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H-Reflexes in Normal Human Infants: Depression of These Electrically Induced Reflexes (EIR's) in Sleep. (27584)

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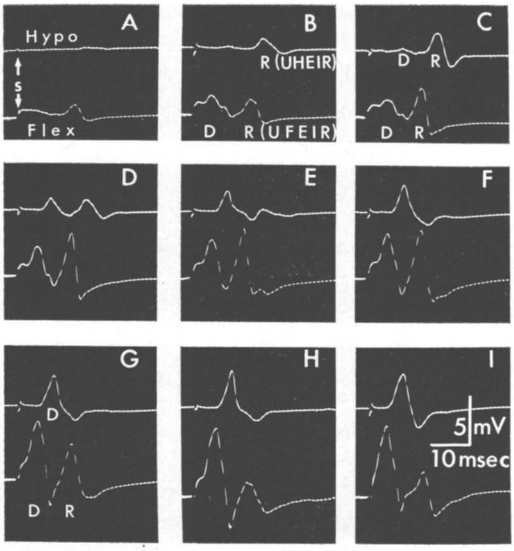
In the normal human adult, weak percutaneous electrical stimulation of the tibial nerve excites low threshold calf muscle afferents which synapse directly on spinal motoneurons to evoke a reflex contraction from the same muscle group. This monosynaptic myotatic reflex, recorded by the action potentials evoked in the muscle, was extensively studied by Magladery *et al.*(1), who named it the H-reflex (after Paul Hoffmann who described it earlier). Thomas and Lambert(2) reported that the H-reflex could be easily elicited in the normal newborn infant by stimulating the ulnar nerve and recording the hypothenar muscles. Their finding that this electrically induced reflex* (EIR) could no longer be obtained in the normal infant over 6 months of age suggested to us its use as one attractive and simple test of the neurological status of the pediatric patient. The value of such testing is indicated in our recent demonstration of aberrant EIR's produced by ulnar nerve stimulation in children, 8 to 14 years old, with Sydenham's Chorea(3).

While using the ulnar EIR in a long-term serial study of growth of the normal infant from birth, as well as in an investigation of various neurological disorders, defective development, and mental retardation of the young patient, we have noted additional points of interest regarding the EIR in 13 normal neonates (1 to 8 days old), some of whom have been reexamined 2 to 4 months later.

* This term, used hereafter, is more descriptive, of more general applicability, and less committed as regards mechanism and functional significance than the designation, H-reflex.

Methods. Subjects were examined while lying undisturbed in the bassinet. Silver cup-shaped disc stimulating and recording electrodes, 6 mm in diameter, were applied to the skin with Bentonite paste and held in place by ¼-inch masking tape. One electrode for stimulating the ulnar nerve was a few cm distal to the axilla, the other at the olecranon groove of the elbow, interelectrode separation being 3.5 to 5 cm. Active recording electrodes were applied over the bellies of forearm flexor, hypothenar, and first dorsal interosseus muscles; indifferent electrodes for these muscle groups were located on the flexor surface at the wrist, and the tip of the fifth and index fingers, respectively. Routinely, square wave pulses of varying voltage, 0.2-0.5 millisecond (msec) in duration, were passed through an isolation transformer and delivered to the stimulating electrodes once per 2 seconds. Muscle action potentials were amplified by conventional biological amplifiers, displayed on a double beam cathode ray oscilloscope, and photographed on 35 mm moving film.

Results. Ulnar-hypothenar (UH) EIR's were easily obtained in all subjects, thus confirming Thomas and Lambert's(2) results. In addition, all subjects presented EIR's from forearm flexor (UFEIR) and dorsal interosseus (UIEIR) muscles upon stimulation of the ulnar nerve. Fig. 1 shows recordings of hypothenar (upper beam) and flexor (lower beam) muscles from a normal 6-day-old baby. These records demonstrate 2 main features



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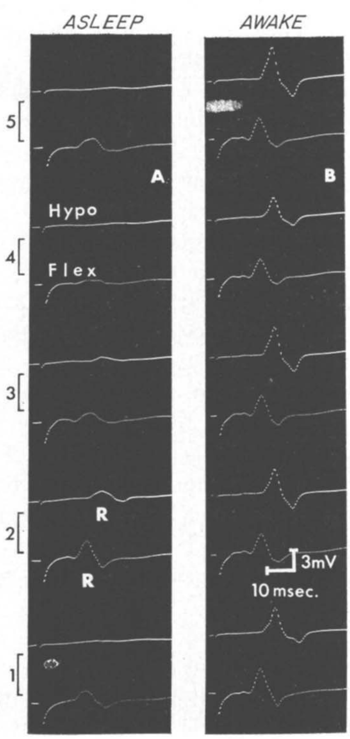

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FIG. 1. Electrically induced reflexes (EIR's) in normal 6-day-old infant. ''R'' potentials produced by ulnar nerve stimulation are reflex responses of hypothenar muscles (UHEIR, upper beam) and flexor muscles of the forearm (UFEIR, lower beam). ''D'' waves are non-reflex, direct muscle responses to nerve stimulation. S is stimulus artifact. Interruptions in potential curves represent intervals of 1 millisecond (msec.). Note lower threshold for R than D; lower threshold of UFEIR compared with UHEIR; increase of D waves as strength of stimulus to ulnar nerve is increased from A to I; and decrease of R potential beyond a certain intensity of stimulation (C-F, upper beam; F-I, lower beam).

