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Therapeutic Strategies in Schizophrenia

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1. Introduction

Schizophrenia is possibly the most notorious of the mental illnesses and the lack of popular understanding of it, with consequent understandable discomfort upon receipt of the diagnosis, persists to the present day. The evolution of terms to describe what is usually understood by health workers in the UK as *learning disability* is a useful illustration of how mental illness generally has come to be understood. :-

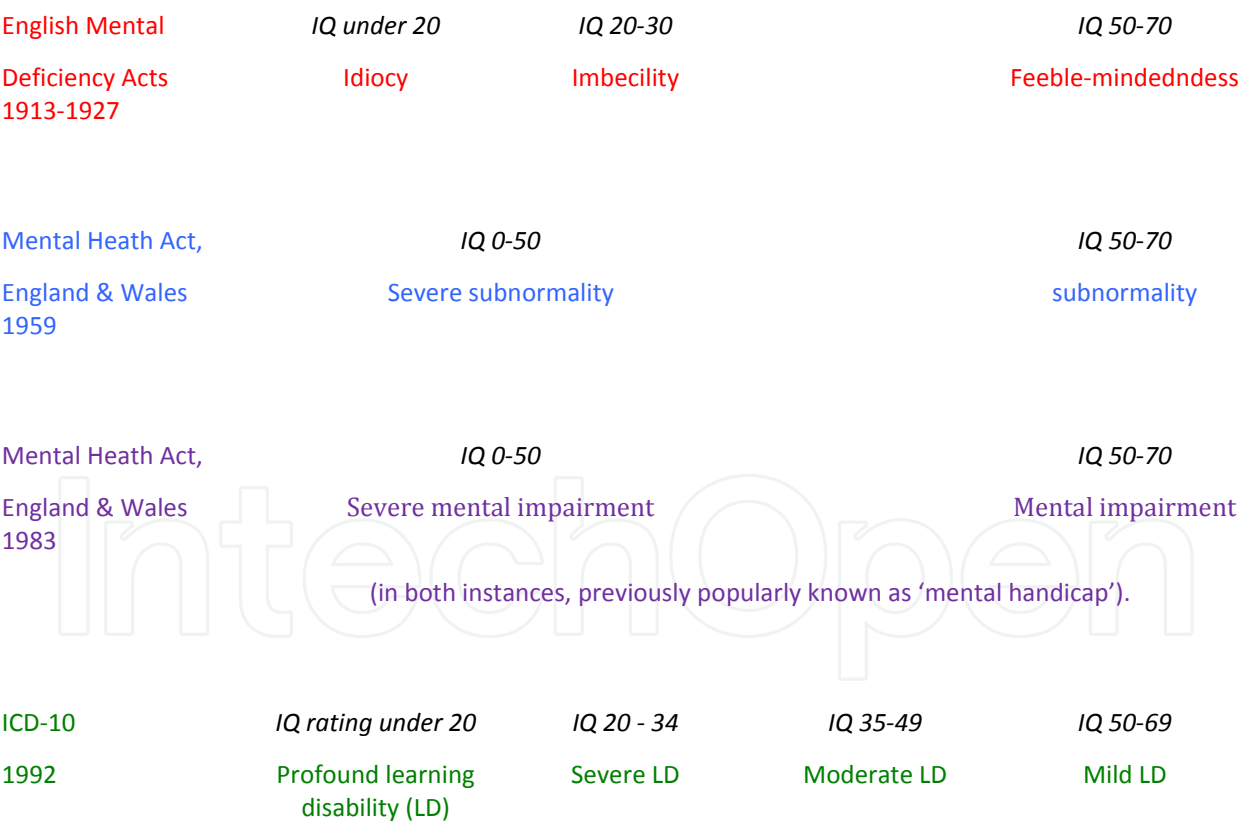


Fig. 1. Progression of statutory understanding of intellectual impairment in the UK.

....Indeed, any condition which affects neurological or intellectual functioning has progressed through an analogous course of understanding. Epilepsy, which is now known to be an abnormality in cerebral neural transmission, was thought of in earlier times to be

perhaps a visitation from God or indicative of shamanic ability. Such lurid explanations are now no longer felt to be appropriate, as more has become known about the underlying pathology. The progression of terms used in the understanding of learning disability is an example of similar development. The progression of understanding of schizophrenia in the 20th century has been aided by inductive appreciation of the *pharmacology* of the illness. This idea will be further considered later on here. Although the progression of knowledge is necessarily contemporaneous on all fronts, public perception of it is undoubtedly affected by the social milieu. Thus, in the progression of understanding of schizophrenia, the first step is that the condition was a result of external forces, such as a result of celestial actions, or of God (in monotheistic cultures). Next, there was an understanding of the importance of direct social factors, such as family and immediate social environment. A reflection upon the psychological effects of these led to the final step in this progression: the role of an affected person's biology. Physiological and ultimately, neurophysiological and biochemical alterations in the disease process are deliberated upon at this final stage of understanding.

Geekie and Read, in 2009, provide an elegant expression of how a *narrative framework* allows a protagonist – such as the affected individual, or society – to *make sense of their experiences*. Thus, in the attempt to understand mental illness, alternative narrative frameworks include:

- madness as a result of *the whim of the deities* (a view prevalent in ancient Greece, for example)
- the same disturbances being understood as the result of one's *life experiences or circumstances*
- " " as a result of *faulty brain chemistry*.

"Within the storytelling framework, we might say that these are all different ways of 'storying' the experience of madness." (1)

...Where "storying" can be understood as placing within a narrative framework in order to make the phenomenon intelligible.

