A STUDY OF SOME PHYSIOLOGICAL MECHANISMS UNDERLYING SUSCEPTIBILITY TO AUDIOGENIC SEIZURES IN MICE*

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One of the difficulties in studying the pathogenesis of epileptiform convulsions is due to the fact that a great variety of apparently heterogeneous causes such as trauma, cerebral edema, anoxemia, and disturbance of acid-base equilibrium may induce convulsions.

If some similarity can be found between various factors such as genetic constitution, biochemical or physiological changes and disturbances, and epileptogenic agents, all of which can bring on convulsive behavior, some progress in the understanding of the pathogenesis of convulsions may be expected.

A fruitful approach to an understanding of the physiology of convulsions may be provided by a study of rabbits and mice genetically predisposed to convulsive behavior in response to auditory stimulation. The extensive literature on these strains has been reviewed by Antonitis, Crary, Sawin and Cohen (4), Bevan (5), Finger (10), Ginsburg (15), and Vicari (27, 28).

At the present time two main approaches are being followed in studies exploring the physiological mechanisms underlying audiogenic seizures. It has been suggested that oxidative processes supplying energy for the nervous system lag behind energy expenditure during convulsive activity. Whether or not this theory is applicable also to audiogenic seizures cannot be decided, since neurochemical studies of the type performed during and after convulsions induced by various pharmacological epileptogens are still lacking in mice suffering from audiogenic seizures (19, 23). However, the protective effect against recurrence of audiogenic seizures exerted by such substances as glutamic acid, glucose, pyruvate, thiouracil, and a number of citric acid cycle intermediates has been interpreted to mean that the differential susceptibility to audiogenic seizures in different strains of mice is a function of different metabolic capacities of the central nervous system (Ginsburg and Hovda (16); Ginsburg, Ross, Zamis and Perkins, (18); Vicari, (27); Vicari, Tracy and Jongbloed, (28)). This view has

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been strengthened by the observation that animals in audiogenic seizure frequently die in respiratory arrest unless saved by artificial respiration. Recently this argument received additional support from the demonstration by Abboed and Gerard (1) that seizure susceptible animals of the DBA strain are characterized by a significant decrease in ATPase activity and in P/O ratio as compared with control strains, and that this metabolic disturbance vanishes along with the audiogenic susceptibility when adulthood is reached.

Another hypothesis has been formulated by Fuller, Easler and Smith (12), Fuller and Smith (13) and by Fuller and Ginsburg (14). These authors suggest that convulsive seizures may be related to a genetically determined unspecified quantitative factor. For lack of a more precise term this factor is referred to as "cortical excitability" or "neuronal permeability".

The study to be reported here was undertaken with the following aims in mind: 1. The authors set out to determine whether in seizure-prone mice there exists a correlation between susceptibility to audiogenic seizures and threshold to convulsions induced by electro-shock; 2. to find out whether certain anti-convulsants which are effective against drug induced seizures are equally potent in protecting against audiogenic seizures. For this purpose the protective effect of the dye trypan blue was studied. This substance was chosen because Aird (2) and Aird and Strait (3) had shown that seizures induced by cocaine and strychnine can be prevented in dogs by pretreatment with vital dyes; 3. to ascertain whether there exists a physiological relationship between anoxia and audiogenic seizures. Interest in this part of the study was aroused by the observation that in some strains, mice suffering from audiogenic seizures invariably die of respiratory failure, unless saved by artificial respiration; 4. In addition, an attempt was made to determine the effects which interference with oxidative processes might have on audiogenic seizures by studying the influence of an agent which uncouples phosphorylation from oxidation. The hormone triiodothyronine was used because this hormone has been demonstrated both in vivo and in vitro to act as an uncoupling agent if present in excess by Lardy and Maley, (20). Since Abboed and Gerard (1) had reported a significant reduction in P/O ratio in brain respiration of animals of the DBA/1 strain, this part of the study seemed especially relevant.

MATERIALS AND METHODS

Mice of the DBA/2 strain susceptible to audiogenic seizures were used. Animals of the C57 BL/10 the A/Jax, and the C3H, strains which are resistant to audiogenic seizures served as controls.

