Corticotropin-Releasing Hormone Receptor 1 Antagonist With or Without Corticotropin-Releasing Hormone Receptor 2 Remain Promising in Relieving Human Acute Psychological Stress and Related Intestinal Hyperpermeability

Li-Yen Tseng, Akio Inui, Chih-Yen Chen

Corticotropin-releasing hormone (CRH) has clinical relevance to stress, feeding behavior, gut motility and immunity. Emerging evidence indicates that two CRH receptor subtypes, receptor 1 (CRH1-R) and 2 (CRH2-R), play pivotal roles in the regulation of these biological functions induced by CRH, depending on which receptor subtypes to be activated. Manipulating and balancing at CRH1-R and CRH2-R has become a novel concept to treat stress-related disorders and gut dysfunction, such as psychological stress and related intestinal hyperpermeability.

© 2015 ACT. All rights reserved.

Key words: Corticotropin-releasing hormone; Intestinal hyperpermeability; Receptor; Stress
mediator of CRH and upstream of cortisol. The measurement of plasma adrenocorticotropic hormone can give us further information. The level of salivary cortisol may reflect both cortisol and salivary secretary capacity, but the latter of which may be affected by stress and sympathetic nervous system.

The results that the intestinal hyperpermeability, but not salivary cortisol concentrations (and/or STAI score), induced by public speech and exogenous CRH was blocked by mast cell stabilizer sodium cromoglycate, may reveal the superiority of CRH receptor antagonists to mast cell blockers in reversing central neuroendocrinological and peripheral gut mucosal barrier dysfunctions (Chen et al[2], 2014). Neuropeptides tend to produce different neurobiological actions depending on which receptor subtype they activate. CRH receptor 1 (CRH1-R) antagonist has been shown to attenuate hippocampal noradrenaline release, visceral perception, adrenocorticotropic hormone release, and anxiety in a rodent model (Saito et al[3], 2005). On the other hand, CRH receptor 2 (CRH2-R) has been demonstrated to induce anxiolytic response via phosphorylation of the transcription factor cAMP response element-binding protein (Creb) but not activation of HPA (Kishimoto et al[4], 2000). Furthermore, CRH1-R has been identified on the cell surface of human intestinal mucosal mast cells, and CRH is reported to activate CD14+ cells to produce tumor necrosis factor-α and induce endothelial barrier dysfunction (Song et al[5], 2013). Using respective agonists and/or antagonists of CRH1-R and CRH2-R in exploring human acute psychological stress and related alteration of intestinal permeability becomes a very intriguing topic.

CONCLUSION

In conclusion, differentially nibbling CRH1-R and CRH2-R remains promising for the management of human acute psychological stress and related intestinal hyperpermeability. The collective evidence can provide useful implications for the future treatment and functional gastrointestinal disorders, such as irritable bowel syndrome.

ACKNOWLEDGEMENTS

The project was funded in part by an intramural grant from Taipei Veterans General Hospital (VGH 94-030) and Yen Tjing Ling Medical Foundation (CI-100-31), Taiwan.

CONFLICT OF INTERESTS

The Author has no conflicts of interest to declare.

REFERENCES


Peer reviewer: Peer reviewer: Yan Teng, Associate Professor, Genetic laboratory of Development and Diseases, Institute of Biotechnology, AMMS, 20 Dongdajie Street, Beijing 100071, China.