr.freeman used a technique called a prefontal lobotomy, in which patient required to go ganeral anesthesia in OT. Dr. Freeman used a stronger version of a leucotome called as orbitoclast. After going through the top of the eye socket, Freeman could enter the prefrontal cortex just by tapping lightly on the orbitoclast with a hammer to break through the thin layer of bone. Then he twirled it to cut through the fibers. After pulling out the orbitoclast, the procedure was repeated on the other side. The transorbital lobotomy took 10 minutes or less. Because it

didn't require drilling through the skull, it could be done by rendering the patient unconscious via electroconvulsive shock.

NUTRITION

Nutrition can play a huge role in improving mental health. If brain is getting the nutrients that it needs, cognition and other mental processing tends to be enhanced. Most studies show that diets high in sugar and saturated fat tend to worsen symptoms and long-term prognosis among individuals with schizophrenia. It is hypothesized that high levels of sugar and saturated fat cause the brain to produce less BDNF (brain-derived neurotrophic factor). BDNF aids in the formation of neural connections and increases are considered beneficial for brain functioning.[95][96][97]

REFERENCE

1. Freudenreich, Oliver (3 December 2012). "Differential Diagnosis of Psychotic Symptoms: Medical "Mimics"". Psychiatric Times. UBM Medica. Retrieved October 2013.
2. American Psychiatric Association, 1994 The Diagnostic and Statistical Manual Revision IV (DSM-IV).
3. Gelder, Michael G; Mayou, Richard; Geddes, John (2005). Psychiatry. New York: Oxford University Press. p. 12. ISBN 978-0-19-852863-0.
4. Yuhas, Daisy. "Throughout History, Defining Schizophrenia Has Remained a Challenge (Timeline)". Scientific American Mind (March 2013). Retrieved 2 March 2013.
5. Murray, Robin; Hill, P. D. (Peter David); McGuffin, P. (Peter) (1997). The essentials of postgraduate psychiatr. Cambridge; New York, NY, USA: Cambridge University Press. p. 231. ISBN 978-0-521-57801-1.
6. Leucht, S; D Arbter; RR Engel; W Kissling; JM Davis (April 2009). "How effective are second-generation antipsychotic drugs? A meta-analysis of placebo-controlled trials" (PDF). Molecular Psychiatry. 14(4): 429–447. doi:10.1038/sj.mp.4002136. PMID 18180760. Retrieved 24 March 2013.
7. Rattehalli, R. D.; Jayaram, M. B.; Smith, M. (5 April 2010). "Risperidone Versus Placebo for Schizophrenia". Schizophrenia Bulletin. 36 (3): 448–449. doi:10.1093/schbul/sbq030. PMC 2879694. PMID 20368309.
8. Fusar-Poli, P.; Deste, G.; Smieskova, R.; Barlati, S.; Yung, AR.; Howes, O.; Stieglitz, RD.; Vita, A.; McGuire, P.; Borgwardt, S (Jun 2012). "Cognitive functioning in

prodromal psychosis: a meta-analysis". Arch Gen Psychiatry. 69(6): 562–71. doi:10.1001/archgenpsychiatry.2011.1592. PMID 22664547.

