Psychosis, Psychopathy and Brain Imaging

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The hierarchy in psychiatric classification

- Organic psychoses – Dementia, Delirium
- Functional psychoses – Schizophrenia, Bipolar disorder
- Depression, Anxiety etc
- Behavioural disorders
- Personality disorders e.g. Anti-social personality disorder
Serial sMRI analysis for Early Differential Diagnosis

Difference Map

Serial Volume loss over 12 months \((O{'B}rien \ et \ al,\ 2001)\)

<table>
<thead>
<tr>
<th></th>
<th>Results</th>
<th>(\Delta)Vol (per yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLB</td>
<td></td>
<td>16 ml (1.4%)</td>
</tr>
<tr>
<td>AD</td>
<td></td>
<td>20 ml (2.0%)</td>
</tr>
<tr>
<td>VaD</td>
<td></td>
<td>19 ml (1.9%)</td>
</tr>
<tr>
<td>Controls</td>
<td></td>
<td>5 ml (0.5%)</td>
</tr>
</tbody>
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Schizophrenia

- Characterised by auditory hallucinations and bizarre delusions, which tend to respond to antipsychotic drugs
- Thought disorder and negative symptoms do not tend to respond
- Lifetime expectancy 1%
- Modal age at onset ~25 years
- Most patients do not work or live independently
- Only a minority are violent
Brain Imaging Diagnosis of Schizophrenia

- Effect size maps (schizophrenia patients vs. healthy controls), for females (A) and males (B), displayed in neurological convention. (C) Effect size maps for males and females combined projected on the outer cortical surface. (D) Average of the 148 images after they were spatially normalized via elastic warping to the template. 3D renderings of anatomical differences found between schizophrenia patients and healthy individuals.
- Red and yellow represent areas of relatively reduced brain tissue volume in patients. Blue areas represent relatively larger brain tissue volumes found in certain deep structures, and could, to some extent, reflect effects of medication. Volume increases were also found in the ventricles, reflecting brain tissue loss and increase of cerebrospinal fluid.
- Christos Davatzikos et al 2005 Archives “Computer-Based Detection of Complex Patterns of Brain Abnormality in Schizophrenia, Using MRI.”
Grey matter changes over time in high risk subjects with symptoms and developing schizophrenia (Job et al 2005)

GMD reductions over time in those at high risk of schizophrenia who had transient or isolated psychotic symptoms.

GMD reductions over time in those 8 people in the high-risk group who have since developed schizophrenia. Green crosshairs indicate reductions in GMD in those 8 people, excluding any change in those 10 high risk subjects who had transient / isolated psychotic symptoms, but did not develop schizophrenia.
fMRI: HR people who got schizophrenia

a. Sentence completion

b. Parametric

Whalley et al 2006
## Predictors of Illness

<table>
<thead>
<tr>
<th>Predictor</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At high genetic risk</td>
<td>21/162</td>
<td>-</td>
</tr>
<tr>
<td>Psychotic symptoms</td>
<td>25</td>
<td>100</td>
</tr>
<tr>
<td>Neuropsych: RAVLT</td>
<td>12</td>
<td>85</td>
</tr>
<tr>
<td>SIS interview</td>
<td>29</td>
<td>98</td>
</tr>
<tr>
<td>RISC questions</td>
<td>50</td>
<td>94</td>
</tr>
<tr>
<td>sMRI: L ITG Δ</td>
<td>60</td>
<td>92</td>
</tr>
<tr>
<td>fMRI: Par + Ling</td>
<td>60</td>
<td>98</td>
</tr>
<tr>
<td>Genetics: COMT</td>
<td>39</td>
<td>93</td>
</tr>
</tbody>
</table>
Putting it into practice with bioinformatics
e.g. using sMR imaging for prediction

- Patient referred by clinician
  - Retrieve baseline scans
    - Submit scans for morphometric analysis
    - If longitudinal changes detected
      - Retrieve demographically matched psychotic patient data with medium term outcome data
      - Compare with patient - prognosis indicator and treatment guide
      - Feedback diagnostic and prognosis indicators to clinician
  - Compare with patient - diagnostic indicator
  - Retrieve demographically matched non-psychotic patient data

- Baseline Structural MRI Scan
  - Store
- 12 Month follow-up structural MRI Scan
  - Store

