



Brain scans could predict patient response to antipsychotic medication

Researchers from the University of Nottingham (Nottingham, UK) and King's College London (London, UK) have identified neuroimaging markers in the brain that could help predict whether or not people with psychosis will respond to antipsychotic medications.

Symptoms in approximately half of young people experiencing their first episode of a psychosis (FEP) do not improve considerably with the initial medication prescribed which increases the risk of subsequent episodes and worse outcome. The ability to identify individuals at greater risk of not responding to medication could help in the search for medication and in personalizing treatment plans.

The researchers of the current study used structural MRI to scan the brains of 126 individuals, 80 presenting with FEP and 46 healthy controls. Participants were assessed with MRI shortly after their FEP, and then again 12 weeks later, to establish whether symptoms had improved following the first treatment with antipsychotic medications.

The authors examined cortical gyrification – the extent of folding in the cerebral cortex – and a marker of how it has developed. The team observed that the individuals who did not respond to treatment had a significant reduction in gyrification across multiple brain regions, in comparison with patients who did respond and with individuals without psychosis. The reduced gyrification was particularly evident in brain areas considered important in psychosis, such as the temporal and frontal lobes. The authors reported that those who responded to treatment

were virtually indistinguishable from the healthy controls.

In the study, the researchers also investigated whether the differences could be explained by the type of psychosis diagnosis (e.g., with or without affective symptoms, i.e., depression or elated mood) and observed reduced gyrification predicted nonresponse to treatment independently of the diagnosis.

One of the researchers, Paola Dazzan (King's College London), commented "Our study provides crucial evidence of a neuroimaging marker that, if validated, could be used early in psychosis to help identify those people less likely to respond to medications. It is possible that the alterations we observed are due to differences in the way the brain has developed early on in people who do not respond to medication compared with those who do."

Dazzan added "There have been few advances in developing novel antipsychotic drugs over the past 50 years and we still face the same problems with a subgroup of people who do not respond to the drugs we currently use. We could envisage using a marker like this one to identify people who are least likely to respond to existing medications and focus our efforts on developing new medication specifically adapted to this group. In the longer term, if we were able to identify poor responders at the outset, we may be able to formulate personalized treatment plans for that individual patient."

Another researcher, Lena Palaniyappan (University of Nottingham), stated "All of us have complex and varying patterns of folding in our brains. For the first time we

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"It is possible that people with specific patterns of brain structure respond better to treatments other than antipsychotics that are currently in use."



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are showing that the measurement of these variations could potentially guide us in treating psychosis. It is possible that people with specific patterns of brain structure respond better to treatments other than antipsychotics that are currently in use.

Clearly, the time is ripe for us to focus on utilizing neuroimaging to guide treatment decisions.”

Sources: Palaniyappan L, Marques T, Taylor H *et al*. Cortical folding defects as markers of poor treatment response in first-episode

psychosis. *JAMA Psychiatry* doi:10.1001/jamapsychiatry.2013.203 (2013) (Epub ahead of print); King's College London press release. Brain scans could predict response to antipsychotic medication: www.kcl.ac.uk/iop/news/records/2013/august/brain-scans-antipsychotic-medication.aspx

New study suggests a way to predict the development of post-traumatic stress disorder

Researchers from the Boston Children's Hospital (MA, USA) have recently published findings that suggest that while most children cannot be shielded from emotionally traumatic events, clinicians can target those who are most vulnerable to developing post-traumatic stress disorder (PTSD).

The team analyzed data of 6483 teen-parent pairs from a survey of the prevalence and correlates of mental disorders in the USA called the National Comorbidity Replication.

The authors observed that 61% of the teens included had been exposed to at least one potentially traumatic event in their lifetime, with 19% having witnessed three or more events, including natural disasters, injuries and interpersonal violence (physical abuse, rape or witnessing domestic violence).

Identified risk factors for trauma exposure included: lack of both biological parents being at home, and pre-existing mental disorders especially ADHD and oppositional defiant disorder. The authors reported that the risk factors most associated with PTSD are female gender, events involving interpersonal violence, and underlying anxiety and mood disorders.

“...while most children cannot be shielded from emotionally traumatic events, clinicians can target those who are most vulnerable to developing post-traumatic stress disorder.”

