Developmental Changes of Axonal Excitability: Refractory Period Measurement in Normal Children

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Summary:

Background: "The absolute refractory" period is the time interval during which the nerve fiber is in capable of conducting another impulse after a conditioning stimulus and the determination of the refractory period distribution in a nerve can give a good idea about the characteristics of the conducting fibers constituting that nerve as it reflects their excitability and could be used as a sensitive indicator for the ability of the nerve fiber to conduct pairs of closely spaced impulses.

Methods: The new collision test was used to measure precisely the absolute motor refractory period and the paired shock technique to measure the absolute sensory refractory period in the ulnar nerves of 167 normal infants and children to identify age related changes in the excitability of the nerve fiber membrane.

Results: These tests showed that changes in the membrane properties of the fastest and the slowest motor and sensory fibers differ with age. Fastest fibers have more prominent and rapid reduction in their absolute refractory periods (increased excitability) at the successive age groups during the period between 6 months to 6years of life, while the slowest ones have more gradual and prolonged membrane changes (as assessed by the dispersion of the refractory periods)

Conclusion: These electrophysiological findings point to a period of rapid increment in the nerve fiber diameter, myelin thickness and the possibility of addition of new functioning nerve fibers during the process of growth and development, since each fiber has its characteristic absolute refractory period from birth.

Keywords: Refractory period, Children, Age related changes, axonal excitability.

Introduction:

"The absolute refractory" period is the time interval during which the nerve fiber is in capable of conducting another impulse after a conditioning stimulus (1). Following the passage of an impulse, an axon becomes totally unexcitable for a period of a fraction of a millisecond (2, 3). During this period the membrane is still depolarized from the preceding action potential and no stimulus, no matter how strong, can initiate a fresh impulse in this region, nor can an impulse generated else where passes through this area. Neither excitability nor conductivity, therefore, are present (4). The reason for this refractoriness is that shortly after the action potential is initiated, the sodium channels become inactivated, and any stimulus applied to these channels at this point will not re-open the inactivated gates unless the membrane is repolorized either to, or almost to, the original resting membrane potential level (3, 5). Because of the refractory period, a nerve fiber cannot be stimulated continuously, thus, the refractory period acts to limit the rate at which nerve impulses can be conducted. In other words the time between impulses can not be less than the absolute refractory period, which is about 1/2500 of a second for the large myelinated nerve fibers (3,6), i.e., they could conduct 2500 impulses per second. Motor fibers rarely have to conduct naturally at rates exceeding 100-150/sec.; sensory fibers under extreme experimental conditions may have to conduct at 300-400/sec. Fibers of smaller diameter recover more gradually and consequently have longer refractory periods so the upper limit of impulse frequency that they can transmit is lower than that of the larger fibers (4). Hence, the determination of the refractory period distribution in a nerve can give a good idea about the characteristics of the conducting fibers constituting that nerve and could be used as a sensitive indicator for the ability of the nerve fiber to conduct pairs of closely spaced impulses. (7) The mean absolute refractory period for the fastest motor fibers was found to be 0.74±0.12msec, while that of the slowest conducting fibers 3.06±0.66msec in adults which were very close to the values obtained for the sensory and mixed nerves (8,9,10). The estimation of the refractory period have proved to be very useful and sensitive in the diagnosis of the disease of the peripheral nerves, especially when there is selective involvement of nerve fibers, where the conventional nerve conduction studies allow only fastest conducting fibers velocities to be recorded, and the more slowly conducting fibers have the onset of their action potential hidden by the

