Chapter 1

Psychosis

1.1 What is psychosis?

Psychiatry has always struggled with terms and definitions. Canvass the opinions of a modern community multidisciplinary team, and there are likely to be a range of opinions on what psychosis actually is [1]. Yet very few will object to the phenomenological perspective, which captures the seriousness of just what is at stake in psychosis. That is because psychosis impacts upon the highest and most personal faculties of the human mind.

In short, psychosis describes a disturbance of perception, thinking, beliefs, or selfhood in which the patient experiences a fundamental transformation in their experience of lived reality. This transformation can be terrifying as in paranoid psychoses or thrilling as in mania. Psychosis can emerge and dissipate quickly or become ingrained in the mind/brain over many months. Some patients seek safety by withdrawing from the world, whereas others attract attention to their mental state through excited, agitated, bizarre, or catatonic behaviour.

1.2 Lack of insight

The most common feature of psychosis is not hallucinations, delusions, thought disorder, paranoia or suspiciousness as is commonly believed but lack of insight [2]. Lack of insight denotes the blind-spot a patient has in regard to the falseness of their new reality and the abnormal nature of their mental state [3]. For some the term 'lack of insight' exemplifies the power imbalance within psychiatry.

Regardless of terminology, the blind-spot is what makes the care of many patients suffering psychosis particularly challenging. Why would anyone take treatment, let alone engage with mental health professionals if they think their experiences are real rather than a manifestation of psychiatric illness.

Advanced Prescribing in Psychosis, First Edition. Paul Morrison, David M. Taylor and Phillip McGuire.

1.3 Causes of psychosis

Mental states have material correlates. For some patients, a material dysfunction is the direct cause of their psychosis. The list of causes includes endocrine disorders (e.g. *thyroid disease*), metabolic disorders (e.g. *porphyria*), auto-immune conditions (e.g. *N-methyl-D-aspartate*, NMDA-*receptor encephalitis*), infections (e.g. *herpes-simplex encephalitis*), epilepsy (e.g. *temporal lobe epilepsy*), nutritional deficits (e.g. *vitamin B12 deficiency*), basal ganglia disorders (e.g. *Wilson's disease*), medications (e.g. *acyclovir)*, dementias (e.g. *Alzheimer's disease*), and most common of all, psychoactive drugs, as causes [4].

The following psychoactive drugs can elicit an acute psychotic episode after a single administration: serotonin $5HT_{2A}$ receptor agonists (e.g. *lysergic acid diethylamide, LSD*), glutamate NMDA channel blockers (e.g. *ketamine),* and cannabinoid CB_1 receptor agonists (e.g. *delta-9-tetrahydrocannabinol, THC*) [5].

Repeated, heavy use of stimulants can elicit a classic paranoid psychosis by impacting upon dopamine signalling (e.g. *methamphetamine*) [5, 6].

Psychosis can occur in the following syndromes: schizophrenia, delusional disorder, bipolar disorder, post-partum psychosis, schizoaffective disorder, and depression. Psychotic experiences can also manifest in severe obsessive compulsive disorder (OCD). There are also brief, acute, full-blown psychotic episodes occurring outwith any of these syndromes, which even in the era before antipsychotic drugs, tended to show a full recovery of insight and restoration of the former reality [7, 8].

Auditory *pseudo*-hallucinations and 'paranoia' can occur in people prone to emotional instability, but insight is maintained, and the prominence of deliberate self-harm in the context of early abuse steers the formulation away from a psychotic disorder [9–11]. Indeed, psychotic-like phenomena including voices and paranoia occur in the general population, but such experiences do not overwhelm the self to the extent that there is a fundamental transformation of lived reality, and should not be over-psychologised as markers of mental illness [12–14].

Robin Murray and Jim van Os have made the elegant observation that, 'the boundaries between normal mentation, common mental disorder and schizophrenia become blurred, if positive psychotic symptoms are used as a distinguisher' [15].

Precise diagnosis might not be possible, but in some cases it is vital. For instance, psychosis arising from antibodies targeting the NMDA-receptor requires urgent immunological treatment [16]. In such cases antipsychotics and psychological therapy are of no value and lead to delays.

Given the multitude of causes of psychosis, patients require a skilled assessment and careful biopsychosocial formulation before treatment, whether pharmacological or psychological, is embarked upon [17].

1.4 Schizophrenia: loss of personality and psychosocial decline

Psychosis and schizophrenia are not synonymous. Only about one in eight patients who experience an acute psychosis will go on to develop schizophrenia over a period of three to five years [18].

Schizophrenia is not a single syndrome [19]. From the outset, the term subsumed a collection of phenotypes [20–22].

Paranoid form, dominated by psychotic symptoms.
Hebephrenic form, dominated by severe thought disorder and bizarre affect.
Catatonic form, dominated by psychomotor signs.
Simple form, dominated by severe psychosocial decline but no psychotic symptoms.

The precise definition and demarcation of schizophrenia is as uncertain as ever, and some authorities have suggested dropping the term altogether because of the associated stigma [23, 24].

On the other hand, there are a proportion of patients who exhibit such marked social decline and loss of personality for whom no alternative descriptor is forthcoming.