There are, of course, multiple possible narrative frameworks. If one is considering the evolution of understanding of schizophrenia, then theological, sociological and biochemical explanatory modes can all be understood as different types of narrative framework. Each attempts to provide a comprehensive explanation for the disorder. Multiple types of explanation exist for many reasons: cultural factors, which include geographical and temporal contexts, as well as educational ones, are perhaps the most important. In this way, the epistemological foundations of an explanatory mode can be easily understood. The existence of several possible types of explanation should lead to the understanding that each relevant branch of knowledge has a contribution to make to the complete understanding of a subject. Different explanations persist because they are useful in their own contexts: therefore, a complete understanding of a subject involves attending to *all* of the potential reasons underlying it. This is summarised in figure 2 on the following page. As this figure shows, it is possible to understand that all factors which influence a mental illness – for our purposes, schizophrenia – can be appreciated as parts of a unified whole, in which every stage will ultimately affect another stage. The appreciation of this interconnected nature of phenomena allows a clinician to provide a *holistic framework* for management of the disorder, and is especially useful when dealing with the mental illnesses.

Continued...

The cerebral appreciation of any event can be summarised, in *extremely* simplified terms as:

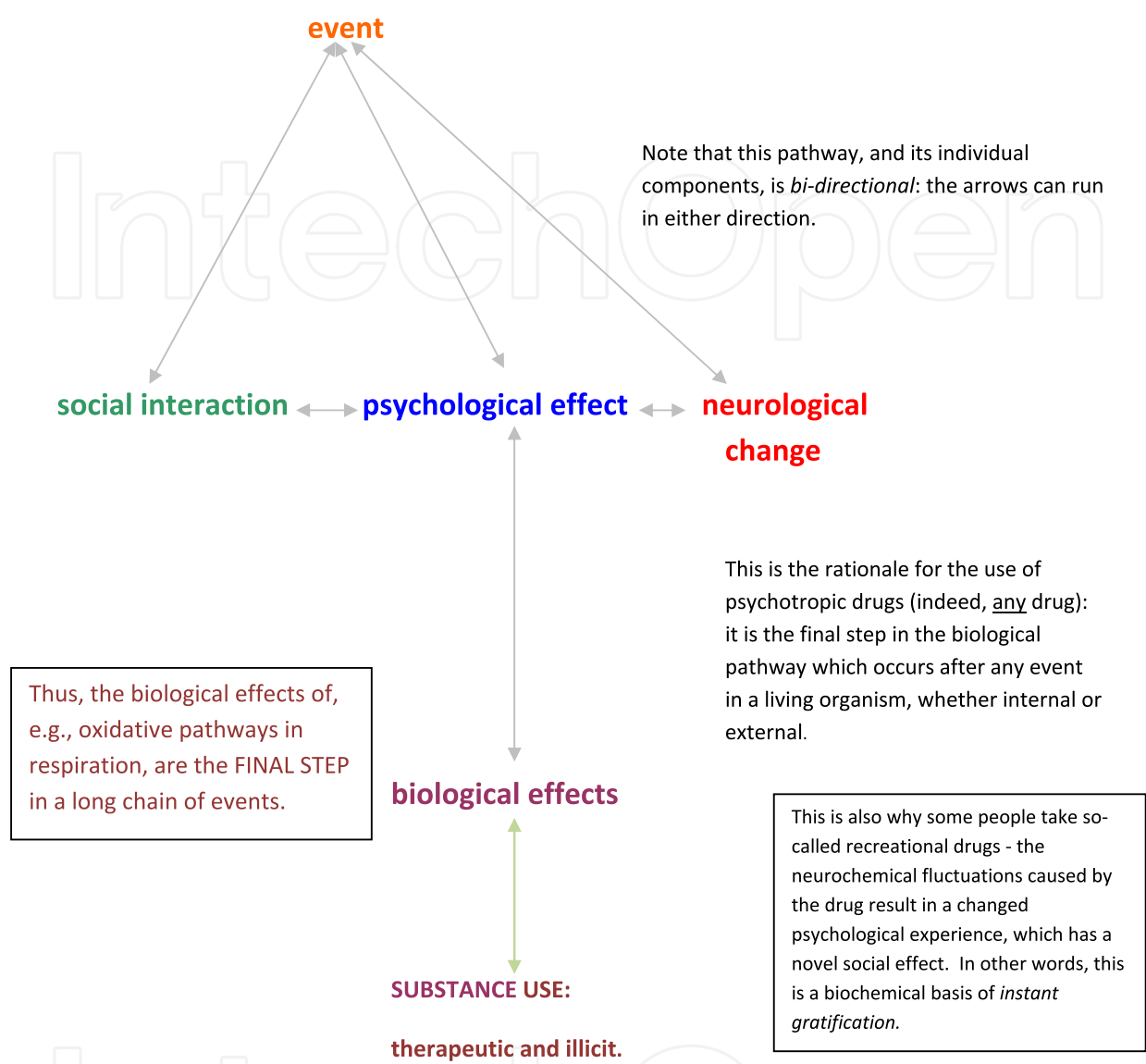


Fig. 2. The interconnected nature of societal, biological and chemical phenomena.