9. Brown, EC.; TAS, C.; Brüne, M. (Jan 2012). "Potential therapeutic avenues to tackle social cognition problems in schizophrenia". Expert Rev Neurother. 12(1): 71–81. doi:10.1586/ern.11.183. PMID 22149657.
10. Harper, Douglas (November 2001). "hallucinate". Online Etymology Dictionary. Retrieved October 15, 2006.
11. Susannah Cahalan. Brain on Fire-My Month of Madness, New York: Simon & Schuster, 2013.
12. http://www.healthline.com/health/depression/catatonic-depression#1
13. http://www.medicalnewstoday.com/articles/192263.php
14. http://psychcentral.com/encyclopedia/thought-disorder/
15. World Health Organization, The ICD-10 Classification of Mental and Behavioural Disorders: Clinical descriptions and diagnostic guidelines (CDDG), 1992.
16. American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR), American Psychiatric Association, 2000.
17. Cardinal, R.N. & Bullmore, E.T., The Diagnosis of Psychosis, Cambridge University Press, 2011, ISBN 978-0-521-16484-9.
18. Shibayama M (2011). "Differential diagnosis between dissociative disorders and schizophrenia". Seishin shinkeigaku zasshi=Psychiatria et neurologia Japonica. 113(9): 906–911. PMID 22117396.
19. Jauch, D. A.; William T. Carpenter, Jr. (February 1988). "Reactive psychosis. I. Does the pre-DSM-III concept define a third psychosis?" Journal of Nervous and Mental Disease. 176(2): 72–81. Doi: 10.1097/00005053-198802000-00002. PMID 3276813.
20. Ohayon, M. M.; R. G. Priest; M. Caulet; C. Guilleminault (October 1996). "Hypnagogic and hypnopompic hallucinations: pathological phenomena?". British Journal of Psychiatry. 169(4): 459–67. doi:10.1192/bjp.169.4.459. PMID 8894197. Retrieved2006-10-21.
21. Sharma, Verinder; Dwight Mazmanian (April 2003). "Sleep loss and postpartum psychosis". Bipolar Disorders. 5 (2): 98–105. doi:10.1034/j.1399-5618.2003.00015.x.PMID 12680898. Retrieved 2006-09-27.

22. Chan-Ob, T.; V. Boonyanaruthee (September 1999). "Meditation in association with psychosis". Journal of the Medical Association of Thailand. 82(9): 925–930. PMID 10561951.
23. Devillieres, P.; M. Opitz; P. Clervoy; J. Stephany (May–June 1996). "[Delusion and sleep deprivation]". L'Encéphale. 22(3): 229–31.
24. Pillmann, Frank; Marneros, Andreas (2004). Acute and transient psychoses. Cambridge, UK: Cambridge University Press. p. 188. ISBN 0-521-83518-6.OCLC 144618418
25. http://www.health24.com/Mental-Health/Brain/Neurological-conditions/12-types-of-psychosis-20130711
26. https://www.kmpt.nhs.uk/conditions/thought-disorder-psychosis/6609
27. Essentials of medical pharmacology by KD Tripathi, 6th
28. www.drugbank.ca/drugs/DB00477
29. Adams CE, Awad G, Rathbone J, Thornley B, Soares-Weiser K (2014). "Chlorpromazine versus placebo for schizophrenia". Cochrane Database of Systematic Reviews. 1(1): CD000284.doi:10.1002/14651858.CD000284.pub3. PMID 24395698.
30. "PRODUCT INFORMATION LARGACTIL" (PDF). TGA eBusiness Services. Sanofi Aventis Pty Ltd. 28 August 2012. Retrieved 8 December 2013.
31. Schotte, A; Janssen PF; Megens AA; Leysen JE (1993). "Occupancy of central neurotransmitter receptors by risperidone, clozapine and haloperidol, measured ex vivo by quantitative autoradiography".Brain Research. 631(2): 191–202. doi:10.1016/0006-8993(93)91535-z. PMID 7510574. Retrieved 21 April 2014.
32. https://www.drugs.com/cdi/haloperidol.html
33. http://www.drugbank.ca/drugs/DB00875
34. Brayfield, A, ed. (13 December 2013). "Haloperidol".Martindale: The Complete Drug Reference. London, UK: Pharmaceutical Press. Retrieved 29 May 2014.
35. "Depixol Tablets 3mg - Summary of Product Characteristics (SPC)". Electronic Medicines Compendium. Lundbeck Ltd. 27 December 2012. Retrieved 20 October 2013.

- Joint Formulary Committee (2013). British National Formulary (BNF) (65 ed.). London, UK: Pharmaceutical Press. ISBN 978-0- 85711-084-8.
- Rossi, S, ed. (2013). Australian Medicines Handbook (2013 ed.). Adelaide: The Australian Medicines Handbook Unit Trust. ISBN 978-0-9805790-9-3.

- Bostwick, JR; Guthrie, SK; Ellingrod, VL (January 2009). "ntipsychotic-induced hyperprolactinemia".Pharmacotherapy. 29(1): 64–73. doi:10.1592/phco.29.1.64. PMID 19113797.
- "FLUANXOL® DEPOT FLUANXOL® CONCENTRATED DEPOT". TGA eBusiness Services. Lundbeck Australia Pty Ltd. 28 June 2013. Retrieved 20 October 2013.

