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Notes on the History of Schizophrenia

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Abstract

Schizophrenia still remains an enigma although it is considered to be among the most common psychiatric disturbances. The word is less than 100 years old but it has probably accompanied mankind throughout its whole history. It was first identified as a discrete mental illness by Emil Kraepelin in 1887, who had used the word dementia preacox to define it. Eugen Bleuler used the word schizophrenia for the first time in 1911. Knowledge of the historic evolution of schizophrenia enables us to understand the different concepts in the comprehension of the pathogenesis of the disease and how the definition, the ideas about its aetiology and its treatment have emerged (German J Psychiatry 2005;8:42-48).

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Introduction

"All the world's mad except thee and me,
and even thee's a little cracked."

— Porter, 1991

Symptoms relating to schizophrenia have been noted since the age of antiquity. A popular belief was that strange behaviour was a result of possession by the devil or assaults from the gods for immoral behaviour (a kind of devine punishment). Ethnographic studies have demonstrated that schizophrenia is present in all existing cultures. Psychotic symptomatology and schizophrenic-like syndromes were clearly present in ancient civilizations. Stone Age skulls have been found with holes made in them. Studies have shown that these holes were made when the person was alive in order to provide a portal for evil spirits to escape from. This process has become known as trepanning. Supernatural explanations remained the dominant theory behind mental illness for many years.

Ancient Ages

Schizophrenia can be traced in written documents to the old Pharaonic Egypt, as far back as the second millennium before Christ. Depression, dementia, as well as thought disturbances found in schizophrenia are described in detail in the Book of Hearts, which is part of the Eber papyrus. Heart and mind seem to have been synonymous in ancient Egypt. The psychical illnesses were regarded as symptoms of the heart and the uterus and originating from the blood vessels or from purulence, faecal matter, a poison or demons. In most cases the Egyptians apparently looked upon the mental diseases as physical illnesses.

Hindu descriptions date back to approximately 1400 BC and can be found in the Atharva Veda, one of the 4 Vedas, which are primary texts of Hinduism. The Vedas contain hymns and incantations from ancient India. It has been posited that health resulted from a balance between 5 elements (Buthas) and 3 humours (Dosas) and that an imbalance between these various elements might result in madness.

A Chinese text entitled The Yellow Emperor's Classic of Internal Medicine, written around 1000 BC, described symptoms of insanity, dementia, and seizures. Demonic or supernatural possession was often implicated as the cause of psychotic behaviours.

A study into the ancient Greek and Roman literature showed that although the general population probably had an awareness of psychotic disorders, there was no condition that would meet the modern diagnostic criteria for schizophrenia in these societies.

At one point, all people who were considered "abnormal", whether due to mental illness, mental retardation, or physical deformities, were largely treated the same. Early theories supposed that mental disorders were caused by evil possession of the body, and the appropriate treatment was then

exorcising these demons, through various means, ranging from innocuous treatments, such as exposing the patient to certain types of music, to dangerous and sometimes deadly means, such as releasing the evil spirits by drilling holes in the patient's skull.

The ancient Greeks took a great interest in the human psyche and especially in madness. Plato who lived in the 5th and 4th centuries BC speaks about two kinds of madness, one with a divine origin and another with a physical origin. The divine madness may create prophets, relieve the generation of impurity, inspire poets, or provoke an intense desire for beauty, according to Plato. The idea of the divine madness was firmly rooted in the Greek culture even before Plato. It also appears in the Greek tragedies, for instance in Heracles by Euripides, from the 5th century BC. But in that tragedy madness ends in catastrophe.

In the Dialogues Plato wrote that "...to think about curing the head alone, and not the rest of the body also, is the height of folly... . And therefore if the head and body are to be well, you must begin by curing the soul." He advanced the idea of unconscious and illogical mental processes, suggesting that all people had a capacity for irrational thinking. He also speculated that "...when the rest of the soul – which is rational, mild and its governing – is asleep, and when that part which is savage and rude, being satisfied with food and drink, frisks about, drives away sleep, and seeks to go and accomplish its practice... that in every one resides a certain species of desires that are terrible, savage, and irregular, even in some that we deem ever so moderate...".

