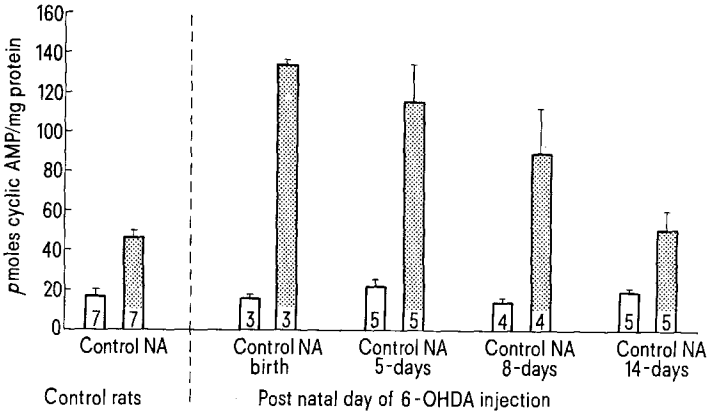

Rats were injected intracranially at various times after birth with either a control solution or 6-OHDA. At 35 days post-partum the animals were sacrificed and the cerebral corties removed, sliced and preincubated at 37 °C for 30 min in Krebs-Ringer bicarbonate buffer. The buffer was changed and the incubations were continued for 15 min at which time NA ($10^{-5}M$) was added. 6 min later the samples were homogenized, cyclic AMP was isolated, measured and expressed as picomoles per mg sample protein. The values in the Figure represent the mean ± SEM and the number of separate experiments are noted at the base of the individual bar graphs.

cerebral cortex of 35-day-old control rats. The cyclic AMP response to NA was 6–9-fold in the animals injected with 6-OHDA at either birth, 5 or 8 days postpartum. No enhanced accumulation of cyclic AMP in response to NA was seen in the incubated cerebral cortices of the animals injected with 6-OHDA at 14 days after birth. In these and earlier studies[3,4] basal levels of the cyclic nucleotide were not affected to any appreciable extent following the intracranial injections of 6-OHDA. In support of previous findings[3,4,16] the 6-OHDA injected rats that demonstrated a 'supersensitive' cyclic AMP response to NA were considerably smaller in size than control injected littermates and did not demonstrate any post-decapitation muscular activity. Moreover, these drug treated animals when handled manifested an increased irritability that was characterized by a fierce attacking behavior similar to that initially reported by PALMER[3] and subsequently described in detail by NAKAMURA and THOENEN[11].

Discussion. From the present experiments it is readily evident that intracranial injections of 6-OHDA at either birth or shortly thereafter lead to a consequent alteration of the receptor moiety of adenyl cyclase in the cerebral cortex when the animals reached the young adult stage. This hyperactive condition of the receptor might reflect an involvement of adenyl cyclase in the underlying molecular mechanisms associated with the phenomenon of adrenergic denervation supersensitivity. Similar investigations using adult rats have described a hyperactive adenyl cyclase following chemical destruction or depletion of adrenergic nerve endings[2–4]. Likewise, additional studies have reported that destruction of catecholamine containing nerve endings leads to supersensitive responses of amphetamine on dopamine receptors[17] and NA actions on isolated atrial and duodenal preparations[18,19].

6-hydroxydopamine appears to selectively destroy adrenergic nerve endings[6,8–11], however, a direct neurotoxic effect on cell bodies has been described[7]. Whether or not these actions of 6-OHDA are permanent in adult or developing animals is subject to considerable debate[9,10,15,17,18,20]. In the rat brain the development of central monoamine containing neurons and respective synaptic connections comes about after birth[9,12,13]. Perhaps in the present study the early injections of 6-OHDA (birth, 5 and 8 days postpartum) destroyed the fetal adrenergic neurons before the capacity to regenerate had appeared. In this case the synaptic inputs that would normally exert a controlling influence on the receptor sites remained absent and the immature hyperactive enzyme persisted throughout development. Conversely, the animals injected at 14 days postpartum may have reached a state of maturation such as to either develop compensatory mechanisms or regenerate sufficient adrenergic nerve endings that would ultimately exert a normal modulating action on the post synaptic adenyl cyclase receptor. These preliminary observations on the development of the adenyl cyclase receptor should provide a framework for further investigation.

Zusammenfassung. Nachweis, dass neugeborene Ratten (bis zum 8. Tag), die intracerebral mit 6-OH-Dopamin behandelt wurden, am 35. Lebenstag eine Überempfindlichkeit gegenüber der Adenylzyklase-stimulierenden Wirkung von Noradrenalin aufweisen.

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Differences in Brain and Body Weights of Mice Caused by Differential Housing[1]

It is becoming increasingly evident that significant differences in the gross and microscopic morphologies of the brains of rodents can be produced by simply changing their housing conditions[2–13]. The changes which differential housing causes in cerebral gross morphology, though slight, can be correlated with more pronounced changes in gross behavior[8,13,14–19], in brain chemistry and metabolism[8,13,15,19,20–26], and in the pharmacological effects

Brain and body weights of isolated and aggregated mice

	Brain weight (g)	Body weight (g)	(Brain wt./Body wt.) (100)
Isolated mice	0.317 ± 0.0014 (245)	22.88 ± 0.20 (296)	1.386 ± 0.013
Aggregated mice	0.308 ± 0.0013 (251)	20.03 ± 0.18 (303)	1.538 ± 0.016
% Difference	2.9	14.2	11.0
p-value	$\ll 0.001$	$\ll 0.001$	$\ll 0.001$

Means ± standard errors; numbers of mice in parentheses.

For calculations of (Brain wt./Body wt.), combined standard errors (CSE) were calculated according to the following equation:

$$\text{CSE} = \pm \sqrt{\frac{\left(\frac{Ba}{A}\right)^2 + b^2}{A}}$$

, in which B = brain weight, A = body weight and ± a and ± b were the respective standard errors of A and B. All p-values were determined using a two-tailed Student's t-test.

and metabolic dispositions of various psycho-active agents such as D-amphetamine and Li^+[18,19,21,27–33]. It has also been shown that marked differences in total body weight can be produced by the exposure of rats or mice to 'isolated' ('impoverished') vs 'aggregated' or 'enriched' environments[7,10,11,21,26,34]. During the past 2 years several studies have been conducted in our laboratory in which the neurochemical effects of differential housing were examined using C-57 Black mice. Since in all of these studies matched, male, weanling littermates were subjected to isolated vs aggregated housing conditions[20] for periods of 4–11 weeks and since body weights and brain (rostral to the inferior colliculi; excluding the cerebellum) weights were carefully recorded, it became possible to compare statistically these parameters between very large populations.

Results shown in the Table indicate, by comparing the brain weights of 245 isolated and 251 aggregated mice, that the brains of aggregated mice are slightly smaller, a difference which could not possibly be shown using small populations of animals. It is shown also that this small difference in brain weight of only 2.9% ($p \ll 0.001$) was correlated with a much greater difference in total body weight (14.2%; $p \ll 0.001$). Further calculations (Table, column 3) indicated that the brain weight/body weight ratio was significantly greater for aggregated than for isolated mice; i. e., the brain, as excised, represented a greater fraction of the total body weight when the mice were subjected to group housing. The difference in this last parameter caused by differential housing may well be of fundamental importance in explaining further the effects which changes in the environment produce on brain chemistry and behavior.

Résumé. Des changements prononcés du poids du corps et du cerveau ont été causés chez des souris en les exposant à des environments différents pendant 4–11 semaines.

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