36. Taylor, D; Paton, C; Shitij, K (2012). The Maudsley prescribing guidelines in psychiatry. West Sussex: Wiley-Blackwell. ISBN 978-0-470-97948-8
37. Schatzberg, AF, Nemeroff, C. The American Psychiatric Publishing Textbook of Psychopharmacology. 4th ed. American Psychiatric Publishing, 2009.
38. Marder SR, Meibach RC. Risperidone in the treatment of schizophrenia. The American Journal of Psychiatry. 1994; 151(6): 825-35.
39. Farde L, Nyberg S, Oxenstierna G, Nakashima Y, Halldin C, Ericsson B. Positron emission tomography studies on D2 and 5-HT2 receptor binding in risperidone-treated schizophrenic patients. Journal of clinical psychopharmacology. 1995; 15(1 Suppl 1): 19S-23S.
40. Wang JS, Zhu HJ, Markowitz JS, Donovan JL, DeVane CL (September 2006). "Evaluation of antipsychotic drugs as inhibitors of multidrug resistance transporter P-glycoprotein". Psychopharmacology (Berl). 187(4): 415–423. Doi: 10.1007/s00213-006-0437-9. PMID 16810505
41. d.com/drugs/2/drug-1644-9274/olanzapine-oral/olanzapine---oral/details#side-effects
42. Naheed M, Green B (2001). "Focus on clozapine". Current Medical Research and Opinion. 17(3): 223–9. Doi: 10.1185/0300799039117069. PMID 11900316.
43. http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=2818
44. Robinson DS (2007). "CNS Receptor Partial Agonists: A New Approach to Drug Discovery". Primary Psychiatry. 14(8): 22–24.
45. Wu Y, Blichowski M, Daskalakis ZJ, Wu Z, Liu CC, Cortez MA, Snead OC (Sep 2011). "Evidence that clozapine directly interacts on the GABAB receptor". Neuro Report. 22(13): 637–41. doi:10.1097/WNR.0b013e328349739b. PMID 21753741.
46. Vacher CM, Gassmann M, Desrayaud S, Challet E, Bradaia A, Hoyer D, Waldmeier P, Kaupmann K, Pévet P, Bettler B (May 2006). "Hyperdopaminergia and altered locomotor activity in GABAB1-deficient mice". Journal of Neurochemistry. 97(4): 979–91. doi:10.1111/j.1471-4159.2006.03806.x. PMID 16606363.

47. Tanahashi S, Yamamura S, Nakagawa M, Motomura E, Okada M (Mar 2012). "Clozapine, but not haloperidol, enhances glial D-serine and L-glutamate release in rat frontal cortex and primary cultured astrocytes". British Journal of Pharmacology. 165(5): 1543–55. doi:10.1111/j.1476-5381.2011.01638.x. PMC 3372736. PMID 21880034
48. Rostami-Hodjegan A, Amin AM, Spencer EP, Lennard MS, Tucker GT, Flanagan RJ (Feb 2004). "Influence of dose, cigarette smoking, age, sex, and metabolic activity on plasma clozapine concentrations: a predictive model and nomograms to aid clozapine dose adjustment and to assess compliance in individual patients". Journal of Clinical Psychopharmacology. 24(1): 70–8. doi:10.1097/01.jcp.0000106221.36344.4d. PMID 14709950
49. "Nuplazid (pimavanserin) Tablets, for Oral Use. U.S. Full Prescribing Information" (PDF). ACADIA Pharmaceuticals Inc. Retrieved 1 May 2016.
50. Friedman, JH (October 2013). "Pimavanserin for the treatment of Parkinson's disease psychosis". Expert Opinion on Pharmacotherapy. 14(14): 1969–1975. doi:10.1517/14656566.2013.819345. PMID 24016069.
51. ACADIA Pharmaceuticals. "Treating Parkinson's disease - Clinical Trial Pimavanserin - ACADIA". Archived from the original on February 25, 2009. Retrieved 2009-04-11.
52. "ACADIA Announces Positive Results from ACP-103 Phase II Schizophrenia Co-Therapy Trial" (Press release). ACADIA Pharmaceuticals. 2007-03-19. Retrieved 2009-04-11
53. "ACADIA Pharmaceuticals Receives FDA Breakthrough Therapy Designation for NUPLAZID™ (Pimavanserin) for Parkinson's Disease Psychosis". Press Releases. Acadia. 2014-09-02.
54. http://www.rxlist.com/nuplazid-side-effects-drug-center.htm
55. https://clinicaltrials.gov/ct2/show/NCT01363349
56. Geffen, Y; Keefe, R; Rabinowitz, J; Anand, R; Davidson, M (September 2012). "Bl-1020, a new γ-aminobutyric acid-enhanced antipsychotic: results of 6-week, randomized, double-blind, controlled, efficacy and safety study.". The Journal of Clinical Psychiatry. 73(9): e1168–74.
57. Biolinerx (Jan 7, 2013). "BioLineRx to Announce Interim Results of Phase II/III Trial for Schizophrenia Drug during week of March 18, 2013". Biolinerx.
58. Intra-Cellular Therapies. "Product Pipeline - Intra-Cellular Therapies". Retrieved 2015-05-19.

