Childhood trauma affects tryptophan metabolism in mood disorder

R. Bonsignori¹, S. Poletti¹, M. Riberto¹, G. Schüetze², C. Locatelli¹, M. Schwarz², F. Benedetti¹.

¹IRCCS Ospedale San Raffaele, Department of Clinical Neurosciences, Milan, Italy. ²Ludwig-Maximilian University, Institute for Laboratory Medicine of Munich University, Munich, Germany.

BACKGROUND

Reduced levels of serotonin have been suggested to be a central factor in the pathogenesis of depression associated to reduced serum level of Tryptophan (Trp) [1]. Indoleamine 2–3 dioxygenase (IDO) and Tryptophan-2,3-Dioxygenase (TDO) convert Trp into kynurenine (Kyn) diverting it from the serotonin synthetic route: TDO is mainly induced by Trp itself and steroids, whereas IDO by inflammation [2]. Childhood maltreatment has been shown to heighten low-grade inflammatory state, with production of pro-inflammatory cytokines and to associate to hypothalamic-pituitary-axis (HPA) hyperactivation, and increased levels of circulating corticosteroids [3,4]. A similar picture is frequently observed in depression. Considering that CM increases the risk of developing a mood disorder and its suggested role in Trp metabolism, we explored if Trp and its breakdown into Kyn could be influenced by CM in a sample of bipolar (BD), major depressive disorder patients (MDD) and healthy controls (HC).

METHOD

Peripheral levels of Trp and Kyn were analyzed in 47 patients affected by mood disorders (32 BD and 15 MDD) and 15 HC. A tryptophan breakdown index (Kyn/Trp) was calculated. Childhood trauma was assessed by using Childhood Trauma Questionnaire (CTQ), which allows to subtype the different abuses: sexual (SA), physical (PA), and emotional (EA), as well as physical (PN) and emotional neglect (EN). In order to explore possible effects of CM on Trp, univariate analyses were performed entering Trp and Trp breakdown as dependent variables, CTQ and its subscales as independent predictors, age, sex and severity of illness as nuisance covariates. All the analyses were conducted separately in the three groups in the context of General Linear Model.

RESULTS

CTQ significantly predicted low levels of Trp in BD (F=6.425; p=0.016). Significant effects were also detected for Trp breakdown index in both MDD (F=5.94; 0.032) and BD patients (F=10.43; 0.003) where high levels of trauma predicted an higher ratio. These effects were also confirmed for the subscales PA (F=5.28; p=0.028), EN (F=9.95; p=0.003), and PN (F=12.41; p=0.001) in BD, and PA (F=6.96, p=0.023), EA=F(6.50; p=0.027), and PN (F=5.44; p=0.039) in MDD. In HC no significant effects were found.

CONCLUSIONS

Results support the pivotal role of early stress in psychiatric disorders: CM reduces the level of Trp in BD and increases its breakdown into Kyn in both BD and MDD. No effects were detected on HC. Lower levels of Trp and higher catabolism into Kyn have been previously observed in depression and our results suggest that CM could contribute to reducing the level of serotonin. These effects would be probably mediated by an increased IDO and TDO enzymatic activity, induced by a HPA hyperactivation, corticoids disruption and proinflammatory response. Notably, proinflammatory cytokines may further cause HPA hyperactivity by disturbing the negative feedback inhibition of circulating corticosteroids on the HPA axis [2].

REFERENCES