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Modification of the Site of Paralysis in Experimental Poliomyelitis.*

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Römer[1] noted that monkeys inoculated intracranially with poliomyelitis virus frequently showed paralysis on the opposite side of the body. This suggested the participation of some decussating pathway in the propagation of the virus, but threw no light on the actual mechanisms which might be thus involved. A demonstration that virus may be routed along known fiber tracts in the central nervous system would go far toward explaining the fact that although the infective agent may enter through the olfactory tract, it usually traverses the entire brain stem without causing serious damage above the cord. Various cytologically distinct areas of the cerebral cortex provide the ideal conditions for such an experiment since their fiber connections with lower centers are sufficiently well known to provide a ready interpretation of the results obtained.

Accordingly 3 representative cortical areas were selected as sites for the introduction of the virus. The first, the so-called motor cortex, known cytologically as area 4 of Brodmann, was chosen because its known lower connections both ascending and descending are predominantly crossed. Next, the visual cortex, area 17 of Brodmann, presented the picture of an area with uncrossed connections. Its relations are with the lateral geniculate body of the same side, a region receiving the optic tracts, but possessing no direct connections with the lower brain stem or cord. The third region selected was the pre-motor cortex, or area 6 of Brodmann. The course of the fibers connecting this field with lower centers is not so well known as in the case of the other cortical areas. It is certain that its descending fibers run outside the pyramidal tract, proceeding as far as the midbrain and pons.[2] Stimulation of area 6 with the cortico-spinal tract eliminated[3] indicates that it is primarily concerned with movements of both arms, although there is a preponderance of crossed representation. Leg movements are

* Supported by a grant from the President's Birthday Ball Committee for Infantile Paralysis Research.

1 Römer, P. H., *Epidemic Infantile Paralysis*, New York, 1913.

2 Levin, P. M., *J. Comp. Neurol.*, 1936, **63**, 369.

3 Tower, S. S. Personal communication.

evoked to a lesser degree, but are obtained on both sides from the cortex of the one side. Area 6 then seems to present a diffusely stimulable surface in which there is no sharp localization for isolated muscles on the opposite side of the body as in the case of area 4.

Thirty-six animals were inoculated; 8 in the visual cortex (area 17), 16 in area 4, and 12 in area 6. The dosage in most cases was 0.2 cc. of 25% suspension of monkey cord containing MV virus. In each case the cortex was exposed and in areas 4 and 6 the regions were delimited by 60 cycle stimulation. The virus suspension was introduced through a 20-gauge needle with a guard to prevent accidental penetration into subcortical tissue. All the animals developed typical poliomyelitis, the paralysis appearing in 5-14 days. The average time elapsed from the date of inoculation until the appearance of paralysis was 7.6 days for area 4, 8.4 days for area 6, and 8.8 days for the visual cortex. The shorter incubation time for the area 4 inoculations may reflect the greater directness of its connections with the spinal cord.

Striking differences in the localization of initial paralysis were noted after inoculation into the three different areas. A crossed initial paralysis appeared in 87% of the inoculations into area 4 (14 cases) with a 13% incidence of uncrossed paralysis (2 cases). The visual cortex inoculations yielded 50% uncrossed paralyses (4 cases) while the remainder were either crossed or balanced on both sides. Inoculation of area 6 gave a little more than half the paralyses on the opposite side (58%) and the remainder either uncrossed or balanced. The experimental data thus correlate amazingly with anatomical and physiological knowledge of the connections involved.

It is possible to make interesting, though at the present time limited, inferences from the incidence of arm and leg paralyses. Inoculation of the visual cortex always gave isolated arm paralysis, with but one instance out of 8 in which the legs also were involved. Likewise area 6 inoculations gave initial arm paralysis in every case but one of the 12, but involved both arms and legs in 5 cases (41%). The sixteen area 4 inoculations were made into a region giving movements of leg or foot upon electric stimulation, and here the incidence of arm paralysis was lower (71%) while the leg paralyses were much more numerous than in other groups (64%). In 4 cases the opposite leg was paralyzed without the arm. Such findings point to a more direct type of virus propagation than that seen after the inoculation of areas 17 and 6. The involvement of the legs without arms suggests that the virus passed through the cervical cord on some system destined to end in the lumbar region. Naturally one thinks of the pyramidal tract in this connection, but it does not represent the only decussating connection with area 4. Thalamo-cortical fibers also end in the region inoculated, so that a relay from the thalamus to the cord via the spino-thalamic tracts or medial lemniscus must also be regarded as a possibility. Further experimental work now in progress is designed to elucidate the separate rôles which these long systems may have in the production of the crossed paralyses. It is thus possible, within certain limits, to alter at will the pattern of paralysis by varying the point at which the virus is introduced into the central nervous system. With this evidence for the propagation of the virus along the lines followed by definite fiber systems it seems possible to analyze the olfactory system for pathways which might be involved after intranasal inoculation.

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Experimental Poliomyelitis Without Paralysis.*

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Preliminary studies on a series of 13 Rhesus monkeys *(Macaca mulatta)* indicate that by section of the olfactory tracts it is possible to confine the activity of poliomyelitis virus after intranasal inoculation to the olfactory bulbs. Previous experiments (Brodie and Elvidge,[1] Schultz and Gebhardt[2]) have shown that monkeys in which both olfactory tracts and bulbs were destroyed did not develop paralysis after introduction of the virus into the nose. These findings, however, give no information regarding the ultimate fate of the virus after such a method of inoculation. The question remains as to whether the virus dies out immediately or may survive in the body—whether it can enter into any reactions with non-nervous tissue, or is capable of conferring any immunity upon its host although the typical picture of clinical poliomyelitis does not appear.

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1 Brodie, M., and Elvidge, A. R., *Science*, 1934, **79**, 235.

2 Schultz, E. W., and Gebhardt, L. P., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 728.