Threshold to Electroshock: In the first set of experiments designed to compare susceptibility to audiogenic seizures with threshold differences to electroshock convulsions, animals of the susceptible DBA/2 strain and the non-susceptible animals of 3 control strains were exposed to electroshock between the 25th to 26th and on the 30th to 31st postnatal day of age respectively.

The following procedure was used: The Offner electroshock apparatus was utilized. In order to establish the relationship between stimulus intensity and elicitation of a tonic convulsive seizure in response to electroshock, mice were tested at 10 hour intervals to allow for full recovery.

The stimulus consisted of a single electroshock of alternating current applied by corneal electrodes for 0.2 seconds between the orbits of the skull to the test animal.
Animals were shocked at the initial trial early in the morning with an intensity of 8 or 9 milliamperes. Those animals which did not respond convulsively were retested 10 hours later with a higher intensity stimulus. The magnitude of the increment at each subsequent stimulation was $1/2$ milliampere. Testing at 10 hour intervals was repeated until a stimulus intensity necessary to elicit a tonic convolution was reached.

Animals which had responded convulsively on the first test at 8 or 9 milliamperes were retested 10 hours later. Stimulation, the intensity of which was decreased by $1/2$ milliampere at each successive shock treatment, was repeated until a stimulus strength was reached at which the animals would no longer respond with a tonic seizure.

No more than 4 separate single shock treatments were administered at 10 hour intervals to any one animal in order to keep the test animals as closely grouped around their respective age means (25 and 30 days respectively) as possible.

The lowest stimulus (in milliamperes) required for tonic seizure was recorded and designated as the threshold-stimulus. Each animal was tested for audiogenic seizures 24 hours after its electroshock threshold was established. Testing for audiogenic seizures was conducted in the following manner: The test enclosure consisted of a tub to which a 100 decibel bell was attached. Mice were placed into this enclosure and subjected to intermittent ringing of a 100 decibel bell for about 2 minutes. Onset of wild running and tonic and clonic convulsions were taken as criteria for audiogenic seizures.

**Protective Effect of Trypan Blue on Audiogenic Seizures:** The second series of experiments was designed to ascertain whether the protection exerted by vital dyes against seizures induced by cocaine and strychnine demonstrated by Airel (2) and Airel and Strait (3) is effective also against audiogenic seizures.

Animals of the DBA/2 strain were used. All animals were tested for audiogenic seizures in the manner described above. Only those animals which had actually suffered a tonic attack, but had been revived by artificial respiration, were retained for subsequent testing. The animals were divided into 2 groups. Group 1 received subcutaneously an injection of 0.02 cc. of a 1 per cent solution of trypan blue per gm. of body weight immediately after recovery from the sound induced attack. Group 2 served as control. The animals in this group were injected with an equal amount of physiological saline solution. On the following day, control and treated groups were retested for audiogenic seizures.

**Audiogenic Seizures and Anoxia:** The third series of experiments was undertaken to test the possibility that there is a correlation between susceptibility to audiogenic seizures and lack of resistance to anoxia. The survival time under anaerobic conditions was measured in 20 day old mice of the DBA/2, the C57BL/10 and the C3H strains by a method described by Fazekas and Himwich (8). Young animals were placed into a transparent sealed glass container into which pure nitrogen gas was pumped, and the survival time under these conditions was measured with the aid of a stop watch.

**Effect of Triiodothyronine on Seizure Patterns:** The fourth series of experiments was designed to test the proposition that excessive thyroid levels by virtue of the action of thyroid hormone as an “uncoupling agent”, might affect the pattern and severity of audiogenic seizures. Newborn mice of the DBA/2 strain were given daily a subcutaneous injection of 0.5 ug of triiodothyronine dissolved in .02 cc of saline and NaOH until the 25th day of age. Each mother was permitted to raise only 6 litter mates to reduce competition for lactation sites. One half of each litter served as controls, and were given saline injections, the other half of the litter were given excess thyroid treatment. After the 12th postnatal day of age animals were tested daily for seizures in the manner described above. The onset, type, and severity of convulsive attacks were recorded. The 12th day was chosen as the starting day for testing because prior to this day most mice do not respond to auditory stimulation (fig. 3).

