Serotonin transporter relationships with response to meditation interventions for PTSD

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Abstract

Background
Mindfulness Based Stress Reduction (MBSR), Transcendental Meditation (TM), and Present-Centered Group Therapy (PCGT), are effective non-pharmacologic treatments for 28-49% of veterans with PTSD. We examined relationships between treatment response, early life trauma and serotonin transporter (*SLC6A4*) polymorphisms known to influence stress sensitivity.

Methods
Veterans with PTSD receiving Meditation [(MBSR (n=50), TM (n=18)], or PCGT (n=52) were enrolled from two separate studies. Participants averaged 58.8±10.8 years of age, n=101 (84%) male, with N=49 (41%) having exposure to early life trauma (e.g. abuse). The PTSD Checklist (PCL) quantified improvements after 9 weeks with 43% responding (≥10pt PCL improvement) to Meditation, and 21% to PCGT. *SLC6A4* promoter (5HTTLPR_L/S_insertion/deletion+rs25531_A/G) polymorphisms defined expression groups [L_AL_A(high) vs non-L_AL_A(low)]. Interventions were examined together and stratified in relation to genotype and trauma.

Results
We identified a main effect of intervention (Meditation vs PGCT) and a 5HTTLPR by childhood trauma interaction with response to Meditation. Those with childhood trauma who were in the high expression (L_AL_A) group were more likely to respond (70% responders) to Meditation than non-L_AL_A individuals (25% responders) (χ^2=5.63, p=0.045). Response rates to Meditation were similar (44-46%) in those without childhood trauma regardless of genotype.

Conclusions
Veterans with PTSD were more likely to benefit from Meditation than PCGT. In those with childhood trauma, greater responses to Meditation were observed in high expression 5HTTLPR groups indicating that serotonin signaling is an important component of Meditation and may be useful in guiding treatment.

Methods

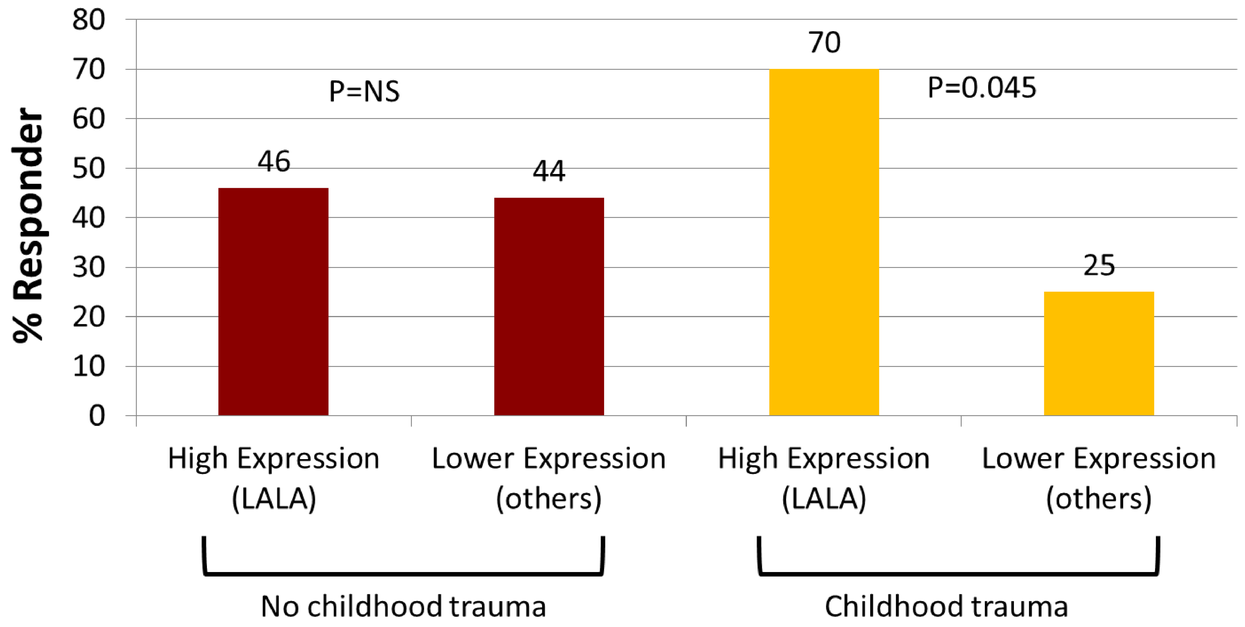
Inclusion Criteria
≥18 years old
Current full PTSD (DSM-IV) or subthreshold PTSD (DSM-IV criterion A1 plus at least one symptom each from criteria B, C, and D with significant impairment)
Agreement not to receive other psychotherapy for PTSD during the study
Stable pharmacotherapy for at least four weeks prior to study entry
No history of seizures or head injury with loss of consciousness > 10 minutes
Available DNA specimen and consent for genetic analyses
Exclusion Criteria
Current substance dependence (except nicotine or caffeine)
Current psychotic disorder
Prominent current suicidal or homicidal ideation
Cognitive impairment or medical illness that might interfere with treatment
Clinical Evaluations
PTSD Checklist (PCL) – Responder status defined as ≥10pt PCL improvement
Clinician –Administered PTSD Scale (CAPS)
Lifetime Events Checklist
Childhood trauma (emotional abuse or neglect, physical abuse or neglect, alcoholic environment)
Interventions (8-weeks duration)
Mindfulness Based Stress Reduction (MBSR) – 8 weekly 2.5 hr group sessions and a day long retreat (total of 9 sessions)
Transcendental Meditation (TM) – 5 group training sessions and 5 individual follow-up meetings
Present-Centered Group Therapy (PCGT) – 9 weekly 1.5 hr group sessions