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discharge of faster units (8). In such disorders and when the clinical involvement of the peripheral nerve is undetectable, the measurement of the distribution of fibers with different conduction velocities in the whole nerve trunk by demonstrating the spectrum of the absolute refractory periods is much valuable (11). Increased refractory periods of sensory and mixed nerves have been reported in diseases of the peripheral nerves (10, 12, 13, and 14). A prolongation of the refractory state appeared to be particularly caused by demyelination (15). Several workers have proposed using the sensory and motor nerve refractory periods as an index of neurotoxicity and as a sensitive method to detect conduction deficits in various nerve disorders, especially when only a small proportion of fibers is abnormal or when the lesion is focal (7,8,11,16,17). Although it is proved that the refractory period measurement reflects the membrane excitability and describes the distribution of fibers of different conduction characteristics, it indicates the limit of both conduction velocity and nerve recovery after depolarization (16, 18). Few studies employed the absolute refractory period measurement to assess indirectly the excitability changes of human nerves during development (19). It was found that the absolute motor refractory period of the fastest (alpha) motor fibers in premature, full term newborns and adults appeared to be a specific functional property of the membrane, independent of post natal development (20). It is reported that already at birth, the absolute refractory period is characteristic for a given group of human nerve fibers, and in each group of nerve fibers the absolute refractory period was not correlated to the growth in fiber diameter (assisted by conduction velocity measurement), as well as it remained rather constant during development (21,22). However, the absolute refractory period of the most excitable fibers (Ia), was found to be smaller than that of the motor fibers independent of the subjects age (23). Therefore it seems to be important to investigate the dispersion of the absolute motor and sensory refractory periods within the peripheral nerve trunk at various ages to define the maturational changes of the various nerve fiber groups constituting that nerve and to establish normal values for each age group during infancy and childhood.

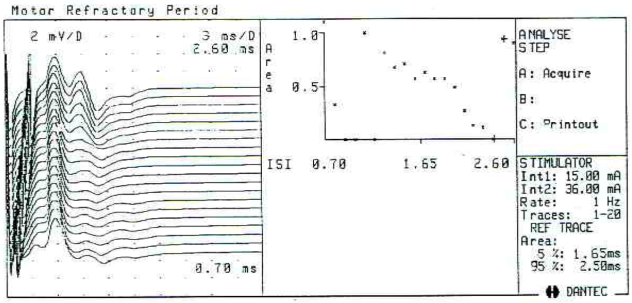
Subjects and Methods:

Subjects

One hundred and sixty seven (167) children below 12 years of age were the subjects of this study. The group included 20 neonates (1-28 days of age), 66 infants (1 month – 1 year of age) and 81 children (2-12 years of age). All the subjects were of full term, normal deliveries, had no family or past medical history of neurological diseases and were normal on physical examination and by assessment of weight, height (length for infants and neonates) and head circumference.

Methods:

The absolute motor refractory period (MRP) was measured in the ulnar nerve using the collision technique. DANTEC Counter-point EMG system was employed, using the motor refractory period assessment program. Two bipolar surface pediatric stimulating electrodes (DANTEC 13L35 or 13L36) were used to stimulate the ulnar nerve at two sites simultaneously. The first stimulating electrode is connected to stimulator A and is placed at the wrist, just over the flexor carpi ulnaris tendon. The second one is connected to stimulator B and is placed on the elbow just distal to the ulnar groove. In both cases, the anode is distally placed and the felt tips were soaked in saline before use to ensure good conduction, the electrodes were placed manually on the skin and a fixating strap (DANTEC 13L38) was used when needed. The Velcro ribbon strap-grounding electrode (DANTEC 13S93) was placed between the distal stimulating site and the active recording electrode after being soaked in saline. A pair of DANTEC 13L20 disposable pediatric surface electrodes was used to record the electrical activity from the abductor digiti minimi muscle. The active recording electrode was placed over the skin at a point mid way between the distal wrist crease and the crease at the base of the fifth digit, at the junction of the dorsal palmer skin. The reference electrode was placed at the base of the fifth digit; both electrodes are connected to the amplifier by the electrode cable (DANTEC 13L02). The skin was cleaned with spirit before application of the electrodes and the electrode paste (DANTEC 15B411) was applied to the contact areas to reduce skin impedance. The ulnar nerve was stimulated by square pulses of a negative polarity and 0.1msec current duration. The intensity was adjusted manually for both stimulation sites (Proximal and distal) to give a maximal muscle responses. Then to ensure supramaximal stimulation the intensity was increased by 50% above that which gave a maximal and stable response. Paired shocks were delivered at the elbow from stimulator B (a conditioning SE_1 and test SE2 stimuli) and a single shock was given from stimulator A at the wrist (SW).



