2 days after the 4th seizure test, approximately half of the animals were adrenalectomized through a midline dorsal incision under pentobarbital anesthesia. Controls were sham-operated. Thereafter, both groups had free access to food and were given a choice between tap water and 0.9% saline to drink. At weekly intervals following the surgery, each animal was tested to determine seizure susceptibility and intensity. Differences between means were tested using a 2-tailed t-test.

Results and discussion. The table shows that neither sham-operation nor adrenalectomy altered the fraction of animals susceptible to sound-induced seizures. The figure shows that neither sham-operation nor adrenalectomy altered seizure intensity in the seizure susceptible rats. Thus, sound-induced seizures in the genetically susceptible rats are analogous to those in genetically susceptible mice to the extent that removal of the adrenal glands does not affect the established seizure patterns in either species. In some other respects these two models differ considerably. For example, seizure intensity in the rat is inversely related to the level of noradrenergic and 5-hydroxytryptaminergic activity in the central nervous system. Dopaminergic tracts, in the rat, are not involved[6]. In the mouse, strong evidence suggests a role for dopamine in seizures whereas the evidence for a role of noradrenaline is more equivocal[5]. The biological basis for sound-induced seizure susceptibility in the rat has not been fully elucidated. However, recent data suggests that at least 2 biological substrates are involved. We believe one substrate to be an abnormality in cochlear function and another to be a deficit in noradrenergic and 5-hydroxytryptaminergic activity in the central nervous system[7].

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Lasting effects of acute dehydration and post-weaning undernourishment on cortical spreading depression in adult rats[1]

A. Vieira-Neto, R.C.A. Guedes[2] and N.R. Teodósio

Dept. of Nutrition, Federal University of Pernambuco, Cidade Universitária, 50.000 Recife-PE (Brazil), 11 September 1980

Summary. Acute dehydration (D) early in life made adult rats less susceptible to cortical spreading depression (SD) than control (C) rats. Post weaning undernourished (U) rats tended to be more susceptible than controls. The association of D and U (DU group) made rats more susceptible to SD than U-rats. It is suggested that this association gives rise to a more complex pathological state than that which would result from the summation of the effects of its components.

The nervous system of undernourished animals appears to have a greater susceptibility to seizures when compared with that of normal animals. The threshold current of electroconvulsive shocks needed to provoke seizures in undernourished rats is significantly lower than that for well-nourished rats, and these seizures are of longer duration[3]. The propagation rate of cortical spreading depression (SD) is increased in rats undernourished from birth until weaning[4] or adulthood[5]. Adult rats undernourished during the nursing period develop hippocampal epileptiform kindling significantly faster than normal animals[6]. In children, undernutrition is often associated with secondary pathologies, which can exacerbate the precarious health condition of the infants. The episodes of systemic dehydration produced by diarrheas are among these pathologies[7], and so undernourishment and dehydration are often associated in childhood. The effects of this association (dehydration + undernutrition) upon brain excitability have not been studied systematically. Rocha[8] reported that acute episodes of dehydration impaired the performance of well-nourished rats in an avoidance-conditioning situation but that the already impaired performance of undernourished rats was not further diminished. In the present work we have studied the effects of dehydration and chronic post-weaning undernutrition on the susceptibility of the cerebral cortex to SD - a phenomenon which is closely associated with epilepsy[9].

Materials and methods. 49 Sprague-Dawley rats of both sexes were divided into 4 groups: C (control, 14 rats), D (dehydrated, 12 rats), U (undernourished, 13 rats) and DU (dehydrated and undernourished, 10 rats). The groups C and D received a normal diet, containing 20% casein as protein source. The groups U and DU were fed a protein-free diet during the 2 weeks after weaning. Subsequent to this period they were fed a diet containing 5% casein. All diets contained about 390 kcal/100 g. 3 sessions of dehydration were performed in the D and DU groups, as described by Rocha[8]. These occurred on the 18th, 21st and 24th days of life. Briefly, 0.2 ml of the laxative, 4-4'-(2-picoliliden)-bis-phenylsulphate, was administered by means of an oesophageal cannula introduced through the mouth. This caused a diarrheic state, with resultant loss of water and electrolytes. After receiving the laxative the rats were maintained without water and food for 10 h. They were weighed before and after each session and those which did not lose at least a mean value of 5% of their body weight in the 3 sessions were not used. The recordings were made when the rats were 60–110 days old. Under anesthesia (urethane, 750 mg/kg + chloralose, 60 mg/kg, i.p.), the animal's head was fixed in a stereotaxic apparatus and 3 trephine holes drilled. SD was elicited by placing a cotton pledget (1-2 mm diameter) soaked in 2% KCl on the cortical surface. Electrocorticograms (ECoG) were performed at 1 point and the slow potential changes (SPC)

