2016

The Tenth Annual Amygdala, Stress, and PTSD Conference: “The Amygdala: Dysfunction, Hyperfunction, and Connectivity”

Eric M. Prager
*John Wiley & Sons, Inc.*

Gary H. Wynn
*Uniformed Services University of the Health Sciences*

Robert J. Ursano
*Uniformed Services University of the Health Sciences*

Follow this and additional works at: [http://digitalcommons.unl.edu/usuhs](http://digitalcommons.unl.edu/usuhs)


[http://digitalcommons.unl.edu/usuhs/172](http://digitalcommons.unl.edu/usuhs/172)

This Article is brought to you for free and open access by the U.S. Department of Defense at DigitalCommons@University of Nebraska - Lincoln. It has been accepted for inclusion in Uniformed Services University of the Health Sciences by an authorized administrator of DigitalCommons@University of Nebraska - Lincoln.
Preface

The Tenth Annual Amygdala, Stress, and PTSD Conference: “The Amygdala: Dysfunction, Hyperfunction, and Connectivity”

Eric M. Prager,1* Gary H. Wynn,2,3,4 and Robert J. Ursano2,3,4

1John Wiley & Sons, Inc., Hoboken, New Jersey
2Center for the Study of Traumatic Stress, F. Edward Hébert School of Medicine, Uniformed Services University of the Health Sciences, Bethesda, Maryland
3Department of Psychiatry, F. Edward Hébert School of Medicine, Uniformed Services University of the Health Sciences, Bethesda, Maryland
4Program in Neuroscience, F. Edward Hébert School of Medicine, Uniformed Services University of the Health Sciences, Bethesda, Maryland

Key words: Amygdala; Stress; Posttraumatic Stress Disorder; Anxiety; Epilepsy; Fragile X Syndrome; schizophrenia; Urbach-Wiethe disease

The Amygdala, Stress, and PTSD Conference, often referred to simply as The Amygdala Conference, is a continuing education conference held each April at the Uniformed Services University (USU) and sponsored by The Center for the Study of Traumatic Stress in collaboration with the USU Department of Psychiatry, USU Neuroscience Program, USU Department of Family Medicine, and The Walter Reed National Military Medical Center Department of Psychiatry. Free and open to the public, this conference brings together nationally and internationally recognized scientists and clinicians to help support the translation of high-quality science into excellent clinical care.

Dedicating an entire conference to the amygdala stems from its neurobiological importance. The amygdala, a pair of almond-shaped clusters of nuclei located medially and deep in the temporal lobe, is a complex structure with variable processes and connections. Adding an additional level of complexity is its internal physiology, which varies between nuclei (Sah et al., 2003). The alterations in these processes as well as the internal physiology are fundamentally important to understanding a range of disorders, which can cause substantial suffering, including increased morbidity and mortality among a wide range of individuals, as well as having substantial impact on families and their communities.

The amygdaloid complex comprises approximately 13 nuclei, including the basolateral complex, medial nucleus, cortical nucleus, central nucleus, and intercalated cell clusters (Krettek and Price, 1978; Lang and Pare, 1998). Each nucleus receives inputs from multiple, yet distinct, brain regions but also has extensive intranuclear and internuclear connectivity. Efferent projections from the amygdala are widespread and include both cortical and subcortical regions (McDonald, 1998; Pitkanen, 2000). The amygdala as a whole comprises primarily glutamatergic pyramidal neurons and, to a lesser extent, GABAergic inhibitory interneurons. However, as in the case of the basolateral complex, GABAergic activity...
we collaborated with the part of the tenth anniversary of the audience beyond the conference attendees. Therefore, as science into excellent clinical care, we had to reach an realized that, to facilitate the translation of high-quality conditions.

might act as a network hub and explained what changes Africa. Dr. Harvey Pollard reviewed how the amygdala associated with an inability to recognize others' fear, while explained how dysfunction in the amygdala may be associated with an inability to recognize others' fear, while Dr. Daniel Stein spoke of trauma and PTSD in South explained how dysfunction in the amygdala may be associated with an inability to recognize others' fear, while Dr. Jacek Debiec provided strong ease was highlighted. Dr. Liberzon spoke about contextual processing of the amygdala in emotional memory and motivational behavior. Dr. Corbin, Alexander Crawford, and Israel Liberzon were among the speakers. Their talks emphasized animal models as well as translational implications in understanding specific disorders. For example, Dr. Corbin spoke about the role of the amygdala in fragile X syndrome, a neurodevelopmental disorder, and Dr. Crawford’s talk emphasized the use of zebrafish as a model for exploring the role of the amygdala in emotional memory and motivational behavior. Dr. Liberzon spoke about contextual processing in PTSD in animal models and in humans.

In 2015, a more clinical and holistic approach to understanding the role of the amygdala in health and disease was highlighted. Dr. Janak and Tye, 2015). Recent evidence, however, has revealed a more essential role for the amygdala than was previously thought. Indeed, excess acetylcholine (ACh) in the amygdala, resulting from the loss of acetylcholinesterase, the catalyzing enzyme for ACh, results in seizure generation after exposure to the nerve agent soman (Prager et al., 2013). Furthermore, excessive activation of the amygdala may contribute to the cluster of PTSD symptoms, including hypervigilance, intrusive memories, and impaired sleep (Diamond and Zoladz, 2016). Alternatively, a failure of the amygdala to function properly may be central to the development of Urbach-Wiethe disease, which impairs fear responses and emotional memory processing (Koen et al., 2016).