**RESULTS**

1. **Threshold to and Lethal Effects of Electroshock:** As shown in Figures 1 and 2 there is a small difference in the threshold to electroshock of the DBA/2 strain, as compared to that of the control strains tested. The threshold to electroshock
FIG. 1. Mean stimulus in milliamperes required to induce tonic convulsions in mice 25 days of age following electroshock applied by corneal electrodes. With each bar, the height of which denotes the mean, is placed $N =$ the number of animals in the group and the value for $p$, calculated by the use of the Student $T$ test. $p =$ the probability of the difference between each control strain and the DBA/2 strain occurring by chance.

FIG. 2. Mean stimulus in milliamperes required to induce tonic convulsions in mice 30 days of age following electroshock applied by corneal electrodes. With each bar, the height of which denotes the mean, is placed $N =$ the number of animals in the group and the value for $p$ calculated by the use of the Student $T$ test. $p =$ the probability of the difference between each control strain and the DBA/2 strains occurring by chance.
Fig. 3. Onset of eye opening startle response and audiogenic seizures in young DBA/2 mice. Experimental animals were injected with 0.5 ug triiodothyronine dissolved in .02 cc of saline starting from birth. Control animals were injected with .02 cc of saline. The startle reaction is a primitive reflex in response to sudden noise. Its onset is probably indicative of the animal's ability to perceive auditory stimuli.

in the 30-day animals is lowest for animals of the DBA/2 strain, followed by those of the C3H, which react similarly to the DBA/2 and is highest for animals of the C57BL/10 strain. A similar pattern exists in 25 day old mice, where C57BL/10 and A/Jax strains served as controls. No clear pattern emerged with respect to differences in threshold between convulsing and non-convulsing animals within the DBA/2 strain. Of greater magnitude is the difference between strains with respect to the lethal effects accompanying electroconvulsions. In a group of DBA/2 mice undergoing convulsions, 65 per cent died in seizures due to respiratory failure in spite of vigorous attempts at artificial respiration, while in a comparable sample of C57BL/10 mice only 25 per cent failed to survive (table 1).
2. Protective Effect of Trypan Blue on Audiogenic Seizures: As indicated in Table 2, pretreatment with trypan blue was effective in preventing the recurrence of a convulsive attack in response to audiogenic stimulations in a group of mice that had given a positive seizure response the previous day to the same type of stimulation. Out of a total of 47 mice treated with trypan blue, only 12 responded with convulsions, while 39 out of 49 saline treated controls went into seizure upon subsequent testing. The protection afforded by the dye lasted for a few days, a period which is roughly equivalent to the time probably required for excretion of a major portion of the dye.

3. Audiogenic Seizures and Anoxia: As indicated in Table 3, the DBA/2 strain is far more sensitive to lack of oxygen than the A/Jax or the C57BL/10 strain. The C3H strain is less resistant to anoxia than the other 2 control strains, but animals of this strain are more resistant to anoxia than mice of the DBA/2

### TABLE 1

<table>
<thead>
<tr>
<th>Strain</th>
<th>DBA/2</th>
<th>C57BL/10</th>
<th>C3H</th>
<th>A/Jax</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Number of Seizing Mice</td>
<td>40</td>
<td>70</td>
<td>25</td>
<td>20</td>
</tr>
<tr>
<td>Number of Lethal Seizures</td>
<td>32</td>
<td>40</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Per Cent of Lethal Seizures</td>
<td>65.3</td>
<td>57.1</td>
<td>32.0</td>
<td>25.0</td>
</tr>
</tbody>
</table>

* Age of mice varies between 25 to 30 days of age.

† Individuals not responding to artificial respiration.

‡ $p$ = the probability of the difference between each control strain and the DBA/2 strain occurring by chance.

### TABLE 2

**Protective Effect of Trypan Blue on Audiogenic Seizures in the DBA/2 Strain**

<table>
<thead>
<tr>
<th>Strain</th>
<th>Experimental</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Individuals Seizing before Treatment</td>
<td>Number of Individuals Seizing after Treatment</td>
<td>Per Cent Seizing after Treatment</td>
</tr>
<tr>
<td>First series</td>
<td>18</td>
<td>5</td>
</tr>
<tr>
<td>Second series</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Third series</td>
<td>16</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>12</td>
</tr>
</tbody>
</table>

* All animals were tested for seizures. Immediately after artificial revival the controls were injected with saline. The experimental was injected with Trypan blue. Both groups were retested for seizure 24 hours after treatment.
PHYSIOLOGY OF AUDIOGENIC SEIZURES