Mean ± SD body and brain weights for the 4 groups of adult rats

Groups	Body weight (g) (90-day-old rats)	Percent of C	Brain wet weight (mg)	Percent of C	Brain dry weight (mg)	Percent of C
Control (C)	198.34 ± 21.05 (5)	100.0	1.515 ± 63 (10)	100.0	325 ± 21 (10)	100.0
Dehydrated (D)	213.82 ± 10.74 (5)	107.8	1.533 ± 77 (12)	101.2	322 ± 18 (12)	99.1
Undernourished (U)	73.62 ± 13.83* (5)	37.1	1.290 ± 135* (13)	85.1	270 ± 20* (13)	83.1
Dehydrated and Undernourished (DU)	41.25 ± 8.02** (6)	20.8	1.178 ± 76*** (10)	77.8	255 ± 16* (10)	78.5

The number of animals is indicated in parentheses; * different from C, $p < 0.001$; ** different from C and U, $p < 0.001$; *** different from C ($p < 0.001$) and from U ($p < 0.03$).

occurring during SD were recorded from 2 points on the cortical surface. Reference electrodes for ECoG and SPC were placed in the neck muscles and on the nasal bone, respectively (see inset of fig. 2). The SPC electrodes were of the Ag-AgCl type, as previously described[10], and the interelectrode distance was about 4–6 mm. The recordings were made continuously throughout 6 h periods. Rectal temperatures were maintained at 35–37 °C. At the end of the experiment the animals were killed with an overdose of anesthetic and the brains (including the cerebellum and excluding the olfactory bulb) were removed immediately and weighed (wet weight). They were then kept at 100 °C and weighed daily until a constant weight was attained (dry weight).

Results. The groups U and DU showed a significant reduction in body weight. Similarly, both the wet and dry brain weights decreased significantly in these 2 groups (table). KCl stimulation at intervals of about 20 min was effective in evoking SD, except in the D group where 60% of the stimulations were ineffective during the 1st h of recording (in 1 rat KCl stimulation was ineffective during all 6 h of the recording period). 'Spontaneous' SD (i.e. SD which appeared without intentional stimulation) was observed more frequently in the U group, about twice as often as in the C group. Calculations of the velocity of propagation of SD were based on the interelectrode distance, checked several times during the recording period, and the time necessary for a SD wave to cross this distance. The mean propagation rates in the U and DU groups tended to be higher than in the C group, the highest rates being observed in the DU rats. The D group however, showed mean rates lower than the other 3 groups (fig. 1). In the U and DU rats, the time to recovery of the ECoG-activity to predepression levels after a SD wave was gradually shortened over the 6 h recording period (fig. 2). Similarly, the incidence of large amplitude spike-like waves increased after the 2nd h or recording.

Discussion. The undernutrition severely affected the growth of the animals, as can be observed from the brain and body weights. The dehydration alone (D group) did not result in any change in the brain weights of adult well-nourished rats; however, when this treatment was associated with undernutrition (DU group), the effects upon brain and body weights were more intense than those seen in the U group. These data suggest that the combined effects of dehydration and unternutrition cannot be regarded merely as the summation of its components. The susceptibility of the cortical tissue to SD was increased in the U and DU groups, as shown by the higher SD propagation rates and the higher incidence of 'spontaneous' SD. These results, as well as the higher incidence of large amplitude waves and the faster return of the ECoG-pattern to the predepression

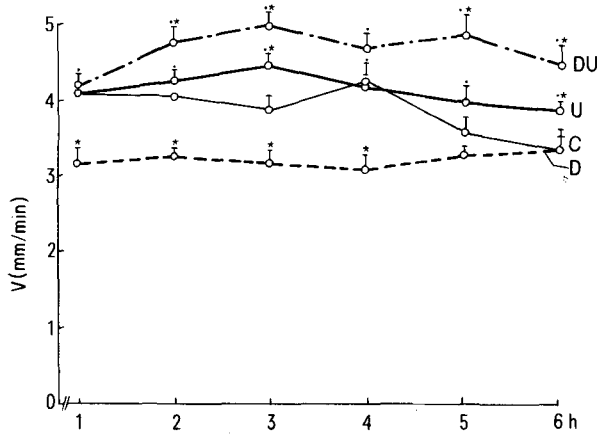

Fig. 1. Velocity of propagation of SD. D, dehydrated; C, control; U, undernourished; DU, dehydrated and undernourished. Vertical bars represent the SE of the mean. Means marked with dots and stars are significantly different from the corresponding D and C means, respectively.

