The role of tryptophan degradation in the association between inflammatory markers and depressive symptoms in chronic dialysis patients

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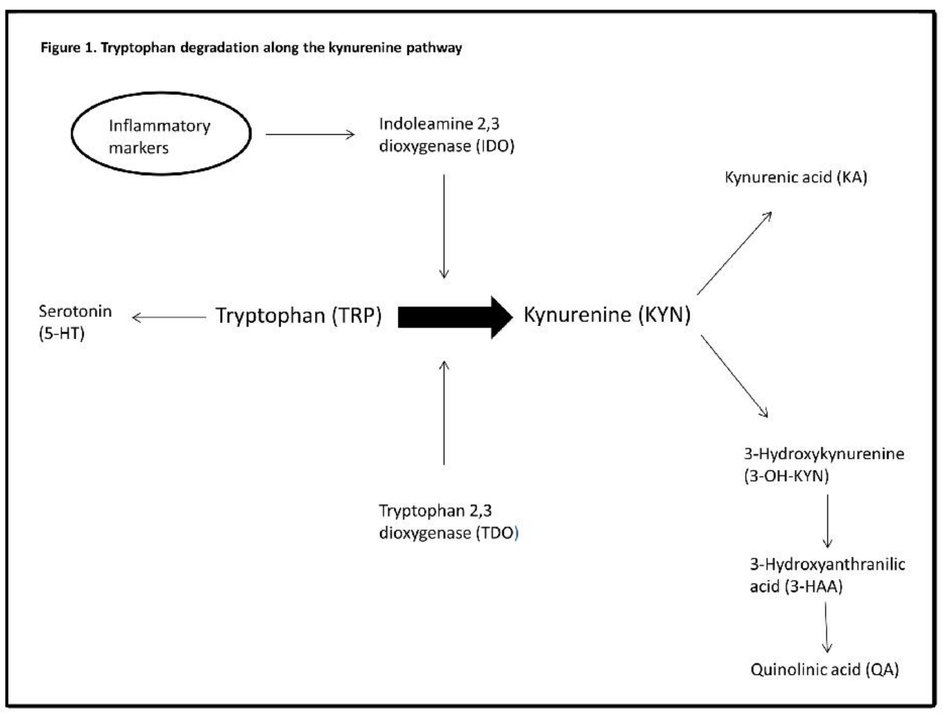
Background and objectives

Among chronic dialysis patients associations have been found between inflammatory markers and depressive symptoms. In this population no studies examined the mechanism linking the association between inflammatory markers and depressive symptoms.

We examined whether tryptophan (TRP) degradation along the kynurenine (KYN) pathway (figure 1) mediates the association between inflammatory markers and depressive symptoms.

Figure 1. Tryptophan degradation along the kynurenine pathway



Methods

490 chronic dialysis patients were selected from DIVERS, a prospective cohort study in 5 urban dialysis centres in The Netherlands.

- **Period:** June 2012 to December 2014. Inclusion and follow-up is ongoing.
- **Inclusion criteria:** age >18, renal replacement therapy for at least 90 days, able to fill out questionnaires. No cognitive disabilities.
- **Measures:**
  - Beck Depression Inventory (BDI): cut-off value ≥ 13
  - Inflammatory markers: IL-1b, IL-6, IL-10, TNFa, HsCRP.
  - TRP, KYN, 3-OH-KYN
  - KYN/TRP ratio x10^3 as a marker for tryptophan degradation
- **Analysis:** Univariate- and multivariate linear regression analysis to determine the association between inflammatory markers and depressive symptoms.

  We adjusted for tryptophan degradation.

Results

- The prevalence of depressive symptoms was 43%.
- Univariate linear regression showed significant associations between HsCRP (β= 0.8 (CI: 0.3-1.3)), and IL-6 (β= 1.2 (CI: 0.3-2.2)), and depressive symptoms (table 2).
- Adjustment for KYN/TRP ratio did not attenuate the association between HsCRP, and IL-6 and depressive symptoms (table 2).

Table 1. Baseline characteristics

	Total sample (N=490)
Age, mean (SD)	64 (15)
Gender, % male	60
TRP, µmol/L (SD)	27.5 (9)
KYN, µmol/L (SD)	4.6 (2)
3-OH-KYN, nmol/L (SD)	168.7 (65)
KYN/TRP x 10^3 (SD)	172.1 (53)
HsCRP, mg/L, median (IQ)	2.4 (0.7-6.8)
IL-1β, pg/mL, median (IQ)	0.06 (0.01-0.41)
IL-6, pg/mL, median (IQ)	2.7 (1.5-4.8)
IL-10, pg/mL, median (IQ)	0.34 (0.13-0.65)
TNF-α, pg/mL, mean (SD)	21.4 (11.8)

Table 2. Association between inflammatory markers and depressive symptoms

Linear regression	Depressive symptoms		
	b (95% CI) Unadjusted	b (95% CI) Adjusted for KYN/TRP	b (95% CI) Adjusted for KYN/TRP and socio-demographics, lifestyle factors and medical variables
HsCRP[L]	0.8 (0.3-1.3)**	0.8 (0.2-1.3)**	0.8 (0.3-1.4)**
IL-1β[L]	-0.1 (-0.5-0.3)	-0.1 (-0.5-0.3)	-0.2 (-0.6-0.3)
IL-6[L]	1.2 (0.3-2.2)**	1.2 (0.2-2.1)*	1.1 (0.1-2.1)*
IL-10[L]	-0.2 (-0.8-0.3)	-0.2 (-0.8-0.3)	-0.1 (-0.7-0.4)
TNF-α	0.01 (-0.1-0.1)	-0.01 (-0.1-0.1)	-0.01 (-0.1-0.1)

Conclusion

- TRP degradation along the KYN pathway does not mediate the association between inflammatory markers and depressive symptoms in this patient population.

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