Press Release: European College of Neuropsychopharmacology conference

Depression history written in the reactions of the brain

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Type of research: peer reviewed/observational study/people

Scientists have found that the more severely patients have been hit by depression across their lifespan, the less they react emotionally to negative faces during current depression. The researchers are now working to understand if this means that serious depression changes the way the brain reacts to emotion over time, or if people with stronger emotional responses to negative faces are less vulnerable to long-term depression. Either may have implications for future patient care. This work is presented at the ECNP conference in Lisbon, after recent publication.

Depression is a major mental health burden, but the direct effect on brain activity is only just beginning to be understood. The brains of depressed patients normally show greater activity in certain areas than those of non-depressed healthy people. Now a group of German scientists have discovered that, while still greater than in non-depressed people, brain activity of patients who are currently depressed and have suffered with prolonged and severe depression is lower than that of patients with less severe and prolonged depression. No specific relation is found between brain activity and previous depression in patients where the depression is no longer present.

The researchers worked with 201 seriously depressed patients and 161 patients who had come out of the period of depression (remitted). Each patient was questioned about the duration and extent of their previous depression, which allowed the researchers to build a tailored depression history. Then during the study, each patient was placed in an MRI scanner, and brain changes were monitored while the patients viewed a series of unsettling images – fearful or angry faces.

Lead researcher Hannah Lemke (*University of Münster)* said:

"We saw that the unsettling images of negative faces caused activity in certain areas of the brain, mostly the amygdala, parahippocampus PHG and Insula, which are areas where emotions are processed. However the extent of the brain activity was different according to the severity and duration of the depression the patient had already suffered. Those patients where the depression had remitted showed a certain level of activity, but those patients where the depression was current exhibited a reduced activity in these brain areas. This differed for each patient, but in general the more severe the depression history, the less responsive their brains were to the photographs".

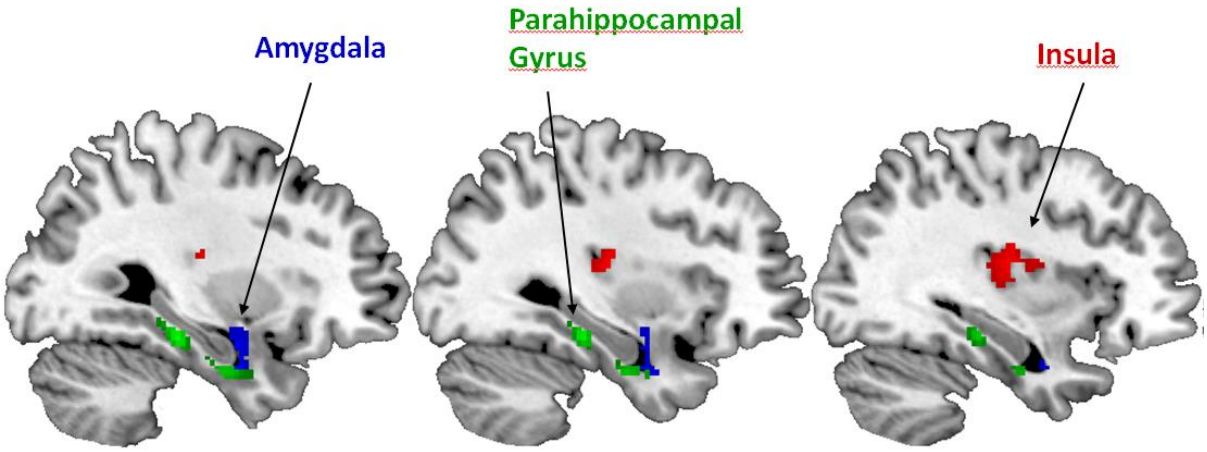

Illustration: MRI scans showing activity in relevant brain areas (Credit: Hannah Lemke)

Hannah Lemke continued:

"In those patients where the depression had remitted the brain response was not related to the previous depression history, which may indicate the importance of disease remission to brain health.

Interpreting this needs more work. It's tempting to think that reduced brain activity is a way the brain copes emotionally with long-term depression, and that maybe the first episode of depression was qualitatively different to the current episode. It seems that underlying brain activity related to the emotional information of serious depression may change over the course of the disease.

But we also need to consider alternative explanations, for example, it may be that people who process emotions in a certain way are more vulnerable to long-term depression. In either case, we are looking at different faces of depression, with different effects and different outcomes. And perhaps future treatment will need to take this into consideration.

This is a big study, so we can be fairly confident in what we have found. Nevertheless, we now need longitudinal studies, where individual depressed patients are followed over a period of years to see how their brain response changes".