STIMULATOR
Int1: 15.00 mA
Int2: 36.00 mA
Rate: 1 Hz
Traces: 1-20
REF TRACE
Area:
5 %: 1.65ms
95 %: 2.50ms

Figure 1: Motor refractory period recording

The interval between the paired elbow stimuli was varied automatically from 0.7 to 2.6msec, in an increment of 0.1msec, per stimulation. Supramaximal stimulation was used for all stimuli, to excite all of the nerve fibers and to ensure a complete block of the first of the paired elbow stimuli (SE_1), which will collide with the antidromic impulse from the wrist (SW). When the motor axons are cleared from the antidromic activity, the impulse of the second elbow stimulus (SE_2) can be transmitted distally, if the axons are excitable after the passage of the conditioning stimulus (2). There fore, only two muscle action potentials were recorded from these three stimuli, due to the blocking of the conditioning shock given at the elbow. These two responses were designated ME_2 (elicited by the test stimulus on the elbow) and (MW) evoked by the stimulus given on the wrist (figure 1). These two potentials were clearly separated and their characteristics can be easily measured. If an F-wave (recurrent discharge of the anterior horn cells after antidromic invasion) was elicited by the test stimulus (SE_2), it can be easily separated from ME2 by the fact that it appeared at the tail end of M E_2, thus not altering its latency. The appearance of the F-wave in the absence of ME_2 can be also easily distinguished from the muscle potentials on the bases of its latency. (9) The peak to peak amplitude of ME_2 is proportional to the number of axons that are no longer refractory when the test stimulus was applied. On the other hand the initial muscle response, ME, evoked by a single supramaximal stimulus at the elbow, represents the total number of axons available in the nerve. Hence, the initial response amplitude recovery of the test response was defined as the return back of the ME_2 to more than 5% of the ME, i.e. 95% cancellation of the maximal muscle action potential amplitude. This is generally easier to determine than the very first [(24)]. The interstimulus interval of the paired shocks at this point represents the minimal absolute motor refractory period (MRP min) for the fastest fibers within the nerve. Full recovery was defined as the return back of the M E_2 amplitude to 95% of that of ME, i.e. 5% cancellation of the maximum muscle action potential amplitude. The interstimulus interval at this point represents the maximal absolute motor refractory period. (MRP max) [(8, 9, 19)]. These two limits of interstimulus intervals (ISI) are calculated. All subjects were lying in supine position on an examination couch, with the arm abducted 10-15^O. Room temperature was monitored and kept constant during the test procedure. The Sensory refractory period (SRP) for the ulnar nerve was measured using the paired shock technique. DANTEC Counter point EMG system was used but employing the sensory refractory period program. A single bipolar surface electrode (DANTEC 13L35 or 13L36) was used to stimulate the ulnar nerve at the wrist after soaking its felt tips in normal saline. The electrode was placed manually just over the flexor carpi ulnaris tendon with the anode distal to the cathode, and it was connected to the stimulator socket A. The fixating strap (DANTEC 13L38) was used when needed. The Velcro ribbon strap-grounding electrode (DANTEC 13S93) was applied between the stimulation and the active recording electrodes after being soaked in saline. Recording was made by the use of a pair of Velcro ribbon surface finger electrodes (DANTEC 13L69) which were placed around the fifth digit, the active is proximal at the base of the fifth digit and the reference electrode is distal. Both were soaked in saline before use to ensure good electrical conduction and are connected to the preamplifier by the electrode cable (DANTEC 13L02). The stimulation was done at one site (the wrist) by square wave shocks of negative polarity, 0.1msec, duration and at a rate of 1HZ. The intensity of the stimulation current was adjusted manually to give maximal stable sensory potentials. Paired stimulation shocks were delivered, the first (SW_1) is a conditioning impulse and the second (SW_2) is the test impulse. The interval between these two stimuli (inter-stimulus interval, ISI) was varied automatically from 0.7 to 2.6msec, in an increment of 0.1 msec. per stimulation. The conditioning SW_1 impulse will result in a sensory nerve action potential, while the response to the test impulse (SW_2) would be absent at the very short inter-stimulus intervals, because it occurs during the refractory period induced by SW_1. Increasing the interstimulus intervals of the paired shocks will result in the appearance of a second sensory nerve action potential, when the axons are excitable, in response to SW_2. i.e. the ISI exceeds the SRP of the fastest fibers (figure 2) the second response amplitude increases gradually to its maximum with the increase of the ISI due to the increment in number of the excitable axons [(2)].

