"Lesions involving a considerable extent of the cortex, but not extending deeply and not implicating the central grey nuclei, produce disturbances which are of relatively short duration and of moderate intensity. Lesions limited to the cortex of one hemisphere, and not extending deeply, may be free from any disturbance."

It is well known that section of a superior or inferior cerebellar peduncle produces rotatory movements, and other motor disturbances, and also that similar disturbances follow removal of one half of the vermis or of one lateral lobe. This second fact may be readily understood when the arrangement of the parts is considered. An examination of Fig. 3 shows that removal of one half the vermis or of one lateral lobe involves a section of the intracerebellar portion of these peduncles. It is also stated that section of the middle peduncles produces somewhat similar symptoms, and since the cerebellar terminations of this peduncle are limited to the lateral lobe, it will naturally be asked why removal of the lateral lobe, which must involve an intracerebellar section of the fibres of this peduncle, should not in like manner produce similar symptoms. In answer to this, I would suggest that many of the results ascribed to section of the middle peduncle are really due to involvement of the upper or lower peduncle or of the cerebello-vestibular tract, or of all of these, during the operation employed for division of the middle peduncle, and that the results of a section limited to the middle peduncle have yet to be determined.

If the views here adduced be well founded, we may expect disturbances of equilibrium to be produced by lesions situated within an area bounded by the intracerebellar path of the two inferior peduncles, of the two superior peduncles, and the dentate nuclei in which the latter arise. This area contains the middle lobe (superior and inferior vermis, the roof nuclei, and the sagittal fibres connecting the latter with the cortex), and the cerebello-vestibular tracts from the roof nuclei to the nucleus of Deiters (Fig. 3). Lesions within this area may produce no such disturbances, provided they are symmetrically situated with reference to the mesial plane, and especially if their growth is so slow that compensation is established *pari passu* with the disturbances they may tend to cause.

On the other hand, lesions situated in the lateral lobes may produce no disturbance of equilibrium provided they are situated entirely external to the intracerebellar paths of the upper and lower peduncles, and of the nucleus dentatus (area of possible latency Fig. 3). If, however, these structures are interfered with, either by pressure or by direct involvement, then the characteristic symptoms of cerebellar disease will be produced, and will depend in their character and amount on the nature and extent of this interference.

Fig. 4. Relation of Deiters's nucleus to the mechanism for conjugate deviation.

If the cerebello-vestibular tract, or Deiters's nucleus, be injured,

then the usual stimuli will not pass either to the anterior cornua of the cord or to the sixth (fourth) or third nuclei. Hence may result the weakness of the same side, the tendency to fall to that side, the impairment of the conjugate deviation to that side, the tendency of both eyes to be directed to the opposite side, and the lateral nystagmus which occurs especially when the eyes are directed towards the same side. A glance at Fig. 2 will show how the spinal symptoms may be produced, since the nucleus of Deiters will not act through the vestibulo-spinal tract and posterior longitudinal fasciculi upon the anterior cornua, and more especially upon that of the same side. The effect on the position and movements of the eyes will be easily understood from Fig. 4, if it be remembered that the sixth nucleus is the nucleus for the conjugate deviation of the eye to the same side, supplying, as it does, not only the external rectus, but also, through the opposite third nucleus and nerve, the internal rectus of the opposite side. A stimulus of Deiters's nucleus, acting on the sixth nucleus, will turn the eyes to the same side; absence of this stimulus will allow the other sixth nucleus to pull the eyes towards the opposite side and will thus weaken the voluntary attempt to look to the same side. On the other hand, lesions which merely irritate but do not destroy the nucleus of Deiters may cause rigidity or spasms of the same side of the body, or such an excess of movement as may cause the body to fall to the other side, and by acting on the sixth nucleus may turn the eyes to the same side.

Luciani, Ballance, and Thomas have also drawn attention to the possible effect which the superior peduncle may exert through the red nucleus and the optic thalamus on the ocular nuclei and the opposite motor nucleus, and it is not my intention to question this influence in producing the symptoms of the cerebellar disease. At the same time, the importance of the nucleus of Deiters as a co-ordinating centre seems too evident to be ignored.

