European College for Neuropsychopharmacology

Scientists discover structure of adult brain – previously thought to be fixed - is changed by treatment

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Not peer reviewed/experimental study/people*

Scientists believe that the structure of the adult brain is generally rigid and incapable of rapid changes; now new work has shown that this is not true. German researchers have shown that in-patient treatment for depression can lead to an increase in brain connectivity, and those patients who respond well to this treatment show a greater increase in connectivity than those who don't.

Presenting the work at the European College for Neuropsychopharmacology Congress in Vienna, lead researcher, Professor Jonathan Repple said:

"This means that the brain structure of patients with serious clinical depression is not as fixed as we thought, and we can improve brain structure within a short time frame, around 6 weeks. We found that if this treatment leads to an increase in brain connectivity, it is also effective in tackling depression symptoms. This gives hope to patients who believe nothing can change and they have to live with a disease forever, because it is "set in stone" in their brain".

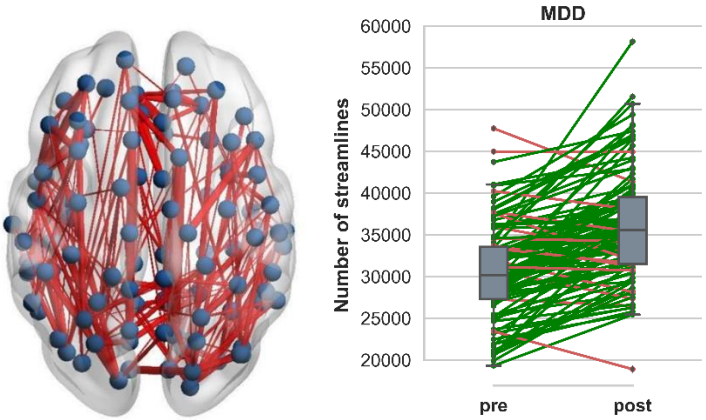
The researchers, working at the University of Muenster in Germany, studied 109 patients with serious depression (Major Depressive Disorder) and compared them with 55 healthy controls. Their brains were scanned using an MRI scanner which had been set up to identify which parts of the brain were communicating with other parts, determining the level of connections within the brain. The patients were then treated for depression, some with electroconvulsive therapy (ECT), some with psychological therapy or medication, some with a combination of all therapies. After treatment they were then rescanned and the number of connections recounted. They were also retested for symptoms of depression.

Professor Repple (now Professor of Predictive Psychiatry at the University of Frankfurt) said:

"*We found that treatment for depression changed the infrastructure of the brain, which goes against previous expectations. Treated patients showed a greater number of connections than they had shown before treatment. Moreover, those who showed the most response to treatment had developed a greater the number of new connections than those who showed little response. A second scan showing that there are no time effects in healthy controls supports our findings that we see something that is related to the disease and more importantly the treatment of this disease*.

We found these changes took place over a period of only around 6 weeks, we were surprised at the speed of response. We don't have an explanation as to how these

changes take place, or why they should happen with such different forms of treatment".



Illustrations: Left, representative map of the affected connections in the brain. The number of these connections increased after treatment. Right, graph showing the increase in the number of connections pre- and post-treatment for clinical depression (credit, Jonathan Repple)

Commenting, Dr Eric Ruhe, Rabdoud University Medical Center, Nijmegen, the Netherlands said:

"This is a very interesting and difficult to perform study in which the authors repeated MRI-scans to reveal changes in structural connectivity over time in patients treated for depression.

The results align very much with our current belief that the brain has much more flexibility in adaptation over (even short) time than was previously thought. Indeed a major idea of what treatment of depression (and other psychiatric illnesses) invoke is plastic changes over time. This has been proposed as a common mechanism for antidepressants, psychotherapy and electroconvulsive therapy. However, the amount of research to elucidate what changes are necessary or specific for response to treatment or remission of the depression is limited. Moreover, the next question is whether different treatments have the possibility to specifically change targeted brain networks or vice versa whether we can use the disturbances in brain-networks as measured in the present study to choose which therapy will be helpful.

