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Schizophrenia

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Introduction

Schizophrenia is a chronic psychiatric disorder found in all races which may lead to lifelong disability. The positive symptoms of schizophrenia, such as delusions, hallucinations and disorganized behaviors, were classically considered to be the main diagnostic criteria of schizophrenia. Now it is found that cognitive impairment and negative symptoms such as poverty of speech and social withdrawal are also major symptoms. The cause of schizophrenia is still unknown but many studies have found possible etiologies that will be discussed below. It is now generally accepted that it is a neuro-developmental disorder that has origins in the prenatal period resulting from the interaction between genetic and environmental factors (Chahl, 2007). The point prevalence of schizophrenia, which is defined as the proportion of a population at a point in time that has the disorder, is 5 per 1000 population. The incidence of schizophrenia is about 0.2 per 1000 per year. A study of incidence (Lieberman, Stroup & Perkins, 2006) from the World Health Organization shows that there is little variation in schizophrenia around the world. The onset of schizophrenia is varied. Hafner and colleagues (1999) suggests that the onset of negative symptoms occurs 5 years before the initial psychotic episode and the onset of positive symptoms is much closer to the first time of hospitalization.

This article provides an introductory review on the causes, symptoms, psychosocial rehabilitation and stigma towards people with schizophrenia based on the literature.

Etiology

Genetics

Three major types of studies are commonly used to explore genetics as an etiological factor of schizophrenia: family studies, adoption studies, and twin studies. In family studies, participants with schizophrenia are compared with participants with no history of schizophrenia who are matched for gender and age (Lieberman et al., 2006). The aim of this type of study is to examine the prevalence of schizophrenia in biological parents. For example, Kendler's study (Kendler, 2000) showed that the first-degree relatives of individuals with schizophrenia were nearly 10 times more likely to suffer from

schizophrenia than the control subjects. These studies provide direct evidence to the fact that genetics is an etiological factor in schizophrenia.

Adoption studies aim to investigate whether environmental factors contribute to the etiology of schizophrenia by investigating the adoptive relatives of the adoptees with and without schizophrenia. Studies revealed that individuals growing up with biological parents were five to six times more likely to get schizophrenia than with adoptive parents (Maxmen & Ward, 1995). Twin studies contrasted pairs of monozygotic twins and dizygotic twins .Similar to other studies, heritability is shown to be an etiology of schizophrenia (Sullivan, Kendler & Neale, 2003). Monozygotic twins have roughly three times the concordance rate of having schizophrenia than dizygotic twins (Maxmen & Ward, 1995).

Substance Use

Studies (Hall & Degenhardt, 2000) suggest that individuals with schizophrenia are more likely to have taken cannabis. It was found people who abuse drugs have mild symptoms of schizophrenia during the premorbid phase. In addition, cannabis can precipitate or even cause an episode of schizophrenia. Dopamine agonists like cocaine and amphetamine can also cause positive symptoms. Furthermore, phencyclidine ("angel dust") and ketamine ("Special K") can cause positive and negative symptoms of schizophrenia (Adler, Malhorta, Elman, Goldberg, Egan, Pickar & Breier, 1999; Lahti, Michaelidis, Parwani, Taminga, 2001; Avila, Weiler, Lahti, Tamminga, & Thaker, 2002).

Biochemistry

Many studies have shown that an excess of subcortical dopamine (DA) resulting from an overstimulation of DA receptors causes positive symptoms of schizophrenia (Chahl, 2007; Carlson, 2007). The main hypothesis in vogue is that there is a hyperactivity of mesolimbic dopamine pathway which projects from dopaminergic cell bodies in the ventral tegmental area (VTA) of the brainstem to axom terminals in the limbic system of the brain, particularly the nucleus accumbens (Stahl, 2000). The level of DA can be affected by other substances, for instance, amphetamines. The abuse of this drug stimulates the release of DA into synaptic clefts of the neural system which then produces a paranoid and psychotic state. However, another study demonstrated that negative symptom in schizophrenia may be related to low dopamine activities in the prefrontal cortex in the brain (Maxmen & Ward, 1995). Weinberger (1988) first suggested that the negative symptoms of schizophrenia are caused by hypofrontality which refers to decreased activity of the dorsolateral prefrontal cortex. Further studies have to be conducted to ascertain the role of dopamine as a plausible cause of schizophrenia.