The ISI at the 5% and 95% cancellation of the maximum sensory nerve action potential amplitude (Maximal and Minimal absolute sensory refractory periods respectively) are calculated. All subjects were lying in supine position on an examination couch, the arm abducted 10^O-15^O, and room temperature was kept constant during the test procedure (25-28 ºC).

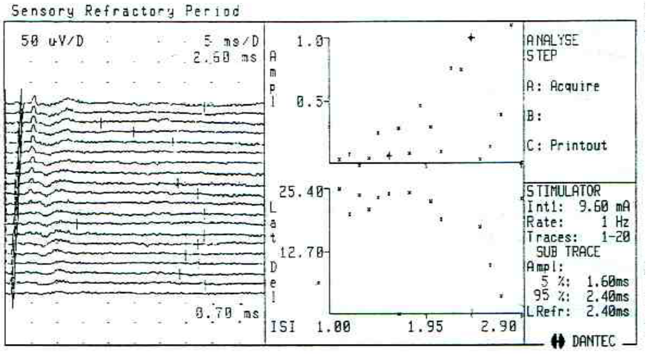


Figure 2: Sensory refractory period recording.

Statistical Analysis:

The arithmetic mean and standard deviation of distribution of each set of the data were calculated. The paired student (t) test was used to compare variables in the same group and the unpaired t-test was used to compare variables of different groups. The level of statistical significance was defined as P value <0.05, which was obtained by comparing the calculated t-value to the tabulated t value at 95% confidence interval and (n_1 + n_2)-2 degrees of freedom. Where n_1 = the number of observations in the first sample and n_2 = the number of observations in the second sample. Regression analysis was chosen as the most powerful tool statistical tool to investigate the effect of age on the measured parameters and to find the correlation. Simple linear regression was used and the correlation coefficient (r) was calculated. Analysis of variance (ANOVA) was done to test the variation significance for each parameter between the different age groups.

Results:

The subjects 167 normal children (79 females and 88 males) were grouped according to age as shown in table 1.

TABLE -1: Age distribution of the subjects

	GROUP NO.	AGE	NO.OF SUSBJECTS
Neonates	Group 1	0-30days(<1 month)	20
Infants	Group 2	1-< 3 months	18
	Group 3	3-< 6 months	15
	Group 4	6-< 9 months	18
	Group 5	9-< 12 months	15
Children	Group 6	1-< 3 years	22
	Group 7	3-< 6 years	21
	Group 8	6-< 9 years	22
	Group 9	9-12 years	16
	Total		167

The Results of Refractory Period Assessment

Minimal motor refractory period (MRPmin): Using the Kimura's collision technique, the motor refractory period measurement showed that during the first 6 months of life the mean minimal absolute motor refractory values decreased in the successive age groups but without statistical differences. From 6 months to<6 years a gradual and statistically significant reduction in the mean MRPmin values was present at the age groups during this period. But after the age of 6 years, there were no statistical differences between the mean MRPmin values of the age groups up to 12 years of age (P>0.05), although an increment in the mean MRPmin is noticed at the age group of 6-<9 years. (Table 2). A significant inverse correlation between age and MRPmin (r=-0.667) existed only between 6 months and 6 years of age (P<0.05).

Maximal motor refractory period (MRPmax):The mean maximal absolute motor refractory period also showed slight changes in the first 6 months of life but without statistical differences between the age groups during this period (P>0.05). From the age of 6 months on the mean MRPmax decreased with statistical significant differences between its values in the successive age groups until at age of <3 years. After which, although the mean MRPmax values continue to decrease, no significant differences could be found between the values in the successive groups up to 12 years (Table 2). A significant inverse correlation between MRPmax values and age (r=-0.628) also present form 6 months to 6 years of age (P<0.05).

