European College of Neuropsychopharmacology (ECNP) – press release

Not so similar after all: depression, but not anxiety, linked with inflammation and metabolic changes

Embargo until: 00.05 CEST (Vienna) Tuesday 15th September 2020

Type of study: not peer-reviewed/observational study/people

Anxiety and depression are often linked and assumed to be closely related, but now research has shown for the first time that depression and anxiety have different biochemical associations with inflammation and lipid (fat) metabolism. This indicates that different, more targeted treatments may be possible to treat anxiety and depression. This work is presented at the ECNP Congress.

Depression and anxiety share several symptoms, have common risk factors, and often they are treated with the same drugs. Over 50% of patients with depression (Major Depressive Disorder) also have a history of anxiety. Nevertheless, psychiatrists classify them as different disorders, although until now it has been difficult to identify biochemical evidence for this.

Scientists from the Netherlands Study of Anxiety and Depression (NESDA) used blood samples from 304 people with current depression, 548 with anxiety, 531 with both depression and anxiety, 807 with remitted disorders, and 634 healthy controls. Using a nuclear magnetic resonance detector they tested for associations between 40 metabolites found in blood and symptoms of depression, and symptoms of anxiety (such as panic, pathological worry, etc.).

"*We have two main findings*", said Hilde de Kluiver, of Amsterdam UMC, "*firstly we found that the depressed group showed evidence of greater inflammation which was not seen in the anxious group. We also found that the depressed group had very different amounts and types of lipid in their blood. For example, depressed people had high levels of triglycerides, but lower levels of omega-3-fatty acids. In contrast, those people who had anxiety disorder had a lipid composition very similar to the healthy control group.*

We also found that those metabolites associated with depression were also associated with the severity of the depression: in other words, if you had more of a lipid associated with depression, your depression tended to be worse".

In recent years, depression has been associated with disturbances in the body's immune system and metabolism, and previous researchers have shown that depressed people tend to have different biochemical markers to those of healthy people. However, no such analysis of such a wide set of markers has been undertaken for anxiety. This work shows, for the first time, that the immune system and lipid metabolism changes in depressed people but not in anxious people.

The researchers hope that these findings will lead to better treatments. "*Our group is now planning to test whether depressed people with altered inflammation might respond to treatment with anti-inflammatory drugs*", said Hilde de Kluiver.

Commenting, Dr Philippe Nuss (Hôpital Saint-Antoine, Paris) said:

"*This is an important finding for several reasons. First it identifies easy-to-measure blood biomarkers characterising a subtype of depression whose underlying mechanism is specific and will probably need an appropriate treatment. It also emphasises the fact that mental disorders should be seen in a whole body perspective where major regulatory physiological systems such as immunity and lipid metabolism are involved. In addition, both immunity and lipids are strongly involved in brain metabolism. It is thus not surprising that Ms de Kluiver's work shows that the severity of depression is greater in patients with more impaired biomarkers*".

Dr Nuss was not involved in this work, this is an independent comment.

ENDS

Notes for Editors

European College of Neuropsychopharmacology (ECNP)

The ECNP is an independent scientific association dedicated to the science and treatment of disorders of the brain. It is the largest non-institutional supporter of applied and translational neuroscience research and education in Europe. Website: www.ecnp.eu

The 33rd annual ECNP Congress – ECNP Virtual - takes place from 12th to 15th September. It is Europe's premier scientific meeting for disease-oriented brain research. In 2020 it is a virtual congress. The regular congress annually attracting up to 6,000 neuroscientists, psychiatrists, neurologists and psychologists from around the world. Congress website: https://www.ecnp.eu/Congress2020 The 2021 congress is scheduled to take place in Lisbon next September.