Prenatal

Apart from the above factors, season of birth has been shown to be related to schizophrenia. A study found that people who are born in winter has 10% higher risk to be schizophrenia (Torrey, Miller, Rawlings, & Yolken, 1997). These findings have been repeatedly shown by different research groups. One possible reason to explain this phenomenon is that the pregnancy time is in the peak of the flu season. This makes them susceptible to suffer from infection which in turn increases the risk of their babies for

schizophrenia. It is also suggested that prenatal development may be highly related to later developed schizophrenia. Malnutrition (Susser, E. S. & Lin, S. P., 1992) and extreme prematurity, hypoxia (i.e., body is deprived of adequate oxygen supply) or ischemia (i.e., restriction of blood supply) may be possible causes of later onset of schizophrenia.

Cerebral Blood Flow

Position emission tomography (PET) was invented in the 80s which allows the investigation of the distribution of specific substances such as glucose and oxygen via the cerebral blood flow. Studies suggested that people with chronic schizophrenia have a lower blood flow to the frontal lobes compared with normal subjects. However, acute and non-medicated individuals showed no significant change (Cutting, 1985). Furthermore, neuropathological studies showed that the volume of the brains especially the frontal lobe of individuals with schizophrenia is reduced when it is compared with those of healthy individuals (Selemon, Kleinman, Herman, & Goldman-Rakic, 2002).

Stress

Psychosocial stress can elevate the level of glucocorticoids (McEwen & Magarinos, 1997). A study showed that increased glucocorticoids and stress reduced the volume of hippocampus in the CA3 region, which is commonly found among individuals with schizophrenia.

Signs and Symptoms

Conventional classification systems divide the symptoms of schizophrenia into positive and negative. Positive symptoms refer to those that cause distortion or excess of normal functions. At the clinical level, positive symptoms command social and medical attention which represent a disruption of functions that are normally present (Cutting 1985). Positive symptoms are distortions or excess of normal thoughts, emotions or behaviors (Weiden, Scheifler, Ross & Diamond, 1999). Examples of positive symptoms include hallucinations, delusions, disorganized behavior and inappropriate affect. They are more easily recognized than negative symptoms which can be seen throughout different phases of schizophrenia even in more stable or acute phase.

Negative symptoms on the contrary often pass without notice. Since they represent impairment of the general intellectual abilities and executive functions, research shows that negative symptoms are more stable than positive ones over time and are less likely to improve over the course of schizophrenia (Addington & Addington, 1991; Hull, Smith, Anthony, Goodman, Kentro, Sepe, Yanulis, & Li, 1997; Pfohl & Winokur, 1982). Arndt and colleagues (1995) have found that negative symptoms were prominent at the time of first episode of schizophrenia and remained generally stable for approximately 2 years. Negative symptoms prevent patients with schizophrenia from leading normal lives, returning to work, attending school, or having normal interpersonal and family relationships. The examples of negative symptoms include alogia (poverty of speech), avolition (lack of motivation), attentional impairment and affective blunting. Since negative symptoms are related to poor premorbid adjustment, structural abnormalities

unresponsive to treatment, and various indicators of neuron-developmental abnormalities, their presence is found to be closely tied to the poor prognosis (Cutting 1985).

Subtypes

Diagnostic and Statistical Manual of Mental Disorders Text Revision (DSM-IV-TR) suggests that there are five subtypes of schizophrenia: paranoid, disorganized, catatonic, undifferentiated, and residual.

Paranoid Type

It is a type of schizophrenia in which individuals are preoccupied with one or more delusions or frequent auditory hallucinations.

Disorganized Type

Individuals with this type of schizophrenia present prominent symptoms of disorganized speech, disorganized behavior, and flat or inappropriate affect.

Catatonic Type

This type of schizophrenia shows motor disturbances ranging from immobility to excessive meaningless activity that are dominated by psychomotor symptoms (Lieberman, 2006).

Undifferentiated Type

Individuals who have a combination of symptoms from other subtypes, but do not meet the criteria for Paranoid, Disorganized, or Catatonic Type are classified as Undifferentiated Type of schizophrenia.

Residual Type

This type of individuals shows absence of prominent delusions, hallucinations, disorganized speech, and grossly disorganized or catatonic behavior. However, individuals lack motivation and interest in day-to-day living (Lieberman, 2006).

Treatment

Medication

Classical antipsychotic medications, such as haloperidol and fluphenazine, act similarly as the dopamine D2 receptor antagonist that binds to the D2 receptor and decreases the amount of dopamine release into the synaptic cleft of the neural system. Classical antipsychotics are reported to be effective treatment of the positive symptoms of schizophrenia. However, the drugs produce serious side effects such as symptoms of Parkinson disease. Moreover, they are relatively ineffective to treat the negative symptoms and cognitive impairment. Recently developed antipsychotics such as clozapine and risperidone block dopamine and serotonin-2 receptors at the same time. These atypical antipsychotics have been shown to have lesser side effects and be efficacious in treating negative symptoms. However, there is no evidence as to the effect

on relieving cognitive impairment. Antipsychotics usually take days or weeks to produce significant effects. Some of these drugs have the sedative effect that tends to go away in seven to ten days. (Chahl, 2007; Lehman, 2004).

