

Introduction:

- With around 50% anxious depression is a major subtype of major depressive disorder (MDD)
- Associated with greater severity, poorer outcome and higher suicidality
- Alterations of the hypothalamic-pituitary-adrenal (HPA) axis are often observed in MDD, especially glucocorticoid receptor (GR) function
- Childhood trauma is known to influence both HPA axis and risk of MDD
- Not clear, if alterations of the HPA axis contribute to anxious depression

Objective:

- GR function in anxious depression dependent on childhood trauma (1)

Methods:

- 144 depressed in-patients (49% females)
- Anxious depression defined by the Hamilton Depression Rating Scale (HAMD) anxiety/somatization factor score ≥ 7 according to Cleary & Guy (2) and previously used in STAR*D (3)
- Blood was taken at 6pm before and 3 hours after 1.5mg dexamethasone ingestion (4, 5)
- Blood: FKBP5 mRNA, cortisol, ACTH, blood count
- Childhood trauma evaluated with the Childhood Trauma Questionnaire (CTQ) (6)

Results:

- Anxious depression affected 78 patients (51.3%) (figure 1 A)
- Anxious depression was associated with:
 - Greater severity (HAMD 29.9 vs 21.5.; $p < 0.001$)
 - Slower response to treatment with antidepressants ($F = 10.946$; $p < 0.001$)
 - Reduced response rate after 4 weeks (52% vs. 75%; $p = 0.022$) (figure 1 B)
 - More previous episodes (9.5 vs. 4.5; $p = 0.023$)
 - Higher rate of previous suicide attempts (39.7 vs. 22.7; $p = 0.05$)
 - Higher rate of family history of depression (79.5% vs. 57.5%; $p = 0.016$)

HPA axis and CTQ findings:

- Childhood trauma was overrepresented in patients with AD (table 1)
- Anxious depressed showed an enhanced GR-induced FKBP5 mRNA expression ($F = 5.128$; $p = 0.03$) (figure 2 A, B)
- and reduced cortisol levels, partly dependent on sexual abuse ($F = 7.730$; $p = 0.006$) and adjusted for FKBP5 risk allele of rs1360780 (figure 2 C, D)
- GR-induced leukocyte response was enhanced in patients with sexual abuse ($F = 7.176$; $p = 0.008$) (figure 3 A, B)
- Emotional neglect had no significant impact on HPA axis function

Comparison of childhood trauma between anxious and non-anxious depressed patients stratified for Childhood Trauma Questionnaire (CTQ) subgroups.

p value	Childhood Trauma Questionnaire		
	Anxious depression	Non-anxious depression	
Total score (± SD)	45.96 (± 15.11)	40.51 (± 14.62)	0.043
Emotional abuse N (%)	41 (53.9)	28 (43.8)	n.s.
Physical abuse N (%)	21 (28.0)	13 (20.3)	n.s.
Sexual abuse N (%)	23 (30.3)	10 (15.6)	0.042
Emotional neglect N (%)	58 (76.3)	37 (57.8)	0.020
Physical neglect N (%)	40 (52.6)	25 (39.1)	n.s.