2. Historical overview of the understanding of schizophrenia

Moskovitz and Heim remind us that it is one hundred years since Bleuler originally proposed the concept of the schizophrenic illnesses, in 1911 (2). In their re-appraisal of Eugen Bleuler’s original concept of ‘Dementia Praecox or the Group of Schizophrenias’, it is noted that Bleuler’s understanding of this illness was a largely inductive one: he spent a great deal of time with his patients at the Burghölzli institute and his understanding of schizophrenia emerged from this immersive observation. This is reminiscent of modern anthropological fieldwork, and indeed, Bleuler’s study was essentially anthropological. This was in marked contrast to the other pioneer of knowledge in schizophrenia, Emil Krapelin. Whereas Bleuler’s understanding was ‘bottom up’ and *inductive*, Krapelin’s was ‘top down’, i.e. theory driven and *deductive*. Both methods of understanding can produce valuable

conclusions. The appropriate task to facilitate a complete understanding is to attempt to bring the multiple sets of theories together in a unified and logical whole. Reference to figure 2, on the previous page, can help with this.

Moskovitz and Heim (2) inform us that the term 'schizophrenia' was effectively coined by Bleuler in 1911. It is perfectly possible that some of the rather vivid explanations noted above were similarly previously used to render a phenomenon resembling schizophrenia intelligible, by placing it within a clear narrative framework.

Romme *et al* (3) discuss the case of perhaps one of the most famous voice-hearers in history, St. Jeanne D'Arc [Joan of Arc]. 'Voice-hearing' here refers to a particular subtype of the psychiatric symptom of auditory hallucination. Auditory hallucination – i.e. hearing audible sounds (including intelligible voices either speaking to or about the affected person) in clear consciousness when there is no physical cause for them – *may* be an important symptom of schizophrenia. In schizophrenic illness, there are often associated ideas which make sense of this symptom; these ideas can solidify into unshakeable associated, consequent delusions. Hence, delusions are performing the *storying* function (1), rendering the psychotic phenomena intelligible to the person who is experiencing them.

Romme *et al* discuss how auditory hallucinations, rather than being dismissed out of hand as an indication of psychosis and thus disregarded, can be actively worked with. This validation of the affected person's symptoms is an important element in that person's eventual recovery. There are several alternative explanations for the phenomenon of voice-hearing. A wry aphorism about this is that if you talk to God, you are religious, whereas if God talks to you, you're schizophrenic. As a clinician, I have always noticed that a psychotic person's delusions are reflective of the current temporal context. The cover of the book by Professor Romme and colleagues about voice-hearing and recovery depicts Jeanne D'Arc in battle. She was a French peasant girl who claimed to hear the voice of God calling upon her to free her nation from English domination. This occurred towards the end of the Hundred Years War (1337-1453). Jeanne D'Arc led her compatriots to many important victories as a result of this 'divine guidance'. After her capture, at the age of nineteen in 1431, she was tried and burned at the stake as a witch. Subsequent regal, then ecclesiastical intervention saw her first declared as a martyr and much later, beatified. In the early twentieth century, she was canonized and as St. Jeanne D'Arc, is one of the five patron saints of France (3). This reflects the importance of the cultural context of auditory hallucinations and their interpretation. In fifteenth century Catholic France, 'hearing the voice of God' could reasonably have been understood as a sign of divine communication. Therefore, the 'divine direction' of Joan of Arc to free her nation from the English in the 1420s would have been unsurprising. In late twentieth and twenty-first centuries in rich industrialised countries, a similar phenomenon would be understood as a sign of psychosis which represents an indication for therapy, most usually pharmacological.

It is worthwhile to briefly reflect upon the history of the treatment of people with mental illness. The profound lack of understanding of, and inability to explain, mental illness led to the majority of people affected by it to be excluded from society: indeed, the archaic term for a psychiatrist is *alienist*, which implies involvement with those outside the usual boundaries of society. A few voice-hearers, such as Jeanne D'Arc, have played important historical roles. The vast majority of others, however, together with their affected fellows, were excluded from society. From the seventeenth century onwards, this was often in large lunatic asylums. Medical involvement in such asylums was confined to treating the physical maladies of the residents. It was not until the mid to late eighteenth century that figures

such as Pinel in Paris and Chiarugi in Tuscany began to advocate the humane treatment of asylum inmates. Pinel, together with his overseer Pussin at the Bicêtre hospital in Paris introduced compassionate reforms in the management of the patients there (4). Their later contemporary Chiarugi, in Tuscany in 1789, asserted that:

“...it is a supreme moral duty and medical obligation to respect the mental patient as a person” (4).

The foundations of the Italian therapeutic movement known as *Democratic Psychiatry* can be seen here. This sequence of events represented an enormous progression in the care of the mentally ill. Pinel later (in 1801) emphatically advocated for the inclusion of mental disorders as a branch of medicine. As a result, he is regarded as the originator of psychiatry as a medical discipline. Thus, we can say – in light of the earlier remarks here- that Pinel *brought psychiatry into the narrative framework of medicine*.

While the introduction of humane treatment of the mentally ill represented a significant advance on previous approaches, the discovery of effective psychotropic medications was really what ‘unlocked the doors of the asylums’. It was not until the discovery of lithium salts as an effective treatment of mania (by Cade in 1949) and the synthesis and subsequent use of chlorpromazine as a major tranquiliser (by Delay and Deniker in 1952) that people who had previously been destined to spend the rest of their lives in asylums could reasonably expect to return to society. Since then, the understanding and development of drug treatments for mental illness has grown apace. The pharmacological appreciation of the nature of schizophrenia began by studying the known chemical effects of the major tranquilisers such as chlorpromazine. Recognition that this drug blocked dopamine receptors - potentially leading to symptoms of iatrogenic Parkinsonism - is what preceded the subsequent explosion of neurochemical understanding of schizophrenia. In this way, by effectively working backwards from the known biochemical effects of a medication, the neuropathology of particular illnesses has come to be appreciated. In other words, inductive reasoning from known psychotropic drug actions led to the understanding of the bases of pathology of these illnesses. Of course, this understanding has continued to grow and some of the consequent latest developments in the neurophysiological field will be considered later on here.

