gic sprouting in this region[15]. In addition, the habenula is of particular interest since it may play a role in the control of feeding[16].

Materials and methods. Timed pregnant Long Evans rats were obtained from Charles River Co. (Boston, MA). A total of 5 litters consisting of 10 pups each, were used in the experiments. 5 pups from each litter were undernourished by depriving access to the mother, with the remaining 5 serving as well-fed littermate controls. Experimental and control groups always contained an equal ratio of male to female pups. The regime of postnatal undernutrition has been characterized and typically leads to a deficit of about 50% b.wt by 21 days (weaning)[17]. Actual weights obtained here were: control 57 ± 1 g, undernourished 29 ± 1 g. From 21-60 days of age all rats were permitted free access to standard laboratory rat chow, which led to growth 'catch-up' to within 5% of the well-fed controls. Actual weights obtained for test and control rats were 360 ± 8 g and 380 ± 4 g, respectively. At 60 days of age, bilateral stria medullaris (SM) lesions were placed in 1 group of test rats and in 1 group of control rats. The remaining were sham-treated animals in which the SM was maintained intact, as previously described[15]. 4 groups were thus obtained: 1. well-fed control, sham treated; 2. well-fed control, lesioned; 3. undernourished-rehabilitated, sham treated; and 4. undernourished-rehabilitated, lesioned. All animals were allowed feeding ad libitum for 4 additional weeks, after which they were sacrificed by decapitation. The brains were frozen immediately in dry ice, and the habenular nuclei were removed by microdissection[15]. Following homogenization in 0.1 N perchloric acid, aliquots were taken for protein[18] and catecholamine[19] assays.

Results. The levels of NE and DA were essentially the same in both sham-treated groups, namely the well-fed controls and the neonatally deprived rats, following nutritional rehabilitation. In response to SM lesions, however, NE increased significantly ($p < 0.01$) in both well-fed controls and deprived rats (table). The NE and DA in the habenula of males and females were identical, therefore results for both sexes were pooled for each experimental group.

Discussion. The increase in NE is most likely to be associated with noradrenergic axons sprouting, rather than with the accumulation of this amine in neuronal terminals. This assumption is based on morphological evidence provided by a recent study, in which proliferating catecholaminergic terminals in the deafferented habenula were visualized by histofluorescence[15]. These data indicate that noradrenergic plastic capacity in the habenula is retained during nutritional rehabilitation. Interestingly, plastic retention has also been reported in the mature cerebellar Purkinje cell dendrites following nutritional recovery[13]. It is not known, however, if other brain regions maintain neuronal plasticity under similar conditions of postnatal undernutrition and recovery. Furthermore, whether or not the newly formed adrenergic synapses are functional, is still an open question. Thus, while early undernutrition appears to have no apparent lasting effect on noradrenergic axon sprouting in the habenula, the possibility is not ruled out that loss of neuronal plasticity is associated with behavioral retardation.

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Variations in cardiac noradrenaline content during sodium loading in hypertension prone and resistant rats

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Summary. The cardiac catecholamine content of Sabra rats and their 2 genetically derived substrains, hypertension prone and resistant rats, was studied by high pressure liquid chromatography and electrochemical detection. Both in the control period and after sodium and DOCA administration the cardiac noradrenaline level is higher in hypertension resistant rats than in Sabra rats, and also higher than in hypertension prone rats. This finding suggests that a reduction of the cardiac sympathetic nervous tone is involved in the genetic resistance to sodium.

Numerous studies suggest an enhanced activity of the peripheral sympathetic system in various models of experimental hypertension. A decrease in the content of endogenous noradrenaline (NA) in the heart has been described in deoxycorticosterone (DOCA) and salt hypertension[1,2]. Both impaired storage[3,4] and increased turnover of noradrenaline[5,6] have been described in the hearts of DOCA-salt hypertensive rats. It has been shown recently that the faster disappearance of endogenous noradrenaline or exogenous labelled noradrenaline observed in vivo in these hypertensive rats should be attributed to an increased release due to enhancement of nerve impulse flow rather than to an impaired storage ability[7]. The relevance of the above abnormalities to hypertension remains uncertain, since spontaneous hypertensive rats appear to have unchanged levels of endogenous noradrenaline, associated with a decreased rate of NA synthesis[8]. Moreover, several studies have suggested that the sodium overload per se

depletes cardiac catecholamines before the development of hypertension when blood pressure is still normal[4,9]. In recent years, we have obtained from the Hebrew University Sabra rats (SB), and 2 substrains that were selectively inbred for their respective sensitivity (substrain H) or resistance (substrain N) to DOCA-salt hypertension[10]. We report herein the results of catecholamine determinations in heart tissue prior to and following DOCA-salt treatment.

