Asian Journal of Psychiatry 46 (2019) 103–104

Contents lists available at ScienceDirect

Asian Journal of Psychiatry

journal homepage: www.elsevier.com/locate/ajp

Letter to the Editor

Neuropeptide Y and resilience to suicide

Neuropeptide Y (NPY) and its receptors are present in the central as well as the peripheral nervous system (Reichmann and Holzer, 2016; Walther et al., 2011). Seven different Y receptors have been described in vertebrates, of which up to 5 (Y1, Y2, Y4, Y5, y6) are present in mammals. In humans, high levels of NPY are found in the basal ganglia, nucleus accumbens, amygdala and the hypothalamus. NPY has been implicated in several biological processes including food intake, anxiety and depression-related behaviors, neuronal excitability and seizures, circadian rhythms, alcohol consumption, neuroendocrine secretions, nociception, and cardiorespiratory functions (Reichmann and Holzer, 2016; Walther et al., 2011). Research data have indicated that NPY is involved in the pathophysiology of different psychiatric and non-psychiatric disorders such as posttraumatic stress disorder (PTSD), anxiety, depression, memory loss, sleep disorders, pain syndromes, and obesity (Crespi, 2011; Reichmann and Holzer, 2016; Walther et al., 2011; Yehuda et al., 2006). For example, studies suggest that a reduction in cerebral NPY function may be associated with depressive symptoms (Crespi, 2011).

Considerable evidence suggests that NPY is involved in the neurobiology of resilience (Reichmann and Holzer, 2016; Sher, 2019a; Walther et al., 2011) which can be defined as the ability to adapt to and overcome adversity and trauma (Sher, 2019a). A number of reports indicate that NPY is crucial for the stress adaptation process, besides other major biological pathways such as the hypothalamic–pituitary–adrenal (HPA) axis and the autonomic nervous system. Accordingly, a concept has been developed, which implicates NPY in the termination of the stress response.

Suicide remains an important and difficult public health issue (Sher, 2019a). Multiple psychosocial aspects contribute to suicidal behavior (Snowdon, 2018; Sher, 2019a). For example, cultural beliefs affect suicide risk (Snowdon, 2018). Also, many neurobiological factors such as the HPA axis or brain-derived neurotrophic factor (BDNF) are involved in the pathophysiology of suicidal behavior (Sher, 2019a; Sonal and Raghavan, 2018).

Several studies indicate that NPY may be involved in the neurobiology of suicide. Widdowson et al. (1992) measured NPY in postmortem brain tissue from victims of suicide and from individuals dying a sudden natural or accidental death, i.e., controls. Concentrations of NPY-immunoreactivity were significantly lower in postmortem frontal cortex and caudate nucleus from suicide victims compared with age-matched controls. Caberlotto and Hurd (2001) found that the Y2 mRNA expression was elevated in layer IV of the dorsolateral prefrontal cortex of individuals who died by suicide.

Westrin et al. (1999) compared plasma NPY levels in patients with mood disorders who had recently made a suicide attempt and healthy controls. NPY levels were lower in recent suicide attempters in comparison to controls. Patients who had repeatedly attempted suicide had the lowest plasma NPY levels. Sandberg et al. (2014) performed lumbar puncture on clinically stable patients with bipolar disorder. NPY-like immunoreactivity in cerebrospinal fluid (CSF) was significantly lower in patients with a history of suicide attempt in comparison to patients who had not attempted suicide prior to lumbar puncture and in patients who made a suicide attempt during the one year follow-up period compared to patients who did not. When compared with healthy controls CSF NPY was lower in patients with mood disorders who had recently attempted suicide. Patients who had repeatedly attempted suicide had the lowest CSF NPY.

Studies conducted over the past 15–20 years indicate that resilience is an important protective factor against suicide risk (Sher, 2019a). Currently, resilience is becoming a focus of suicide research and prevention. Studies suggest that low resilience is related to a dysregulation in stress response and the development of emotional dysregulation and psychopathology, including suicidal behavior (Sher, 2019a). Promoting resilience may reduce suicide risk in the general population, in groups at elevated suicide risk, and among high-risk individuals.

Probably, resilience partially mediates effects of the NPYergic system on suicidality. It is also possible that some effects of NPY on suicidality are independent of resilience. NPY abnormalities might be biomarkers of suicide risk.

