Stress Biomarkers and In-Session Exposure to Nightmare Content: Results from a Pilot Trial of Nightmare Deconstruction of Reprocessing

Patricia T. Spangler,[1,2] James C. West, [1] Catherine L. Dempsey,[1,2] David M. Benedek,[1] Jessica Gill, [3] Xianzhang Hu,[1] Rebecca Kwasinski, [4] Brent Winslow,[4] Lei Zhang[1]

[1] Uniformed Services University, Bethesda, MD, [2]Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Bethesda, MD, [3]Johns Hopkins University, Baltimore, MD, [4]Design Interactive Inc. Orlando, FL

INTRODUCTION

Nightmares are prevalent in service members and veterans.[1,2] They impact mental health and daytime function[3] and are often resistant to evidence-based treatments.[4] Trauma activation is a mechanism of change in PTSD exposure treatments.[5] Thus, a treatment that uses exposure to nightmare content to activate trauma memories could facilitate recovery. Cardiovascular activity (CVA) and electrodermal activity (EDA) can be monitored in session as objective evidence of trauma activation.[6] Peripheral blood biomarkers including BDNF, TNF-α, and IL-10, have been used to investigate treatment response in PTSD patients. This single-arm pilot trial tested Nightmare Deconstruction and Reprocessing (NDR)[7] for trauma-related nightmares. Aims were to test the potential efficacy of NDR and the feasibility of biomarker data collection.

METHODS

Service members and veterans (*N*=11) with post-trauma nightmares were recruited at Walter Reed National Military Medical Center. They received 8 sessions of NDR over 8 weeks. Potential efficacy was determined by change from baseline to 1-month follow up in self-reported nightmares and insomnia. Objective measures of change included CVA and EDA collected with the Empatica E4 wristband. Blood samples were taken immediately after Visits 0, 1, and 7 to test for differences in expression of BDNF, TNF-α, and IL-10.

RESULTS: SIGNALS OF TREATMENT RESPONSE

Psychometric Outcomes

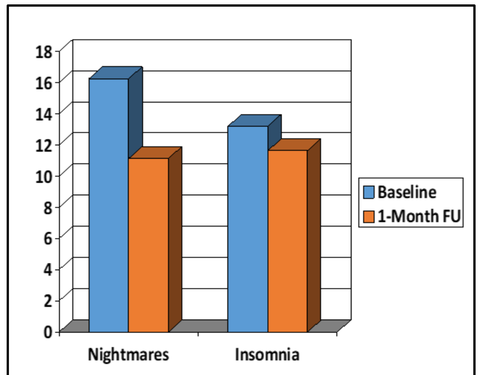

Figure 1. *Psychometric outcome results for N=11 participants show a large pre- to post-treatment effect for nightmare severity (d=0.93) on the Disturbing Dreams and Nightmare Severity Index and a small effect for sleep disturbance (d=0.41) on the Pittsburgh Sleep Quality Index.*

In-Session Cardiovascular Activity

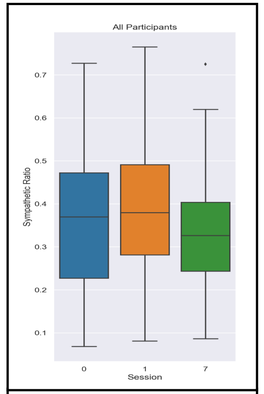

Figure 2a*. Sympathetic nervous system activity increased at Visit 1 (First in-session exposure to nightmare) and decreased by Visit 7 (final exposure).*

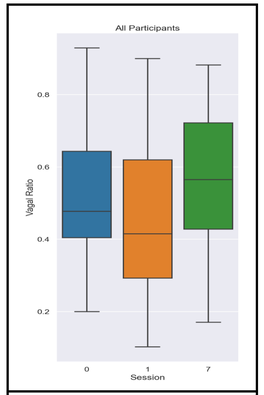

Figure 2b. *Vagal tone (parasympathetic activity) decreased from Visit 0 to Visit 1 and then increased by Visit 7 to a level higher than at Visit 0.*

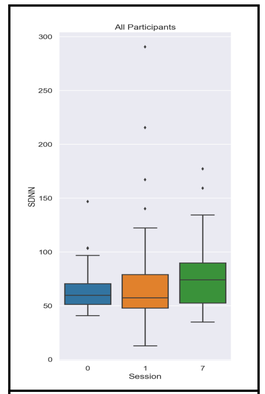

Figure 2c. *Standard deviation of interbeat interval of normal sinus beats (indicating resilience against stress) increased by Visit 7.*

