Serotonin transporter gene polymorphism, platelet serotonin concentration and sleep disturbances in veterans with post-traumatic stress disorder

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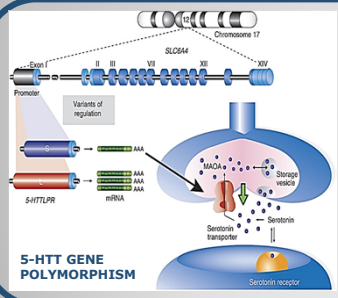
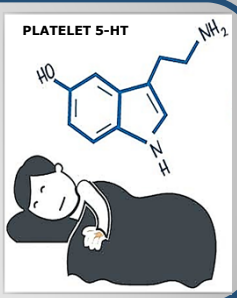
INTRODUCTION: Post-traumatic stress disorder (PTSD) is a complex psychiatric disorder, which develops after exposure to traumatic experience(s). Sleep disorders, such as nightmares and insomnia, are hallmarks of PTSD. Although the neurobiological basis of PTSD is not fully elucidated, this disorder most likely results from complex interactions between genetic and environmental factors. It has been suggested that serotonin (5-HT) system, due to its important role in controlling mood, arousal, and sleep, is involved in the development of PTSD symptoms.



Several studies have investigated the association of functional 5-HTTLPR polymorphism in the 5-HT transporter (5-HTT) gene, with sleep disturbances, however the findings are contradictory. The function of 5-HTT is re-uptake of 5-HT into presynaptic neuron or platelets, and 5-HTTLPR modulates the transcriptional activity of 5-HTT gene, influencing mRNA and protein levels. Since platelets and 5-HT neurons share similar biochemical processes, such as intake, storage, release and degradation of 5-HT, and expression of 5-HTT and some 5-HT receptors, the concentration of platelet 5-HT may be used as a peripheral marker of certain PTSD symptoms. The aim of the study was to investigate the association of 5-HTTLPR and platelet 5-HT concentrations with sleep disorders in Croatian war veterans with PTSD.



MATERIALS AND METHODS: Croatian male, medication-free war veterans with PTSD (N=393), with or without comorbid depression and various sleep disturbances, were evaluated using the Structured Clinical Interview (SCID) based on DSM-IV criteria, the Hamilton Rating Scale for Anxiety (HAMA), the Hamilton Depression Scale (HDRS) and the Clinician Administered PTSD Scale (CAPS). Veterans with PTSD were subdivided according to sleep disturbances in those with or without insomnia and other sleep disturbances (nightmares, interrupted sleep). Genomic DNA was extracted from peripheral blood using a salting out method. Genotyping was performed using polymerase chain reaction (PCR) and DNA fragments were separated on a 2% agarose gel and visualized. 5-HT concentration was determined spectrofluorimetrically in platelets isolated from platelet rich plasma by series of centrifugations. All data were evaluated using GraphPad Prism version 4.00.

Table 1. The distribution of 5-HTTLPR genotypes in PTSD veterans without or with comorbid depression divided by values of early insomnia according to scores on Item 4 of HDRS scale

Item 4 of HDRS scale (scores)		0	1	2
PTSD		No insomnia	Early insomnia 1	Early insomnia 2
5-HTTLPR	LL carriers, n (%)	4 (6.5 %)	32 (51.6)	26 (41.9)
	S carriers, n (%)	7 (7.3 %)	68 (70.8)	21 (21.9)
χ^2 =7.33, df=2, p=0.026				
PTSD with comorbid depression		No insomnia	Early insomnia 1	Early insomnia 2
5-HTTLPR	LL carriers, n (%)	3 (5.2)	34 (58.6)	12 (36.2)
	S carriers, n (%)	3 (2.7)	63 (56.8)	45 (40.5)
χ^2 =0.86, df=2, p=0.650				

RESULTS: Significantly higher frequency of the LL genotype of the 5-HTTLPR polymorphism in 5-HTT gene compared to S carriers and significantly higher platelet 5-HT concentrations were detected in veterans with PTSD with early insomnia compared to veterans with PTSD without early insomnia. Other sleep disturbances were not associated with 5-HTTLPR genotypes or platelet 5-HT concentration in veterans with PTSD with or without comorbid depression.

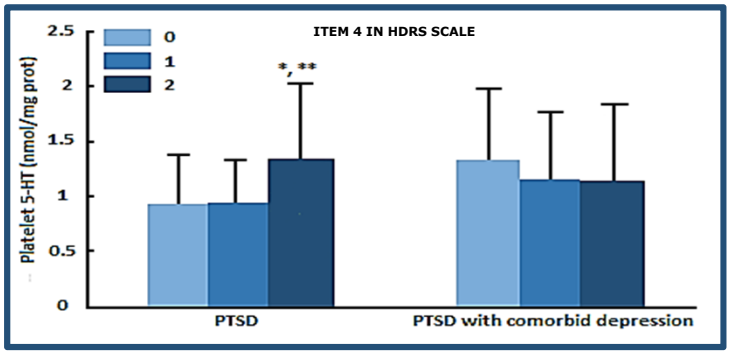


Fig 1. Platelet 5-HT concentration in veterans with PTSD and PTSD veterans with comorbid depression divided by values of early insomnia (Item 4,HDRS scale). p=0.015 vs. veterans with PTSPs with 0 scores **p<0.001 vs. PTSD veterans with 1 score (Tukey's test)

CONCLUSION: Our results suggest the role od 5-HT system in early insomnia in veterans with PTSD. Further studies with larger groups should clarify the association of 5-HTTLPR and platelet 5-HT with sleep disturbances in PTSD. This work was supported by Croatian Science Foundation grant IP-2014-09-4289.