The complexity of the amygdala has understandably resulted in an impressive array of invaluable research with strong clinical implications. The 2014 and 2015 Amygdala Conference themes were from “Bench to Bedside” and “Of Mice and Man,” respectively. The significance of these 2 years, in particular, was the emphasis of translational research and clinical application. In 2014, Joshua Corbin, Alexander Crawford, and Israel Liberzon were among the speakers. Their talks emphasized animal models as well as translational implications in understanding specific disorders. For example, Dr. Corbin spoke about the role of the amygdala in fragile X syndrome, a neurodevelopmental disorder, and Dr. Crawford’s talk emphasized the use of zebrafish as a model for exploring the role of the amygdala in emotional memory and motivational behavior. Dr. Liberonz spoke about contextual processing in PTSD in animal models and in humans.

In 2015, a more clinical and holistic approach to understanding the role of the amygdala in health and disease was highlighted. Dr. Jacek Debiec provided strong evidence that offspring learn adaptive and maladaptive behaviors, such as anxiety, from their parents and that this may lead to significant increases in amygdala activity. Dr. Abigail Marsh reviewed various theories concerning the role of the amygdala in perceiving fearful expressions and explained how dysfunction in the amygdala may be associated with an inability to recognize others’ fear, while Dr. Harvey Pollard reviewed how the amygdala might act as a network hub and explained what changes in this network reveal about normal and pathological conditions.

After concluding last year’s Amygdala Conference, we realized that, to facilitate the translation of high-quality science into excellent clinical care, we had to reach an audience beyond the conference attendees. Therefore, as part of the tenth anniversary of the Amygdala Conference, we collaborated with the Journal of Neuroscience Research to create this Special Issue entitled “The Amygdala: Dysfunction, Hyperfunction, and Connectivity.”
during development, are more likely to have a hypoactive amygdala as a result of damage or dysfunction. Animal models have also been used to understand early developmental and intergenerational mechanisms. Debiec and Sullivan (2014) have previously shown that rodents acquire maternal fear through social learning at birth via an amygdala–dependent mechanism. In this Special Issue, Chang and Debiec (2016) show that the mother–to–infant transmission of fear in preweaning rats is also associated with a significant increase of activity in multiple subcortical brain regions beyond the amygdala.

Although it is also known that stress throughout childhood is associated with structural changes in the brain, Evans et al. (2016) provide new translational evidence from human subjects that exposure to chronic stress via cumulative risk exposures during childhood leads to larger amygdala volumes and elevated amygdala reactivity in adulthood. However, structural changes do not occur only as a result of chronic stress. In a Letter to the Editor, Williams et al. (2016) find clear neuroarchitectural changes in the basolateral amygdala but not the centromedial amygdala of schizophrenic patients.

Although a substantial portion of the issue is devoted to translational research, this issue also provides a series of studies and reviews examining how different diseases lead to changes in synaptic transmission and the importance of animal models in the development of novel therapies. Prager et al. (2016) provide an overview of the GABAergic inhibitory system within the amygdala in health and disease. The authors discuss mechanisms that modulate inhibitory synaptic transmission within the basolateral complex and how different deficits in inhibitory synaptic transmission contribute to various disorders. One such disorder that is discussed is fragile X. Studies have found pathological changes in GABAergic neurotransmission in this neurodevelopmental disorder, leading to alterations in the excitatory/inhibitory balance in local circuits, including the amygdala (Paluszkiewicz et al., 2011). In an original research article, Martin et al. (2016) target tonic inhibitory transmission to treat neurophysiological symptoms such as anxiety in a fragile X model. They find that application of a novel agonist targeting extrasynaptic GABA_A receptors rescues inhibitory neurotransmission in the amygdala and improves the excitatory/inhibitory balance. Changes in excitatory neurotransmission are also discussed. In another original research article, Klein et al. (2016) find that, after a mild traumatic brain injury (TBI), excitatory synaptic transmission is increased. Exposing animals to stress prior to TBI was found to lead to a significant decrease in excitatory synaptic transmission after TBI.

In an excellent summary article, Mears and Pollard (2016) discuss the complex network that is the brain and the role of the amygdala as a hub in health and disease. Their article explains how graph theory has been applied to study structural and functional networks in the brain. Some brain networks are highly connected hubs, which play an essential role in information processing because of their high connectivity and centrality. The amygdala may be considered a network hub because it is considered one of the most highly connected regions of the brain. Changes in the nodal properties of the amygdala are present in depression but may also be present in other neurological diseases. The authors rightfully conclude this inaugural issue by suggesting that focusing operational attention on the amygdala network and its associated functional and anatomical systems will contribute to the development of new tools to predict, diagnose, and design individualized treatment strategies for a broad range of neurological and psychiatric disorders.

This Special Issue, rather than representing a culmination of 10 years of conferences, is the beginning of further efforts to communicate this excellent science to other researchers and clinicians. Moving forward, we are excited about our next conference, the 11th annual Amygdala, Stress, and PTSD Conference: The Effects of Stress and Loss/www.amygdalaPTSDconference.org. We will hear presentations from five esteemed scientists, including Stephen Suomi, Patrizia Casaccia, Naomi Simon, Michael Fanselow, and David Krantz, each of whom will speak about different biological mechanisms underlying stress, loss, fear, and downstream effects of PTSD. We will take this opportunity to continue our collaboration with The Journal of Neuroscience Research through the In Focus Section, which is a collection of articles that focuses on updating a particular subject within neuroscience.

ACKNOWLEDGMENTS
We thank Dr. Joshua Plotkin and Dr. Caterina Cuhna for their critical input and revisions to this article.

CONFLICT OF INTEREST STATEMENT
The authors declare that there are no conflicts of interest.

ROLE OF AUTHORS
All authors take responsibility for the integrity and accuracy of this article. Drafting of the manuscript and critical revisions of the article: EMP, GHW, RJU.

REFERENCES


