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Brain scans could predict response to antipsychotic medication

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

In approximately half of young people experiencing their first episode of a psychosis (FEP), the symptoms do not improve considerably with the initial medication prescribed, increasing the risk of subsequent episodes and worse outcome. Identifying individuals at greatest risk of not responding to existing medications could help in the search for improved medications, and may eventually help clinicians personalize treatment plans.

In a study published today in *JAMA Psychiatry*, researchers used structural Magnetic Resonance Imaging (MRI) to scan the brains of 126 individuals – 80 presenting with FEP, and 46 healthy controls. Participants had an MRI scan shortly after their FEP, and another assessment 12 weeks later, to establish whether symptoms had improved following the first treatment with antipsychotic medications.

The researchers examined a particular feature of the brain called "cortical gyrification" - the extent of folding of the cerebral cortex and a marker of how it has developed. They found that the individuals who did not respond to treatment already had a significant reduction in gyrification across multiple brain regions, compared to patients who did respond and to individuals without psychosis. This reduced gyrification

was particularly present in brain areas considered important in psychosis, such as the temporal and frontal lobes. Those who responded to treatment were virtually indistinguishable from the healthy controls.

The researchers also investigated whether the differences could be explained by the type of diagnosis of psychosis (eg. with or without affective symptoms, such as depression or elated mood). They found that reduced gyrification predicted non-response to treatment independently of the diagnosis.

Dr Paola Dazzan from King's College London's Institute of Psychiatry, and senior author of the paper, says: "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 to those who do."

She continues:"There have been few advances in developing novel anti-psychotic drugs over the past 50 years and we still face the same problems with a sub-group 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."

Dr Lena Palaniyappan from the University of Nottingham adds: "All of us have complex and varying patterns of folding in our brains. For the first time we 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 utilising neuroimaging to guide treatment decisions."

Psychosis is a term used to indicate mental health disorders that present with symptoms like hallucinations (such as hearing voices) or delusions (unshakeable beliefs based on the person's altered perception of reality, which may not correspond to the way others see the world). Psychotic episodes are present in conditions such as schizophrenia and bipolar disorder.

Approximately 1 in 100 people in England have at least one episode of psychosis throughout their lives. In most cases, psychosis develops during late adolescence (15 or above) or adulthood. Treatment involves a combination of antipsychotic medication, psychological therapies and social support. Many people with psychosis go on to lead ordinary lives and for about 60% of people, the symptoms disappear within 12 months from onset. However, for others, treatment is less straightforward and many do not respond to the initial antipsychotic treatment prescribed by their doctor. Early response to antipsychotic medication is known to be associated with better outcome and fewer subsequent episodes, and intervening early with effective treatments is therefore important.

More information: Palaniyappan, L. et al. 'Cortical folding defects as markers of poor treatment response in first episode psychosis' *JAMA Psychiatry*, 2013.

Provided by King's College London