The fact that the observed changes over time could not be associated with a form of treatment is a pity, but as the authors themselves suggest a topic for further research. First these results should be replicated in independent samples which hopefully is going to happen soon. Second further elaboration on this approach would be daunting and should be supported firmly as this work might help to bridge the current gap between neuroscience and evidence based patient care".

This is an independent comment, Dr Ruhe was not involved in this study.

This work is presented at the 35th European College of Neuropsychopharmacology annual conference, which takes place in Vienna and online from 15-18 October, see

https://www.ecnp.eu/Congress2022/ECNPcongress. Up to 5000 delegates are expected to attend. The ECNP is Europe's main organisation working in applied neuroscience.

*Press release labelling system for journalists, see https://tinyurl.com/3kww75hy for details

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Notes for Editors

Abstract

P.0979 Effective in-patient treatment is associated with an increase in structural brain connectivity in severely depressed patients

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Background: Altered brain structural connectivity has been implicated in the pathophysiology of major depressive disorder (MDD). However, little is known whether these changes are stable over time and therefore might represent a biological predisposition, or whether these are state markers of current disease severity and change dynamically with effective treatment.

Human white matter network ("connectome") analysis via network science can be used to examine the link between altered brain connectivity and MDD treatment in a longitudinal design. To this end, T1-weighted magnetic resonance imaging (MRI) and diffusion-weighted imaging (DWI) were applied twice in MDD patients undergoing in-patient treatment (baseline + 6-weeks follow up).

This study investigates (1) whether alterations in global network organization is impaired in patients with MDD, (2) whether in-patient treatment including pharmacological, psychological and neurostimulation interventions is linked to changes in structural brain connectivity and (3) whether changes relate to changes in depression symptomatology. We hypothesize impaired structural connectivity that increases after effective inpatients treatment.

Methods: One hundred seventy-eight subjects – 109 subjects diagnosed with current MDD and 55 healthy controls (HC) - participated in the present study. Fifty-six depressed patients were treated with electroconvulsive therapy (ECT) and 67 received in-patient treatment without ECT. Here, grey matter T1-weighted MRI was used to define nodes and DWI-based tractography to define the connections – or edges – between the nodes creating a structural connectome.

Based on the resulting connectivity matrices, network-based-statistic (NBS) was employed to identify subnetworks to investigate (1) differences in connectivity

strength between MDD and HC at baseline, (2) that change over time in MDD patients undergoing multimodal treatment, and (3) that show an association between changes over time in connectivity and changes over time in depressions symptom severity measured with the Hamilton Depression Ratings Scale.

Results: There was a significant time (pre vs. post)-by-group (MDD vs. HC) interaction ($p_{FWE} < 0.05$; NBS t-thresholds = 1.5, component sizes: 404 edges), which was driven by the following pattern of results: MDD patients showed reduced connectivity strength at baseline compared to healthy controls ($p_{FWE} < 0.05$; NBS t-thresholds = 1.5, component sizes: 486 edges). MDD patients showed a significant increase of connectivity strength over time ($p_{FWE} < 0.05$; NBS t-thresholds = 1.5, component sizes: 225 edges), an effect that was not detected in HC.

Moreover, a significant subnetwork, where an increase of connectivity strength was associated with a decrease in depression symptom severity, was identified in MDD patients ($p_{FWE} < 0.05$; NBS t-thresholds = 1.5, component sizes: 304 edges). These effects were independent of treatment choice, suggesting a nonspecific effect that cannot be traced back to ECT.

Conclusion: We demonstrate an alleviation of structural brain disconnectivity in MDD patients after successful antidepressive treatment, which is most prominent in those patients that show the greatest reduction in depressive symptomatology. This pattern of results suggests neuroplastic mechanisms involved in the successful treatment of depression and should be investigated as a potential treatment target in future studies.

References

No conflict of interest