FIG. 2. Two-day-old normal infant. A. Asleep. B. 1 min. after spontaneous awakening. Increased UHEIR (upper) and UFEIR (lower) in B. Intensity of 5 successive stimuli to ulnar nerve in A and B are identical. Stimulus frequency, 1 per 2 sec ; time marks, 0.5 msec.

of the EIR (labelled "R" in the figures): (1) Its low threshold, which usually allows it to be uncovered (Fig. 1A-B) before many motor fibers are excited to produce a non-reflex direct muscle response (labelled "D" in the records); (2) Its reduction in amplitude as intensity of nerve stimulation is increased beyond a certain level (Fig. 1C-F, upper beam; Fig. 1F-I, lower beam), because of antidromic blockade. These features of the EIR have been discussed in detail elsewhere(1,3).

Threshold for elicitation of UFEIR is lower than that of UHEIR (Fig. 1). The former also has a lower threshold than that of the UIEIR. The UHEIR usually appears very slightly before the UIEIR as the strength of stimulus to the ulnar nerve is gradually increased. UFEIR's may be obtained over a much wider range of stimulation intensities to the nerve than either UHEIR or UIEIR (Fig. 1), the latter two being about equal in this respect.

We observed repeatedly that, even when the shock applied to the nerve remained constant, all 3 EIR's varied considerably in amplitude at different times during the observation session. Further, they all varied concomitantly in the same direction *i.e.,* when the UFEIR was large, so were the UHEIR and UIEIR's, and *vice-versa.* This is the situation in Fig. 2A, where the response to 5 identical successive shocks at 2-second intervals is shown. This 2-day-old infant was asleep during the sequence, but awakened spontaneously before Fig. 2B was recorded, a minute after the tracings of Fig. 2A were photographed. The increase in size of EIR's from both muscles, as well as their greater constancy, is apparent in the waking state. Similar potentiation of EIR could also be obtained if the sleeping infant were aroused

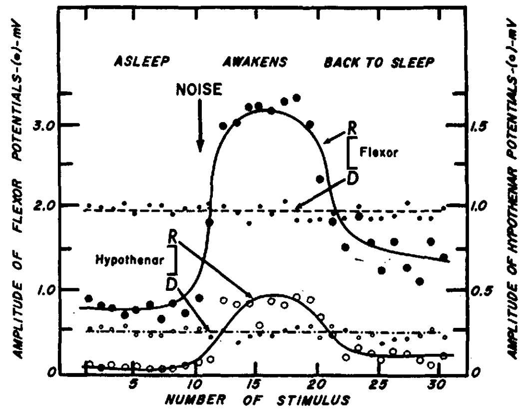

FIG. 3. One-day-old normal infant, asleep at start of recording, awakened by loud noise at arrow, and gradually returning to sleep thereafter. Thirty successive, identical stimuli delivered once every 2 sec. to ulnar nerve. D wave unaltered throughout.

from sleep by intentional sensory stimulation by noise, light, pinch, etc. Fig. 3 represents this graphically for another neonate, awakened by a sudden, loud noise. It shows, in addition, that the non-reflex, direct muscular response to stimulation of motor nerve fibers (D potential) is unchanged throughout. EIR's were also present in the subjects reexamined at 2-4 months of age. Depression of EIR in sleep, and accentuation in wakefulness or arousal was striking, as in the neonatal period.

Discussion. The fact that 3 ulnar EIR's are now known to exist in the normal newborn and disappear with age suggests that these reflexes represent widespread generalized infantile reactions which are inhibited during maturation. They may reappear as a result of nervous system dysfunction of diverse etiology, sufficiently damaging to disrupt the normal tonic inhibition from above. Examples of such results, *e.g.*, are classical upper motor neuron disease(4,5), Sydenham's Chorea(3), inborn metabolic errors (6), certain congenital defects, and some types of mental retardation (unpublished). Probably additional abnormal occurrence of EIR's may be uncovered as the test is extended to other areas of pediatric neurology.