Genetic Analyses
DNA samples were obtained from EDTA-treated whole blood and standardized to a working concentration of 10ng/ul
PCR amplification of genomic regions covering *SLC6A4*_5HTTLPR were performed with the following primer sets: 5HTTLPR Forward Primer 5'-FAM-CTGAATGCCAGCACCTAACCCCTAATGT-3'; 5HTTLPR Reverse Primer 5'- GGGGAATACTGGTAGGGTGCAAGGAGAA-3'; *SLC6A4*_5HTTLR amplicons produce fragment sizes of 341bp for the small or "S" allele (14 repeats), or 383bp for the large or "L" allele (16 repeats). *SLC6A4*_VNTR STin2 amplicons produce fragment sizes of 345bp for the 9 repeat allele, 360bp for the 10 repeat allele, or 390bp for the 12 repeat allele. In order to determine the status of *SLC6A4*_rs25531 (g.28564346 A>G), *SLC6A4*_5HTTLPR amplicons were digested with MspI which cleaves at the CCGG restriction site to produce fragment sizes of 285bp for the S_A allele, 328bp for the L_A allele, and 155bp for the L_G and S_G alleles
*SLC6A4*_5HTTLPR high vs lower expression groups (L_A/L_A vs others) were used for analyses in relation to clinical data and treatment outcomes

Demographic and clinical characteristics

Characteristic	All (n=128)	MBSR (n=53)	TM (n=21)	PCGT (n=54)
Age (Std Dev)	58.4 (10.5)	57.8 (10.5)	58.4 (13.6)	58.9 (69.4)
% Male	84%	81%	76%	91%
% White	85%	81%	95%	91%
PCL Total Baseline	61.2 (12.1)	63.8 (11.6)	63.2 (8.8)	57.8 (13.0)
PHQ-9 Total	15 (5.3)	15.6 (5.2)	15.7 (4.7)	14.1 (5.6)
% With any childhood trauma	41%	43%	37%	48%
% 5HTTLPR High Expressor (L_A/L_A)	27%	34%	14%	26%

Responder to meditation (MBSR or TM) by childhood trauma history and serotonin transporter genotype



Primary Findings

- We identified a main effect of intervention (Meditation vs PCGT) and a 5HTTLPR by childhood trauma interaction with response to Meditation.
- High expressing serotonin transporter genotypes were associated with better symptom response to mediation interventions for PTSD, but only in those with a history of childhood trauma.

Discussion

This is the first study to characterize the relationships between serotonin transporter promoter (5HTTLPR) genotypes, childhood trauma, and response to meditation interventions for PTSD. Prior studies have examined the 5HTTLPR in relation to cognitive behavioral therapy and response to sertraline for PTSD, identifying less response in lower expressing genotypes (Bryant 2010 PMID: 20434135; Mushtag 2012 PMID: 21962566). Our results are consistent with these prior studies, and additionally suggest that adverse early life events may moderate relationships between 5HTTLPR genotype and treatment outcomes. The influence of early life trauma suggests that epigenetic relationships with treatment response to PTSD interventions requires further study.

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