Many consider that psychosocial decline and loss of personality are the hallmarks of schizophrenia [25]. Essentially the same meaning is conveyed by the term, *negative symptoms,* originally formulated in nineteenth-century neurology to describe the loss of a function which is normally present in health. In schizophrenia the loss encompasses; drive, motivation, ambition, emotion, conversation, interests, family life, friendships, romantic relationships, and intellectual life [26–28].

A proportion of patients present with negative symptoms from the outset. Indeed, the drift towards psychosocial withdrawal and personality decline can precede a psychotic episode by several years [25].

Negative symptoms carry much more prognostic and diagnostic weight than the positive symptoms. Negative symptoms are commensurate with poorer long-term outcomes [29].

Schizophrenic patients with prominent negative symptoms are amongst the most psychosocially disabled, but sometimes the absence of risk alerts means that they can often be overlooked [30, 31]. Indeed, the absence or relative paucity of 'voices' and 'paranoia' in the overall clinical picture can even lead inexperienced workers to judge that there is no evidence of a mental disorder.

A relatively common error is the misdiagnosis of an autistic disorder. The negative syndrome of schizophrenia and autistic disorders are characterised by impaired social interaction. A key distinguishing feature is that autism is manifest before the age of three years, whereas a schizophrenic decline emerges in adolescence/early adulthood.

One concern, which has arisen, is that there may be a tendency towards under-recognition and under-treatment of severe and enduring mental illness, such as negative syndrome schizophrenia, and over-responding to relatively mild psychological problems [32].

1.5 Bipolar disorder

Bipolar disorder is a lifelong, episodic illness with high heritability [33] Bipolar I is defined by mania. In mania, there is an absence of insight, the cardinal feature of psychosis [33].

Bipolar patients typically recover insight between manic episodes, in that they can take a rationale perspective on their previous mental state and judge correctly that their experience of lived-reality at the time of crisis was pathological [34, 35].

Bipolar I is diagnosed after one episode of mania. Mania is characterised by a discrete period of at least one week of: persistently elevated or irritable mood; increased self-esteem or grandiosity; decreased need for sleep; more talkativeness than usual or pressure to keep talking; flight of ideas or subjective experience of racing thoughts; distractibility; increased goal-directed activity, or excessive involvement in pleasurable activities with high potential for painful results.

Bipolar II is diagnosed after one episode of hypomania + one episode of depression. Hypomania ('mini-mania') is recognised as mania which is not severe enough to cause a marked impairment in psychosocial functioning, psychosis, or to require hospitalisation. Periods of hypomania lasting one to four days are more common than prolonged episodes [36].

In the *Diagnostic and Statistical Manual of Mental Disorders* (DSM5), the presence of increased activity is a requirement for mania/hypomania. Increased activity can differentiate mania/hypomania from other illnesses [37].

1.6 Cannabis, synthetic cannabinoids, and psychosis

Clinicians who treat psychosis will be familiar with the range of patients who present with problems arising from cannabis use [38]. At least one-quarter of all new cases of psychotic illness in South London are attributable to high-potency 'skunk' cannabis [39].

Compared to traditional cannabis, skunk is high in the pro-psychotic molecule THC, but contains negligible amounts of another molecule called cannabidiol (CBD). The balance is important as CBD inhibits the psychotic effect of THC [40]. CBD also appears to have therapeutic effects in schizophrenia [41].

Acute cannabinoid psychoses are typically paranoid or manic in flavour. Less commonly, there can be hebephrenic features or motor signs such as posturing and bizarre gestures [42].

Some patients go through an acute psychosis as a result of high potency cannabinoids, but return to their lives, chastened by the intensity of their experience. Others abstain for a period, but dabble again, going through a relapse. A significant proportion of patients simply refuse to accept that cannabis has a negative impact on their mental health, and continue using the drug on a regular basis.

Two very large studies from Scandinavia found that about 50% of patients who present to emergency services with a cannabis elicited psychosis will go onto become long-term psychiatric patients [43, 44].

THC, is a partial agonist at the CB_1 receptor. The synthetic cannabinoids ('spice') are full agonists at the CB_1 receptor and have much stronger effects on the psyche, eliciting intense, florid psychoses [45]. Synthetic cannabinoids can also have a pronounced effect on heart rate and blood pressure.

An emerging concern is that the synthetic cannabinoids may be so powerful as to overwhelm the stabilising properties of antipsychotic medication.

The synthetic cannabinoids are not detected in standard drug screens, and over 150 molecules are available. Markers of synthetic cannabinoids use include confusion, slurred speech, excessive sweating, tachycardia and hypertension [46].

Complications of synthetic cannabis use include renal failure, pulmonary damage, myocardial infarction, seizures, and stroke [46].

Synthetic cannabinoids have emerged as a major problem in UK prisons [47].

Around one in seven cannabis users in the population meet criteria for dependence. High-potency cannabinoid preparations appear to have more propensity for addiction. There is a cannabis withdrawal syndrome, which resembles nicotine withdrawal. Cravings and psychomotor agitation peak at days 3–4 and diminish over 14 days [48].

Many patients who are able to sustain abstinence can make a significant recovery. The challenge, of course, is in persuading patients that the downside of their drug use far outweighs any residual upside.

In many US states and in Canada, cannabis has been legalised for recreational or medical use. Products that are high in THC with negligible CBD concentrations can be readily purchased. There are worries that cannabis-related psychiatric problems could increase in North America with the change in legislation [49].