It is by no means claimed that the above described mechanism is as yet so fully understood as to be capable of explaining all the symptoms of cerebellar disease, but it, at least, affords a working hypothesis on which the most characteristic and frequent among them may be interpreted.

REFERENCES.

- ¹ *Proceedings of the Royal Society of Edinburgh*, xvii, 1883-1884, p. 26.
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ON THE PHYSIOLOGICAL ACTION OF CHOLINE AND NEURINE.*

BY
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THE cerebro-spinal fluid removed from cases of brain atrophy, particularly from cases of general paralysis of the insane, produces when injected into the circulation of anæsthetised animals (dogs, cats, rabbits), a fall of arterial blood pressure, with little or no effect on respiration. This pathological fluid is richer in proteid matter than the normal fluid, and among the proteids, nucleo-proteid is present. The fall of blood pressure is, however, due not to proteid, nor to inorganic constituents, but to an organic substance which is soluble in alcohol. This substance is precipitable by phosphotungstic acid, and by chemical methods was identified as choline. The crystals of the platinum double salt, which, when crystallised from 15 per cent. alcohol, are characteristic octahedra, form the most convenient test for the separation and identification of this base.

The nucleo-proteid and choline doubtless originate from the disintegration of the brain tissue, and their presence indicates that possibly some of the symptoms of general paralysis may be due to auto-intoxication; these substances pass into the blood, for the cerebro-spinal fluid functions as the lymph of the central nervous system. We have identified choline in the blood removed by venesection from these patients

Abstract of a Paper read before the Royal Society on April 20th, 1899.

during the convulsive seizures which form a prominent symptom in the disease.

Normal cerebro-spinal fluid does not contain nucleo-proteid or choline, or if these substances are present, their amount is so small that they cannot be identified. Normal cerebro-spinal fluid produces no effect on arterial pressure; neither does the alcoholic extract of normal blood or of ordinary dropical effusions.

The presence of choline in the pathological fluids will not explain the symptoms of general paralysis; for instance, it will not account for the fits just referred to. Its presence, however, is an indication that an acute disintegration of the cerebral tissues has occurred. If other poisonous substances are also present, they have still to be discovered.

Our proof that the toxic material we have specially worked with is choline rests not only on chemical tests, but also on the evidence afforded by physiological experiments; the action of the cerebro-spinal substance exactly resembles that of choline. Neurine, an alkaloid closely related to choline, is not present in the fluid; its toxic action is much more powerful, and its effects differ considerably from those of choline.

PHYSIOLOGICAL ACTION OF CHOLINE.

The doses employed were from 1 to 10 c.cm. of a 0.2 per cent. solution, either of choline or of its hydrochloride. These were injected intravenously. The fall of blood pressure is in some measure due to its action on the heart, but is mainly produced by dilatation of the peripheral vessels, especially in the intestinal area. This was demonstrated by the use of an intestinal oncometer. The limbs and kidneys are somewhat lessened in volume; this appears to be a passive effect, secondary to the fall in general blood pressure. The drug causes a marked contraction of the spleen, followed by an exaggeration of the normal curves, due to the alternate systole and diastole of that organ.

The action on the splanchnic vessels is due to the direct action of the base on the neuro-muscular mechanism of the blood vessels themselves; for after the influence of the central nervous system has been removed by section of the spinal cord, or of the splanchnic nerves, choline still causes the typical fall of blood pressure. The action of peripheral ganglia was in other experiments excluded by previous intravenous injection of a solution of nicotine.

Section of the vagi produces no effect on the results of injecting choline. We have obtained no evidence of any direct action of the base on the cerebral vessels. Choline has little or no action on nerve trunks, as tested by their electrical response to stimulation. This aspect of the subject has been taken up by Dr. Waller and Miss Sowton, who will publish their results fully in a separate paper. Choline has no effect on respiration.

The effect of choline soon passes off, and the blood pressure returns to its previous level. This is due partly to the great dilution of the substance injected by the whole volume of the blood, and may be partly due to the excretion of the alkaloid, or to its being broken up into simpler substances by metabolic processes. We could not find it in the urine.