Courtesy: John Ainsworth PsyGrid
CaliBrain

Admin UI

Consent Register

Dataset Metadata

Link Controller

Cleaned, Pseudonymised Research Data Sets

Linker

Provenance and audit

NeuroGrid

NeuroPsyGrid

MRC Medical Research Council

The University Of Edinburgh

Newcastle University

Manchester

Imperial College London

University of Cambridge

Institute of Psychiatry at the Maudsley
Anti-social personality disorder

- DSM-IV (TR) diagnostic criteria for ASPD are a pervasive disregard for the rights of others since the age of 15, as indicated by three (or more) of:
  - failure to conform with respect to lawful behaviors…;
  - deceitfulness…;
  - impulsivity or failure to plan ahead;
  - irritability and aggressiveness, e.g. repeated physical fights or assaults;
  - reckless disregard for safety of self or others;
  - consistent irresponsibility, ….failure to work or honor financial obligations;
  - lack of remorse, as indicated by being indifferent to or rationalizing having hurt, mistreated, or stolen from another.

- Psychopathy is characterized by an abnormal lack of empathy combined with strongly amoral conduct, masked by an ability to appear outwardly normal.

- Antisocial personality disorder is diagnosed via behavior and social deviance, whereas psychopathy includes affective and interpersonal personality factors.
Brain dysfunction and crime?

- Brower & Price (2001) Neuropsychiatry of frontal lobe
dysfunction in violent and criminal behaviour: a critical review. J
Neurol Neurosurg Psychiatry. 2001 Dec;71(6):720-6.....associations
between aggressive dyscontrol and brain injury, especially involving
the frontal lobes.....between frontal lobe dysfunction and increased
aggressive and antisocial behaviour. Focal orbitofrontal injury is
specifically associated with increased aggression. Deficits in frontal
executive function may increase the likelihood of future aggression,
but no study has reliably demonstrated a characteristic pattern of
frontal network dysfunction predictive of violent crime.

imaging findings in antisocial, violent, and psychopathic
individuals: a meta-analysis. Psychiatry Res. 2009 Nov
30;174(2):81-8. ..in 43 structural and functional imaging studies, and
the results show significantly reduced prefrontal structure and function
in antisocial individuals...localized to the right orbitofrontal cortex,
right anterior cingulate cortex, and left dorsolateral prefrontal cortex.
Psychopathy as a neurodevelopmental disorder?

• A characteristic course – disadvantaged early upbringing, conduct disorder, truancy, substance misuse, recidivism

• A recognisable syndrome with cognitive deficits (externalising behaviours, failure to learn from experience, social cognition deficits) and brain imaging correlates

• Better to offer treatment to criminals than punishment (cf Samuel Butler’s ‘Erewhon’)

Temporal lobe dysfunction on social cognition in ex-prisoners correlates with autistic features

Group difference for approachability versus gender judgement

Cluster of significant difference in left middle temporal gyrus
P=0.039 (corrected), KE=97, Z=3.84; controls < prisoners

Correlation between MTG activation and AQ scores
People with impulsive or antisocial traits have an exaggerated response to anticipated reward

- Buckholtz JW et al. *Nat Neurosci*. (2010) used positron emission tomography (PET) to assess the relationship between traits associated with psychopathy and dopamine release following amphetamine administration in 30 normal volunteers.
- They found a strong correlation between higher scores related to impulsive or antisocial characteristics on the psychopathic personality inventory and dopamine release.
- Additionally, functional magnetic resonance imaging of 24 individuals (18 of whom also underwent PET testing) indicated that those with such traits had a greater neurological response to the anticipation of a monetary reward.
- Individuals with substance abuse problems also have demonstrated a similar pattern of excessive reward response. A hypersensitive reward system may underlie both substance abuse and psychopathy.
Neuroimaging in court !!

• As evidence in mitigation e.g. for the ‘reality’ of auditory hallucinations
• To ‘read minds’
• To verify pain, PTSD, other medico-legal complaints
• Detection of malingering
• “No Lie fMRI”
• ‘False memories’ check
• Understanding criminal behaviour
• Predicting responsiveness to treatment, punishment
Conclusions

• Structural and functional neuro-imaging tests are amongst the strongest predictors of schizophrenia (and dementia) – almost to the point where they could be used as early diagnostic aids – prompting ethical questions about the desirability of that information at certain levels of risk and potential treatment.

• Large stores of such information, in imaging and genetic databases, is highly desirable scientifically but raises issues about consent, anonymisation and potential mis-use.

• Psychopathy and crime is associated with structural and functional abnormality of the brain but that does not necessarily explain it, let alone signify treatability or predictive value.

• Neuro-imaging evidence has already been presented in courts, and this is scientifically premature …

• …but we need to start thinking about the ethical issues…