Psychosocial Treatment

The ultimate goal of psychosocial rehabilitation is to attain recovery by helping individuals obtain employment, gain independence, improve quality of life, and facilitate interpersonal relationships. The interventions of rehabilitation include facilitating symptom management skills, training social skills, and improving cognitive performance.

"Evidence based practice" (EBP) refers to health services that are bolstered by a plethora of randomized clinical trials performed by different research groups in multiple research sites (Torrey, Rapp, van Tosh, McNabb & Ralph, 2005). It would be even better if the outcome of a particular intervention has been confirmed by meta-analysis which is an increasingly popular statistical tool. A well recognized way of implementing evidence based practice is through the development of guidelines for the best practice. With this consent, a number of indicators for determining if a particular intervention may be regarded as evidence based have been put forward for the past few years. The most influential set of criteria are the Schizophrenia Patient Outcomes Research Team (PORT) treatment recommendations (Lehman & Steinwachs, 1998). It is part of the huge PORT program initiated by the Agency for Healthcare Research and Quality (AHRQ) of the Department of Health and Human Services, with a view to compiling the scientific literature on the efficacy of treatments for various medical conditions, to examine various prevailing treatment practices, to develop scientifically based treatment recommendations and practice guidelines, and to evaluate effects to disseminate knowledge to improve care (Lehman et al., 2004). Under the above criteria, only a few of the treatment practices have shown to have well-established scientific base and empirical evidence, which include Cognitive Behavioral Therapy (CBT), Family Interventions (FI), Assertive Community Treatment (ACT), Social Skills Training (SST) and Supported Employment (SE) (Tsang, Siu & Lloyd, in press).

Cognitive behavioral therapy (CBT) is "an active, problem-oriented treatment task that seeks to identify and change maladaptive beliefs, attitudes, and behaviors that contribute to emotional distress" (Reinsecke, Ryan, & Dubois, 1998). It was initially developed to treat depression and anxiety (Beck, 1976; Haddock et al., 1998). Recently, it has been used as a supplement to pharmacotherapy for people with schizophrenia and bipolar disorders (Gould, Mueser, Bolton, Mays, & Goff, 2001). Cognitive behavioral therapy can help reduce the level of hallucinations and delusions of people with psychotic disorders, and their level of social disability and risk of relapse (Bustillo, Lauriello, Horan, Keith, 2001; Glynn, 2003). Cognitive behavioral therapy assumes that symptom or problem is manifested and maintained by the mediation of cognitive and environmental processes. It modifies those processes by teaching the individuals with more adaptive cognitive and behavioral skills (Haddock, Tarrier, Spaulding, Yusupoff, Kinney, & McCarthy, 1998). Kingdon, Turkington and Beck. (1993) illustrated the two-pronged approach of CBT. First, testing the validity of potential irrational beliefs by logical reasoning is the first step of this approach. Management strategies such as

problem-solving or distraction would be developed if the symptoms could not be eliminated via logical reasoning. Modalities such as psychoeducation, cognitive reconstruction, and skills trainings are integrated in the CBT programs (Kingdon, & Turkington, 1994). Cognitive behavioral therapy can be run in individual and group formats. Its effectiveness in reducing psychotic symptoms of participants has been demonstrated in a volume of clinical trials (Clark & Samnaliev, 2005; Gould, Mueser, Bolton, Mays, & Goff, 2001; Lehman et al., 2003). It is especially promising to manage delusions and auditory hallucinations (Glynn, 2003). Although CBT has promising effects on symptom control among people with schizophrenia and bipolar disorders (Garety, Fowler, & Kuipers, 2000; Jones, 2004; Otto, Reilly-Harrington, & Sachs, 2003), its beneficial effects on relapse prevention, reduction of number of hospital admissions, and promotion of social functioning are limited (Dickerson & Lehman, 2006).