Table – 2: The results of motor refractory period (MRP) assessment

Age groups	MRP min msec	MRP max msec	Δ MRP msec
1 < 1 month	1.71±0.14	2.28±0.17	0.57±0.09
2 1-<3 months	1.7±0.15	2.29±0.17	0.59±0.09
3 3-<6 months	1.6±0.17	2.2±0.13	0.60±0.05
4 6-<9 months	1.3±0.13 *	2.0±0.14 *	0.70±0.07 *
5 9-<12 months	1.09±0.17 *	1.9±0.18 *	0.80±0.16 *
6 1-<3 years	0.9±0.21 *	1.79±0.15*	0.88±0.1 *
7 3-<6 years	0.72±0.02 *	1.71±0.17	1.05±0.12 *
8 6-<9 years	0.77±0.09	1.7±0.11	0.93±0.19
9 9-12 years	0.74±0.14	1.69±0.14	0.94±0.21

Values are in mean ± SD.
MRPmin=minimal motor refractory period.
MRPmax=maximal motor refractory period.
MRP=the difference between maximal and minimal motor refractory periods.
*** =Significant level (P<0.05) related to preceding group.**
ΔMRP= the difference between the maximal and minimal absolute refractory periods (dispersion of the absolute motor refractory periods).

The mean values of the differences between the MRPmax and MRPmin (ΔMRP) are also calculated for each age group. It showed no statistical differences between the values for the age groups from birth to 6 months of age, in spite of the little increment from 0.57-0.09 msec. to 0.6-0.05msec.during this period (P>0.05). After the age of 6 months, the mean ΔMRP increased with significant statistical differences between the values of the successive age groups (P<0.05) reaching a maximal value at the age group of 3-<6 years (Table 2). After the age of 6 years, although the mean ΔMRP showed little decrement, no statistical differences exist between the mean values for the age groups (P>0.05) A significant correlation between age and ΔMRP (r=0.632) was present only from 6 months to 6 years of age (P<0.05).

Minimal sensory refractory period (SRPmin): The mean minimal absolute sensory refractory period, measured by the paired shock technique is found to decrease slightly in the successive age groups during the first 6 month of life, but with out statistical significant differences (P>0.05) between the age groups during this period. Between 6 month and 6 year of age, the mean SRPmin decreases more rapidly and with significant differences between the mean values of the age groups (P<0.05). From 6 years on, the mean SRPmin values showed no statistical differences (Table 3). The correlation coefficient between age and SRPmin values was –0.388 during the first 6 months (P>0.05), and –0.759 from 6 months to 6 years of age (P<0.01). Then r=0.294 up to 12 years of age (P>0.05).

Maximal sensory refractory period (SRPmax): The mean maximal absolute sensory refractory period values remained statistically without differences between age groups in the first 6 months of life. After this period the mean SRPmax decreases with significant differences between the mean values of different age groups up to one year. Then after, a gradual and continuous reduction is present until the age group of 9-12 years. However, no significant differences were found between the mean SRPmax values of the age groups after the age of 3 years (Table 3).The correlation coefficient was 0.207 between age and SRPmax values up to the age of 6 months (P>0.05), after which a significant inverse correlation was present between the two (r=-0.582) till the age of 6 years (P<0.05). There after no correlation existed (r=-0.129).

TABLE – 3: The results of the sensory refractory period (SRP) assessment

Age groups	SRP min msec	SRP max msec	ΔSRP msec
1 < 1 month	1.47±0.15	2.04±0.18	0.56±0.085
2 1- < 3 months	1.46±0.15	2.05±0.18	0.58±0.107
3 3- < 6 months	1.42±0.16	2.01±0.12	0.59±0.13
4 6- < 9 months	1.11±0.16 *	1.83±0.16 *	0.71±0.04 *
5 9-< 12 months	0.9±0.12 *	1.7±0.18 *	0.80±0.11 *
6 1- < 3 years	0.78±0.02 *	1.66±0.19	0.88±0.09 *
7 3- < 6 years	0.64±0.09 *	1.59±0.17 *	0.95±0.13 *
8 6- < 9 years	0.62±0.08	1.59±0.18	0.9±0.2
9 9-12 years	0.63±0.14	1.52±0.2	0.88±0.24