The platonic ideas of a connection between madness and prophecy recur in the ancient Israel. The highly esteemed religious prophets were often regarded as mad because of their odd utterances and deviant clothes and Behavior. The same conceptions later appear in the Koran in the Islamic countries. Even if the Muslim nursing ward sometimes used brutal procedures the Orthodox Islam did not give as much support to exorcism as Christianity did, and surely not as an alternative to medical treatment. The word Majnun is the Muslim word for mad or possessed while a jinn is a supernatural spirit. According to Koran a jinn may lie behind a mental illness.

Even in Greece the relation between madness and genius survived. The written collection *Problemata* is usually attributed to Aristotle who lived in the 4th century BC. One of the written documents begins with the question "How come that all men distinguished in philosophy, statesmanship, poetry or art are melancholics and some of them to such an extent that they are affected by the illnesses originating from the black bile (melaines choles), of which the story of Heracles tells us?". The author himself answers that the black bile may influence mood and behaviour by among other things cold and heat. In favourable circumstances this may lead to great achievements, while otherwise the result may be madness. But contrary to Plato the author does not believe in any madness of a divine origin.

The influence from Hippocrates is obvious in the citation from *Problemata*. Hippocrates, the "father of medicine", was partly a contemporary with Plato. He has given rise to the Hippocratic Collection. In one of the documents, "The Holy Disease", the author objects to the opinion that illnesses like epilepsy, madness and confusion are caused by the gods. Instead he argues that „...only from the brain spring our pleasures, our feelings of happiness, laughter and jokes, our pain, our sorrows and tears.... This same organ makes us mad or confused, inspires us with fear and anxiety...". Then the author describes the famous humoural pathology, a model to explain the origin of the diseases as a disturbance of the balance of the humours that is the body fluids. This model groups the humours into blood, phledge, yellow bile and black bile. According to the humoural pathology an imbalance of the body fluids may influence the brain and provoke madness. The disturbance is caused by a complex co-operation between the outer environment and interior physical factors, including inheritance. The humours are coupled to the four elements of air, water, fire and earth. The blood is warm and wet like the air, the phledge is wet and cold like water, the yellow bile is hot and dry like fire, and the black bile is dry and cold like earth. Moreover, the ages of man and the changes of the seasons play a role. Diseases are cured through correcting the imbalance with the help of diet or lifestyle. For instance, if an illness is caused by too little blood the body shall be provided with wet and heat. Later the four humours were also related with temperament. Blood is connected with sanguine, phledge with phlegmatic, yellow bile with choleric and black bile with melancholic temperament. Different methods of emptying the body of fluids were also added, such as blood-letting, purgatives, vomiting and purulence.

Hippocrates wanted to build his theories on a rationalistic and empirical basis. In that he continued the tradition of the ionic Greek philosophers who wanted to explain nature in a rational way. Hippocratic medicine draws a sharp line between knowledge and belief. It clearly criticizes the methods of magicians and quacks even in the treatment of mental diseases, which are considered to be biologically rooted. However, no official view existed on the origin of diseases in antiquity, and there were often other opinions among the laymen than among the academics. The belief that mentally ill persons were possessed by devils was widely spread. Humoural pathology competed with astrology, magic and occultism, which played an important role in the popular tradition. Apart from the academically educated physicians there were a lot of other persons, for instance priests, who tried to cure the ill with an arsenal of different therapies, such as medical herbs, gymnastics, magic and exorcism. In the holy temples academic treatments were mixed with religious rites.

The origins of many enlightened treatments may be found in the Greek and Roman period. Asclepiades advocated the use of music and invented a swinging bed designed to relax the agitated patient. He regarded mental disorders as stemming from emotional disturbances (passions of sensation). Cicero rejected the Hippocratic bile theory stating that emotional factors could cause physical illness. He believed that man could help with his own cure through philosophy. Soranus, in the 2nd century, suggested that patients should be housed in light and airy facilities. He believed that corporal punishment should not be used, and emphasized the importance of the physician's relationship with the patient and believed that it was important to understand the social environment to gain a full understanding of the patient. Therapeutic inter-

ventions by the Romans tended to be humane and emphasis was placed on warm baths, massage, and diet. Other treatments at this time were not as enlightened and benign, including shocks by electric eels. Cornelius Celsus suggested that starvation, fetters, and flogging would help to stir up the spirit. He justified these means on the belief that the anger of the gods caused these maladies.

