2015

Use of Oxytocin as a Preventative Treatment for PTSD

Laurel V. Kovalchick
Virginia Commonwealth University

Use of Oxytocin as a Preventative Treatment for PTSD

Laurel Kovalchick, Virginia Commonwealth University
Mentor: Professor Mary Boyes

Abstract

Posttraumatic stress disorder (PTSD) is a disorder triggered by experiencing a traumatic event. PTSD causes recurrent flashbacks of memories that lead to over-consolidation that prevents extinction of emotional and physiological responses to the memory. Because individuals can respond differently to trauma, no measures are currently practiced to prevent PTSD. By studying the changes in the brain before and after PTSD diagnosis, it can be hypothesized that treatments that regulate the hypothalamic-pituitary-adrenal (HPA) axis activity may prevent PTSD. Risk of developing PTSD is associated with abnormal cortisol and norepinephrine levels and altered HPA axis functioning after trauma. New research on how stress alters the HPA axis has opened up the opportunity to prevent PTSD in high-risk patients. Oxytocin regulates the HPA axis by inhibiting amygdala activity and the fear response. Stress is also reduced by increased benefit received from social support. After reviewing previous studies on oxytocin, PTSD, and the HPA axis, it was concluded that regulation of the HPA axis by oxytocin may prevent PTSD by inhibiting memory over-consolidation and by reducing physical damage to the brain caused by abnormal hormone levels. Oxytocin is suitable for pharmacological studies because oxytocin can reach the central nervous system through intranasal spray application with minimal side effects. Oxytocin's anxiolytic qualities and ability to alter HPA axis function call for more research to evaluate its potential pharmacological applications. More research is needed on regulation of the HPA axis to prevent PTSD and the duration and dosage of oxytocin treatments necessary to achieve sufficient HPA regulation.

Introduction

PTSD is a mental health disorder associated with maladaptive fear response, excessive anxiety, hyperarousal, avoidance, and flashbacks. Symptoms can last for month or years, and typical treatments involve a combination of psychotherapy and medications like antidepressants and anti-anxiety drugs.

Patients with PTSD show evidence of dysregulated hypothalamic-pituitary-adrenal (HPA) axis resulting in lower levels of cortisol. Long term stress causes excessive secretions of norepinephrine that may lead to harmful physical changes in the brain and body, such as atrophy of the hippocampus and elevated blood pressure. While PTSD symptoms often do not begin for months following trauma, changes in hormones may begin much sooner.

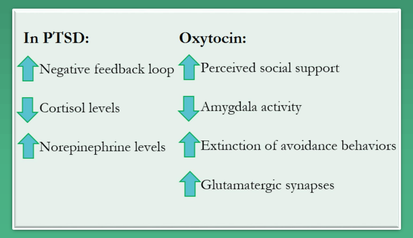
Currently, PTSD is only diagnosed and treated after symptoms included in the DSM occur. Previous research has found several risk factors for PTSD including genetics and abnormal hormone levels following trauma, and these factors could be used to target and treat high-risk individuals. Preventing PTSD would not only stop symptoms from occurring, but it would also prevent the damages caused by the altered hormone levels.

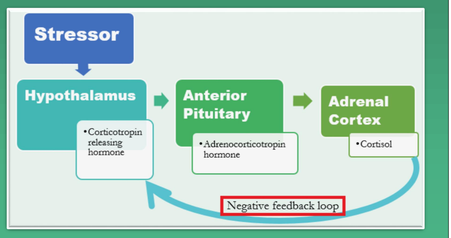
Pharmacological treatments that regulate the HPA axis may be effective in preventing PTSD. Oxytocin was chosen as the focus of research in this study because it can be delivered to the central nervous system in a nasal spray with minimal side effects.

Results

Changes in the brain caused by PTSD
- Increased negative feedback in HPA axis
  - Lowers circulating cortisol levels to limit over-activation
    - Effort to maintain homeostasis
- Sympathetic nervous system over activation
  - Elevates norepinephrine levels
- Happen before PTSD onset