TABLE 3

Strain Differences of Survival Time under Anaerobic Conditions following Exposure to pure Nitrogen

<table>
<thead>
<tr>
<th>Time of Exposure to Pure Nitrogen</th>
<th>DBA/2 Mice Dying of Resp. Failure</th>
<th>C3H Mice Dying of Resp. Failure</th>
<th>C57BL/10 Mice Dying of Resp. Failure</th>
<th>A/Jax Mice Dying of Resp. Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Per cent</td>
<td>Number</td>
<td>Per cent</td>
</tr>
<tr>
<td>10 seconds</td>
<td>38</td>
<td>71.7</td>
<td>5</td>
<td>25.0</td>
</tr>
<tr>
<td>15 seconds</td>
<td>15</td>
<td>28.3</td>
<td>10</td>
<td>50.0</td>
</tr>
<tr>
<td>20 seconds</td>
<td>1</td>
<td></td>
<td>5</td>
<td>25.0</td>
</tr>
<tr>
<td>25 seconds</td>
<td>1</td>
<td></td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Total number of animals tested*</td>
<td>53</td>
<td></td>
<td>20</td>
<td></td>
</tr>
</tbody>
</table>

* For each strain the total number of animals was obtained from at least four different litters.

strain. As already mentioned above, the incidence of respiratory failure following electroshock treatment is far greater in animals of the DBA/2 strain than in the 3 other control strains tested (table 1).

4. Effect of Triiodothyronine on Seizure Pattern: Treatment of newborn mice with thyroid hormone starting at birth produced the changes normally associated with hyperthyroidism, such as acceleration of the rate of maturation. Animals generally were more excitable and alert; increment in body weight was slowed; mortality was high. Only rarely did hyperthyroid animals survive beyond the 30th day of age.

Treatment of newborn mice with thyroid hormone in a strain of DBA/2 mice highly inbred for audiogenic seizures (seizure incidence 90 per cent) advanced the onset of seizure susceptibility by 3 to 4 days (fig. 3). Untreated animals of the DBA/2 strain rarely responded to auditory stimulation with convulsive behavior before they had reached the 18th day of age. Most of the hyperthyroid DBA/2 animals convulsed as early as the 14th day of age when exposed to the ringing of a 100 decibel bell. Treatment with exogenous thyroid hormone, however, had little noticeable effect on the pattern or severity of audiogenic seizures, in this strain, nor did it induce audiogenic seizures in three control strains tested, which are genetically resistant to such seizures.

DISCUSSION

1. Threshold to Electroshock of the Audiogenic Seizure Strain: A small difference in response to electroshock could be demonstrated between the animals of the DBA/2 strain and animals of the control strains (A/Jax, C3H and C57BL/10) which were tested. The possibility that the differences in response to electroshock might be related to differences in weight between the strains tested seems un-
likely because the magnitude of the difference remains constant in the 2 different age groups, which were tested, i.e., the 25 day old and the 30 day old animals (figs. 1 and 2). No such difference in threshold to electroshock could be discerned within the DBA/2 strain itself between animals which were susceptible to audiogenic convulsive seizures and those animals within that strain which were resistant to such convulsions. The observation that the animals of the DBA/2 strain, which is a strain characterized by susceptibility to audiogenic seizures, have also a lower threshold to convulsions which are induced by electroshock, than do mice of 3 strains normally resistant to audiogenic seizures, is of interest, and might lend some support to the hypothesis of a lowered “neuronal threshold” advanced by Fuller, Easler and Smith (12), Fuller and Smith (13), and Fuller and Ginsburg (14).

2. Protective Effect of Trypan Blue: Aird (2) and Aird and Strait (3) reported that vital acid dyes such as trypan red exert protective action against epileptiform seizures induced by strychnine and cocaine in animals, as well as against epileptic attacks in man. These dyes are generally assumed not to have any depressant effect on the nervous system if administered by themselves. In fact they are normally prevented from entering the brain tissue proper by the blood-brain barrier, the existence of which has been deduced in part from the observation that dyes such as trypan blue fail to appear in adult nervous tissue after injection into the blood stream. These observations, as well as the additional demonstration by these authors that in animals treated with trypan red the amount of injected cocaine reaching the brain (measured spectrophotometrically) is only one third or less of that of the controls, were interpreted by Aird (2) and Aird and Strait (3) to mean that the protective action of the dye is related to its action on the permeability of the blood-brain barrier. Since cocaine is an exclusively centrally acting epileptogen, the possibility of a peripheral action of the dye on the cocaine was ruled out. Our own observation, that pretreatment with dye protected susceptible animals against recurrence of audiogenic convulsions, could be interpreted along similar lines. It has been shown (Spiegel and Spiegel (22)) that during seizures induced by metrazol and insulin the permeability relations in the vascular bed supplying brain tissue, are altered.