The lower threshold of UFEIR's than of those from hand muscles may be related to the fact that the former are supplied by nerve fibers in the ulnar trunk which are larger than those innervating the latter (Hodes *et al.*) (7). It is also possible that spinal flexor moto-neurons are more excitable, and/or less easily inhibited by supraspinal impulses than are those neurons supplying the distal muscle groups.

Thomas and Lambert(2) recorded as "equivocal" the reflex status of 9 of their 58 normal subjects who ranged in age from 3 days to 5 months. One possible cause of equivocation with regard to presence or absence of EIR would be the failure to control the state of consciousness. A subject in deep sleep might conceivably show insignificant EIR's when, in fact, unmistakable low threshold reflexes might be obtained if the subject awakened or were aroused. It should also be noted that proper attention to this important variable might well be decisive in establishing a correct evaluation of the EIR when used as a test in individuals with suspected central nervous system dysfunction.

Summary. 1. Three H-reflexes, 2 of which have not been described previously, have been obtained in 13 normal human neonates when the ulnar nerve was stimulated. These electrically induced reflexes (EIR's) were demonstrated by muscle action potential recordings from the flexor muscles of the forearm (UFEIR), the hypothenar (UHEIR) and the first dorsal interosseus muscles (UIEIR) of the hand. 2. The UFEIR had a lower threshold than either the UIEIR, or the previously described UHEIR. 3. All 3 EIR's were reduced in amplitude in neonates and in those subjects reexamined 2 to 4 months later, as the infants fell asleep. They were restored by spontaneous arousal or by waking induced by sensory stimulation with sound, light, or touch.

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Effects of Gum Guar, Locust Bean Gum and Carrageenan on Liver Cholesterol of Cholesterol-Fed Rats.* (27585)

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Our previous studies(1) indicate that pectin N.F. when fed at a 5% level in the diet largely counteracted the increment in liver cholesterol and liver total lipids induced by cholesterol feeding in the rat. Other roughage or bulk-forming materials such as cellulose, agar, sodium alginate, protopectin and calcium silicate (Micro-Cel) were ineffective in this regard. Data are presented here indicating that Gum Guar, Locust Bean Gum and carrageenan also have significant activity in counteracting the increment in liver cholesterol and liver total lipids induced by cholesterol feeding in the rat.

Procedure. The basal ration consisted of sucrose, 61%; casein,[†] 24%; cottonseed oil, 10%; salt mixture,[‡] 5%; and the following vitamins per kg of diet: thiamine hydrochloride, 20 mg; riboflavin, 20 mg; pyridoxine hydrochloride, 20 mg; calcium pantothenate, 60 mg; nicotinic acid, 100 mg; ascorbic acid, 200 mg; biotin, 4 mg; folic acid, 10 mg; p-aminobenzoic acid, 400 mg; inositol, 800 mg; 2-methyl-1,4 naphthoquinone, 5 mg; vit B_{12}, 150 μg; choline chloride, 2 g; vit A, 5000 U.S.P. units; vit D_2, 500 U.S.P. units; and alpha-tocopheryl acetate, 100 mg. Tests were conducted with rats fed the basal ration, the basal ration + 1% cholesterol, and the basal ration + 1% cholesterol + the various supplements indicated in Table I. The cholesterol and test supplements were incorporated in the basal ration in place of an equal amount of sucrose. Fifty-six male rats of the Holtzman strain with an average body wt of 43.6 g (range 38 to 50 g) were divided into 7 comparable groups of 8 each, placed in metal cages with raised screen bottoms (2 or 3 rats per cage), and provided the test diets and water *ad libitum*. Animals were fed on alternate days and all food not consumed 48 hours after feeding was discarded. Body weights were recorded weekly. After 28 days of feeding, the rats were anesthetized with sodium pentobarbital, and blood was withdrawn from the aorta into a heparinized syringe. Livers were excised, blotted to remove excess blood, weighed and stored in a freezer until analyzed. Lipid was extracted from the livers by the method of Thompson *et al.*(2), and cholesterol was determined on liver and plasma by the method of Nieft and Deuel(3). Total lipids were determined gravimetrically on an aliquot of the liver extract.

Results. The increment in liver cholesterol and liver total lipid induced by cholesterol feeding in the rat was largely counteracted by the concurrent feeding of Gum Guar, Locust Bean Gum or carrageenan at a 10% level in the diet. The effects of these supplements were similar to, although slightly less marked than, that of a comparable amount of pectin N.F. Cholesterol feeding also induced a slight increment in plasma cholesterol levels which was partially counteracted by concurrent feeding of pectin N.F. and several of the other test supplements. Differences between the various groups however were not statis-

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† Vitamin-Free Test Casein, General Biochemicals, Inc., Chagrin Falls, Ohio.

‡ Hubbell, Mendel and Wakeman Salt Mixture, General Biochemicals, Inc., Chagrin Falls, Ohio.