3. Current pharmacological and neurophysiological knowledge about schizophrenia

As indicated above, the first instances of this were arrived at by inductive reasoning about the mechanisms of action of the earliest widely-available psychotropic drugs. In the process of obtaining supplementary information about this knowledge, areas requiring further investigation have, of course, been opened up. Some of these were to further understand the pharmacological mechanisms and some of this work has necessarily explored the underlying neuropathology of schizophrenia. In the process of doing so, further therapeutic avenues became apparent. Miyamoto *et al* (5) wrote a comprehensive review of pharmacological treatments for schizophrenia in 2005. Important work had already been carried out on the detailed neurophysiology and pathology of the disease: in my opinion, the most significant findings were about the importance of sensory gating (6, 7) and of the roles of *excitotoxicity* (8) and *apoptosis* (9) in the presentation of, and progression of this disease. Site-specific dopamine receptor activity can be influenced *either* by (e.g.) interneuronal sensory gating *or* by a simple dose-response effect: in the latter case, a high

receptor density implies that low doses of the particular agent will affect that receptor. In contrast, a low receptor density requires a higher dose of binding agent. For example, the second-generation antipsychotic agents sulpride and amisulpiride have differing biological profiles at different doses. These drugs bind to dopamine D2 receptors in the temporal lobe cortex at low doses, conferring their excellent antipsychotic activity. At higher doses, these agents bind to D2 receptors in the corpus striatum, causing difficult extra-pyramidal side effects -again, including iatrogenic Parkinsonian symptoms (5). Therefore, this implies that D2 receptors are at a high density in the temporal cortex, but at a lower density in the striatum, which explains the dose-response effect. At other sites, such as area CA3 of the hippocampus, interneuronal sensory gating is the phenomenon which determines post-synaptic D2 activity (10).

Miyamoto *et al* (5) remind us that for any antipsychotic drug to be clinically effective, it *must* display occupancy of cerebral dopamine D2 receptors. As we have already seen, the particular site of the involved D2 receptor is important. To reiterate, this can be partly determined physiologically (e.g. pre-synaptically), or physically, by the ratio of available drug to available receptor site.

Dopamine receptor blockade was the main mode of action of the first-generation antipsychotic drugs: however, the therapeutic window available for this is extremely narrow. The optimal level of cerebral D2 receptor occupancy classically lies only between 65% to 70%. Below this, there is often no clinical response – although there are a few affected people who *will* show a therapeutic response to very low doses of antipsychotic drug. Above this level of receptor occupancy, symptoms of iatrogenic Parkinsonism, such as tardive dyskinesia, become a real problem. This is further complicated by the fact that chronic treatment with the first-generation ('typical') antipsychotic drugs causes a homeostatic increase of D2 receptors (5). Of course, chronic treatment is the most usual clinical scenario. Ken Steele, a now deceased, well-known advocate of service users' rights in the United States, summarised this succinctly. –

"...Just as a diabetic needs to take insulin to control diabetes, a schizophrenic must remain on medication- each and every day. It's a question of maintenance. ...Schizophrenia is a disease that *can* be controlled, but not yet cured. " (11, original emphasis)

Steele correctly emphasised the chronic nature of pharmacological treatment for schizophrenia. Although he was writing in 2001, the position is unchanged today, some 10 years later: schizophrenia remains "...a disease that *can* be controlled, but not yet cured".

Empirical experience with the first generation of antipsychotic drugs showed that the D2 receptor model clearly could not explain the whole pathological picture of schizophrenia. Work was therefore understandably directed towards trying to find out more about this, because it became apparent that *schizophrenia is not simply a process of excessive dopaminergic activity centred on the cerebral D2 receptors*. In order to further elucidate the neuropathology of schizophrenia, one important branch of work has investigated the role of *sensory gating* in schizophrenia (6, 7, 10, 12). Sensory gating is the process where the conscious mind devotes the majority of its attention to the task which it is directly presented with. Other sensory stimuli are deemed irrelevant while the task in hand is focussed on. A formal definition is given by Potter *et al* (12): "... Sensory gating refers to the *pre-attentional* habituation of responses to repeated exposure to the same sensory stimulus." [my emphasis].

A further explanation of this is given by Conway in 2009 (10):

"...Efficient sensory gating allows a person to 'screen out', or ignore background stimuli, such as the noise of a ventilation motor, or traffic outside a window. If the person is unable

to do this, as in acute schizophrenia, the now intrusive stimulus may acquire a delusional significance. This is explicable by the pathological cerebral functioning which occurs in schizophrenia: delusions may represent a conscious attempt by the person to comprehend the contemporaneous neurophysiological events in his/her brain. Correctly functioning sensory gating stops the possible misinterpretation of cerebral events."