59. Snyder GL, Vanover KE, Zhu H, Miller DB, O'Callaghan JP, Tomesch J, Li P, Zhang Q, Krishnan V, Hendrick JP, Nestler EJ, Davis RE, Wennogle LP, Mates S (2015). "Functional profile of a novel modulator of serotonin, dopamine and glutamate neurotransmission". Psychopharmacology (Berl.). 232(3): 605–21. doi:10.1007/s00213-014-3704-1. PMC 4302236. PMID 25120104
60. Li P, Zhang Q, Robichaud AJ, Lee T, Tomesch J, Yao W, Beard JD, Snyder GL, Zhu H, Peng Y, Hendrick JP, Vanover KE, Davis RE, Mates S, Wennogle LP (2014). "Discovery of a tetracyclic quinoxaline derivative as a potent and orally active multifunctional drug candidate for the treatment of neuropsychiatric and neurological disorders". J. Med. Chem. 57(6): 2670–82. doi:10.1021/jm401958n. PMID 24559051.
61. Intra-Cellular Therapies, Inc. (2015). "Intra-Cellular Therapies Announces Further Analyses of the Phase 2 Clinical Trial of ITI-007 in Schizophrenia at the 168th Annual Meeting of the American Psychiatric Association". GlobeNewswire, Inc.
62. Intra-Cellular Therapies, Inc. (2013). "Intra-Cellular Therapies Announces Positive Topline Phase II Clinical Results of ITI-007 for the Treatment of Schizophrenia". PRNewswire.
63. http://revivapharma.com/about-us/
64. Newman-Tancredi, A. (May 2007). "F15063, a potential antipsychotic with D2/D3 antagonist, 5-HT1A agonist and D4 partial agonist properties: (I) in vitro receptor affinity and efficacy profile". British Journal of Pharmacology. 151(2): 237–52. doi:10.1038/sj.bjp.0707158. PMC 2013955. PMID 17375087.
65. http://schizophrenia.com/glycine.htm#1
66. Tanahashi S, Yamamura S, Nakagawa M, Motomura E, Okada M (Mar 2012). "Clozapine, but not haloperidol, enhances glial D-serine and L-glutamate release in rat frontal cortex and primary cultured astrocytes". British Journal of Pharmacology. 165(5): 1543–55. doi:10.1111/j.1476-5381.2011.01638.x. PMC 3372736. PMID 21880034.
67. Xi D, Li YC, Snyder MA, Gao RY, Adelman AE, Zhang W, Shumsky JS, Gao WJ (May 2011). "Group II metabotropic glutamate receptor agonist ameliorates MK801-induced dysfunction of NMDA receptors via the Akt/GSK-3β pathway in adult rat prefrontal cortex".Neuropsychopharmacology. 36(6): 1260–74. doi:10.1038/npp.2011.12. PMC 3079418.PMID 21326193.
68. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3331508/
69. https://www.ayurtimes.com/rajat-bhasma-silver-ash/