The use of family intervention (FI) in psychosocial rehabilitation is to reduce the relapse rate and enhance the social adjustment of people with psychotic disorders, and to reduce their caregivers' stress and burdens in caring them. Behavioral, psychodynamic, psychoeducation, and supportive models are commonly used in family interventions (Glynn, 2003). Effective family interventions consist of psychoeducation, problem-solving, crisis management, and crisis intervention (Dixon & Lehaman, 1995; Lehman et al., 2003). Multiple family groups or individual family members could conduct in family intervention. It is suggested that the use of multiple family groups is more effective, and offers additional benefits of increased social supports among members. (Glynn. 2003; Mcfarlane, Dushay, Stastny, Deakins, & Link, 1996). The effectiveness of family interventions in the reduction of symptoms relapse, improvement of individuals' functioning, reduction of family burdens, and promotion of family subjective wellbeing have been well verified by randomized controlled trials (Dixon, Adams, & Lucksted, 2000; Klingberg et al. 1999; Lehman et al., 2003; Pharoah, Mari, Rathbone, & Wong, 2006). It was reported that the relapse rate of individuals who had participated in family intervention was 24%, which was significantly lower than those who had not received the treatment with the relapse rate of 64% (Mueser and Glynn 1998). It has also been shown that the implementation of family interventions in psychiatric rehabilitation could also enhance medication compliance, and improve the coping skills and knowledge of family members to take care of their mentally ill relatives (McFarlane, Dushay, Stastny, Deakins, & Link, 1996; Pharoah, Mari, Rathbone, & Wong, 2006). Moreover, the durable effect of long term family intervention is supported by empirical evidence (Mueser & Glynn, 1998; Tarrier, Barrowclough, Porceddu, & Fitzpatrick, 1994). The beneficial effects of family interventions could be sustained after the termination of services (Tarrier, Barrowclough, Porceddu, & Fitzpatrick, 1994).

Assertive community treatment (ACT) is a community-oriented intensive case management approach of treatment and support delivery (Dhillon & Dollieslager, 2002; Lehman et al., 2003; Mueser, Bond, Drake, & Resnick, 1998; Philips et al. 2001). The development of ACT is responsive to the deinstitutionalization movement of psychiatric rehabilitation. The key objectives of this treatment are to reduce the hospital admission rate among individuals with high risk of suffering, and to enable them to have proper utilization of mental health services (Antai-Otong, 2003; Marshell & Lockwood, 1998).

One of the key features of this treatment is multidisciplinary team work. The team consists usually of 10 to 12 mental health professionals, including a case manager, occupational therapist, nurse, or other related experts like psychiatrists, psychologists and social workers. The caseload of staff members is generally low. This is to make sure that staff members have the capacity to cope with the intensive needs of service recipients (Phillips et al., 2001). The service is delivered on a 24-hours basis with no arbitrary time limit and is tailor-made to meet the individualized needs of participants. A 10% to 85% reduction on hospitalization rate was reported among participants who had engaged in ACT programs (Latimer, 1999). In addition, individuals with serious symptoms and functional impairments demonstrated more prominent outcomes in ACT programs. (Phillips et al. 2001). However, consensus regarding its effectiveness in promoting competitive employment, social functioning and symptoms management have not been demonstrated (Marshall & Lockwood, 1998; Mueser, Bond, Drake, & Resnick, 1998).

The objectives of social skills training in psychiatric rehabilitation are to promote the social functioning of individuals, and to enhance their specific skills in identifying and solving problems in social relationships, daily life, work, and leisure. (Lauriello, Bustillo, & Keith, 1999). The key elements of social skills training include warm-up activities, behaviorally based instructions, demonstration, corrective feedback, and homework assignments (Lehman et al., 2003; Wallace et al., 1980).

Tsang and colleagues (1996; 2001) have developed a structural work-related social skills training (WSST) programs for people with psychotic disorders in view of the importance of social skills in the workplace. In this program, participants are required to learn social skills in handling general and specific work-related situations in addition to practicing basic social skills and basic social survival skills (Tsang & Pearson, 1996). Tsang and Pearson (2001) conducted a randomized controlled trial to test the effectiveness of the WSST program. The study suggested that the participants had better social competence than those who received standard treatment without WSST. In addition, the competitive employment rate of participants of WSST program reached 46.7%. WSST is commonly used as a part of psychiatric rehabilitation programs in Hong Kong, Australia and Germany (Tsang & Cheung, 2005).

It is suggested (Becker et al., 1998) that skills training programs should be tailored for the required skills of a particular job. Cheung and Tsang (2005) developed a Job-specific Social Skills Training (JSST) program for this purpose. Sins sales is found to be one of the common occupations for people with psychotic disorders (Tsang, Ng & Chiu, 2002), JSST program is specifically designed for individuals who plan to be a salesperson (Tsang & Cheung, 2005). According to their study, the integration of the JSST and WSST could raise the employment rate to 70.3%.