Material and methods. Male rats of the Hebrew University Sabra strain (SB), and hypertension prone (H) and resistant (N) substrains, aged 8 weeks, were used. All rats were uninephrectomized. 10 days later, half of each group received DOCA (Percorten®, Ciba; 20 mg/kg, at weekly intervals) and salt (1% NaCl solution to drink). They were studied 4 weeks later. Systolic blood pressure was determined by tail plethysmography after heating on the day before the experiment. Hearts were quickly removed and the atria were dissected, frozen at −180 °C, weighed and homogenized in 0.4 N $HC10_4$ containing 10^{-5} M ascorbic acid. Analysis of catecholamine content was performed by high pressure liquid chromatography and electrochemical detection according to the method of Keller et al.[11] with minor modifications (Le Quan-Bui et al., in preparation). This method allows the direct, rapid and accurate measurement of catecholamines in quantities as low as 5×10^{-14} moles. Statistical analysis was performed using the unpaired Student t-test.

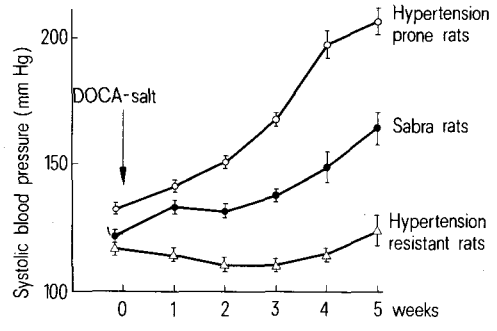

Fig. 1. Blood pressure changes induced by DOCA-salt administration in hypertension prone and hypertension resistant substrains compared to the original Sabra strain (mean ± SEM from 6–16 determinations).

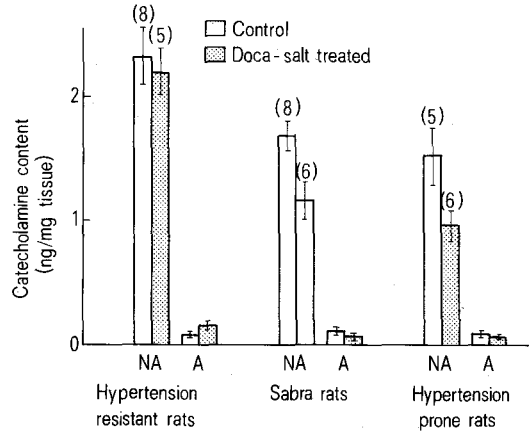

Fig. 2. Atrial noradrenaline (NA) and adrenaline (A) content in hypertension prone and resistant substrains compared to the original Sabra strain, with and without a 4-week DOCA-salt treatment. The number of rats studied is given in brackets. Results are expressed as mean ± SEM.

Results and discussion. The time-course variations in systolic blood pressure of Sabra, hypertension prone and hypertension resistant (N) rats after DOCA-salt administration are shown in figure 1. The absence of any blood pressure variation in N rats contrasts with the moderate increase observed in SB and with the large increase observed in H rats. The variations of atrial catecholamine content are represented in figure 2. Both noradrenaline and adrenaline were detectable. The concentration of adrenaline was about 20 times lower than that of noradrenaline. The concentration of NA in atria of untreated hypertension resistant rats was significantly higher than that of SB and H rats ($p < 0.05$ and $p < 0.02$ respectively). Following DOCA-salt treatment, there was a significant decrease in the NA content of SB and H rats ($p < 0.02$ and $p < 0.05$). This reduction agrees with previous reports[1,2,9] which established the role of sodium loading in lowering the cardiac noradrenaline content. In contrast, NA levels did not change after DOCA-salt treatment in the atria of hypertension resistant rats. NaCl intake, which has been shown to be similar in hypertension prone and resistant rats, both prior to and following administration of DOCA[12], cannot explain this difference. These animals are thus characterized by their insensitivity to sodium loading both in terms of blood pressure and the activity of their cardiac neuronal sympathetic endings suggesting that these 2 phenomena may be linked. Such a dependence of DOCA-salt hypertension upon the activity of adrenergic cardiac nerves has recently been reported[13]. The anomaly in catecholamine metabolism observed in atria from hypertension resistant rats, both untreated or DOCA-salt treated is not limited to the heart and has been found in other tissues[14] (Devynck and Le Quan-Bui, unpublished observations) suggesting that the reduction of the sympathetic activity is a diffuse process. Depletion of endogenous catecholamines usually leads to an increased response to catecholamines[15,16]. Conversely, the elevated catecholamine levels in N rats should lead to a decreased response. This may be in part responsible for their marked resistance to manipulations that normally cause hypertension in other strains.

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