Abstract P.721 Metabolomic profiles discriminating anxiety from depression

H. De Kluiver[1], R. Jansen[1], Y. Milaneschi[1], M. Bot[1], E.J. Giltay[2], R. Schoevers[3], B.W.J.H. Penninx[1]

[1]Amsterdam UMC- Vrije Universiteit Amsterdam, Psychiatry, Amsterdam, The Netherlands ; [2]Leiden University Medical Center-Leiden University, Psychiatry, Leiden, The Netherlands ; [3]University Medical Center Groningen- University of Groningen, Psychiatry, Groningen, The Netherlands

Background: Depression has been associated with immuno-metabolic disturbances, such as alterations in metabolomic markers [1]. Depressive and anxiety disorders are often comorbid diagnoses and these disorders are suggested to share etiological mechanisms [2,3]. We therefore investigated whether metabolomic alterations related to depression are also seen in anxiety disorders, and which clinical characteristics of these disorders are related to metabolomic alterations.

Methods:

Data were from the Netherlands Study of Depression and Anxiety (NESDA), including 304 subjects with only current depressive disorders, 548 with only anxiety disorders, 531 with comorbid depressive and anxiety disorders, 897 with remitted disorders, and 634 healthy controls. Forty metabolites from a proton nuclear magnetic resonance metabolomics panel were analysed, comprising measures of lipids, amino acids and inflammation. First, we examined differences in the forty metabolomic markers across groups using ANCOVAs, and corrected for multiple testing based on the Benjamini-Hochberg procedure. For each marker that differed significantly across groups at a False Discovery Rate (FDR) <.05, a linear regression

analysis was run in order to examine which of the patient groups (remitted, current purely anxious, current purely depressed and current comorbid groups) exactly differed from controls. Second, we assessed whether severity measures of depression (i.e., severity of depressive symptoms) and anxiety (i.e., severity of anxious arousal symptoms as common in panic and generalized anxiety disorders, phobic avoidance and pathological worry) were related to the forty tested metabolomic markers by performing a linear regression for each metabolite-characteristic combination and accordingly adjusting for multiple testing.

Results:

Of the forty examined markers, thirteen differed significantly across groups. As compared to healthy controls, most alterations (n=7) in metabolomic markers were found in the group with only a depression, reflecting an inflammatory and an atherogenic-lipoprotein-related (e.g. glycoprotein acetyls: Cohen's d=0.12, $p=1.58*10^{-3}$; apolipoprotein B: Cohen's d=0.08, $p=3.45*10^{-2}$ and VLDL cholesterol: Cohen's d=0.08, $p=3.91*10^{-2}$) profile. The comorbid group showed a somewhat attenuated but similar pattern of deviations (n=3). No metabolomic alterations were found in the groups with only anxiety disorders and remitted disorders. Significant associations (FDR<.05) with clinical characteristics were found, with a stronger signal for depression severity than for the anxiety severity measures. The majority of metabolites associated with the presence of depression diagnosis were also associated with depression severity. Only higher levels glycoprotein acetyls were associated with both the anxious arousal and the phobic severity measure and no markers were found to be associated with pathological worry.

Conclusion:

While substantial biological similarities between anxiety and depression have been seen, this study suggests that altered inflammatory and atherogenic-lipoprotein-related metabolomic profiles may primarily be associated with the current depression presence and severity, and not with anxiety presence nor severity. This study confirms the involvement of immuno-metabolic disturbances in depression. In future research, we will further investigate whether metabolomic markers are differentially linked to specific symptoms of depression. This study confirms the involvement of immuno-metabolic disturbances in depression. In future research, we will further investigate whether metabolomic markers are differentially linked to specific symptoms of depression.

References

[1] Bot M., Milaneschi Y., Al-Shehri T., Amin N., Garmaeva S., Onderwater G.L.J., et al., 2020. Metabolomics Profile in Depression: A Pooled Analysis of 230 Metabolic Markers in 5283 Cases With Depression and 10,145 Controls. Biol Psychiatry 87(5), 409-418. [2] Kaufman J., Charney D., 2000. Comorbidity of mood and anxiety disorders. Depress Anxiety 12(S1), 69-76. [3] Wray N.R., Ripke S., Mattheisen M., Trzaskowski M., Byrne E.M., Abdellaoui A., et al., 2018. Genome-wide association analyses identify 44 risk variants and refine the genetic architecture of major depression. Nat Genet 50(5), 668-681.

No conflict of interest