Study for the neural molecular basis and clinical application in vasopressin treating pain

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1 Introduction

Pain, which is one of the most common medical symptoms, affects human beings greatly. According to the incomplete statistics, the annual loss due to the pain is over one trillion U.S. dollars in the United States.

Arginine vasopressin (AVP), also known as antidiuretic hormone (ADH), is mainly synthesized in the hypothalamic paraventricular nucleus (PVN) and supraoptic nucleus (SON), transported to the neurohypophysis by the hypothalamus-pituitary axis for storage, and released into the body circulation where it influences physiological functions such as the water and electrolyte balance. Recent studies have proven that AVP also plays an important role in the pain regulation.

2 Materials and Methods

This project was founded by the National Natural Science Foundation and the Army Major Research Programs. Pioneered the technologies of the push-pull perfusion in the awake animal nucleus and the nucleus receptor knockout, combining with many research tools of molecular biology and neuroscience, we explored the neural molecular mechanism of AVP regulating pain systematically. Using the multi-center clinical study, we determine the Program of Intranasal AVP Treatment of Migraine.

3 Results

3.1 Clinical Trials

The analgesic site of AVP modulating pain was found in the animal experiments. The law of intranasal AVP treatment of migraine was worked out in the multi-center clinical studies. The results showed that intranasal 400 ng AVP had a role in 96.4% of migraine patients effective including 75.0% complete response; 200 ng AVP in 89.3% of migraine patients effective including 46.4% complete response; and 100 ng AVP in 60.7% of migraine patients effective including 28.6% complete response. The Program of Intranasal AVP Treatment of Migraine should be determined as administered one per six hours and 200-400ng every time.

The Program of Intranasal AVP Treatment of Migraine has been used to treat nearly 30,000 migraine patients with a good effect in more than 500 hospitals and clinics all over the country.

3.2 Neurobiological Research

The project studied the neural molecular mechanism of AVP regulating pain in the different levels from a whole body to a molecule. The results showed that ① The brain, not spinal cord and peripheral AVP could regulate pain; ② AVP that regulated pain was synthesized and released in the PVN, not SON; ③ AVP in the PVN was transported to the periaqueductal gray (PAG), nucleus raphe magnus (NRM) and caudate nucleus (CdN); ④ AVP in the PAG enhanced the synthesis of Leucine-enkephalin (L-Ek), Methionine-enkephalin (M-Ek) and β-endorphin (β-Ep) rather than dynorphin A1-13 (DynA1-13); ⑤
AVP induced the serotonin (5-HT) release in the NRM and the acetylcholine (Ach) release in the CdN; and 5-HT and Ach in the spinal cord could influence the endogenous opiate peptides to regulate pain.

4 Discussions

The project has published 23 papers including 20 papers were published in famous SCI journals such as Brain Research, Brain Research Bulletin, Life Sciences, Neuroscience Research, Neuroscience Letters, Peptides, Regulatory Peptides and Neuropeptides. The cumulative impact factor was 46.160. The papers were cited 811 in total including 614 times by the famous SCI journals such as Journal of Neurosciences, Pain and Journal of Physiology. The single paper was cited 93 times in maximum. The paper titled “Arginine vasopressin is an important regulator in antinociceptive modulation of hypothalamic paraventricular nucleus in the rat” was one of the most downloaded articles in the neuropeptide field in the first quarter of 2007.

The Shanghai Investigation and Check Committee of Medical Science has confirmed that the Program of Intranasal AVP Treatment of Migraine is the first application and the neural molecular mechanism of AVP regulating pain systematically is the first time to clarify in the world.

REFERENCES


