Combination therapy might be beneficial in schizophrenia

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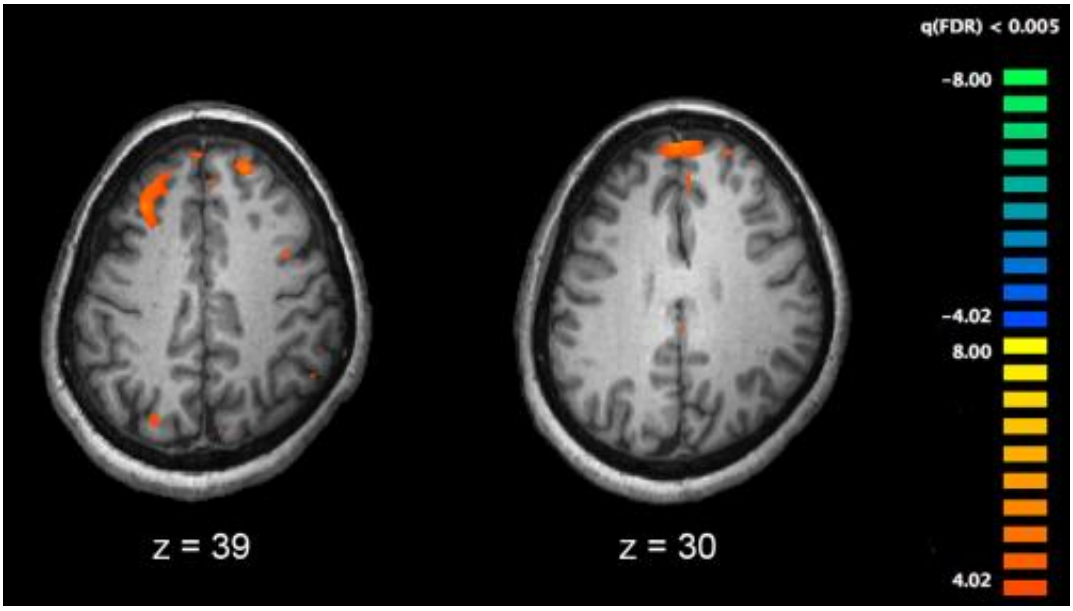

Functional magnetic resonance imaging (fMRI) and other brain imaging technologies allow for the study of differences in brain activity in people diagnosed with schizophrenia. The image shows two levels of the brain, with areas that were more active in healthy controls than in schizophrenia patients shown in orange, during an fMRI study of working memory. Credit: Kim J, Matthews NL, Park S./PLoS One.

Combining certain types of two antipsychotic agents in the maintenance treatment of schizophrenia is associated with a lower risk of relapse than using monotherapy. This is suggested in a paper published by researchers at Karolinska Institutet in the journal *JAMA Psychiatry*. The current

treatment guidelines should modify their categorical recommendations discouraging all antipsychotic polypharmacy, according to the researchers.

The effectiveness of antipsychotic combination therapy in schizophrenia relapse prevention is controversial, and use of multiple agents is generally believed to impair physical well-being. But the evidence for this is weak and antipsychotic polypharmacy is widely used.

Now researchers at Karolinska Institutet in Sweden have conducted a large registry based study to see if there is any difference in the risk of relapse in schizophrenia when patients use antipsychotic polypharmacy compared to monotherapy.

The study was based on more than 62,000 patients; all persons with schizophrenia treated in the inpatient setting during 1972-2014 in Finland. The researchers then followed the patients to see to what extent they were rehospitalised for psychiatric care, which was used as a marker for relapse. The median follow-up time was 14.1 years and to avoid bias each patient was used as his or her own control (so called within-individual analysis).

The results show that antipsychotic polypharmacy in general was associated with a slightly lower risk of psychiatric rehospitalisation than monotherapy. They do however not indicate that all types of polypharmacy are beneficial. Combining aripiprazole with clozapine was associated with the best outcome, with a 14-23 per cent lower risk of rehospitalisation compared to clozapine alone; which was the monotherapy associated with the best outcomes.

Current treatment guidelines state that antipsychotic monotherapy should be preferred and polypharmacy should be avoided if possible. This study should change that view, according to first author of the study, Jari

Tiihonen, specialist doctor and professor at Karolinska Institutet's Department of Clinical Neuroscience.

"Our results indicate that the current treatment guidelines should tone down their categorical recommendations discouraging all antipsychotic polypharmacy. The evidence of superiority of polypharmacy might be sparse, and should be replicated in other countries, but there is no evidence at all on superiority of monotherapy over polypharmacy in the maintenance treatment of schizophrenia," says Jari Tiihonen.

More information: Jari Tiihonen et al. Association of Antipsychotic Polypharmacy vs Monotherapy With Psychiatric Rehospitalization Among Adults With Schizophrenia, *JAMA Psychiatry* (2019). DOI: 10.1001/jamapsychiatry.2018.4320

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