From Ancient Ages to the Medieval Period

The ancient view on the origin, symptoms, and treatment of diseases is summarized in a medical handbook written by the physician Aretaios in the 2nd century AD. This handbook contains a systematic classification of the psychical illnesses. The most important diagnoses are phrenitis, hysterical suffocation, melancholy and mania. Phrenitis corresponds to an acute and temporary state of febrile confusion. Hysterical suffocation implies anxiety diseases, while melancholy comprises depressions and schizophrenic states of withdrawal and chronic deterioration. Mania corresponds to modern mania in manic depressive illness, as well as schizophrenic states of excitement and agitation. The instructions for treatment followed the rules of humoural pathology. Aretaios was the first to suggest that the origin of mental disorders might not be specifically localized. He also believed that premorbid personality might play a role in the aetiology of mental disorders.

The humoral pathology was taken over by the Greek physician Galen in the 2nd century AD. He believed that mental diseases could be the result of a disorder in the brain or the secondary result of the disorder of another organ. Galen exerted a great influence over Arabic as well as European medicine, and he was an important authority until the beginning of the 19th century. The theory of the four body fluids survived just as long.

Byzantine physician Alexander of Tralles (6th century A.D.) handles mental diseases as an independent medical topic. The Arabic physician Ibn Rabban at-Tabari (9th century A.D.) wrote a medical book containing a separate chapter on diseases of the brain. The belief that demons lie behind mental diseases became more influential when Christianity entered. In most cases mental diseases were believed to be of demonic origin, taking also into consideration the fact that Christianity did not give much importance in the present life but in the life in another world. It is possible that early Christian saints who heard voices and saw visions were in fact having hallucinations. However their experiences were treated as divine ones rather than demonic

Medieval Era

In the middle ages the scholars at the Universities seem to have had a rational and scientific attitude towards madness, but outside them people seemed to believe that it was a trial or a punishment from God. In 15th century Europe hallucinations and delusions were seen as a proof that someone was possessed. Many women were thought to be witches and were burnt at the stake.

In the medieval era many mentally ill persons were congregated near churches where they found shelter and protection by monks and priests. As medical notions again gained momentum, institutions became popular. Although confinement was not a new idea, it grew in popularity in the 16th century. Chains and stocks employed to quell the spirit of demons were slowly abandoned as medical thinking began to quash the notion of possession.

The 17th century saw the beginnings of psychiatric hospitals in Europe. With these hospitals came attendants and medical supervisors and the birth of psychiatry. But the ideas of early psychiatrists made no more sense than those who had tried to cure the mentally ill before them. It was widely believed in the asylums that the way to cure someone was to shock them. Early shock methods included pinning patients down and pouring cold water on their faces until they were nearly drowned, or strapping patients to chairs so that they lost sensation and became calm

The Pioneers of Psychiatry

Beginning in the 1700s, increased emphasis was placed on detailed and accurate descriptions of abnormal mental processes and states. Philippe Pinel, a French physician considered to be one of the founders of modern psychiatry, argued for an objective medico-philosophical approach to psychological disorders. He advocated that "...only symptoms that are manifest to the senses through external signs, such as the speech, strange gestures, the expression of certain bizarre and uncontrolled emotions...are taken into account. Why not, therefore, bring into this part of medicine, as into its other parts, the method used in all the branches of natural history?". He distinguished a deteriorating psychological "dementia" from other states including idiocy, mania, and melancholia.

Jean Etienne Esquirol, a student of Pinel, defined hallucinations in a way that is similar to current terminology. They were described as an "intimate conviction of a sensation actually perceived, while no external object capable of exciting that sensation is accessible to the senses". He also identified "monomania", a clinical syndrome similar to modern descriptions of paranoid schizophrenia.