Javanbakht (7) notes that there is a "...fronto-limbic imbalance..." which he proposes as one of the causes of disrupted sensory gating. I would propose that *excitotoxicity* (8) is perhaps the cause of this imbalance: excitotoxicity represents the consequence of unremitting neuronal stimulation. One result of this is that the content of affected neurones is exhausted and the resultant cellular debris is catabolised by astrocytes. These latter cells are acting, in effect, as cerebral macrophages, clearing the non-functional cellular material produced as a result of *apoptosis* (9). Repeated exacerbations of schizophrenia result in repeated instances of apoptosis, ultimately leading to the cortical (frontal) atrophy typical of chronic schizophrenia. Therefore, a functional fronto-limbic imbalance could be caused by excitotoxic, apoptotic tissue loss in the (pre) frontal cortex. The especially aggressive pathological process which underlies schizophrenia is exemplified by the fact that negative symptoms – which are a possible consequence of cerebral hypofunction caused by actual apoptotic neuronal loss – can be seen in a first attack of schizophrenia (10).

Unremitting cortico-limbic stimulation can be prevented by correctly functioning sensory gating (6, 7, 10, 12, 13). Here, *nicotinic activation*, especially of hippocampal area CA3 (10, 13) will prevent this unremitting stimulation, and its apoptotic consequence (9). The operative nicotinic receptor – the $\alpha 7$ receptor in area CA3 of the hippocampus – (7, 10, 13) desensitises very quickly. Short bursts of nicotinic enhancement, such as that provided by cigarette smoking (10, 13) – or theoretically by nicotine chewing-gum – would, importantly, allow a *transient normalisation of dysfunctional sensory gating*. Therefore, the notoriously heavy cigarette-smoking rate of people with schizophrenia, an attempt at self-medication, (10, 13, 14, 15, 16, 17) might be preventable and thus, important health benefits could be afforded to this vulnerable patient group if the role of nicotinic transmission is remembered (10).

The search for more efficient antipsychotic medication was stimulated, in part, by the experience of the limited efficacy of antipsychotic drugs which had existed hitherto. Certainly the currently available antipsychotic agents represent a great advance on their earlier predecessors, although they are not without difficult side-effects of their own. This simple fact tells us that our understanding of schizophrenia remains incomplete. It was noted above how a relatively simple entity such as dose-response can give an indication about comparative site-specific receptor density. Such working hypotheses can now, fortunately, be confirmed or refuted with the help of powerful neuroimaging techniques such as positron emission tomography (PET scanning), single-photon emission computed tomography (SPECT scanning), or functional magnetic resonance (fMRI) scanning. However, perhaps the most important factor with regard to pharmacological treatments for schizophrenia is to emphasise *the necessity for lifelong continuation of medication* such that the inherent pathology is not allowed to progress. Attention is again drawn to Ken Steele's quote (11): schizophrenia is exactly analogous to diabetes, but the schizophrenic illness process affects the brain.

4. Psychological approaches to the management of schizophrenic illness

Of course, pharmacological treatments are not the only option in schizophrenia. Remembering the importance of holistic treatment – for any illness – one should consider

non-medication based adjunctive managements as part of a treatment package. Following on from the statement immediately above, any illness which affects the brain will also consequently affect the mind, thus allowing the possibility of psychological treatments. (This rubric also includes the *social manipulations* employed therapeutically in this illness.) These have proved to be particularly successful in schizophrenia when employed as part of a treatment programme including appropriate pharmacological and social adjustments. Not only does psychological treatment provide a useful adjunct to pharmacological treatment, it has been shown to lower the maintenance medication requirement in this illness (18). In a thoughtful 2004 paper about the efficacy of cognitive behaviour therapy (CBT) for psychotic illness, Tarrier and Wykes performed a meta-analysis of 20 randomised controlled trials of CBT compared to treatment as usual. They found that 14 of these trials had at least "...a small [positive] effect size, and 3 a large [positive] effect size" (18). These authors drew the cautious conclusion that CBT for psychosis was thus able to reduce positive symptoms in schizophrenia (and therefore the need for antipsychotic medication).

A large contributor to this was the effect of *listening to the affected person's symptoms*. The value of listening to symptoms really cannot be overemphasised, principally because of two important issues:

- the validation of an affected person's experience and
- assessment of the current progression of pathology.

Barker *et al* (19) noted that in their study, both the affected people themselves and their immediate social contacts were "not heard by professionals", and their beliefs and opinions about the illness process were discounted. Nine years later, Owens *et al* (20) identified "...an existing dearth of evidence on service users' experiences of mental health services." This implies that subjective experience of the affected person in mental illness continues to be ignored. The importance of listening to symptoms is that they can clearly tell the observer about the likely coincident pathology. The table on the next page is produced from a first-hand account of the progression of schizophrenia (21), which I have correlated with the likely coincident neuropathology.

Thus, one of the most useful features of the psychological approaches to the management of schizophrenia is *validation of the affected person's experience*. As one can see from the following table, by listening to the affected person, a clinician obtains a very clear expression of the likely current pathology. The first-hand effect of *not* listening to an affected person's symptoms is neatly summarised in the following quote, from a mental health academic who had spent twelve months being detained in hospital under the Mental Health Act, with schizophrenia. -

"...My strange religious beliefs were perhaps quite rightly classified as delusional and discounted...but this left me with the impression that my experiences...were also being discounted..." (24, my emphasis)

The point made above and in Figure 3, about the importance of listening to the content of hallucinatory voices perhaps reminds us of perhaps how short-sighted this person's clinicians were. As another example of the importance of listening, the testimonial data collected by Barker *et al* is sobering for a therapeutic readership. -

"...They all said the same things: you're hallucinating, they said. I thought: what's caused this? So they said the damaged area of the head, this bit round here [*no indication of area given in transcript*], that's all I was told, really."

