PREFERENTIAL ACCUMULATION OF [\(^3\)H] CORTICOSTERONE IN CHICK BRAIN DURING EMBRYONIC DEVELOPMENT

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In the present study, we examined the distribution of [\(^3\)H]corticosterone ([\(^3\)H]B) in chick embryonic brain during development using two different routes of administration: intracerebral and intraocular. After injection of 1 \(\mu\)Ci into the brain of 8-day embryos, [\(^3\)H]B was preferentially accumulated in the retinas, whereas regions such as cerebral hemispheres, optic tecta, and midbrain showed lower amounts of [\(^3\)H]B. In 14-day embryos, a slightly higher amount of [\(^3\)H]B was found in retinas and midbrain in comparison with other regions of the brain. After injection into the eye, [\(^3\)H]B seemed to easily diffuse to brain regions and to preferentially accumulate in the opposite eye and very slowly diffused to other brain areas. The accumulation of the hormone in the retina parallels the presence of hormone receptors reported by others. A correlation between the preferential accumulation of hormone and its action is proposed.

INTRODUCTION

There is ample evidence that some hormones participate in the maturational processes of the central nervous system (CNS) both in animals and man. Although a great deal is known about the mechanism of action of thyroid hormones in the development of the central nervous system (CNS), the role played by steroid hormones is still unclear. Steroid hormones exert excitatory or inhibitory effects, depending on the degree of brain maturation at the time of hormone administration (1). Cortisol and

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estradiol, when administered to developing rats, accelerate CNS myelinogenesis (2); cortisol administration decreases brain GABA levels when given to rats after 8 days postnatally (3). Other studies have shown that accumulation of norepinephrine into cultured explants of chick embryonic cerebellum is lower when cortisol is present in the medium (4). More recent evidence has demonstrated that steroid hormones influence neurogenesis and cell proliferation (5–7). These findings support the view that corticosteroid hormones play a role in neuronal growth and differentiation and presumably also in neurotransmitter maturation. However, there is no information available of direct in vivo effects of steroid hormones on neural tissues thought to be affected by the hormone during development. In addition, no data are available about the accessibility of the hormone to different regions of the developing brain where the hormone is thought to have an effect. The possibility is proposed that the action of the hormone is not only dependent on the presence of receptors on the cell but also on the availability of the hormone in a region of the brain at a critical moment of neuronal maturation. Thus, in this paper we examined the distribution of corticosterone administered intracerebrally or intraocularly to the chick embryo in an attempt to determine whether localization of the hormone can be correlated with known actions of the hormone. A preliminary account of this work has been presented (8).

**EXPERIMENTAL PROCEDURE**

Chick embryos of 8, 11 and 14 days of incubation were exposed through a window in the egg shell and injected with 1 μCi of [3H]corticosterone (New England Nuclear, specific activity 58.9 Ci/mmol). The hormone was dried under vacuum and then resuspended into a 1:10 ethanol–saline solution. After the hormone injection, the window was tightly sealed with parafilm and the eggs were returned to the incubator. One, 2, and 5 hr after injection the embryos were killed by decapitation and the different regions of the brain (cerebral hemisphere, optic tecta, midbrain, and retinas) rapidly dissected. The tissue was put into a scintillation vial containing 3 ml of dichloromethane and shaken at room temperature overnight as described by McEwen et al. (9). One ml of the extracted material was counted in 10 ml of PPO–POPOP at 35% efficiency. The radioactivity in each brain area was expressed as percent of total radioactivity recovered. We have assumed that the radioactivity recovered is predominantly [3H]corticosterone. In their early studies McEwen and associates (9), using thin-layer chromatography, found that at 4 hr after [3H]corticosterone administration intraperitoneally in rats 70–80% of the radioactivity recovered was in the corticosterone spot and a very small proportion of the total radioactivity was recovered as 11-dehydrocorticosterone. Grosser (10) has reported that 11β-hydroxycorticosterone is a metabolite found in the adult mouse brain. In other studies of uptake of [3H]corticosterone, using neural explants removed from 14- or 16-day embryos and cultured, we found that at up to 6 hr of incubation 80–90% of radioactivity was corticosterone and the remaining was 11-dehydrocorticosterone as identified by thin-layer chromatography (11). In view of the