In addition to identification of specific symptoms, attempts were made to divide the clinical landscape into syndromes sharing both clinical features and course. Benedict Augustin Morel in his 1860 "Traite des Maladies Mentales" (Treatise on Mental Illness) was the first to use the term dementia praecox (demence precoce). He characterized a previously asymptomatic adolescent boy who became progressively more withdrawn and "degenerated into a state of dementia." The boy also expressed homicidal thoughts towards his father. He differentiated idiocy, a defect state apparent in early life from the deteriorating process associated with dementia praecox. This latter syndrome presented later in life and was potentially reversible. Morel postulated that some of these pathological states may be inherited, and

reflected a familial form of degeneration. In support of this, he reported on a psychotic child whose mother had been insane and grandmother had been eccentric. Other symptom complexes identified included delusional states (France) and paranoid states, as described by the German physician Vogel in 1764. In 1868 Kahlbaum characterized a pattern of abnormal motor tension which he referred to as "katatonia" or catatonia.

Johann Christian August Heinroth outlined 48 distinct disease entities and thereby epitomized the general inability to develop straightforward, reliable criteria. He derided biologically oriented theorists as viewing the human mind "as a cadaver which one could cut to pieces with a knife, or as a chemical compound which could be broken down into elements, or as a mechanical contraption, the workings of which one could calculate with the help of mathematics." These theoretical controversies and confusion lead Heinrich Neumann to reject all systems of classification and suggest that it was necessary "to throw overboard the whole business of classifications" to bring order to the field. He suggested that "there is but one type of mental disturbance, and we call it insanity." Nevertheless, despite the intermittent sense of frustration and confusion, classificatory efforts continued unabated.

From Kraepelin to Bleuler

The 19th century saw an explosion of information about the body and mind. Evidence was mounting that mental illness was caused by disease in the brain after a link had been found between general paresis of the insane and syphilis. Psychiatry had found its place in the medical world. Organic aetiologies of mental illness were adopted and separate illnesses identified. There were several fragmented descriptions of schizophrenia. Psychiatrists noted that many of their young patients had grandiose delusions or developed unusual postures, while others developed mental deficiency and mania. But no connection was made between the symptoms.

In 1851 Falvet first described a 'Folie Circulaire' or cyclical madness, and some twenty years later Hecker referred to a 'Hebephrenia', or a silly, undisciplined mind after Hebe, goddess of youth and frivolity (1871). Soon after, in 1874, Kahlbaum referred to both catatonic and paranoid disorders of the mind, the term catatonia describing a movement disorder characterized by a mannequin-like muscle stiffness associated with unusual postures and a pervading fear. Then in 1878 Emil Kraepelin, perhaps auspiciously, combined these various 'disorders' into a single disease entity which he termed dementia praecox, or 'dementia of early onset' reflecting a decline of cognitive processes which he divided into four subtypes - simple, marked by slow social decline concomitant with apathy and social withdrawal; paranoid, with its attendant fear and 'persecutory' delusions; hebephrenic and catatonic, characterized by a poverty of movement and expression. Kraepelin named the disorder 'dementia praecox' (early dementia) to distinguish it from other forms of dementia (such as Alzheimer's disease) which typically occur late in life. He used this term because his studies focused on young adults with dementia. Kraepelin noted that patients with this condition showed emotional dullness, loss of inner unity and that they would at times laugh or cry without apparent reason, and that the symptoms worsened with time.

The inevitable inexactitudes of this emerging science continued with the dawn of the 20th Century when in 1908 Eugen Bleuler criticized the use of the term dementia praecox, arguing for an absence of evidence supporting a global dementing process. It was Bleuler who first coined the divisive term 'schizophrenia' in 1911. Bleuler defined schizophrenia with his four "A's", referring to the blunted Affect (diminished emotional response to stimuli); loosening of Associations (by which he meant a disordered pattern of thought, inferring a cognitive deficit), Ambivalence (an apparent inability to make decisions, again suggesting a deficit of the integration and processing of incident and retrieved information) and Autism (a loss of awareness of external events, and a preoccupation with the self and one's own thoughts). Bleuler was also the first to describe the symptoms as "positive" or "negative."

The word „schizophrenia" comes from the Greek roots schizo (split) and phrene (mind) to describe the fragmented thinking of people with the disorder. His term was not meant to convey the idea of split or multiple personality. Since Bleuler's time, the definition of schizophrenia has continued to change, as scientists attempt to more accurately delineate the different types of mental diseases. Without knowing the exact causes of these diseases, scientists can only base their classifications on the observation that some symptoms tend to occur together.