Reported subjective experience: verbatim quotes from Snyder (21).	Comment, including when relevant, possible operative neuropathology.
<i>"I developed schizophrenia gradually over a period of nine years, with the most severe symptoms appearing when I was twenty-eight years old."</i>	This puts his probable age of onset at nineteen years old . Late adolescence is the typical age of onset for the schizophrenic illnesses, which require sufficient maturity in the affected neural pathways before the pathology can express itself .
<i>"I cannot think of anything physical or psychological that could have triggered a change in my mental state. I had wonderful, supportive parents, relatives and friends, and I had a wonderful childhood."</i>	The onset of a psychotic illness is, more often than not, triggered by an event which anyone would find severely upsetting. The course of the illness can be further exacerbated by ongoing social or psychological stressors. Mr. Snyder is fortunate in that neither of these apply to him, suggesting that his illness had a very strong neurological basis which, if coupled with the above stressors, may well have been much more severe. This is an example of the genetic heterogeneity of schizophrenic phenotypes.
<i>"Somewhere between the ages of nineteen and twenty-one, I was exposed to the mathematical idea of fractals...I thought I was going to discover some incredible and fabulous mathematical principle that would transform the way we view the universe...Even though I had no evidence to substantiate my self-image, I knew in my heart that I was just like Einstein..."</i>	Here, Mr. Snyder is clearly using a manic defence to make sense of his progressive excessive mesolimbic dopaminergic discharge . A manic defence is where the affected person adopts a grandiose explanation for (e.g.) their coincident cerebral pathology. Grandiosity can also be a feature of transient hyperdopaminergia , as seen both in acute schizophrenia and acute mania, or in hypomania.
<i>"At about...twenty-two, I had my first significant paranoid episodes...I started to think about images from horror movies where an insane man breaks into the house and kills everyone...later...I hurt my leg and...feeling very vulnerable ...the nurse might try to infect me with the AIDS virus by injecting me with a tainted needle..."</i>	Here, this gentleman is describing what the progression of hyperdopaminergic discharge feels like. By now he may well have suffered some excitotoxic cell damage (8). However, because he was fortunate in having numerous effective social supports and was well-engaged in treatment , his illness was not allowed to progress to any significant extent and thus it is probable that any excitotoxic cell loss (8) was consequently limited .
<i>"In my second psychotic episode, I experienced for the first time what I can confidently say were auditory and visual hallucinations...At the time, these hallucinations seemed real to me, absolutely real...my family tried to get me medical help. Medications were prescribed, but I</i>	The aggressive nature of the underlying pathology of Mr. Snyder's illness is clearly demonstrated here. The onset of auditory hallucinations may well have been have a consequence of disrupted sensory gating (6,10). The lack of insight , e.g. the lack of acceptance of a psychiatric illness, is common for people affected by severe psychoses. To paraphrase

<p>refused to take them. I didn't believe anything was wrong with me... – those pills were for crazy people!"</p>	<p>Nelson (22), hallucinatory voices and their consequent belief systems are as real and rational to the affected person as the fact that I happen to have two arms and two legs. This is what makes schizophrenia such a problematic illness to treat: like all the mental illnesses, it profoundly alters one's experience of reality. As such, the protagonists' reality at the time has to be actively worked with in order for this person to move forward productively.</p>
<p>"After several months I finally decided to take the medication (Geodon) [=ziprasidone]...I developed a severe case of depression...I wanted to die rather than continue to experience this feeling...At the end of my second year taking Geodon, I began to experience severe akathisia. This unusual type of anxiety is the worst emotional experience I have ever experienced in my entire life..."</p>	<p>Depression is a very common part of the pathological progression of schizophrenia: it's appearance is so common that it may well be an intrinsic consequence of the underlying pathology- possibly due to excitotoxicity (8) caused by apoptosis (9). Akathisia is a type of physical restlessness which is uncontrollable: the affected person has, scatologically, extremely severe 'ants in their pants'.</p>
<p>"My doctor switched my medication to Zyprexa [=olanzapine], and the akathisia gradually diminished...I now believe that I have fully recovered from schizophrenia, and I realise that my recovery is owed entirely to medication...I did not pursue any type of psychoanalysis. I simply took the medication..."</p>	<p>The idiosyncratic nature of a person's response to treatment is well-demonstrated here. Both ziprasidone and olanzapine are newer antipsychotic medications, which generally have far fewer side effects than their older precursors. In spite of this, ziprasidone – which reputedly has much less tendency to cause weight gain than the commonly-used olanzapine – didn't prove suitable for Mr Snyder. The fact that he "did not pursue any type of psychoanalysis" and still recovered is attributable to this gentleman's excellent social supports. This is in marked contrast to other first-hand accounts, e.g. Steele (11) and Schiller (23): although Mr. Steele was markedly lacking in social support, Mr. Snyder was not. This again indicates the idiosyncratic nature of responses to therapeutic efforts in schizophrenia. A likely explanation is that there is a continuum of severity along the spectrum of schizophrenic illness.</p>

Fig. 3. (above) The probable relationship between symptoms experienced in schizophrenia and causative pathology.

...and:

"...they just didn't want to listen to the patients' side at all: they would make their diagnoses and that was it."

(Both verbatim quotes from Barker *et al* [19]; my addition to first quote.)

...Again, referring especially to the last comment, the success of the psychological managements of schizophrenia, with their essential *validation* of a person's symptoms is unsurprising. As has been stated earlier here, it can clearly be seen that delusions are an attempt by the affected person at storying their experience (1). Another, equally important facet of the psychological approaches is the degree of *empowerment* that they afford the affected person (24). *Education* about the nature of the illness and how an affected person can recognise a potential worsening of symptoms and act to prevent an exacerbation is extremely important. Employment of psychological techniques of management as part of a treatment programme for schizophrenia can render consumption of antipsychotic medication an emphatic choice for the affected person rather than passive compliance- the latter is unfortunately the usual situation.

