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Review

Screening of central functions of amino acids and their metabolites for sedative and hypnotic effects using chick models

Mitsuhiro Furuse *

Laboratory of Regulation in Metabolism and Behavior, Faculty of Agriculture, Kyushu University, Fukuoka 812-8581, Japan

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ABSTRACT

The chick has a practical advantage in the screening process in that chicks require only small quantities of drugs. The chick separation stress paradigm has traditionally been recognized as a valid form of anxiolytic screening. Further, chick behavior involving standing motionless with eyes closed or sitting motionless with head drooped is nearly always associated with electrophysiological sleep.

When centrally administered, some DNA-encoded L-α-amino acids, as well as some DNA-non-encoded amino acids, such as metabolites of L-α-amino acids, D-amino acid and β-amino acid, have shown sedative and/or hypnotic effects in chicks. The effects of some of these amino acids have subsequently been confirmed in humans.

In conclusion, the chick model is convenient and useful for screening central functions of amino acids and their metabolites for hypnosis and sedation.

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1. Introduction

In modern society, most people have been subjected to numerous physical and mental stresses at various points in their lives. These stresses cause a variety of conditions, including insomnia, adjustment disorder, alcohol dependence and depression. Therefore, clarification is needed of the control mechanisms of stress, such as the induction of sleep and sedation.

In 1999, it was reported that the organization of the human genome is closer to that of the chicken than it is to that of the mouse; this finding was achieved by adding comparative mapping results from a range of vertebrates (Burt et al., 1999). The total number of autosomal conserved segments is interesting from an evolutionary point of view.

The chick separation stress paradigm has traditionally been used as a biobehavioral assay, and it is recognized as a valid form of anxiolytic screening. Chicks feel comfortable in crowds, but they become stressed when isolated. This social separation stress increases spontaneous activity in chicks as well as their distress

* Fax: +81 92 642 2954.
E-mail address: furuse@brs.kyushu-u.ac.jp

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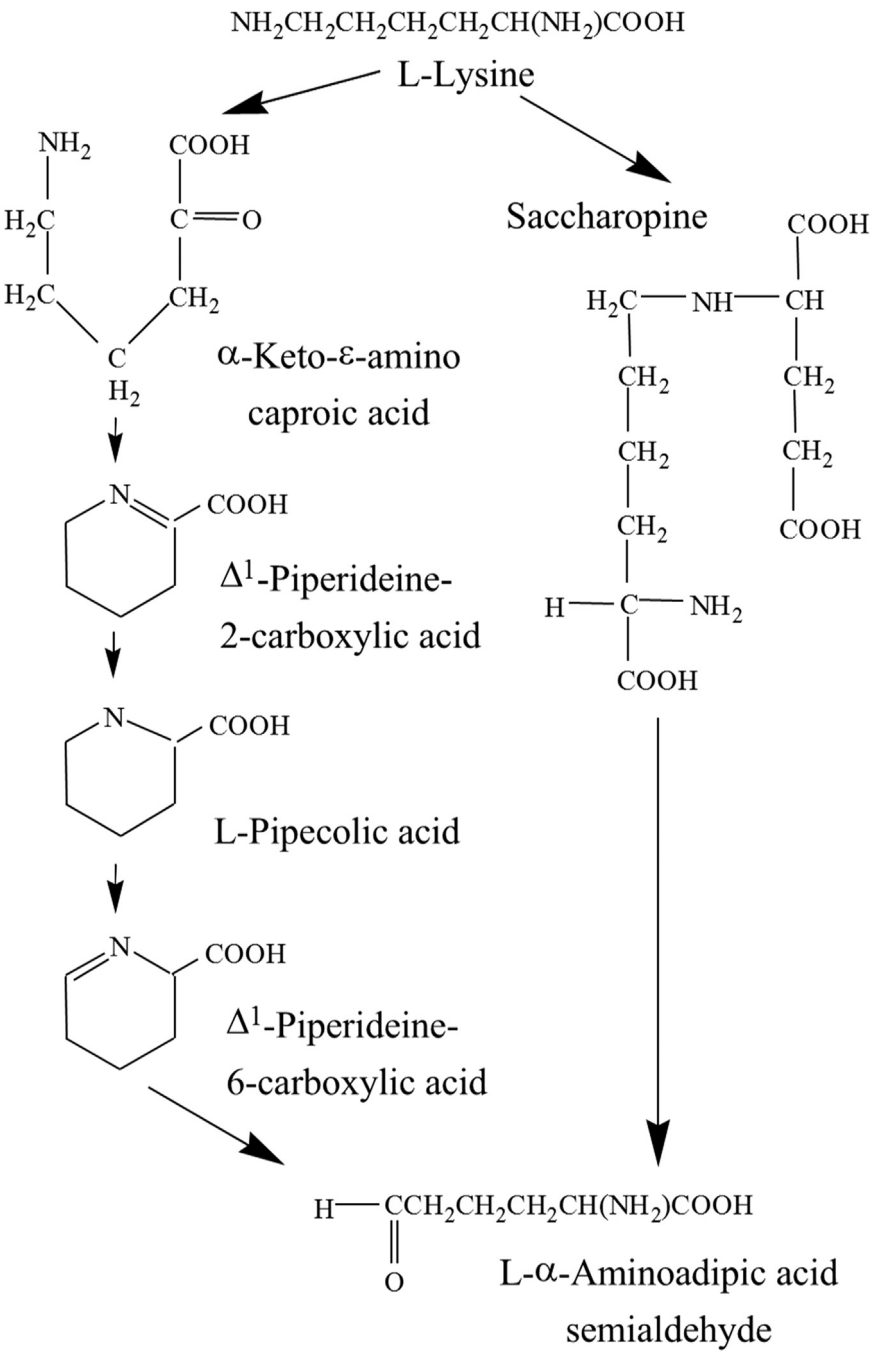

Fig. 1. Metabolic pathways of L-Lys in the body.

vocalizations (DVs). Various drugs having an anxiolytic action in rodent models of anxiety also showed anxiolytic effects in this chick separation stress model (Feltenstein et al., 2003, 2004).

On the basis of the method developed by van Luijtelaar et al. (1987), the chick behaviors were classified into four categories: (1) active wakefulness; (2) standing/sitting motionless with eyes open; (3) standing motionless with eyes closed; (4) sitting motionless with head drooping (sleeping posture). van Luijtelaar et al. (1987) demonstrated that the sleeping posture and sitting/motionless with eyes closed were nearly always associated with electrophysiological sleep (90.5% of the time). Therefore, in experiments involving neonatal chicks, results involving the sleeping posture can be taken to indicate electrophysiological sleep.

Davis et al. (1979) developed the chick head holder, which provides a quick, accurate method of delivering a solution to the brain of the young chicken. Using this holder, the effects on feeding behavior of neuropeptides and neurotransmitters were widely investigated in neonatal chicks (Furuse, 2002; Furuse et al., 2007; Cline and Furuse, 2012).

Further, these chick models possess a practical advantage in that chicks require only small quantities of drugs in the screening process (Watson et al., 1999).

During stressful conditions, the free amino acid pattern has been found to be modified in the brains of neonatal chicks. Hamasu et al. (2009a) reported that in the telencephalon, in the isolation-induced stress group compared with the control group, L-glutamine (L-Gln) was significantly higher, whereas γ-aminobutyric acid (GABA), L-arginine (L-Arg), and L-proline (L-Pro) were significantly lower, following 30 min restraint. In the diencephalon, L-alanine (L-Ala), L-Arg, L-asparagine (L-Asn), L-aspartic acid