Both Bleuler and Kraepelin subdivided schizophrenia into categories, based on prominent symptoms and prognoses. Over the years, those working in this field have continued to attempt to classify types of schizophrenia. Five types were delineated in the DSM-III: disorganized, catatonic, paranoid, residual, and undifferentiated. The first three categories were originally proposed by Kraepelin. These classifications, while still employed in DSM-IV, have not shown to be helpful in predicting outcome of the disorder, and the types are not reliably diagnosed. Many researchers are using other systems to classify types of the disorder, based on the preponderance of "positive" vs "negative" symptoms, the progression of the disorder in terms of type and severity of symptoms over time, and the co-occurrence of other mental disorders and syndromes. It is hoped that differentiating types of schizophrenia based on clinical symptoms will help to determine different aetiologies or causes of the disorder.

Other clinicians also advocated a hierarchical system of symptom classification like Bleuler's. In 1959 Kurt Schneider termed the core features "first-rank" symptoms. These symptoms included

a) Hearing one's thoughts spoken aloud
b) Auditory hallucinations commenting on one's own behaviour
c) Thought withdrawal, insertion and broadcasting
d) Somatic hallucinations, or the experience of one's thoughts as being controlled or influenced by outside

Manifestation of one 1st rank symptom in the absence of organic disease, persistent affective disorder or drug intoxication was sufficient for the diagnosis of schizophrenia. 2nd rank symptoms included other forms of hallucinations, depressive or euphoric mood changes, emotional blunting, perplexity, and sudden delusional ideas. When first-rank symptoms were absent, schizophrenia might still be diagnosed if a sufficient number of second-rank symptoms were present. Although the Schneiderian criteria have been criticized as being non-specific, they have been incorporated into clinical diagnostic tools such as the Research Diagnostic Criteria (RDC) and Diagnostic and Statistical Manual of Mental Disorders (DSM) classificatory systems.

Influenced by the psychoanalytic theory of Freud and others, many researchers of the mid-20th century focused on the relationship between family dynamics and the onset of schizophrenia. Specifically, researchers emphasized the quality of the mother-child relationship as crucial to the development of schizophrenia. The type of parent thought to induce schizophrenia was termed a schizophrenogenic mother. Another view, called the Double-Bind Theory, was proposed by Bateson in the mid 1950s. So-called double-bind situations were thought to be an important contributing factor to the development of schizophrenic thought disorder. Influenced by Bleuler's theory, and in the face of a body of data suggesting that schizophrenia was heritable, Meehl discussed the interaction of genetics and environment in aetiology of schizophrenia. Meehl emphasized the symptoms of thought disorder, interpersonal aversiveness, anhedonia, and ambivalence. Schizotaxia, or a neural integrative deficit, was the only inherited factor emphasized by Meehl. Schizotaxia interacts with what an individual has learned from the environment, and results in a personality organization called schizotype. Thought disorder, interpersonal aversiveness, anhedonia, and ambivalence are learned by schizotaxic individuals. Only a small number of schizotaxic individuals were thought to develop schizophrenia. Meehl proposed that the mother-child relationship played a role in the ultimate development of schizophrenia However; contemporary research has not implicated the mother-child relationship, nor double bind situations as causal factors in schizophrenia.

Treatment of Schizophrenia

Once schizophrenia had been defined, the next challenge for the medical profession was to find an effective treatment.

The cause of schizophrenia was still unknown, so the first half of the 20th century saw trial and error treatments, many of which were painful and unsuccessful.

Fever therapy was one such treatment. It was noted that people with schizophrenia recovered slightly when their temperature was high, so psychiatrists experimented by inducing fevers in their patients, often by injecting sulphur and oil, or causing abscesses. Other failed but fashionable treatments included gas therapy, sleep therapy, insulin therapy, electroconvulsive treatment and lobotomies.

Chloral hydrate in 1869 and barbiturates in 1903 gave some relief to the anxiety and sleep disturbances of psychotics but did nothing for their hallucinations and other psychotic symptoms.

