The effect of postnatal undernourishment on epileptiform kindling of dorsal hippocampus[1]

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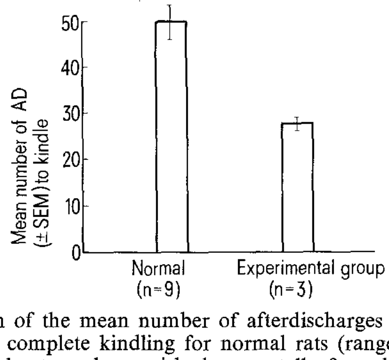
Summary. Rats were undernourished postnatally from birth through 20 days of age. They were subsequently tested for susceptibility to motor seizures kindled in hippocampus in adulthood. Compared to littermate control animals the postnatally undernourished rats were more susceptible to the kindling treatment. We conclude that early postnatal undernourishment has a permanent effect on susceptibility of the hippocampus to electrically-induced seizures.

Several effects of undernourishment on central nervous system electrical activity have been identified in the rat. Alterations in the electroencephalogram (EEG) from sensorimotor and visual cortex[3] and from the hippocampus[4] have been reported. Both sensory evoked cortical potentials[4-7] and potentials evoked by electrical stimulation of the brain[4,8,9] exhibit unusually long latencies in young undernourished rats. This effect diminishes with age. Similar changes have been seen in protein-calorie malnourished human infants[10]. There is also evidence that seizure thresholds can be altered by undernourishment. Seizure thresholds in both septum and hypothalamus are decreased following starvation[11], as is the response to electroconvulsive shock[12]. The rate of propagation of KCl-induced cortical spreading depression is enhanced[13]. The response to electroconvulsive shock (ECS) is greater in protein malnourished rats, even in adulthood[4,14], although these animals are less susceptible to kindling of the amygdala than controls[4,15]. Thus undernourishment has been found to both increase and decrease seizure susceptibility, depending upon the seizure-inducing agent used. To further investigate the effects of postnatal undernourishment on seizure-related mechanisms in adult rats, we have kindled both normal and previously undernourished rats. Kindling is a model of epilepsy in which an epileptic focus is created by delivering repetitive, low intensity, electrical stimulation to a susceptible brain area[16]. This results in the development, over a series of stimulations, of both behavioral and EEG manifestations of seizure activity. Kindling can be considered complete when the subject has experienced 3 consecutive tonic/clonic convulsions with loss of postural control.

Materials and methods. Suckling pups of Long Evans mother rats were undernourished by an increasingly severe regime of daily isolation from the mother, beginning with 2 h on day 2 postnatal, and increasing daily to a maximum of 10 h/day by the 2nd week[17,18]. Littermate control rats remained in the home box. At 21 days of age (weaning) the undernourished rats averaged $58.2 \pm 1.9\%$ (SEM) of the weight of their littermate controls. Following weaning all rats received normal lab chow ad libitum. By day 60 the previously undernourished rats averaged $83 \pm 4.2\%$ (SEM) of the weight of littermate controls as a result fo growth 'catch-up'. At this time all rats were anesthetized with nembutal (50 mg/kg, i.p.) and implanted bilaterally in area CA_1 of dorsal hippocampus with bipolar twisted nichrome wire electrodes (125 µm). Leads from the electrodes and from a grounding pin (embedded in the nasal sinus) were inserted into an Amphenol connector which was then cemented to the skull. After a 2-week recovery period, kindling stimulations consisting of 1 sec trains of 60 Hz, 1 msec, 400 µA monopolar pulses were delivered by a Grass Model 4 stimulator every 2 h for 12 out of every 24 h until kindling was complete. The 1st session commenced at 07.00 h. The EEG was monitored on a Grass Model 6 Electroencephalograph for several minutes preceeding the stimulation and following it until electrical activity returned to normal. Following the completion of kindling, rats were sacrificed to allow histological verification of electrode placement. The following results are based upon a final control group of 9 rats and an experimental group of 3.

Results. In agreement with previous reports[16,19], control rats required an average of 50 ± 3.7 (SEM) afterdischarges (AD-induced by the electrical stimulation) to kindle. The exhibited the characteristic gradual development of seizure intensity both behaviorally and electrically. In contrast, all 3 previously undernourished rats kindled prior to the 1st kindling success among the controls. These rehabilitated undernourished rats required an average of only 27.6 ± 1.1 (SEM) ADs to kindle, a significantly faster rate ($p < 0.01$, Mann-Whitney U-test, one-tailed) than controls (figure). There were no significant differences between the groups in the average duration of AD per stimulation or in the duration of AD in the final stage of kindling. There was a tendency for the rehabilitated rats to progress through the intermediate stages of kindling more quickly and more reliably than the controls. Thus an experimental rat, once it had achieved a later stage of kindling, progressed to the next stage rather than reverting to an earlier one. This group exhibited an average of 0.7 ± 0.5 (SEM) reversals during kindling. Control rats, on the other hand, exhibited an average of 4.1 ± 1.2 (SEM) reversals before kindling was completed.