The inference that the so-called “blood-brain barrier” may be one of the physiological factors, which is altered in animals of strains susceptible to convulsive seizures, as compared with animals of strains more resistant to audiogenic or other seizures, may merit further investigation.

3. Audiogenic Seizures and Anoxia: The observation that DBA mice suffering from audiogenic seizures invariably die of respiratory failure unless saved by artificial respiration has been reported by all investigators who have worked with this strain. This has suggested to some authors that the genetic constitution of mice susceptible to seizures affects in some way the respiratory centers or the general metabolic capacity of the brains of these animals. Our own observations lead us to similar conclusions. Results summarized in Table 1 clearly indicate that animals of control strains in which tonic seizure was induced by electroshock could almost always be revived by artificial respiration, while 65 per cent of the
DBA/2 mice suffering seizures, died as a consequence of respiratory failure in spite of vigorous attempts at artificial respiration. This confirms recent findings of Torchiana and Stone (24) who reported a significantly higher mortality following electroconvulsions in 3 strains of mice, which were also susceptible to audiogenic seizures, as compared with animals of strains resistant to audiogenic seizures.

Furthermore, the demonstration of a significant difference in anaerobic survival time between animals of a number of seizure resistant control strains and animals of the seizure susceptible DBA/2 strain seems to provide additional justification for the assumption that either the physiology of the respiratory centers or the metabolic activity of the brain tissue is somewhat altered by the genetic constitution in mice of the DBA/2 strain (table 3).

On the other hand Fuller, Easler and Smith (12) have shown that the death rate following audiogenic seizures is determined by genes which segregate independently from the genes predisposing to seizures. Frings, Frings and Kivert (11) have shown that there are striking interstrains differences in death rates following seizures in different strains of mice susceptible to audiogenic seizures. These conflicting results might perhaps be reconciled by assuming that the genes predisposing to seizures although not identical with the gene loci influencing respiratory capacity, might perhaps be closely linked with the latter. Our own data presented here as well as the findings reported by Torchiana and Stone (24) that the incidence of respiratory failure following electroconvulsions is significantly higher in three strains of mice, which are also subject to audiogenic seizures as compared with mice of strains which are resistant to such seizures, suggests the existence of some relationship between these 2 events.

4. Effect of Triiodothyronine on Seizure Patterns: The interpretation of the effect of thyroid hormone as an agent which uncouples phosphorylation from cellular oxidation (Lardy and Maley (20)) must take into consideration conflicting opinions as to the effect of this hormone on oxygen consumption of nervous tissue. Fazekas (7) and Fazekas, Graves and Alman (9) claim that nervous tissue in contrast to most other tissues does not respond by an increase in oxygen consumption to thyroxine treatment. Pretreatment of exogenous thyroid hormone of newborn mice accelerated the onset of audiogenic seizures only in those young DBA/2 mice, whose genetic constitution makes them susceptible to such seizures in the first place. This is part of a general action of thyroid hormone, which consists in speeding up maturation (fig. 3) and is not at all a specific effect on induction of audiogenic seizures.

The further evaluation of the data presented here will have to await an unequivocal demonstration of the effect of excess thyroid hormone on the P/O ratio of nerve cells.

CONCLUSIONS AND SUGGESTIONS FOR FURTHER RESEARCH

The present study has demonstrated that mice of the DBA/2 strain differ from mice of the C57BL/10, the A/Jax and the C3H strain by: 1. a somewhat lower threshold to electroshock stimulation; 2. a greater incidence of total respiratory failure following electroshock, and 3. a much lower resistance to anoxia.
The present study has further demonstrated that an agent which inhibits the passage of centrally acting convulsant drugs from the cerebral circulation into brain tissue, also protects against the recurrence of audiogenic seizures in the DBA/2 strain of mice inbred for susceptibility to such seizures. The suggestion has been advanced that perhaps physiological factors affecting the rate of penetration and exchange of material from capillaries into cerebral tissue, i.e. the so-called "blood-brain barrier," may be altered in strains of mice susceptible to convulsive seizures.

