

European College of Neuropsychopharmacology – press release

[Sexual abuse as a child changes the body's biochemical response to stress](#)

For immediate release, Tuesday 9th October 2018

Type of study: Peer-reviewed; observational study; people

Barcelona, 9th October: Anxious Depression, often resulting from childhood trauma, causes body changes which mean that standard depression treatments are often ineffective, according to new research presented at the ECNP in Barcelona (*see also publication note, below).

Major Depressive Disorder (MDD) affects up to 20% of Europeans, and around half of these people have “anxious depression” (psychological anxiety like high levels of anxiety and nervousness, plus somatic anxiety, such as gastrointestinal symptoms); which is associated with greater severity, poorer outcomes, and higher possibility of suicide. Now scientists have concluded that the biochemistry of patients with MDD and anxious depression is different, and that patients with anxious depression need to be treated differently. In addition, patients with anxious depression who have undergone sexual abuse or neglect as a child have a tendency to have a changed biochemistry.

The team worked with 144 patients with MDD. A subgroup of 78 patients were identified as having anxious depression, and these patients showed a greater severity of symptoms, and a poorer response to treatment than patients with general MDD. They found that 30% of the patients with anxious depression had suffered sexual abuse as children (versus 16% with ‘normal’ depression, MDD), and 76% suffered from emotional neglect (versus 58% with ‘normal’ depression).

This difference was also reflected in how their bodies reacted to stress hormones.

As research leader Dr Andreas Menke (University Hospital Wuerzburg) said;

“We could show that childhood trauma is clearly overrepresented in patients with anxious depression, especially sexual abuse. In addition, we showed that patients with anxious depression have a heightened sensitivity to stress-hormones such as glucocorticoids (cortisol), whereas major depression is more or less associated with a reduced sensitivity to stress-hormones. In addition, we observed that patients who have experienced childhood sexual abuse have more reactive immune cells. This is a surprising finding, because this is not found in anxious depressive patients in the absence of childhood abuse or trauma. We suspect that this is because the type of trauma these patients have experienced in early life has conditioned their immune system to react differently.

In practical terms, the difference we see between the biochemical responses would explain why anxious depressed patients have a worse outcome compared to non-anxious depressed patients with the standard treatment approaches. This really means that, for a significant subgroup of depressed patients, the standard drugs just don't work sufficiently well, thus we have to find alternatives.”

Commenting, Professor Brenda Penninx (Amsterdam UMC) said:

“This is an interesting study suggesting that anxious depression and/or childhood trauma may identify a specific depressed patient group where glucocorticoid receptor function is dysregulated. However, whether this truly explains worse outcomes to standard treatment – as now indicated by

the study authors – needs to be formally tested in a larger study before we can think about it affecting clinical practice”.

Dr Penninx was not involved in this research, this is an independent comment.

*This work is based on the peer-reviewed paper *Childhood trauma dependent anxious depression sensitizes HPA axis function*, which will appear in the December 2018 edition of the journal *Psychoneuroendocrinology* [https://www.psyneuen-journal.com/article/S0306-4530\(18\)30481-5/fulltext](https://www.psyneuen-journal.com/article/S0306-4530(18)30481-5/fulltext) None of the comments in this press release are in the published paper.

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Notes for Editors

Please mention the ECNP Congress in any story resulting from this press release.

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The 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 31st annual ECNP Congress takes place from 6nd to 9th September in Barcelona. It is Europe's premier scientific meeting for disease-oriented brain research, annually attracting between 4,000 and 6,000 neuroscientists, psychiatrists, neurologists and psychologists from around the world. Congress website: <https://2018.ecnp.eu/>

Conference abstract

Childhood trauma dependent anxious depression sensitizes HPA axis function (Poster number 555)

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Introduction:

Anxious depression is a common subtype of major depressive disorder (MDD) and is associated with greater severity, poorer outcome and higher suicidality. Alterations of the hypothalamic-pituitary-adrenal (HPA) axis, especially of the glucocorticoid receptor (GR) function, are often observed in MDD. Childhood adversity is known to influence both the HPA axis and the risk of MDD. However, it is not clear if alterations of the HPA axis also contribute to the development of anxious depression. Therefore we investigated GR function in anxious depression dependent on childhood adversity.

Methods:

We enrolled 144 in-patients (49% females) with a moderate to severe depressive episode (Hamilton Depression Rating Scale (HAM-D) ≥ 14). Anxious depression was defined using the HAM-D anxiety/somatization factor score ≥ 7 according to Cleary & Guy 1977 and previously used in STAR*D. Blood draws were performed at 6pm before and 3 hours after 1.5 mg dexamethasone (dex) ingestion for measurement of FKBP5 mRNA expression, cortisol, ACTH and blood count to assess the function of the HPA axis and the immune system in the first 5 days after hospital admission. Childhood adversity was evaluated using the Childhood Trauma Questionnaire (CTQ). The CTQ differentiate childhood adversity in sexual abuse, physical abuse, emotional abuse, emotional neglect and physical neglect.

Results:

We identified 78 patients (51.3%) with anxious depression who showed a greater severity (HAM-D 29.9 vs. 21.5; $p < 0.001$) and slower response to treatment with antidepressants ($F = 10.946$; $p < 0.001$) and a reduced response rate after 4 weeks (52% vs. 75%; $p = 0.022$). Anxious depressed patients had more previous episodes (9.5 vs. 4.5; $p = 0.023$), higher rate of previous suicide attempts (39.7 vs. 22.7; $p = 0.05$) and higher rate of positive family history of depression (79.5% vs. 57.5%; $p = 0.016$). Thus the sample is comparable to other cohorts investigating anxious depression. In our sample, anxious depressed patients were more often exposed to sexual abuse (30% vs 16%, $p = 0.04$) and emotional neglect (76% vs. 58%, $p = 0.02$) than patients with non-anxious depression. Anxious depressed patients showed an enhanced GR-induced FKBP5 mRNA expression ($F = 5.128$; $p = 0.03$) and reduced cortisol levels, partly dependent on sexual abuse ($F = 7.730$; $p = 0.006$) and adjusted for FKBP5 risk allele of rs1360780. In addition, the GR-induced leukocyte response was enhanced in patients with sexual abuse ($F = 7.176$; $p = 0.008$). Emotional neglect had no significant impact on HPA axis function or immune system. Of note, the single-nucleotide polymorphisms (SNP) rs1360780 was not associated with anxious depression or childhood abuse, however, the sample size may be not large enough to exclude significant effects.

Conclusion:

In conclusion, anxious depression in dependence of childhood trauma is associated with heightened sensitivity of the HPA axis and the immune system which should be considered for the evaluation of treatment algorithms and targets. Hence, agents targeting FKBP5 may be a treatment options specifically for patients suffering from anxious depression.