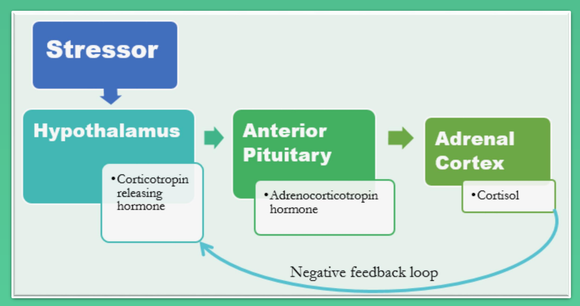
Oxytocin's ability to regulate the HPA axis
- Increases perception of social support
- Inhibits the stress response
  - Inhibits amygdala activity
  - Decreases levels of adrenocorticotropic hormone
- Facilitates extinction of avoidance behaviors
- Enhances plasticity of glutamatergic synapses
  - New connections promote extinction





Background

In a properly functioning HPA axis, a stressor prompts the release of corticotropin releasing hormone from the hypothalamus. This hormone causes a circulation in the levels of cortisol, a steroid glucocorticoid hormone. Cortisol influences memory and the release of norepinephrine from the adrenal medulla. The elevated levels of cortisol trigger a negative feedback loop in the HPA axis.



Oxytocin is a peptide hormone that acts as a neurotransmitter. The hypothalamus synthesize oxytocin naturally, and the pituitary releases this hormone in to the bloodstream Administration of oxytocin in humans has mostly been through intravenous infusion or nasal spray, and it has been commonly used to induce labor and enhance lactation

Conclusion

Due to the physical damages caused by HPA dysregulation in PTSD, preventative treatments should be used for patients at risk of developing PTSD. Intranasal oxytocin should be studied as a preventative pharmacological treatment because of its ability to regulate the HPA axis's response to a stressor and its lack of harsh side effects in short-term treatments. Excessive secretions of norepinephrine may cause atrophy of the hippocampus and dysregulation of the HPA axis can also lead to cardiovascular disease through increases in blood pressure. Not only would oxytocin treatments prevent the occurrence of harsh side effects, but regulation of the HPA axis would also prevent the physical damages associated with PTSD.

Works Cited

Bakermans-Kranenburg, M. J., & van IJzendoorn, M. H. (2013). Sniffing around oxytocin: Review and meta-analyses of trials in healthy and clinical groups with implications for pharmacotherapy. *Translational Psychiatry*, *3*(5):1-14. doi:10.1038/tp.2013.34

Cain, C. K., Maynand, G. D., & Kehne, J. H. (2012). Targeting memory processes with drugs to prevent or cure PTSD. *Expert Opinion*, *12*(9):1323-1350. doi:10.1517/13543784.2012.704020

Frijling, J. L., van Zuiden, M., Koch, S. B., Nawjin, L., Goslings, C., Luitse, J. S. …& Olff, M. (2014). Efficacy of oxytocin administration early after psychotrauma in preventing the development of PTSD: Study protocol of a randomized controlled trial. *BMC Psychiatry*. *14*(92):1-11. doi:10.1186/1471-244X-14-92.

Jones, T. & Moller, M. D. (2011). Implications of hypothalamic-pituitary-adrenal axis functioning in posttraumatic stress disorder. *Journal of the American Psychiatric Nurses Association*, *17*(6):393-403. doi:10.1177/1078390311420564.

MacDonald, E., Dadds, M. R., Brennan, J. L., Williams, K., Levy, F., & Cauchi, A. J. (2011). A review of safety, side-effects and subjective reactions to intranasal oxytocin in human research. *Psychoneuroendocrinology*, *36*(8):1114-1126. doi:10.1016/j.psyneuen.2011.02.015.

Parker, K. J., Buckmaster, C. L., Schatzberg, A. F. & Lyons D. M. 2005. Intranasal oxytocin administration attenuates the ACTH stress response in monkeys. *Psychoneuroendocrinology*, *30*:924-929. doi:10.1016/j.psyneuen.2005.04.002.

Smith, A. S. & Wang, Z. (2014). Hypothalamic Oxytocin Mediates Social Buffering of the Stress Response. *Biological Psychiatry*, *74*(4)281-288. doi:10.1016/j.biopsych.2013.09.017.

Wingenfeld, K., Whooley, M.A., Neylan, T. C., Otte, C., & Cohen B. E. (2015). Effect of current and lifetime posttraumatic stress disorder on 24-h urinary catecholamines and cortisol: Results from the mind and your heart study. *Psychoneuroendocrinology*. *52*:83-91. doi:10.1016/j.psyneuen.2014.10.023.

Acknowledgements

I would like to thank Professor Mary Boyes and HONR 200 TA's Abby Burns, Bethany Echerd, and Maheen Khan for their helpful guidance throughout my research.

Further information: kovalchicklv@vcu.edu