The animals of the DBA/2 strain of mice which we tested belonged to a subline highly inbred for susceptibility to audiogenic seizures. The evaluation of any of the observations reported here of the physiological properties of the DBA/2 strain in terms of their relationship to the convulsive behavior also characterizing the animals of this strain will have to await the demonstration of the presence of similar physiological properties in convulsing animals of other strains of mice. Such a study is now in progress on two lines inbred for audiogenic seizures: a Swiss Albino line, and a line of CE mice.

Treatment with excess thyroid hormone advanced the onset of the audiogenic seizure response to an earlier age than that at which this behavior normally begins to occur. However, such treatment does not bring on convulsions in animals of strains which lack the full genetic background conveying seizure susceptibility (Nelson (21)).

Our failure to demonstrate a specific relationship between excess thyroid hormone concentration and induction of convulsive audiogenic seizures in mice in no way rules out the possibility of endocrine involvement in bringing about his syndrome.

There is a growing amount of evidence that the endocrine balance in animals subject to audiogenic seizures is altered. Chai (6) has shown that the thyroid activity of the seizure susceptible DBA strain is twice as high as that of all other inbred strains which he tested. Conversely, protective action of the anti-thyroid drug thiouracil on audiogenic seizures was reported by Vicari, Tracy and Jongbloed (28). Vicari (25) has demonstrated audiogenic seizures in a strain of Jackson mice (CE strain) with a high incidence of adrenal-cortical tumors, and furthermore she has shown that the onset of seizure susceptibility roughly coincides with the development of these tumors. Experiments to analyze more fully the influence of the endocrine system on convulsive behavior in general and audiogenic seizures in particular are now in progress.

**SUMMARY**

Mice of the DBA strain (lines 1 and 2) typically respond with clonic and tonic convulsive seizures upon exposure to the continuous ringing of a 100 decibel bell over a 2 minute period, whereas mice of the C57BL/10, the A/Jax, and the C3H strain do not respond convulsively to loud audiogenic stimuli. This difference in susceptibility to sound-induced seizures between animals of the DBA strain and those of a number of strains which are resistant to such seizures has been ascribed to a multigenic difference.
The present study adds the following data: Mice of the audiogenic seizure susceptible DBA/2 strain have a lower threshold to seizures induced by electroshock, than do mice of the C57BL/10, A/Jax, and C3H strains, which are normally resistant to audiogenic seizures.

Vital dyes, such as trypan blue, which protect against cocaine and strychnine-induced seizures, also protect against recurrence of audiogenic seizures.

Young DBA mice are characterized by a lower resistance to anoxia and a higher incidence of respiratory failure following electroshock stimulation, than are mice of the C3H, A/Jax, and C57BL/10 strains.

Triiodothyronine, which presumably uncouples phosphorylation from oxidation, does not change the seizure pattern of susceptible mice, in response to audiogenic stimuli. Treatment of young DBA/2 mice with triiodothyronine merely advances to an earlier age the onset of the period during which susceptible animals will respond convulsively to audiogenic stimulation.

REFERENCES

19. Gurdiian, E. S., Webster, J. E. and Stone, W. E.: Cerebral Metabolism in Metrazole
Convulsions of the Dog. Proc. of Ass. for Res. in Nervous & Mental Dis., 26:
184-204, 1946.
20. Lardy, H., and Maley, G. F.: Metabolic Effects of Thyroid Hormone. Recent Progress
21. Nelson, Eric: Effect of Thyroxin on Audiogenic Seizures in DBA/2, C57BL/6 and BD
23. Stone, W. E., Webster, J. E. and Gurdiian, E. S.: Chemical Changes in the Cerebral
290, 1959.
1952.

AWARD

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36th Annual Meeting of the American Association of Neuropathologists was
awarded to Drs. H. D. Webster, D. Spiro, B. Waksman and R. D. Adams for
"Phase and Electron Microscope Study of Experimental Diphtheritic Neuritis
in Guinea Pig Sciatic Nerves".