70. http://www.top10homeremedies.com/home-remedies/home-remedies-for-schizophrenia.html
71. http://www.top10homeremedies.com/home-remedies/home-remedies-for-schizophrenia.html/2
72. https://area1255.blogspot.in/2015/11/the-multiple-mechanisms-of-action-of.html
73. Sarris, J; Panossian, A; Schweitzer, I; Stough, C; Scholey, A (December 2011). "Herbal medicine for depression, anxiety, and insomnia: a review of psychopharmacology and clinical evidence". European neuropsychopharmacology. 21(12): 841–860. doi:10.1016/j.euroneuro.2011.04.002. PMID 21601431.
74. http://www.top10homeremedies.com/home-remedies/home-remedies-for-schizophrenia.html/3
75. http://herbalsatt.blogspot.in/2011/05/30-sarpgandha.html
76. http://www.ihomeopathic.com/2015/01/schizophrenia-treatment-with.html
77. http://www.rotem-center.co.il/sites/default/files/pdf/jcm93_57schizophrenia.pdf
78. Kingston, Jennifer A. (28 July 2010). "Nostrums: Aromatherapy Rarely Stands Up to Testing". The New York Times. Retrieved 29 December 2010.
79. Nagourney, Eric (11 March 2008). "Skin Deep: In Competition for your Nose". The New York Times. Retrieved 29 December 2010
80. Mathrani, Vandana (17 January 2008). "The Power of Smell"
81. Prabuseenivasan, Seenivasan; Jayakumar, Manickkam; Ignacimuthu, Savarimuthu (2006). "In vitro antibacterial activity of some plant essential oils". BMC Complementary and Alternative Medicine. 6: 39. doi:10.1186/1472-6882-6-39. PMC 1693916. PMID 17134518
82. "Organic Bath Oil". Plaisirs. Retrieved 11 October 2011.
83. "Complementary, Alternative, or Integrative Health: What's In a Name?". NCCIH Pub. No. D156. National Center for Complementary and Integrative Health (NCCIH), National Institutes of Health (NIH), US Dept. of Health and Human Services (US HHS). May 2002. Archived from the original on 2005-12-08. Retrieved 2006-07-11.
84. http://www.ncbi.nlm.nih.gov/pubmed/15846692
85. http://www.schizophrenia.com/family/ect1.html
86. http://www.webmd.com/depression/electroconvulsive-therapy?page=2
87. National Institute of Neurological Disorders and Stroke. Deep brain stimulation for Parkinson's Disease information page. Retrieved November 23, 2006.

88. McIntyre CC, Thakor NV (2002). "Uncovering the mechanisms of deep brain stimulation for Parkinson's disease through functional imaging, neural recording, and neural modeling". Crit Rev Biomed Eng. 30(4–6): 249–81. doi:10.1615/critrevbiomedeng.v30.i456.20. PMID 12739751.
89. Herrington TM, Cheng JJ, Eskandar EM (2016). "Mechanisms of deep brain stimulation". J. Neurophysiol. 115(4–6): 19–38. doi:10.1152/jn.00281.2015. PMC 4760496. PMID 26510756.
90. García MR, Pearlmutter BA, Wellstead PE, Middleton RH (2013). "A Slow Axon Antidromic Blockade Hypothesis for Tremor Reduction via Deep Brain Stimulation". PLoS ONE. 8(9): e73456. doi:10.1371/journal.pone.0073456. PMC 3774723. PMID 24066049.
91. http://www.nimh.nih.gov/health/topics/brain-stimulation-therapies/brain-stimulation-therapies.shtml#part_152880
92. https://www.bsneny.com/content/dam/COMMON/Provider/Protocols/T/prov_prot_20150.pdf
93. http://jpma.org.pk/full_article_text.php?article_id=1448
94. http://science.howstuffworks.com/life/inside-the-mind/human-brain/lobotomy1.htm
95. http://www.ncbi.nlm.nih.gov/pubmed/15041037
96. http://www.ncbi.nlm.nih.gov/pubmed/20196981
97. http://www.ncbi.nlm.nih.gov/pubmed/15682652