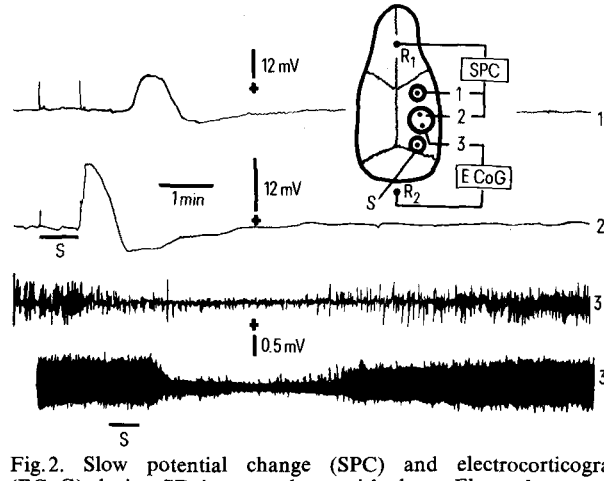

Fig. 2. Slow potential change (SPC) and electrocorticogram (ECoG) during SD in an undernourished rat. Electrode arrangement is shown in the inset. Records 1–3 were taken simultaneously. Recording 3' was taken 4 h later. Comparing record 3' with 3, note in the former the faster return of the ECoG-pattern to the predepression levels after SD, as well as the higher incidence of large amplitude waves. S, stimulation with KCl.

levels after SD, indicate that the cortical tissue in the U and DU groups was in a state of higher neuronal excitability than that of the control animals; this was more evident in the DU group. A possible explanation for the higher propagation rate of SD in undernourished animals could be, as suggested[4], the impairment of myelination caused by undernutrition[11]. Cellular[12-14] as well as neurochemical[3,15] alterations observed during undernutrition may also have contributed to the increased cortical excitability reported here. In addition, epileptiform activity associated with higher SD propagation rate and higher incidence of 'spontaneous' SD has been described in adult rabbits submitted to an acute alteration of the extracellular ionic environment[10]. Clinical[16] and experimental[17,18] evidence shows that the metabolism of water and electrolytes is disturbed during undernutrition. It is thus possible that dehydration, when associated with undernutrition, has a physiopathological significance different from that observed in the well-nourished condition. This possibility, specifically concerning brain excitability, seems to be supported by the present results. In conclusion, the present results show that dehydration early in life makes adult rats, undernourished after weaning, more susceptible to cortical SD, the opposite effect being observed in well-nourished animals. Since dehydration was performed early in life, and the effects on SD were observed in the adult animals, it is clear that a long-lasting change must have occurred in the brain. Additional studies are clearly warranted to reveal the underlying mechanisms, the effects of which have been observed in the present study. The experimental model described here may be useful for that purpose. It would also interesting to investigate the association between undernutrition and disturbances in body water and electrolyte contents observed in children[19,20], in order to detect any possible effect of such an association on brain excitability.

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Relationship between glucose absorption and villus height in ageing

L. Jakab and L. Pénzes

Gerontology Center, Semmelweis Medical School, H-1428 Budapest (Hungary), 6 June 1980

Summary. There is a diminution of D-glucose absorption in the aged rat which is partly due to the decrease of the length of the villi.

The role of ageing in sugar absorption from the intestine has already been discussed by numerous authors[1-5]. However, there are discrepancies because of the different indices used. According to the literature, the number of villi does not change with age[6-11]. Therefore we decided to study whether the height of the villi changes during senescence and if so, in how far these changes influence their functional role, i.e. glucose absorption.

We used a low sugar concentration (4 mM), firstly to limit passive diffusion, and secondly because hardly any data are available on the absorption of this relatively low luminal sugar concentration. We also wanted to simulate the conditions in the aged small intestine, where lower intraluminal glucose concentrations may occur owing to reduced disaccharidase efficiencies[5].

Materials and methods. Young (6-month-old), adult (12-month-old) and aged (24-month-old) female Wistar rats were used. The animals were fasted overnight before the experiment. After Nembutal® anaesthesia the abdominal cavity was opened and the Musacchia[12] method applied. The small intestine was washed with Krebs-Henseleit bicarbonate saline and 6 cm segments prepared from the duodenum (D), jejunum (J) and ileum (I). 1.5 ml 4 mM D-glucose solution was introduced into each of the segments and the cavity clamped. Special care was taken to maintain the appropriate ambient temperature during the experiment. After 20 min the loops were emptied, the luminal content collected and centrifuged, and the glucose concentration determined according to Hultman[13], Hyvärinen and Nikkilä[14]. The sugar absorbed was related to the wet intestinal weight (segment-length in cm and 20 min). The wet weight/segment-length ratio was found to be constant during ageing, i.e. it does not alter the rate of absorption itself. A Carl Zeiss microprojecting device was used for the microscopical evaluation of the length of the villi.

Results. Figure 1 shows that glucose absorption was highest in the jejunum of young rats while it was less high in the duodenum and ileum. Identical findings were recorded in adults, and similar values were found in the duodenum and jejunum in the old rat. Less absorption was observed in the