LETTER TO THE EDITOR

Shailendra Kapoor, *Private practice, Mechanicsville, VA, USA*

STNFR1 AND IT'S CONTRIBUTORY ROLE IN THE EVOLUTION AND PROGRESSION OF DIFFERENT PSYCHIATRIC DISORDERS

Dear Editor,

The recent article by Morley et al provided for highly interesting and thought stimulating reading (1). A significant co- relationship EXISTS between soluble TNF-alpha receptor1 (sTNFr1) levels and the evolution and progression of a number of different psychiatric disorders.

A significant association has been seen between sTNFr1 levels and the cognitive/ affective aspect of depression (2). This is especially more pronounced in patients with coexisting comorbidities such as congestive heart failure. Higher levels are also noticed in patients with depression secondary to "post-traumatic stress disorder" (3). A significant association is also seen between the age of the patients with major depression and the corresponding sTNFr1 levels. Similarly, elevated sTNFr1 levels have been noted in patients with bipolar disorder. Barbosa et al in a recent study have shown a significant impact of the duration of bipolar disorder on sTNFr1 levels (4). Simultaneous up- regulation of leptin expression is seen in these patients (5). Interestingly, serum sTNFr1 levels in bipolar patients with frank manic symptoms are much higher than in bipolar patients with euthymia. A similar relationship has been noted in patients with underlying obsessive compulsive disorder. For instance, the severity of compulsive symptoms such as repetitive hand washing bears a close association with serum sTNFr1 levels (6).

Similarly, elevated sTNFr1 levels in the CSF have been noted in patients with Alzheimer's disease. A significant association has been seen between CSF sTNFr1 levels and CSF TNF- α converting enzyme (TACE) levels (7). Similar elevations have been noted in patients with "mild cognitive impairment". A significant association is also seen between CSF levels of sTNFr1 and CSF levels of tau as well as A β 40 in these patients (8). The risk of progression from "mild cognitive impairment" to frank Alzheimer's disease is significantly accentuated with up- regulation if serum sTNFr1 expression (9). Not surprisingly, a significant association is seen between CSF sTNFr1 levels and β -site APP-cleaving enzyme 1 activity

in these patients (10). A close association also exists between serum sTNFr1 levels and schizophrenia. Resistance to therapeutic intervention is more likely in those with comparatively higher sTNFr1 levels (11).

Similar elevation in sTNFr1 levels has been noted in patients with certain neurological disorders such as Parkinson's disease (12). The above examples further corroborate the fact that disturbances in inflammatory processes involving sTNFr1 contribute to the evolution and progression of a number of psychiatric disorders.

References

1. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. *J Nutr Health Aging* 2012;16:601-8.
2. Kupper N, Widdershoven JW, Pedersen SS. Cognitive/affective and somatic/affective symptom dimensions of depression are associated with current and future inflammation in heart failure patients. *J Affect Disord* 2012;136:567-76.
3. Grassi-Oliveira R, Brietzke E, Pezzi JC, Lopes RP, Teixeira AL, Bauer ME. Increased soluble tumor necrosis factor-alpha receptors in patients with major depressive disorder. *Psychiatry Clin Neurosci* 2009;63:202-8.
4. Barbosa IG, Huguet RB, Mendonca VA, et al. Increased plasma levels of soluble TNF receptor I in patients with bipolar disorder. *Eur Arch Psychiatry Clin Neurosci* 2011;261:139-43.
5. Barbosa IG, Rocha NP, de Miranda AS, et al. Increased levels of adipokines in bipolar disorder. *J Psychiatr Res* 2012;46:389-93.
6. Fontenelle LF, Barbosa IG, Luna JV, de Sousa LP, Abreu MN, Teixeira AL. A cytokine study of adult patients with obsessive-compulsive disorder. *Compr Psychiatry* 2012;53:797-804.
7. Jiang H, Hampel H, Prvulovic D, et al. Elevated CSF levels of TACE activity and soluble TNF receptors in subjects with mild cognitive impairment and patients with Alzheimer's disease. *Mol Neurodegener* 2011;6:69,1326-6-69.
8. Bai L, Song N, Yu J, et al. Elevated Plasma Levels of Soluble TNFRs and TACE Activity in Alzheimer's Disease Patients of Northern Han Chinese Descent. *Curr Alzheimer Res* 2013;10:57-62.
9. Diniz BS, Teixeira AL, Ojopi EB, et al. Higher serum sTNFR1 level predicts conversion from mild cognitive impairment to Alzheimer's disease. *J Alzheimers Dis* 2010;22:1305-11.
10. Buchhave P, Zetterberg H, Blennow K, Minthon L, Janciauskiene S, Hansson O. Soluble TNF receptors are associated with Abeta metabolism and conversion to dementia in subjects with mild cognitive impairment. *Neurobiol Aging* 2010;31:1877-84.
11. Noto C, Gadelha A, Belangero SI, et al. Circulating levels of sTNFR1 as a marker of severe clinical course in schizophrenia. *J Psychiatr Res* 2013;.
12. Scalzo P, Kummer A, Cardoso F, Teixeira AL. Increased serum levels of soluble tumor necrosis factor-alpha receptor-1 in patients with Parkinson's disease. *J Neuroimmunol* 2009;216:122-5.