Resilience may mean not only that someone responds to stress more adaptively, but that someone actively creates a world in which stressful situations are less likely to take place (Sher, 2019b). Therefore, I have recently proposed to term this ability to create a stress-free world “primary resilience” while the ability to adapt well in the face of stress and adversity can be called “secondary resilience” (Sher, 2019b). It is interesting to hypothesize that NPY may affect both primary and secondary resilience to stress-related disorders and suicidal behavior.

The implications of NPY in resilience and suicidal behavior make the NPYergic system a promising target for the development of novel therapeutic interventions to prevent suicidal behavior. These may include NPY administration and the development of medications targeting NPY receptors. It is probably necessary to explore and develop NPY family related small ligands as promising drug candidates for the treatment of suicidality.

Financial disclosure

No financial support was provided for the preparation of this article.

Declaration of Competing Interest

None.

Acknowledgements

None.

https://doi.org/10.1016/j.ajp.2019.09.029
Received 21 September 2019
1876-2018/ © 2019 Elsevier B.V. All rights reserved.

References

Caberlotto, L., Hurd, Y.L., 2001. Neuropeptide Y Y(1) and Y(2) receptor mRNA expression in the prefrontal cortex of psychiatric subjects. Relationship of Y(2) subtype to suicidal behavior. Neuropsychopharmacology 25 (1), 91–97.

Crespi, F., 2011. Influence of Neuropeptide Y and antidepressants upon cerebral monoamines involved in depression: an in vivo electrochemical study. Brain Res. 1407, 27–37. https://doi.org/10.1016/j.brainres.2011.05.033.

Reichmann, F., Holzer, P., 2016. Neuropeptide Y. A stressful review. Neuropeptides 55, 99–109. https://doi.org/10.1016/j.npep.2015.09.008.

Sandberg, J.V., Jakobsson, J., Pålsson, E., Landén, M., Mathé, A.A., 2014. Low neuropeptide Y in cerebrospinal fluid in bipolar patients is associated with previous and prospective suicide attempts. Eur. Neuropsychopharmacol. 24 (12), 1907–1915. https://doi.org/10.1016/j.euroneuro.2014.10.006.

Sher, L., 2019a. Resilience as a focus of suicide research and prevention. Acta Psychiatr. Scand. 140 (2), 169–180. https://doi.org/10.1111/acps.13059.

Sher, L., 2019b. Primary and secondary resilience to stress-related disorders and suicidal behavior. Aust. N. Z. J. Psychiatry 13 (Sep), 4867419876698. https://doi.org/10.1177/0004867419876698. [Epub ahead of print].

Snowdon, J., 2018. Differences between patterns of suicide in East Asia and the West. The importance of sociocultural factors. Asian J. Psychiatr. 37, 106–111. https://doi.org/10.1016/j.ajp.2018.08.019.

Sonal, A., Raghavan, V., 2018. Brain derived neurotrophic factor (BDNF) and suicidal behavior: a review of studies from Asian countries. Asian J. Psychiatr. 33, 128–132. https://doi.org/10.1016/j.ajp.2018.03.004.

Walther, C., Mörl, K., Beck-Sickinger, A.G., 2011. Neuropeptide Y receptors: ligand binding and trafficking suggest novel approaches in drug development. J. Pept. Sci. 17 (4), 233–246. https://doi.org/10.1002/psc.1357.

Westrin, A., Ekman, R., Träskman-Bendz, L., 1999. Alterations of corticotropin releasing hormone (CRH) and neuropeptide Y (NPY) plasma levels in mood disorder patients with a recent suicide attempt. Eur. Neuropsychopharmacol. 9 (3), 205–211.

Widdowson, P.S., Ordway, G.A., Halaris, A.E., 1992. Reduced neuropeptide Y concentrations in suicide brain. J. Neurochem. 59 (1), 73–80.

Yehuda, R., Brand, S., Yang, R.K., 2006. Plasma neuropeptide Y concentrations in combat exposed veterans: relationship to trauma exposure, recovery from PTSD, and coping. Biol. Psychiatry 59 (7), 660–663.

Leo Sher[a,b,*]

[a] *James J. Peters Veterans' Administration Medical Center, Bronx, NY, USA*

[b] *Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY, USA*

E-mail address: Leo.Sher@mssm.edu.

[*] Corresponding author at: James J. Peters VA Medical Center, 130 West Kingsbridge Road, Bronx, NY 10468, USA.