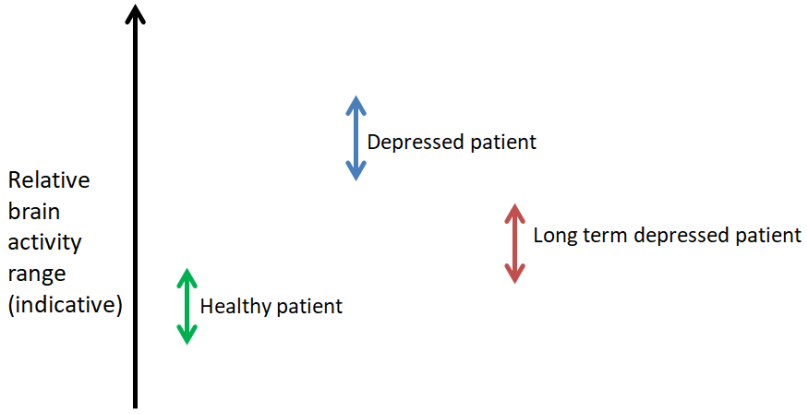

Diagram: relative brain activity – indicative only

Commenting, Dr Carmine Pariante, Professor of Biological Psychiatry at King's College London, said:

"This study confirms how profoundly the brain of patients is affected by major depression. A number of mechanisms can explain these findings, all relevant to the further understanding of depression, as this biological signature could be either a risk factor for, or a consequence of, more severe and chronic depression. Moreover, future studies should clarify if these effects are driven more by the maximum severity of depression, the chronicity of depression, or the exposure to antidepressants; and clarify the molecular mechanisms underpinning these functional changes".

The 34th ECNP Annual conference takes place in Lisbon and online from 2-5 October, see https://www.ecnp.eu/Congress2021/ECNPcongress . The European College of Neuropsychopharmacology is Europe's main organisation working in applied neuroscience.

This press release includes work which appeared in *Biological Psychiatry:CNNI*, June 2021. see *https://www.sciencedirect.com/science/article/abs/pii/S2451902221001488?via%3Dihub*

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Notes for Editors

Conference abstract: P.0365 Associations between abnormal brain function during emotion processing and lifetime disease course in major depressive disorder

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Introduction: Brain functional alterations in the amygdala, parahippocampal gyrus (PHG) and insula during emotional processing are frequently reported in patients with major depressive disorder (MDD) [1]. However, evidence for functional correlates of emotion processing and MDD trajectories is sparse. Early age of onset was associated with increased amygdala responsiveness during processing of sad face stimuli [2]. In a two-year prospective study, a decrease of activation in the insula during processing of happy faces has been found following remission [3], and in another prospective study, symptom improvement was associated with increased amygdala and hippocampus activation during positive and negative

word encoding [4]. However, no study has investigated lifetime disease characteristics and brain functional correlates of negative emotion processing in MDD. Thus, the present study aimed to investigate associations between lifetime disease course and brain function during a negative emotional face processing task in a large and well-characterized sample of MDD patients. We further investigated effects of remission status on the relationship between brain responsiveness and MDD trajectories.

Methods: In N=362 MDD patients (MDDacute: N=201, mean age: 36.05 years, SD=13.50, 66.17% female; MDDremitted: N=161, mean age: 35.75 years, SD=12.58, 73.91% female) brain activation was investigated during a negative emotional face processing task at a 3-Tesla MRI scanner. Patients' lifetime disease course was characterized by two components scores named Duration of Illness and Hospitalization as previously established [5]. First, general activation of the amygdala, PHG and insula during processing of fearful faces were examined. Second, in multiple regression analyses, brain responsiveness in the amygdala, PHG and insula were associated with both components of disease course. All analyses were controlled for age, sex, antidepressant medication intake and current depression severity.

Results: The face processing task could elicit strong bilateral activations in the amygdala, PHG and insula as expected (all p>015). In the MDDremitted sample the insula effect was only found in the right hemisphere. The component Hospitalization revealed negative associations with the right amygdala, right PHG and right insula (all p<.018) in the MDDacute sample. No significant assocations between Duration of Illness and brain responsiveness in the MDDacute sample emerged. Furthermore, remitted patients did not show any associations between disease course and brain functional alterations.

Conclusion: Processing of negative emotional faces elicited strong activations in the limbic system, more precisely the amygdala, PHG and insula. Higher lifetime hospitalization scores were associated with decreased brain activation in the face processing network comprising the amygdala, PHG and insula during processing of negative face stimuli in patients with acute depression, whereas no such correlations were found in the remitted MDD sample. Our study provides first evidence of brain functional correlates of emotion processing and lifetime disease course during acute depressive episodes. These findings can give new implications for treatment of patients with more severe disease course and more frequent and longer hospitalizations.References

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No conflict of interest