Misunderstanding madness: Deciphering Schizophrenia
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Disorders of Mental Health: From Discovery to Recovery
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What is madness?
What is madness?

madness

Pronunciation: /ˈmadnis/

noun
the state of having a serious mental illness

extremely foolish behaviour:
the bank bailout was madness

a state of wild or chaotic activity:
Trying to ram the Dail with a cement truck

With apologies to the Oxford English Dictionary
Psychotic Disorders

Disorders with impaired *reality testing* affecting perception, thinking and behaviour

delusions
- paranoid, reference, grandiose, guilt, religious

hallucinations
- auditory, visual, somatic, gustatory, olfactory
Psychosis in the population

Fig. 4. Psychosis: variation along a continuum.

Psychotic experiences (8%)

Psychotic symptoms (4%)

Psychotic disorder (3%)

Van Os et al, 2009
Psychotic Disorders

1. Brief psychotic disorders
   1. Substance induced disorders
   1. General medical causes
   1. Mood disorders
   2. Schizophrenia (and related disorders)

Fig. 4. Psychosis: variation along a continuum.
How are different types of psychotic disorder diagnosed?
Diagnostic criteria for Schizophrenia

A. *Characteristic symptoms:* Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated):

1. delusions
2. hallucinations
3. disorganized speech (e.g., frequent derailment or incoherence)
4. grossly disorganized or catatonic behavior
5. negative symptoms, i.e., affective flattening, alogia, or avolition

*Note:* Only one Criterion A symptom is required if delusions are bizarre or hallucinations consist of a voice keeping up a running commentary on the person's behavior or thoughts, or two or more voices conversing with each other.

B. *Social/occupational dysfunction:* For a significant portion of the time since the onset of the disturbance, one or more major areas of functioning such as work, interpersonal relations, or self-care are markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement).

C. *Duration:* Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or two or more symptoms listed in Criterion A present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).
Schizophrenia

1. Increased family history of schizophrenia and other (particularly) psychotic disorders
2. Identified genetic risk factors (individual genes, but each of small effect on risk)
3. Older fathers (related to increased rate of genetic mutations in sperm)
4. Increased rates of prenatal health problems (e.g. maternal infection)
5. Perinatal complications (e.g. birth related problems)
6. Neurodevelopmental deficits (e.g. delayed walking, talking)
7. History of childhood trauma
8. History of cannabis use (particularly early onset group of cannabis users)
9. Risk of social stress/marginalization on developing brain
10. Duration of untreated psychosis
11. Onset typically in early twenties
12. About 20% have only one episode, 50% have recurrent episodes, 30% continuous illness
13. Effective treatments for some symptoms (e.g. antipsychotic medications, psychotherapy)
14. But not for others (e.g. motivational, concentration and memory problems)
15. Significant health consequences (>20 year average reduction in life expectancy)
How could the theatre of the mind be generated by the machinery of the brain?

Charles Bonnet (1760)
Is schizophrenia one disease process?
Association within a family of a balanced autosomal translocation with major mental illness

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Abstract

282 pedigrees in the MRC Cytogenetics Registry, Edinburgh, with familial autosomal anomalies were examined for the presence of associated mental illness. In one large pedigree there were 23 cases of mental and/or behavioural disorders meeting Research Diagnostic Criteria. 34 of the 77 family members available for cytogenetic analysis carried a balanced translocation t(1;11)(q13;q21). Psychiatric diagnoses had been recorded for 16 of the 34 members with the translocation compared with only 5 of the 43 without it. The lod scores (against chance linkage of the translocation with mental illness) were greatest when the mental disorders in the phenotype were restricted to schizophrenia, schizoaffective disorder, recurrent major depression, and adolescent conduct and emotional disorders. Although the mental illness in this family may not be typical of that in the general population, the findings suggest that the q21-22 region of chromosome 11 may be a promising area to examine for genes predisposing to major mental illness.
Genes contain instructions for making proteins.

Proteins act alone or in complexes to perform many cellular functions.
Duplications at PAK7
Protein activated kinase-7 (PAK7)

The gene is expressed in the brain
From a small family of genes involved in key aspects of brain development
PAK 7 is involved in regulation of communication between brain cells
This communication is critical to how we learn
PAK7 may be part of a regulatory mechanism also involving DISC1

Localization
Expression controlled by neuronal activity

Brandon & Sawa, Nat Rev Neurosci 2011
Deciphering Schizophrenia

Psychotic experience is more common than most people think
A smaller group of people have psychotic disorders
These can be brief or enduring (schizophrenia is example)

Help and treatment is available for people with schizophrenia

The brain is science’s greatest challenge
Progress is being made in understanding the brain
Most particularly in how we interact with the world

This is informing our understanding of mental disorders
Understanding can reduce stigma
We can develop better diagnostics and treatments
Acknowledgements