The team also assessed risk factors associated with a lack of recovery of PTSD or risk factors associated with 'chronicity',

including underlying bipolar disorder, exposure to an additional traumatic event, living in poverty and being native to the USA.

The findings led the authors to speculate that interventions designed to prevent the development of PTSD in teens exposed to potentially traumatic experiences should be targeted at victims of interpersonal violence with pre-existing fear and distress disorders, whereas interventions to reduce the chronicity of PTSD should attempt to prevent secondary potentially traumatic experiences.

Source: McLaughlin K, Koenen K, Hill E *et al*. trauma exposure and posttraumatic stress disorder in a national sample of adolescents. *J. Am. Acad. Child Adolesc. Psychiatry* 52(8), 815.e14–830.e14 (2013).

Is cognitive impairment still a global problem?

A recent study carried out by researchers at the National Institute of Mental Health (MA, USA) examined the extent to which the cognitive deficits associated with schizophrenia are generalized across domains, potential moderator variables and whether the pattern of cognitive findings reported in schizophrenia has remained consistent over time, and across cultural and geographic variation.

The authors identified relevant publications from 2006 to 2011 through keyword searches, including studies that compared the cognitive performance of adult schizophrenia patients and healthy controls; based schizophrenia diagnoses on contemporary diagnostic criteria, reported

information sufficient to permit effect size calculation, were reported in English and reported data for neuropsychological tests falling into at least three distinct cognitive domains. A total of 100 studies were identified, and effect sizes (Hedge's *g*) were calculated for each cognitive variable.

The authors reported that patients with schizophrenia scored significantly lower than controls across all cognitive tests and domains (grand mean effect size, *g*: 1.03). Individuals demonstrated larger impairments in the domains of processing speed (*g*: -1.25) and episodic memory (*g*: -1.23). The authors also demonstrated few inconsistencies when grouped by geographic region.

The results of the study extend from 1980 to 2006 of a substantial, generalized cognitive impairment in schizophrenia, demonstrating that this finding has remained robust over time despite changes in assessment instruments and alterations in diagnostic criteria, and that it manifests similarly in different regions of the world despite linguistic and cultural differences.

Source: Schaefer J, Giangrande E, Weinberger D, Dickinson D. The global cognitive impairment in schizophrenia: consistent over decades and around the world. *Schizophr. Res.* doi:10.1016/j.schres.2013.07.009 (2013) (Epub ahead of print).

Tracking tactics: can a digital tablet help with medication adherence in schizophrenia?

Researchers from New York State Psychiatric Institute (NY, USA) have conducted a study that could help improve medication adherence in patients suffering from bipolar disorder or schizophrenia through the ingestion of a digital tablet alongside their normal medication.

“Patients were given a digital tablet, to ingest alongside their regularly prescribed medication, consisting of an ingestion sensor that was embedded in a tablet containing a pharmacologically inert substance.”

In a 4-week observational study, 12 adults with bipolar disorder and 16 adults with schizophrenia on a stable regimen of oral medication utilized a digital health feedback system (DHFS) to assess medication adherence. Patients were given a digital tablet, to ingest alongside their regularly prescribed medication, consisting of an ingestion sensor that was embedded in a tablet containing a pharmacologically inert

substance. The formulation of the digital tablet allowed ingestion sensor separation and activation by stomach fluids after ingestion, followed by communication of a unique identifying signal from the ingestion sensor to an adhesive sensor worn on the torso that automatically logged the date and time of each digital tablet ingestion. The primary objective of the study was to compare the accuracy of DHFS in confirming digital tablet ingestion versus a method of directly observed ingestion.

A total of 96% patients completed the study. The mean adherence rate to the DHFS was 74%, which was 94% accurate in detecting ingestion of medication. The authors reported that 67% of doses were taken within 2 h of the prescribed dosing time. The most common adverse event was minor skin irritation, which occurred at the site of the wearable sensor in five subjects (18%), which did not lead to early discontinuation and no adverse events occurred due to the ingestion sensor. The authors reported that no subjects developed worsening of psychosis attributable to use of the DHFS.

The authors concluded that the DHFS provided a novel means of confirming medication ingestion and tracking selected physiologic parameters, and that it was generally well tolerated by patients.