Psychological treatments for schizophrenia include an array of possibilities (18, 22, 25, 26): cognitive behavioural therapy [in its many variations] personal therapy, psychotherapy [again, with many variations of type] and compliance therapy. All of the psychotherapeutic approaches overlap to some degree. A particularly important ingredient of the psychological therapies for schizophrenia is the degree of empowerment of the affected person: these therapies rely on the agency of the affected person in the maintenance of their own health. As has been indicated above, validation, together with empowerment are two very important contributors to the improvement in, and maintenance of, ego strength. To reiterate an earlier assertion here, the establishment of a robust *therapeutic alliance* between the affected person and the treating team is a significant positive contributor to the eventual success of the treatment. The proven success of methods such as cognitive therapy for schizophrenia is undoubtedly partly attributable to the affected person's experiences being listened to or validated (19, 20, 23). In cognitive therapy, the affected person him/herself becomes the agent of therapeutic change. One facet of cognitive therapy for schizophrenia involves the affected person actively challenging a delusional belief. As an example, it is not uncommon for a person suffering from acute schizophrenia to believe that they are evil. (Hence an acute attack of schizophrenia can include depressive aspects which are experienced as delusional beliefs, or as persecutory hallucinatory voices.) In cognitive therapy, the protagonist would be advised to challenge this psychotic expression of experience by (e.g.) asking the hallucinatory voice to provide evidence for their statement. The affected person is taught how to provide evidence to the contrary. Hence, *dysfunctional thoughts are confronted*. This is the general principle of cognitive therapy, wherever it is used.

To pursue this hypothetical example further:

Hallucinatory voice: "You're evil."

Affected person: "No I'm not. I do voluntary work at the local charity shop twice a week and they really like me there."

... and here, the importance of appropriate *social manipulations* as a therapeutic tool becomes evident.

To combat dysfunctional thoughts, as in this example, the person must have enough *ego strength* to be able to do so. This is the aim of the whole treatment package, but especially applies to psychological techniques used in management. The ability to challenge delusional beliefs in cognitive therapy or in psychotherapy for psychosis depends on good ego-

strength in the affected person. Therefore, at first glance, it might seem counter-intuitive to employ psychotherapeutic methods in schizophrenia where one of the core pathological features is a disruption of the protagonists' individuality (and thus, by definition, ego-strength). However, in common with all therapies for all illnesses, the aim of treatment is to arrest – or, at the very least, alleviate – the disease process. Psychotherapeutic approaches for schizophrenia centre upon maintaining the affected person's ego-integrity. Psycho-education is thus an immensely important part of the treatment process. If the affected person can understand the need for continued medication and further, if they are able to use psychological techniques to combat a resurgence of symptoms should these arise, the combination is, again immensely empowering. It is thus unsurprising that the eventual dose of maintenance medication can be lowered (18).

Interested readers are referred to the wealth of excellent practical texts for cognitive therapy in schizophrenia, such as Nelson (22). While cognitive therapy has often been successfully used to aid compliance with medication, we have seen here that effective therapy of this kind with a well-engaged service user is known to reduce the required dose of maintenance medication. This is undoubtedly because the affected person can react in a therapeutic manner to the resurgence of symptoms. Other approaches to the presence of hallucinatory voices in schizophrenia include using distraction techniques: some affected people find that listening to music on a personal stereo blocks or drowns out their hallucinatory voices.

As proponents of psychotherapy for the psychoses readily agree, psychotherapy is not a suitable treatment option for everyone affected by schizophrenia. Again, this is perfectly intelligible: while there are treatment approaches which are generally applicable – such as the employment of a drug which has some dopamine D2 antagonism as an antipsychotic measure – each treatment regime must ideally be individually tailored as far as possible. One is referred again to figure 2, to be reminded of the holistic picture in treatment of mental illness. The importance of the holistic picture is emphasised in a review edited by Gleeson, Killackey and Krstev (27): within this review, the assertion is that a therapeutic alliance between proponents of the biochemical and psychodynamic models of schizophrenia is long overdue. Several essays within the review echo this sentiment.

5. Social manipulations in the treatment of schizophrenia

Social and psychological manipulations for illness overlap to a slight degree, most obviously in their therapeutic effects. The theoretical example of combating dysfunctional beliefs in the cognitive treatment of schizophrenia above indicates how important social conditions are. Remembering (from figure 2) that social events produce physiological changes, it is essential to consider a person's social situation when attempting to optimise their functional capacity. Therefore, the affected person must be in a stable and appropriate living situation: the high frequency of serious mental illness in the homeless and vulnerably housed population is testament to the importance of the 'home' situation. While some people with schizophrenia are able, with regular medication and regular clinical review, to maintain paid employment, not everyone is in this position. The usefulness of the attention of a social worker, or similarly qualified professional who has expertise in negotiating fields such as finance, housing and employment, is evident. Active feedback between all specialist practitioners about an affected person is essential: this is the model of the old *Community Mental Health Team* (CMHT) in the UK. The usefulness of this particular model is that a single group of practitioners gets to know the ill person well, and is aware of factors which may alleviate, or

aggravate their illness. The current (2011) fragmentation of care in the UK therefore can be potentially unhelpful for the affected person. It is well-recognised that the CMHT can become a surrogate family for the person with a chronic illness such as schizophrenia. In this context, perhaps it is useful to reminisce upon the work of Leff *et al* (28), who described the importance of *expressed emotion* (EE).

