SCHIZOPHRENIA and PSYCHOSES

Schizophrenia is a diagnosis which includes psychoses symptoms
Greek - Skhizen (to split) Phren (mind)
Splitting of the mind or it’s function – NOT a split personality.

Psychoses can be a descriptive term for a group of symptoms characterised by thoughts and emotions which are disconnected from reality
Outline

- Epidemiology
- Aetiology
- Clinical features
- Treatment
- Prognosis
Epidemiology

- Incidence/prevalence
  - Life time risk 1%
  - Annual incidence 15-20/100 000
  - Prevalence 0.5 -1 %

- Similar statistics across all cultures  WHO 1973

- Peak onset
  - Men: 15-25 years
  - Women 25-35 years
  - Similar rates in men and women
Aetiology: Gene-environment threshold hypothesis

Several susceptibility genes + Early environment events (Obstetric paediatric effects on brain) → Leads to increased vulnerability (neuromotor delay, cognitive impairment, social anxiety) → Psychosis

Social factors → Drug misuse
Lifetime risk of schizophrenia - established through family, twin and adoption studies
Rate of schizophrenia in adopted away children higher if had biological parent with Schizophrenia

Children raised by an adoptive parent with schizophrenia do not have an increased rate

Polygenic mode of transmission
Aetiology Peri-natal exposure

- Higher rates of pregnancy and birth complications in people who develop schizophrenia

- Maternal infection
  - Higher rates in winter births
  - Exposure to influenza epidemics in 2nd trimester may increase risk (Small studies, highly controversial)

- Obstetric complications
  - Low birth weight
  - Prematurity
  - Subtle hypoxic-ischaemic CNS / neuronal damage ?

- A neuro-developmental disorder?
Brain abnormalities

- Not diagnostic for Schizophrenia
- Reduced whole brain volume
- Enlarged lateral and third ventricle
- Bilateral reduction hippocampal and amygdala volume
- Abnormal cerebral blood flow
- Aberrant connectivity between synapses and dendrites “disconnectivity syndrome”
- Dopamine theory
  - Imbalance of serotonin-dopamine in pre-frontal cortex
  - Glutamate deficiency (Dopamine imbalance)
- EEG abnormalities especially after evoked potentials
VENTRICULAR SIZE
Epidemiology: Social factors

- More people with SCZ in lower socio economic class
- Social adversity in childhood may increase risk of SCZ
- Higher rate of admission with SCZ in urban areas
- Higher rates of schizophrenia in those born in urban areas
  - Social drift versus social causation hypothesis
Epidemiology: Social factors

- Higher incidence in recent immigrants (e.g. 2nd generation African-Caribbean immigrants)
  - ? Selective migration of vulnerable individuals
  - ? Related to lower socio-economic status
  - ? Exposure to risk factors in early
  - ? Possible racial discrimination
Aetiology: **Social factors**

- Adverse life events trigger illness onset and relapse, but are not causal
- High expressed emotions can lead to relapse (critical comments, hostility, over-involvement)
- Drug misuse
  - Cannabis component cause but not sufficient alone
  - Most illicit drugs increase serotonin and dopamine and can give symptoms of psychosis short-term
Pathophysiologicl Theory

Hyperactive mesolimbic pathways

VTA → Nucleus accumbens

Responsible for positive symptoms

Hypoactive mesocortical pathways

VTA → frontal cortex

Responsible for negative symptoms

http://www.nature.com/nm/journal/v7/n10/images/nm1001-1099-F1.gif
# Symptoms

<table>
<thead>
<tr>
<th>Premorbid</th>
<th>Prodromal</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtle motor, linguistic and social dysfunction Jones et al 1994</td>
<td>Functional decline, odd ideas, eccentric interests, changes in affect, unusual speech and bizarre perceptual experiences</td>
<td>Delusions, hallucinations, thought disorder, bizarre behaviour</td>
<td>Flattening of affect and volition, amotivation, anhedonia and attentional impairment Different classifications: ICD 10 and DSM IV</td>
</tr>
</tbody>
</table>
Definition F20 Schizophrenia  ICD 10

Symptoms **lasting for at least one month** (at some time during most of the days)

**At least one** of the following:
- Thought echo/insertion/withdrawal, or thought broadcasting
- Delusions of control/passivity phenomena; delusional perception
- Hallucinatory voices giving running commentary or discussing patient between themselves (3rd person), or other types of hallucinatory voices coming from some part of the body
- Persistent delusions of other kinds that are culturally inappropriate and impossible

**Or at least two** of the following:
- Persistent hallucinations in any modality when accompanied by delusions (which may be fleeting or half-formed) without clear affective content, or when accompanied by persistent over-valued ideas
- Neologisms, breaks or interpolations in the train of thought, resulting in incoherence or irrelevant speech
- Catatonic behaviour
- "Negative" symptoms (Flattening of affect and volition, amotivation, anhedonia and attentional impairment)

**Exclusion** criteria (Differential diagnosis)
- Manic or depressive episode
- Organic brain disease or alcohol- or drug-related
### Schizophrenia Sub-types