“...tools that can assist patients and caregivers to play a more informed role in their own healthcare offer an opportunity to improve adherence.”

The authors commented that since a large proportion of nonadherence is not wilful conscious refusal to take medication, tools that can assist patients and caregivers to play a more informed role in their own healthcare offer an opportunity to improve adherence.

Source: Kane J, Perlis R, Dicarlo L, Au-Yeung K, Duong J, Petrides G. First experience with a wireless system incorporating physiologic assessments and direct confirmation of digital tablet ingestions in ambulatory patients with schizophrenia or bipolar disorder. *J. Clin. Psychiatry* doi:10.4088/JCP.12m08222 (2013) (Epub ahead of print).

First episode psychosis: addressing multiple substance abuse should be top priority

Researchers from the Queensland University of Technology (Brisbane, Australia) have recently published a study suggesting that addressing multiple substance-use disorder (SUD) should be a key aim for treatment in people with a first episode psychosis (FEP) who report substance use.

In the study, researchers reviewed the medical files of 432 FEP patients using a standardized file audit for baseline comorbid substance-use disorder. Predictors of reduction/cessation of substance use at follow-up were examined using logistic regression analyses.

The researchers predicted a reduction/cessation of substance use by baseline measures reflecting higher education, employment, accommodation with others, cannabis-use disorder only (rather than poly-SUDs), better global functioning and better premorbid social and occupational functioning, later age at onset of psychosis and a diagnosis of nonaffective psychosis through univariate analyses. In multivariate analysis, cannabis-use disorder alone, and better premorbid social and occupational functioning remained significant predictors.

Although noting that further longitudinal research on recovery from SUD and FEP is needed to disentangle directions of influence and identify key targets for intervention, the authors concluded that addressing SUDs, and social and occupational goals in people with FEP may offer opportunities to prevent SUDs becoming more severe or entrenched.

Source: Rebgetz S, Conus P, Hides L *et al.* Predictors of substance use reduction in an epidemiological first-episode psychosis cohort. *Early Interv. Psychiatry* doi:10.1111/eip.12067 (2013) (Epub ahead of print).

Highly familial: offspring of depressed parents more likely to develop psychiatric disorders

A recent study assessing whether offspring of parents with bipolar disorder (BD) would be at increased risk for BD and other comorbid disorders common to BD, such as anxiety and substance use, relative to the offspring of parents with major depressive disorder (MDD) by researchers at the New York State Psychiatric Institute (NY, USA) suggests that adverse experiences in childhood are associated with an increased risk for psychopathology in the offspring of people with BD or MDD. The researchers also examined whether the offspring of parents with BD versus those with MDD were at greater risk for externalizing disorders (i.e., conduct disorder, ADHD or antisocial personality disorder).

Researchers studied parents with mood disorders and their offspring. The team administered the Structured Clinical Interview for DSM-IV Axis I Disorders to adult offspring in order to establish

the presence of psychopathology. Offspring aged 10–18 years were assessed using the School Aged Schedule for Affective Disorders and Schizophrenia, Present and Lifetime version. Additionally, parents of children under the age of 10 years completed the Child Behavioral Checklist.

The authors observed no difference in hazard of mood disorders in the offspring of parents with BD compared with the offspring of parents with MDD. However, the researchers noted a number of other parent and offspring characteristics that increased the risk of mood, anxiety, externalizing and substance-use disorders in the offspring, including self-reported childhood abuse in the parent or offspring, offspring impulsive aggression and the age at onset of parental mood disorder.

Discussing their results, the authors suggest that mood disorders are highly

familial, a finding that appears independent of whether the parent's condition is unipolar or bipolar, which suggests considerable overlap in the heritability of MDD and BD. The authors postulated that although parental characteristics had a limited influence on the risk of offspring psychopathology, reported childhood adversity, be it in the parent or child, is a foreshadowing of negative outcomes. The reported risk factors extend previous findings, and are consistent with diathesis–stress conceptualizations.

Source: Oquendo M, Ellis S, Chesin M *et al*. Familial transmission of parental mood disorders: unipolar and bipolar disorders in offspring. *Bipolar Disord*. doi:10.1111/bdi.12107 (2013) (Epub ahead of print).

– All stories written by Dominic Chamberlain

About the News

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