EE is understood as the level of critical comments and hostility toward the affected person from a particular carer. Also, the degree of emotional over-involvement of that carer is noted (28, 29). Since these topics were first considered, from the late 1950s onwards, high EE has been repeatedly and reliably shown to be associated with a higher relapse rate of schizophrenia. With the moves towards care in the community of mentally ill people, people with long-term mental illnesses living in residential facilities essentially have statutory replacements for their biological families. Therefore, the principles of EE are similarly applicable. While the degree of EE can be reduced with appropriate staff training, many care personnel in residential facilities are amongst the least trained (29). Previous studies in this area have found that critical personally directed comments towards people with schizophrenia were due to an attribution of dysfunctional behaviours directly to the affected person, rather than to their illness. Psycho-education about the nature and natural history of schizophrenia is therefore a great help for all those closely involved with it: patients, carers and staff members. One of the effects of education is a reduction in EE due to a better understanding of the illness process.

Many of the social aspects of a person's situation are the pragmatic ones, e.g.

- Can they care for themselves independently, or do they need help with tasks such as eating regularly and maintaining personal hygiene?
- Do they have enough money to live on?
- Are they eligible for state benefits?
- Are they able to work, and if so, how does this affect any benefits?
- Do they have secure tenancy of their homes?

One can see that a social worker, or similarly trained professional, is ideally placed to answer these concerns. Remembering the holistic package of treatment which should ideally be provided for the person with schizophrenia, the significant potential reduction in stress makes an important contribution to the maintenance of well-being.

6. Future developments in the treatment of schizophrenia

Unfortunately, constraints of space do not permit a full discussion here of potential future developments in schizophrenia. With respect to future drug developments, the reader is referred to the excellent review by Miyamoto *et al* (5). The pharmacology section above has already mentioned the potential usefulness of nicotinic adjuncts to the treatment of schizophrenia. My particular interest is in the use of substances such as nicotine chewing-gum to provide the short-term enhancement of sensory gating which would normalise the dysfunction seen in schizophrenia (10). The sustained activation of nicotinic receptors such as that provided by nicotine patches is probably unsuitable, because the involved receptors - the $\alpha 7$ nicotinic receptors in the hippocampus - desensitise quickly (13, 30). Galantamine is an $\alpha 7$ ligand which allosterically modulates the receptor to increase neurotransmission (30, 31). The potentiation of nicotinic transmission would therefore be potentially expected to transiently improve the sensory gating deficit intrinsic to schizophrenia and thus improve symptoms (6, 7, 10). The recognition of the importance of nicotinic neurotransmission in

schizophrenia has led to the investigation of drugs such as galantamine as potential therapeutic agents for schizophrenia; indeed, symptomatic improvement was seen with the addition of galantamine to the therapeutic regime in two very small samples of patients (29, 30). Enhancement of glutamatergic transmission is another area in which pharmacological effort may be directed in the search for new drug treatments for schizophrenia. Noting the remarks above about the importance of holistic treatments in mental illness, an obvious direction for future treatments in schizophrenia is greater multidisciplinary involvement. Recent legislative changes in the UK, with the amendment of the Mental Health Act 1983 in 2007, pay attention to this. The senior clinician in charge of a service user's treatment used to invariably be the consultant psychiatrist. Under the new Mental Health Act, the person in overall charge of the service user's care is the *responsible clinician* (RC). The RC can be any of the *approved clinicians* (ACs):

- a registered medical practitioner
- a registered mental health nurse (including registered learning disability nurse)
- a registered occupational therapist
- a chartered clinical psychologist, and
- a registered social worker (32)

The widening of professions eligible for the senior role of responsible clinician is a reflection of greater multidisciplinary involvement in the delivery of care to the service user. Thus, more effort is directed towards holistic care, which is important.

This emphasis provides a useful point at which to close this chapter. One is reminded that especially in the mental illnesses, as in all illness, phenomena are interconnected. In consequence, change at any point on the pathway of causative/therapeutic events can have potential profound effects on all other stages in the pathway.

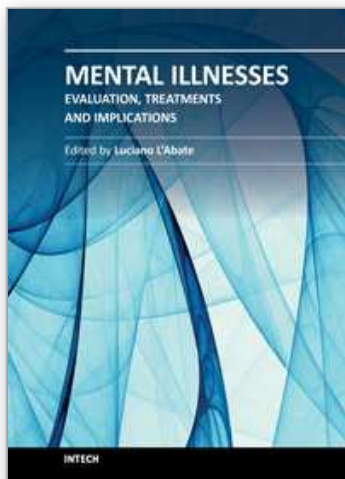
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In the book "Mental Illnesses - Evaluation, Treatments and Implications" attention is focused on background factors underlying mental illness. It is crucial that mental illness be evaluated thoroughly if we want to understand its nature, predict its long-term outcome, and treat it with specific rather than generic treatment, such as pharmacotherapy for instance. Additionally, community-wide and cognitive-behavioral approaches need to be combined to decrease the severity of symptoms of mental illness. Unfortunately, those who should profit the most by combination of treatments, often times refuse treatment or show poor adherence to treatment maintenance. Most importantly, what are the implications of the above for the mental health community? Mental illness cannot be treated with one single form of treatment. Combined individual, community, and socially-oriented treatments, including recent distance-writing technologies will hopefully allow a more integrated approach to decrease mental illness world-wide.

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