

Ontogenic Changes in Ulcerogenic Cinchophen Effect in Neuroendocrine Cells during Postnatal Rat Brain Development.

Hisaka Jingu^{1,2*}, Misae Ohta² and Noriyuki Koibuchi^{1,2} ¹Department of Physiology, Gunma University School of Medicine, Maebashi, Japan, ²CREST, Japan Science and Technology Corporation.

Cinchophen (2-phenyl-4-quinolinecarboxylic acid), a quinine derivative that has been used as an analgesic, causes gastric and duodenal ulcer. Such uleceration may be caused by activation of the hypothalamo-pituitary-adrenal system. Thus, we have been using cinchophen as a stressor. Recently, many investigators focus on the effect of stress hormones on brain development. Our system can be used to examine such effect. We hypothesized that perinatal exposure to glucocorticoid by cinchophen treatment may induce structural changes in brain. In particular, cinchophen exposure during critical period may induce serious changes. However, such critical period is not known yet. On the other hand, it is well known that Fos is expressed in nuclei of activated cells after various kinds of stimuli. To study the ontogenic change in stress sensitivity during postnatal brain development, we examined the ontogenic changes of Fos expression in the paraventricular nucleus of the hypothalamus (PVN), hippocampus, and the central nucleus of the amygdala in the rat brain after intraperitoneal injection of cinchophen as a stressor. Expressions of Fos-immunoreactive neurons were identified by immunohistochemistry using postnatal day (P)7, P10, P15, P21, and P60 rats. After P10, Fos was induced by cinchophen in the PVN. These results suggest that there may be a critical period for stress sensitivity during neurological development.