Discussion. Previously undernourished rats were significantly more susceptible to hippocampal kindling than normally nourished littermate controls. This is in agreement with reports that protein malnourished rats are more susceptible to the effects of ECS[4,14]. It is in contrast to the finding that protein malnourished rats take longer to kindle in response to stimulation of the amygdala[4,15]. This may represent a real difference between the functional properties of the amygdala and the hippocampus. It also may be due to a difference in the effects of undernourishment on these 2 limbic areas. We know from previous work[17,18] that this regime of postnatal undernutrition results in a lasting depression in myelin synthesis, although the myelin is of



Comparison of the mean number of afterdischarges (AD ± SEM) required to complete kindling for normal rats (range 34–67) and experimental rats undernourished postnatally from birth through 20 days of age (range 26–30). The previously undernourished rats kindled significantly faster ($p < 0.01$, Mann Whitney U-Test, one-tailed) than the control rats.

normal composition[20,21]. Thus although it is clear that limbic structures are affected by undernourishment, they may not all be affected in the same way.
The undernourished rats kindled in this study were allowed a long period of rehabilitation before kindling commenced. The clear enhancement of the kindling may, therefore, be an indication of a permanent effect of undernourishment on seizure-related processes in hippocampus. In view of the presumed importance of the hippocampus in many functions, including emotional behavior, learning, and memory, the effect of early undernutrition on quickening of hippocampal kindling encourages further investigation.

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Effets de la vision sur la réponse tonique vibratoire d'un muscle ou de ses antagonistes chez l'homme normal[1]

Effects of vision on tonic vibration response of a muscle or its antagonists in normal man

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Summary. In normal man, a vibratory stimulus applied to tendon of arm muscles can induce either a tonic motor response in the vibrated muscle or in its antagonists depending upon presence or absence of visual feedback from the arm (perception of position vrs.perception of an illusive motion). Spinal motor effects of inputs from muscle spindle afferents elicited by vibration can be modified by the perceptive events experienced by the subject.

De très nombreux travaux[2-4] ont montré que, chez l'homme, l'application d'une vibration sur le tendon d'un muscle entraîne une réponse musculaire tonique du muscle vibré, et un relâchement simultané de ses antagonistes. Cette réponse est interprétée comme une mise en jeu du circuit myotatique liée à l'activation spécifique, par le stimulus vibratoire, des afférences musculaires d'origine fusoriale[5-8]. Par ailleurs, dans le domaine perceptif, les résultats de Goodwin et al.[9] montrent que la vibration d'un muscle conduit, en l'absence de vision directe du membre stimulé, à la perception d'un mouvement illusoire. Cette perception serait évoquée par les afférences issues du muscle vibré et interprétée, par le système nerveux central, comme une étirement du muscle stimulé.
Nos propres résultats sont en accord avec l'ensemble de ces données. Toutefois, nous avons pu montrer[10,11] qu'une vibration ménagée des tendons des muscles du biceps brachial et triceps brachial, chez l'homme normal au repos et en l'absence de vision du membre vibré, non seulement entraînait la perception de mouvements illusoires (la vibration du triceps entraîne une sensation de flexion et celle du biceps une sensation d'extension) mais surtout faisait naître des activités E.M.G. dans les muscles antagonistes.
De telles réponses ne semblent pas avoir été précédemment décrites et restent de toutes façons difficilement interprétables dans le cadre des théories classiques sur l'organisation réciproque.
C'est dans le but de mieux connaître ces réponses E.M.G. paradoxales que nous avons entrepris d'étudier les effets de la vision sur les conditions de leur apparition et de leur maintien.
Matériel et méthodes. L'étude a porté sur 12 sujets humains adultes. Chaque sujet est assis confortablement dans un fauteuil, la main et l'avant-bras droits reposant sur un support mécanique horizontal fixe (conditions isométriques vérifiées par enregistrements potentiométriques permettant la détection d'un mouvement d'une amplitude supérieure à 0,2°). L'angle du coude est de 90° ou 110°. La tête étant maintenue immobile, le sujet peut en ouvrant les yeux, soit voir son avant-bras et sa main, soit voir seulement l'environnement. Les vibrations mécaniques (amplitude: 0,2 à 0,5 mm; fréquence: 70 Hz), appliquées au niveau des tendons distaux des muscles biceps ou triceps brachial, sont délivrées à l'aide d'un marteau électromagnétique LDS (type 201). Les électromyogrammes des muscles biceps brachial et triceps brachial, et le clignement palpébral, indicateur de la date d'ouverture ou de fermeture des yeux, sont enregistrés à l'aide d'électrodes de surface par dérivations bipolaires. La sensation de mouvement est appréciée par interrogation verbale du sujet (direction, présence/absence).
Résultats. La vibration continue du tendon distal du biceps brachial (figure 1) induit une réponse E.M.G. dans le triceps brachial lorsque le sujet a les yeux fermés. Cette