If the animal has been given a hypodermic injection of morphine and atropine prior to the administration of the ether or A.C.E. mixture, the effect produced by choline is a rise of arterial pressure, accompanied by a rise of the lever of the intestinal oncometer. We consider this observation of some importance, for it shows how the action of one poison may be modified by the presence of another. This has some bearing on general paralysis, for the arterial tension in that disease is usually high, not low, as it would be if choline were the only toxic agent at work.

PHYSIOLOGICAL ACTION OF NEURINE.

The doses employed varied from 1 to 5 c.cm. of a 0.1 per cent. solution. These were injected intravenously.

Neurine produces a fall of arterial pressure, followed by a marked rise, and a subsequent fall to the normal level. Sometimes, especially with small doses, the preliminary fall may be absent. Sometimes, especially with large doses, by which presumably the heart is more profoundly affected, the rise is absent. The effect of neurine on the heart of both frog and mammal is much more marked than is the case with

choline; in the case of both choline and neurine, the action on the frog's heart is antagonised by atropine.

The slowing and weakening of the heart appear to account for the preliminary fall of blood pressure; in some cases this is apparently combined with a direct dilating influence on the peripheral vessels. The rise of blood pressure which occurs after the fall is due to the constriction of the peripheral vessels, evidence of which we have obtained by the use of oncometers for intestine, spleen, and kidney. After the influence of the central nervous system has been removed by section of the spinal cord, or of the splanchnic nerves, neurine still produces its typical effects. After, however, the action of peripheral ganglia has been cut off by the use of nicotine, neurine produces only a fall of blood pressure. It therefore appears that the constriction of the vessels is due to the action of the drug on the ganglia; in this, it would agree with nicotine, coniine, and piperidine. Section of the vagi produces no influence on the results of injecting neurine. In animals anaesthetised with morphine and atropine, injection of neurine causes only a rise of blood pressure, which is accompanied with constriction of peripheral vessels.

Neurine produces no direct results, so far as we could ascertain, on the cerebral blood vessels. Neurine is intensely toxic to nerve trunks (Dr. Waller and Miss Sowton). It produces a marked effect on the respiration. This is first greatly increased; but with each successive dose the effect is less, and ultimately the respiration becomes weaker and ceases altogether. The animal can still be kept alive by artificial respiration.

The exacerbation of respiratory movements will not account for the rise of arterial pressure; the two events are usually not synchronous, and an intense rise of arterial pressure—due, as previously stated, to contraction of peripheral blood vessels—may occur when there is little or no increase of respiratory activity or during artificial respiration.

As confirmatory of Cervello's statement that neurine acts like curare on the nerve endings of voluntary muscle, and to which he attributes the cessation of respiration, we may mention that after an animal has been poisoned with neurine asphyxiation causes little or none of the usual convulsions.

The full paper contains references to previous work on the subject, and complete details of the methods used, and the cases investigated; it is illustrated by reproductions of numerous tracings.

[Note added April 20th, 1899.—It should be mentioned that in the case of brain atrophy referred to the cerebro-spinal fluid was removed soon after death. Since the foregoing abstract was written we have, however, by the kindness of Dr. Turner, had the opportunity of examining two specimens removed during life by lumbar puncture, and the results of our experiments with these corroborate the conclusions previously arrived at.]

TRAUMATIC EPILEPSY, STATUS EPILEPTICUS : TREPHERING : RECOVERY.

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THE following case is a good example of what may be accomplished by an exploratory operation in an apparently hopeless case.

J. A., aged 25, labourer, was admitted into the Mill Road Infirmary, Liverpool, in an unconscious condition on September 2nd, 1898. Ten months previously he had fallen a distance of 18 feet upon his forehead. He was picked up unconscious and taken to a hospital, where he remained in an unconscious state for six days. He slowly recovered, and was discharged improved after six weeks. He resumed his work after a few months, and appeared in his usual health until two weeks before his admission here, when he was suddenly seized with a "fit." The fits continued at intervals for ten days. On the day before admission he had fifteen "fits" in rapid succession.

On admission the man was quite unconscious; his face was flushed, his pupils were unequal, the right dilated and fixed; there appeared to be some slight left facial paralysis, and the left arm and left leg were a little more flaccid than the right. The deep reflexes were present. There was no scar or other