Values are in mean ±SD.
SRPmin= minimal sensory refractory period.
SRPmax= maximal sensory refractory period.
Δ SRP = the difference between the maximal and minimal sensory refractory periods.
***= Significant level (P<0.05) related to preceding age group.**

The difference between the maximal and minimal absolute sensory refractory periods (dispersion of the absolute sensory refractory periods): The mean of the differences between the SRPmax and SRPmin (ΔSRP), for each age group was calculated and statistically verified (Table 3). In spite of its increment, the mean ΔSRP showed no significant differences between the age groups up to 6 months to age. However, from 6 month to 6 years of age, the mean ΔSRP increases (with significant differences between the successive age groups) (P<0.05). From 6 years on, there were no significant differences between the mean ΔSRP values at the successive age groups (P>0.05) in spite of the slight reduction observed in these values during this period. A significant correlation was only present between age and ΔSRP values(r=0.672) from 6 months to 6 years of age (P<0.05).

Discussion and Conclusion:

Electrophysiology includes non-invasive, simple and reliable methods that can be used to evaluate the functional changes of the nervous system and can even give an idea about its structural background (2, 25). In this study, we utilized some of these electrophysiological tests to assess the maturational changes, from the functional point of view, in the peripheral nerves of our neonates, infants and children. These may help to follow up the normal process of development and growth. By knowing the normal values and their pattern of progress with age, these testes can also aid to diagnose any deviation form the normal, as early as possible, which in turn helps in the management and correction of these defects, if possible. To study the nerve excitability changes during maturation and to discriminate clearly between nerve fibers of different membrane characteristics, the motor and sensory absolute refractory periods were assessed. With the development of the refractory period measurements as a potential tool in clinical neurophysiology, it has become increasingly important to study fully the characteristics of this phase of axonal membrane excitability (8, 9, 13, 24), because it is a very sensitive measure that can detect early changes in nerve function (7). The value of the absolute refractory period measurement is that it is a quantitative description of the changes in nerve excitability (16), and it provide data that can give information not only about the alterations in nerve functions according to the maturational changes with age, but also about the changes of the different fibers within the peripheral nerve. Moreover, these methods are non-invasive electrical measurement that can investigate functionally important nerves, which other wise, are inaccessible for morphological evaluation. The mean absolute motor refractory period assessment for the ulnar nerve in the studied subjects showed different pattern of maturational changes with age, for the fastest motor fibers than for the slowest ones. We found that the mean minimum absolute motor refractory period (representing the fastest fibers of the nerve) reduced very slightly in the age groups during the first 6 months of life, indicating a minor increase in the membrane excitability of the nerve fibers that can be due to the increase in the myelination process during this period (18). However, in the age groups from 6 month to 6 years, the reduction in the minimal absolute refractory period was more evident and significant. This reflects a predominant increase in the membrane excitability that can not be attributed to the increase in myelination alone, and since it was found that the absolute refractory period is characteristic for a give group of human nerve fibers (21) and it is a specific functional property of the membrane of each nerve fiber (20), it seems that during this period (6 months to 6 years of life) there is an electrophysiological evidence that process of structural maturation in the peripheral nerve trunks could involve, in addition to the increase in nerve fiber size and the increase in myelin sheath thickness, the addition of new myelinated nerve fibers with increasing membrane excitability. This finding is supported by the histological evidence of an increase in the number of the myelinated fibers during the early years of life (26, 27). In our study, the minimal absolute motor refractory period remained rather constant after the age of 6 years indicating a complete functional and structural maturity for the fastest motor nerve fibers. While the mean maximal absolute motor refractory period (representing membrane excitability changes of the slowest conducting motor nerve fibers) showed a slight insignificant reduction in the values of the age groups up t 6 months of age, after which, there was a significant reduction in the mean values of the age groups up to 3 years of age. Those changes can also be explained by the structural maturation changes in the slowest conducting motor fibers with age (i.e. increase diameter, myelin thickness and fiber number) but the continuation in the reduction of the mean MRPmax values in the age groups after the third year of life, indicate a more gradual functional and structural maturation in the slowest than in fastest conducting fibers of the same peripheral nerve. This can be explained by the fact