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MEETING ABSTRACT

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Age-dependent sensitivity to glucocorticoids in the developing mouse basolateral nucleus of the amygdala

Peter Koppensteiner[1,2,3], Shu Aizawa[1], Daisuke Yamada[1,3], Tomohiro Kabuta[1], Stefan Boehm[2], Keiji Wada[1,3] and Masayuki Sekiguchi[1,3,*]

[1]*Department of Degenerative Neurological Diseases, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Tokyo, Japan;* [2]*Department of Neurophysiology and Neuropharmacology, Center for Physiology and Pharmacology, Medical University of Vienna, Austria;* [3]*CREST, Japan Science and Technology Agency, Saitama, Japan*

Background: Experiences of severe trauma during childhood are thought to be risk factors for developing mental disorders, such as anxiety and mood disorders, later in life. Correspondingly, exposure of rodents to early-life stress has been shown to affect neuronal circuitry and emotional behavior in adulthood, indicating a significant impact of stress on brain development. One current hypothesis proposes that the developing central nervous system is more sensitive to environmental influences, such as stress, than the adult. To test this hypothesis, we compared long-lasting effects of systemic corticosterone (CORT) administrations in two distinct early developmental periods.

Methods: We performed whole-cell patch clamp recordings of brain slices of C57BL/6J mice, contextual fear conditioning and extinction behavioral testing, as well as quantitative real-time PCR experiments.

Results: Mice exposed to early-neonatal CORT treatment on postnatal days (PD) 2–4 exhibited strongly enhanced excitability of neurons of the basolateral nucleus of the amygdala (BLA) in early adolescence and displayed impaired extinction of contextually conditioned fear memory, a type of behavior in which the BLA plays an important role. Furthermore, gene-expression of NMDA receptor subunits as well as calcium-activated K^+ channels was reduced in the amygdala. In contrast, exposure to the same CORT concentrations in a late-neonatal period (PD17–19) did not significantly affect BLA electrophysiology or extinction learning in adolescence.

Discussion: Glucocorticoid exposure in early-neonatal life appears to affect the development of passive membrane properties of amygdala neurons and lead to increased amygdala excitability in adolescence. Our findings indicate that the treatment with glucocorticoids in early postnatal days could be a suitable model to study the mechanisms that link early-life stress and psychiatric disorders. Furthermore, our results emphasize the importance of a stress-free environment, especially in early developmental periods, as these periods appear to be highly sensitive to stress hormones. We therefore conclude that the early-neonatal period presents a window of opportunity for CORT to induce long-lasting alterations in amygdala electrophysiology and related behavior.

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*Corresponding author e-mail: *elec1@ncnp.go.jp*