Table 1

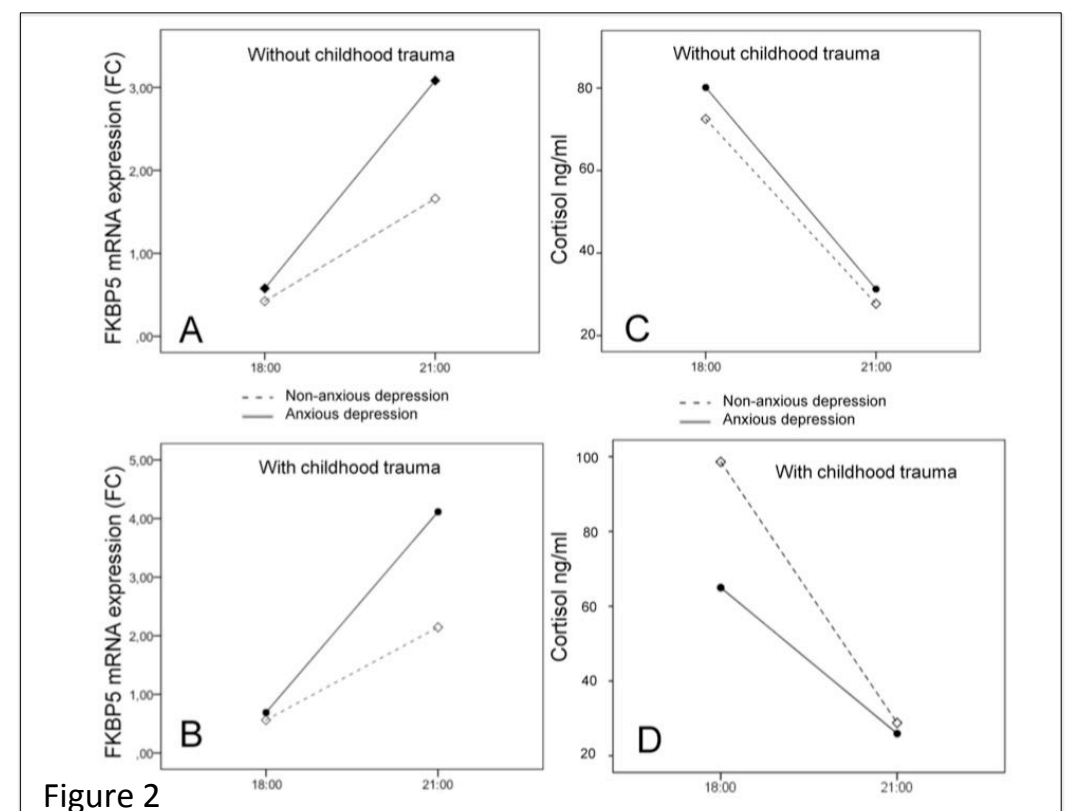


Figure 2

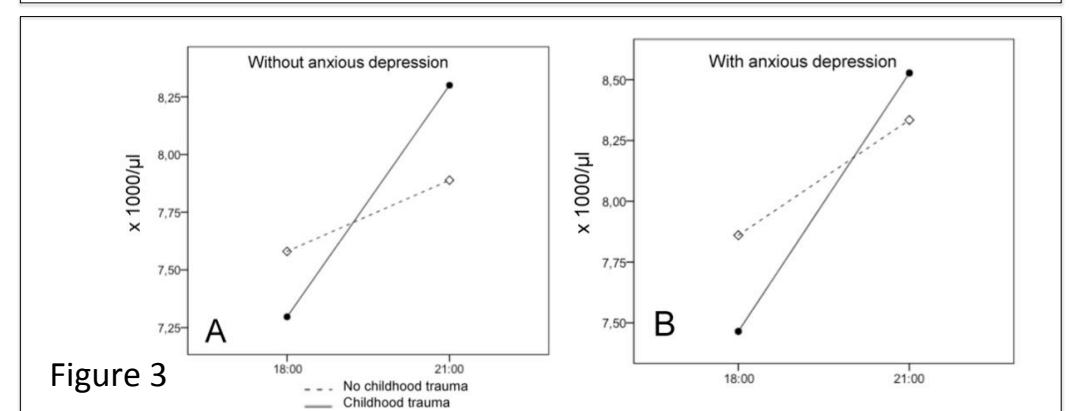


Figure 3

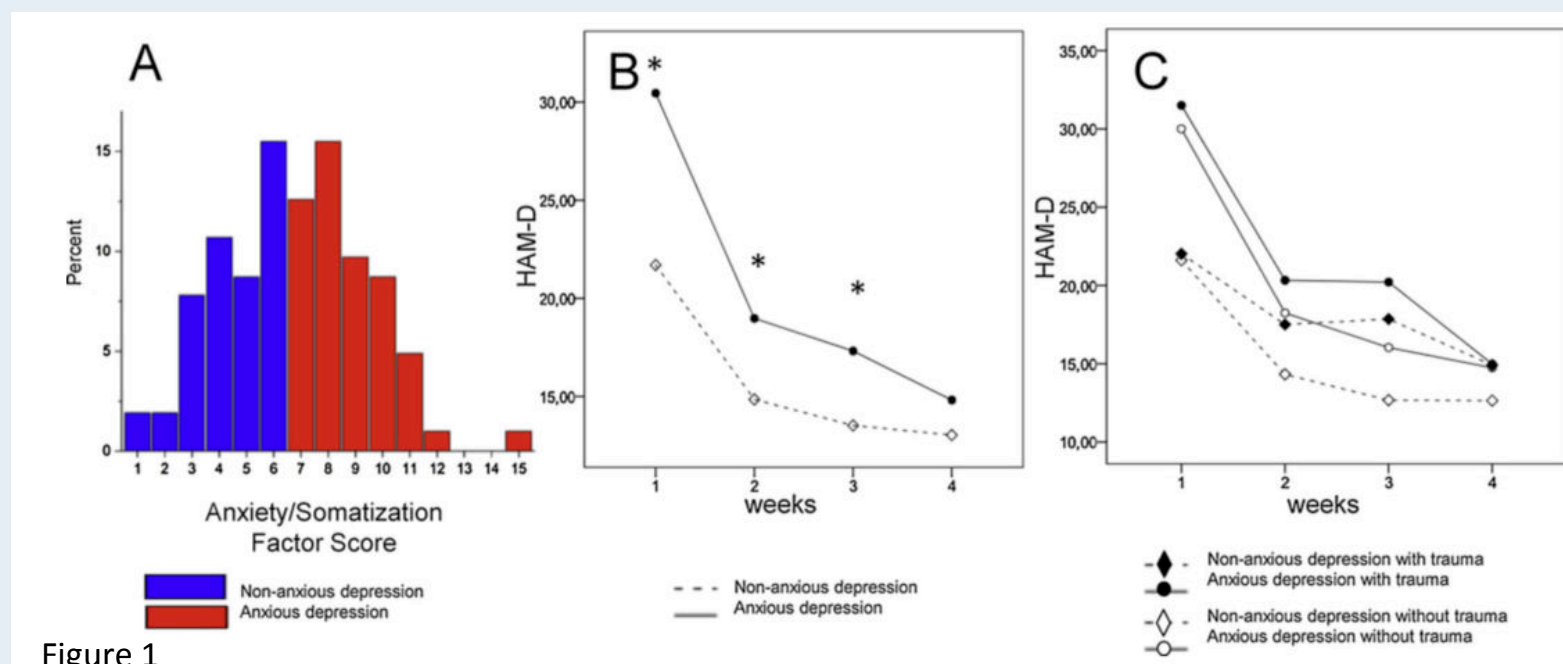


Figure 1

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.

References:

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 (4) Menke A, Arloth J, Putz B, et al. Neuropsychopharmacology. 37(6):1455-1464, 2012
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