that myelination increases proportionally with the increase in fiber diameter (28), and the diameter of larger fibers increases faster and more than the diameter of the smaller ones, thus, resulting in rapid and bigger changes in fastest fibers and gradual maturational changes in the slowest fibers. The differences in the maturational changes between the fastest and the slowest conducting fibers, as assessed by the absolute motor refractory periods, showed statistically insignificant changes in the age groups during the first 6 months of life, indicating a parallel progression in the myelination and fiber diameter of the fastest and slowest fibers during this period. After this period the values of the mean difference between the maximal and minimal MRP increased significantly in the age groups up to 6 years of age, which reflect that the functional maturation is more rapid in the fastest conducting fibers than the slowest ones, as the mean MRPmin values reduce much in the successive age groups than the mean values for the MRPmax, during this period. From 6 years on, there is a slight in significant reduction in the mean ΔMRP which is explained by the nearly constant mean MRPmin values and the slight continuous reduction in the mean MRPmax values in the successive age groups. Changes in the mean ΔMRP with age also shows that the period of rapid maturational changes is during the first 6 years of life in our pediatric population as regarding the peripheral nerve fiber membrane excitability and gave evidence for the assertion that the thickest fibers are predominately involved during this period. There are few measurement of the absolute motor refractory period of normal human peripheral nerves, however the mean values for the MRPmin and MRPmax in our work for the children after the age of 6 years did not differ than the reported values for normal adults (8, 15, 22, 24). But we could not find in the available literature such measurements neither for children under the age of 6 years nor for infants and neonates. The results of the absolute sensory refractory period assessment for the ulnar nerve showed that the pattern of nerve fiber excitability changes with age also differ in the fastest sensory fibers than in the slowest ones in the same nerve trunk. Where the mean SRPmin, reflecting the absolute refractory period of the fastest fibers) showed an in significantly reducing values in the age groups up to 6 months of age, after which, the mean SRPmin values showed evident and significant reduction. These findings indicate that the maturation for the fastest sensory fibers in the first 6 months of life corresponds to the increase in fiber diameter and to the process of myelination (18) while the more prominent membrane excitability changes, fiber diameter and myelin thickness, Similarly to the motor fibers of the ulnar nerve, the slowest conducting fibers, showed a significant reduction in the mean values for their absolute refractory period (SRPmax) for the age group up to 3 years of age, after which, the mean SRPmax values continued to decrease in significantly indicating a more gradual maturational process for the slowest fibers than that for the thickest (fastest) conducting fibers. The mean values of the differences between the maximal and minimal absolute sensory refractory periods (ΔSRP), representing the maturational differences between the fastest and the slowest sensory fibers in the ulnar nerve trunk, remained with no statistical differences between the age groups in the first 6 months of age, representing also a parallel structural maturation for both fiber types at this period. Form 6 months to 6 years of age, the mean ΔSRP values increased significantly, since the reduction in the mean SRPmin values is much more than that of the mean SRPmax values in the age groups at this period, indicating a more rapid increase in the fiber diameter and myelin thickness in the fastest fibers than the slowest conducting ones, as well as, the possibility of addition of new myelinated fibers with faster conduction characteristics. Carpenter and Bergland (1975) studied the developmental changes of the distribution according to the size of the myelinated fibers in nerve trunks and found that the difference between the size of the largest and the smallest myelinated fibers increased gradually with maturation. Schröder, et al., (1978) have reported the development changes of the sural nerve, and observed that the difference in the size of the large and small fibers was more prominent in older infants than newborn babies. These histological findings support electrophysiological findings that maturation proceeds at rates in nerve fibers of different diameters in the same nerve trunk. The mean ΔSRP values showed also an insignificant reduction at the age groups after the age of 6 years due to the relatively constant mean SRPmin and the slightly reduced SRPmax at this period, representing an earlier completion of functional and structural maturation for the fastest sensory fibers than the slowest fibers.Our values for the minimal absolute SRP for the children after the age of 6 years are in agreement with those reported by Tackmann and Lehmann, 1974 for adults using the same paired shock technique and for the absolute sensory refractory period values reported by Hopf, et al., (1975) and Lowitzsch and Hopf, (1973) which may indicate a complete functional maturity in our studied sample at this period.

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