The first antipsychotic medication came on the market in the 1950s. Chlorpromazine was discovered by a surgeon looking to find an anaesthetic which could control cardiorespiratory shock. He noted that the cocktail of sedating, hypnotic and narcotic drugs caused his patients to become indifferent; he described the effect of the drug as a 'chemical lobotomy' and recommended it to his psychiatric colleagues. Within ten years of chlorpromazine hitting the market, over twenty other antipsychotic drugs were in the pipeline. It was soon noted that these drugs caused numerous side effects; tremors, restlessness, loss of muscle tone and postural disorders (EPS) and so the group of drugs earned their name – neuroleptics.

The pharmacological breakthrough came when new 'atypical' antipsychotics appeared on the scene, clozapine was one of the first. Clozapine was not a new drug; it had been around since the 1960s, but due to fears that it caused a severe blood disorder-agranulocytosis, it did not hit the UK or US markets until 1990. The new atypical drugs were deemed 'cleaner' than the old neuroleptics, and although not side effect free, they were an improvement on the old medications. Other advantages were that the new drugs helped to alleviate some negative symptoms of schizophrenia, not just the positive ones. They also worked in patients who had shown little response to the old neuroleptics.

While the pharmacological revolution of the 50s and 60s was happening, a new wave of ideas from America was reaching Europe. The ideas that Freud introduced at the turn of the century were starting to have an impact. The psychoanalytical approach was proving popular in the treatment of mental illness. It was felt that exploring people's childhood experiences and unconscious desires would help to alleviate mental suffering.

Counselling and behavioural therapy became increasingly popular, and as a result of de-institutionalisation and care in the community, such therapies became an essential part of the treatment strategy for people with schizophrenia. Controlling symptoms with medications was only one half of the equation, enabling individuals with schizophrenia to function in society was paramount. Cognitive behavioural therapy was used to teach people basic skills such as personal hygiene and money management. Psychotherapy was used to help people distinguish between what was real and unreal.

Evolving Concepts on Schizophrenia

One of the problems with investigating disorders such as schizophrenia is that the tools available in the past to evaluate subtle, small changes in the brain have been rather crude. Thus most of the work done in the past century to investigate brain structural abnormalities in schizophrenia was based on methods that were crude, prone to error, and it therefore did not further our knowledge and understanding of brain abnormalities in schizophrenia. This is not to say, however, that structural brain abnormalities were not thought to underlie the symptoms observed in schizophre-

nia. In fact, early documentation of abnormal brain structures from post-mortem studies of schizophrenia led to the formulation of quite specific hypotheses concerning the relations between brain and behaviour.

These early studies, however, were hampered by inconsistent findings, crude measurement techniques, and carefully methodologically controlled studies often led to negative findings. This turn of events led many investigators to conclude that there were no structural brain abnormalities observed in schizophrenia that could not also be seen in normal controls. Progress in this area of research thus came to a near standstill and it was not until 1976, with the advent of computed tomography (CT), that the first CT study of schizophrenia reported abnormally large lateral ventricles in schizophrenic patients. This one study led to numerous CT studies which confirmed abnormalities in the brains of schizophrenic patients, and this one study led to a renewed interest in investigating such abnormalities in schizophrenia.

The early CT studies evaluated only ventricular size and did not evaluate local regions of interest nor could grey and white matter be differentiated. With the advent of MR imaging, grey and white matter could be evaluated and thus a new tool was added. In 1984, the first MR study of schizophrenia was reported in the literature. Many studies followed, but most were based on magnets with a field strength less than 1.0,and the slice thickness was often 1 cm or more. Moreover, there were no methods for evaluating grey and white matter throughout the brain.

The first study to use contiguous slices of the entire brain (1.5 mm coronal and 3 mm axial), was done by a group and the findings were reported in the New England Journal of Medicine, August, 1992. Here, the results that were reported included small but important grey matter volume reduction in schizophrenic patients, compared to controls, in the amygdala-hippocampal complex, in parahippocampal gyrus, and in superior temporal gyrus, on the left. The latter changes were also correlated with disordered thinking and were thus suggestive of a disturbance in an important neural circuit involved in verbal processing and consolidation of information that involve both the amygdala-hippocampal complex and the superior temporal gyrus.

Through the knowledge of history can we understand the roots of schizophrenia and its historical evolution. Both of them are extremely helpful for the understanding of the disease itself.

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