<table>
<thead>
<tr>
<th>Sub-type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paranoid schizophrenia</td>
<td>Delusions or hallucinations prominent</td>
</tr>
<tr>
<td>Hebephrenic schizophrenia</td>
<td>Flattening, shallowness, incongruity or inappropriateness of <strong>affect</strong></td>
</tr>
<tr>
<td><strong>Behaviour</strong></td>
<td>which is aimless and disjointed</td>
</tr>
<tr>
<td><strong>Thought disorder</strong></td>
<td></td>
</tr>
<tr>
<td>Catatonic Schizophrenia</td>
<td>For a period of at least two weeks one or more of the following <strong>psychomotor disturbances</strong>:</td>
</tr>
<tr>
<td></td>
<td>(1) Stupor or mutism or (2) Excitement</td>
</tr>
<tr>
<td></td>
<td>(3) Posturing, (4) Negativism</td>
</tr>
<tr>
<td></td>
<td>(5) Rigidity or (6) Waxy flexibility</td>
</tr>
<tr>
<td></td>
<td>(7) Command automatism</td>
</tr>
<tr>
<td>Simple schizophrenia</td>
<td>Insidious but progressive <strong>negative symptoms</strong></td>
</tr>
<tr>
<td></td>
<td>No overt psychotic symptoms prior</td>
</tr>
<tr>
<td>Residual</td>
<td>Negative symptoms with clear cut positive symptoms in the past</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>Criteria for Schizophrenia but none of the above sub-types</td>
</tr>
</tbody>
</table>
Differential Diagnosis

- Organic syndromes.
- Drug induced states.
- Mood disorders with psychotic features.
- Delusional disorders.
- Personality disorders.
Prognosis

- ~22% of patients have one episode only (complete remission)
- ~32% episodic remittent
- ~8% impairment after first episode (stable deficit)
- ~38% impairment increasing after each episode
- Relapse 60-80% in 5 years
- ~10% commit suicide
- Reduced life span by 10 years
Management

- Physical
- Psychological
- Social
- Rehabilitation & Recovery
Treatment: Medication

- Medication effects (and side effects)
  - Blockage of different receptor types
  - To target positive and negative symptoms, cognitive performance and non-specific symptoms and behaviour
    - Dopamine D2 receptors (extra pyramidal side effects)
    - Muscarinic-anticholinergic receptors (Constipation, drowsiness, dry mouth, blurred vision)
    - Alpha 1 adrenergic receptors (hypotension, dizziness)
    - Histaminic receptors (weight gain, drowsiness)

- Oral or injection (short or long acting)

- Adjunctive medication
  - Anti depressants, mood stabilizers, tranquilizers
PET image showing dopamine receptor binding in the basal ganglia

Fig. 2 (a) PET image showing dopamine receptor binding in the basal ganglia; (b) measurements of D<sub>2</sub> receptor occupancy made using PET illustrate how occupancy increases with increasing antipsychotic dose. With permission of Professor P. Grasby. Part (a) appears in colour in the online version of this article (accessible via http://apt.rcpsych.org).

Woolley, J. et al.
# Treatment: Medication and other medical

<table>
<thead>
<tr>
<th>Medication</th>
<th>Examples</th>
<th>Some Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical antipsychotics</td>
<td>Haloperidol, Flupenthixol, Fluphenazine, Pipothiazine, Zuclopenthixol</td>
<td>Extra pyramidal Sexual side effects Weight gain</td>
</tr>
<tr>
<td>Atypical new generation antipsychotics</td>
<td>Risperidone, Olanzapine, Amisulpiride, Quetiapine, Aripiprazole</td>
<td>Less EPSE Metabolic syndrome Some weight gain</td>
</tr>
<tr>
<td>Treatment resistance</td>
<td>Clozapine (Blocks more selective)</td>
<td>Agranulocytosis Myocarditis Cardiomyopathy Pulmonary embolism Sexual side effects Weight gain</td>
</tr>
</tbody>
</table>

In life threatening situations or extreme treatment resistance: ECT
NICE GUIDELINES - Acute episode

- Decide antipsychotic with the service user and carer if appropriate.
- Most suitable medication - consider the relative potential of individual antipsychotics to cause extra pyramidal side effects (such as akathisia), metabolic side effects (such as weight gain), and other side effects (including unpleasant subjective experiences).
- Trial of the medication at optimum dosage for 4–6 weeks.
NICE GUIDELINES

- Offer CBT and family intervention.
- High risk of relapse if medication is stopped in 1–2 years.
- Offering depot/long-acting injectable antipsychotics- service users prefer
  -avoiding covert nonadherence
NICE GUIDELINES

Symptoms have not responded adequately to treatment:
- review the diagnosis
- adherence to antipsychotic medication
- psychological treatments
- other causes of non-response, for example co-morbid substance or alcohol misuse, concurrent use of other prescribed medication, or physical illness.
NICE GUIDELINES

- Clozapine-if symptoms have not responded adequately despite sequential use of at least two different antipsychotics, one of which should be a non-clozapine second-generation antipsychotic.
- Not responded adequately to an optimised dose of clozapine - other possible causes of non-response and measure therapeutic drug levels before offering a second antipsychotic to augment clozapine.
- An adequate trial of augmentation may need to be up to 8–10 weeks.
Treatment – cont. -
Comprehensive multi-disciplinary approach

- **Social**
  - Integrated care plan approach (person-centred)
    - Care co-ordinator, individual care plan, recovery plan
  - Occupational therapy

- **Psychological**
  - Psycho education and relapse signature
  - CBT
  - Family work
  - Art therapy

- **Rehabilitation**
  - Social skills training
  - Carer’s assessment
  - Monitor physical health
References

- WHO. report of the International Pilot Study of Schizophrenia 1973
- Jones et al British Cohort Birth study 1946 Lancet 1994
- NICE guidance Schizophrenia Updated March 2009
- McDonald C. and Murray R. Early and late environmental risk factors for schizophrenia Brain Research Reviews 200;130-7
- Cannon M. et al Evidence of Early-childhood, pan-developmental impairment specific to schizophrenifrom disorder