Individual placement and support (IPS) is a specific model of supported employment (SE) that aims at helping people with psychotic disorder to obtain competitive employment. The SE model has seven key principles that include:

1. seeking competitive employment
2. conducting a rapid job search
3. integrating mental health services
4. emphasizing individuals' preference
5. implementing continuous and comprehensive assessment
6. providing time-unlimited support
7. conducting benefits counseling

Research results show that the IPS model could improve short-term employment of people with psychotic disorders (Drake et al., 1999; Lehman et al., 2002). Bond (2004) noted that nearly half of participants still cannot obtain employment under the IPS model. Therefore, vocational researchers have integrated skills training elements into the IPS model in order to augment its treatment outcomes (Cook et al., 2005; McGurk, Mueser, & Pascaris, 2005; Tsang, Chan, & Wong, under review). An Integrated Supported Employment programme (ISE); (Tsang, 2003) was developed by combining the IPS model and the Work-related Social Skills Training (WSST). An RCT (Tsang, 2007) reported that ISE participants obtained a competitive employment rate of 78.8%, which was significantly higher than 53.6% for IPS participants. Meanwhile, the job tenure of ISE participants was significantly longer than that of IPS participants. The number of job terminations among the ISE group was 0.34 ± 0.81, which was significantly lower than 1.76 ±1.92 of IPS group. As to the reasons for job terminations, 25.0% of IPS participants were related to interpersonal problems such as poor relationships with supervisor and co-workers, whereas only 7.7% of ISE participants were due to interpersonal problems.

Stigma and Discrimination

A study by Tsang, Chan & Cheung, 2003 shows that family members feel ashamed of having a mentally ill relative. Many of them express embarrassing feelings when going out with their mentally ill relatives. It was found that this attitude in the family also existed in the society. For instance, people would change seats on public transport when they realized that the nearby passenger behaved as a mentally ill person. The most common stereotype in relation to schizophrenia at work is the perception of dangerousness (Tsang, Angell, Corrigan, Lee, Shi, Lam, Jin, Fung, 2007). Employers stigmatize individuals with mental illness thinking they may create accidents or mistakes, may have unreliable attendance, and may contaminate the work atmosphere (Tsang et al., 2007). Historically, individuals with schizophrenia were isolated from the community. Therefore, employers are very likely to reject an applicant with acknowledged schizophrenia since applicants have already been stereotyped.

Individuals who are self-stigmatized are likely to avoid engaging in appropriate help-seeking behaviors (Fung, Tsang & Corrigan, under review). This reduces their treatment adherence that may prevent the recovery of people with schizophrenia (Swanson et al., 1997). Fung, Tsang and Corrigan (under review) suggest that the goal attainment program (GAP); (Ng and Tsang, 2002) and motivational interviewing (MI); (Miller, 1982) that help people with schizophrenia develop realistic life goals and insight are promising interventions to improve treatment participation. They also propose cognitive behavioral therapy (Holmes & River, 1998; Kingdon & Turkington, 1991) to normalize

the individual's stigmatized ideas. A self stigma reduction program is now being developed in Tsang's group.

Directions for Future Research

Continuous research efforts are needed to explore schizophrenia so as to elucidate the neurobiological mechanism of the disease and provide better psychiatric services to clients. Although second generation antipsychotics have lesser side effects and are more effective in treating negative symptoms than the classical antipsychotic medications, evidence does not support a significant effect on cognitive impairment. Continuous efforts in pharmaceutical research have to be maintained so as to develop third generation antipsychotics that may improve cognitive and functional impairment on top of its efficacy to reduce positive and negative symptoms.

Apart from scientific and medication research, research on psychosocial rehabilitation is urgently needed that helps individuals obtain employment, improve independence, and thus enhance their quality of life (Tsang 2006). Although Integrated Supported Employment (ISE); (Tsang, 2003, 2007) has been shown to be the most effective approach in terms of employment rate and job tenure, further enhancement is needed particularly to help participants retain their jobs. One of the strategies is to further improve its efficacy by merging it with cognitive remediation.

Finally, it is common for individuals with schizophrenia or other severe mental illnesses to be stigmatized. This happens in family, work, and community settings. Individuals with schizophrenia have a greater level of self-stigma if they assign greater responsibility to themselves for causing their illness (Mak & Wu, 2006). They may avoid socialization, do not comply with medication and psychosocial treatments, and thus block their recovery (Fung, Tsang & Corrigan, under review). In view of this, the authors' team is currently developing strategies to remove their self-stigma and hence engage them actively in the rehabilitation process.

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