In-Session Electrodermal Activity

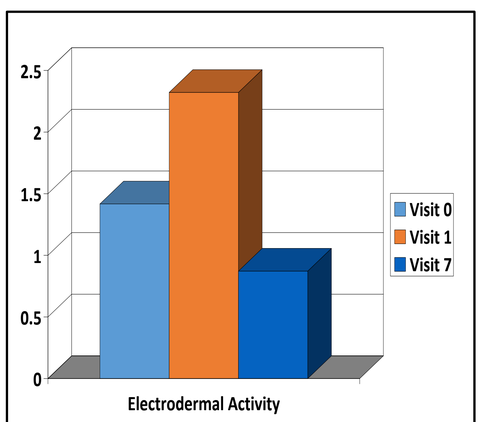

Figure 3. *Electrodermal results show that the highest mean EDA (reported in microsiemens) occurring in Visit 1, (μS=3.378) at first exposure to nightmare content and then a decrease at Visit 7 (μS=1.089).*

Post-Session Serum Expression

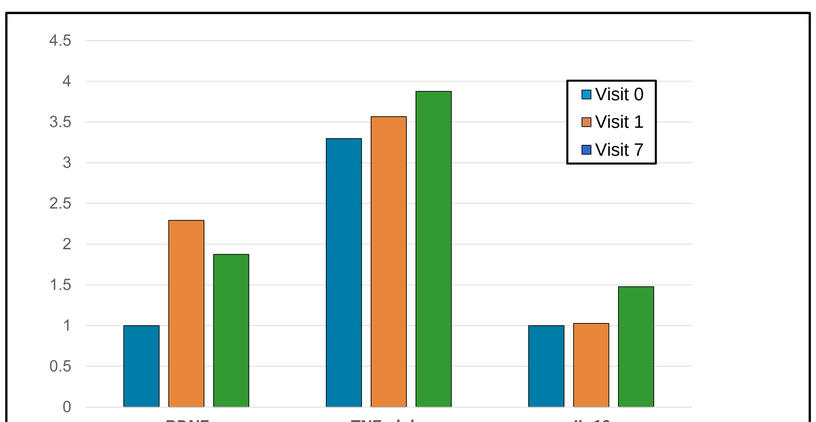

Figure 4. *Results of serum expression of blood samples taken at Visits 0, 1, and 7. Assay results of BDNF, tumor necrosis factor-alpha, and interleukin-10 show a significant difference in BDNF expression from Visit 0 (M= 1.00, SD = .88) to Visit 1 (M=2.29, SD= 1.72), t(21)= -2.24 , p =.03, with a large effect (d=0.94). Between visit difference in TNF-α and IL-10 were not significant.*

DISCUSSION

With a large effect for decrease in nightmares and a small effect for insomnia, our results provide a signal of NDR's potential efficacy for treating trauma-related nightmares. CVA and EDA results indicate that data collected from the Empatica wristband data are feasible markers of in-session stress related to nightmare exposure. Significant results for BDNF indicate it may be a valid marker in future studies. These results provide a rationale for conducting the next phase of investigation, which is comparing process and outcome for NDR (exposure) and the NightWare device (non-exposure) treatments for trauma-related nightmares.

REFERENCES

1. Creamer JL et al. Nightmares in U.S. military personnel w sleep disturbances. *J Clin Sleep Med*. 2018;14(3):419-426. doi:10.5664/jcsm.6990
2. Pruiksma KE et al. A pilot randomized controlled trial of cognitive behavioral treatment for trauma-related nightmares in active duty military personnel. *Journal of clinical sleep medicine*. 2020; 16(1), 29-40. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7053000/
3. Simor P, Pajkossy P, Horváth K, Bódizs R. Impaired executive functions in subjects with frequent nightmares as reflected by performance in different neuropsychological tasks. *Brain and Cognition***.** 2012;78(38):274-283. http://dx.doi.org/10.1016/j.bandc.2012.01.006.
4. Schnurr PP et al. Residual symptoms following PE and present-centered therapy for PTSD in female veterans and soldiers, *Depress Anxiety.* 2019;36(2):162–169.
5. Kida S. Reconsolidation/destabilization, extinction and forgetting of fear memory as therapeutic targets for PTSD. *Psychopharm.* 2019;236: 49-57. doi: 10.1007/s00213-018-5086-2. Epub 2018 Oct 29. PMID: 30374892.
6. Maples-Keller JL et al. Changes in trauma-potentiated startle, skin conductance, and heart rate within prolonged exposure therapy for PTSD in high and low treatment responders. *J Anxiety Disord*. 2019;68:102147.
7. Spangler PT, West JC. Nightmare deconstruction and reprocessing for PTSD nightmares. In: Vermetten E, Germain A, Neylan T, Eds. *Sleep and combat-related posttraumatic stress disorder.* New York: Springer; 2018; 311-16. https://doi.org/10.1007/978-1-4939-7148-0_27

ACKNOWLEDGMENTS

We thank Teotimo Andrada, Clinical Coordinator, Walter Reed National Military Medical Center Sleep Disorders Center, for his work on this study.