Short Notes and Clinical Cases.

A NOTE ON THE ACTION OF BULBOCAPNINE.

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THE recent work of de Jong and Baruk on the experimental production of catatonia in animals by means of bulbocapnine throws light on the condition of catalepsy. The first important fact discovered is that bulbocapnine can produce effects in the higher animals corresponding to those of catalepsy in man, but cannot produce such effects in the lower vertebrates (frogs, snakes, lizards, fish), *which lack a neocortex*. Furthermore, as stated by de Jong and Baruk, in an animal whose cortex has been removed bulbocapnine does not cause catalepsy. This indicates that the catalepsy-producing effect of bulbocapnine occurs through a specific action of the drug on the cerebral cortex. In fowls, which have but a rudimentary neocortex, the catalepsy is incomplete and unstable. In moderate doses bulbocapnine has the unique effect of producing catalepsy. What is the physiological process at work here?

We must assume that in catalepsy there is primarily a blocking of sensory nerve-impulses in the central nervous system. That this is so is indicated by the fact that one may stick a pin into the flesh of a cataleptic person without any visible response. Generally speaking, to obtain a change of position of a limb or of the body in a cataleptic, *mechanical force* must be used, whereas in a normal person a nervous stimulus such as a pinprick or a slight pressure is sufficient. The long maintenance of one position by a cataleptic also suggests a complete isolation of the motor centres of the central nervous system from external stimuli.

In *sleep* there is also an isolation of the motor centres of the brain from external stimuli, but it is more of a partial isolation, for an individual may frequently move in his sleep from an obvious external cause. Also, the isolation of the motor centres in sleep is easily broken down by any slight stimulus which awakens the individual. The physiological process at work here is, according to Pavlov, a general inhibition of the cerebral cortex, descending to the subcortical motor centres.

Catalepsy, as well as sleep, is apparently caused by a change in the cerebral cortex, and in catalepsy that change would appear to consist of a

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general cortical inhibition, but without descent to the subcortical centres, thus allowing the muscles to maintain contraction. In the catalepsy of human beings, the cortical inhibition differs further from that of sleep by being stable and persistent in character, thus more or less permanently shutting off the motor centres from external stimuli, but not causing them to enter into a state of inhibition such as occurs during sleep. It seems, therefore, that bulbocapnine *has a selective action on sensory elements of the brain*, thus isolating the animal from the external world (cf. 'l'animal perdre le contact avec le milieu extérieur'—de Jong and Baruk), and depriving it of 'l'initiative motrice.' Muscular action remains in the cataleptic, but it is static in character, the stimuli for dynamic muscular action having been cut off by the cortical inhibition. Mechanical force is therefore necessary to change the position of the cataleptic, and the opposition of the tonic contractile muscular action to the outside mechanical force gives us the 'negativism' of catalepsy.

With smaller doses of bulbocapnine than those which cause catalepsy, de Jong and Baruk state that in the higher animals 'sleep' is produced. However, the term 'sleep' applied to the conditions observed is perhaps somewhat misleading, for it is applied to conditions where there does not appear to be inhibition of the lower motor centres—as judged by the animal's maintaining positions of muscular strain (cf. the 'Penseur de Rodin'), instead of reclining in a relaxed position as in ordinary sleep. The importance of this point is that if small doses of bulbocapnine did inhibit the subcortical motor centres, then why should larger doses leave these lower motor centres uninhibited, permitting the muscles to retain the tonic contraction of catalepsy? However, as the animals apparently do not 'go to sleep' in the usual fashion with small doses of the drug, that is, do not recline with relaxed muscles, we may say that the action of bulbocapnine on these animals is confined to the cortex, which must be in a state of unstable inhibition, easily broken by the external stimulus that 'awakens' the animal.

With larger doses of bulbocapnine than those which produce catalepsy the signs of *hyperkinesis* are observed, that is, movements of a stereotyped and mechanical character, or sudden violent movements, that may be equally suddenly arrested by a further state of catalepsy. If bulbocapnine is a drug which causes cortical inhibition, as appears probable, then the signs of hyperkinesis with large doses of the drug may also be due to inhibition—of other parts of the central nervous system. It is to be noted that in animals lacking a neocortex (fish and reptiles), signs of hyperkinesis—of rapid and mechanical-like movements—are caused by bulbocapnine (large doses). May it not be that in these lower animals bulbocapnine has a selective action on the sensory elements of the brain,

as in the higher animals? On account of the absence of a neocortex catalepsy is not produced. But why do we get the movements of hyperkinesis? Surely because the proprioceptive sensory impulses would be interfered with in a selective action of the drug on the sensory elements of such a brain. In the brain of the higher animals, a special organ, the neocortex, exists to deal in particular with stimuli from the external world. Proprioceptive stimuli can be dealt with by lower portions of the brain while the cortex is in a state of inhibition, as appears to be the case in catalepsy. In the lower animals, on the other hand, which lack a neocortex, all sensory impulses, including the proprioceptive, pass to a brain which cannot deal in a special area with impulses from external stimuli. Hence in such a brain a drug affecting these impulses from external stimuli would also be likely to affect the more closely intermingled proprioceptive impulses, thus throwing the muscular system out of equilibrium, and resulting in movement.

In the catalepsy of the higher animals, where only the cortex appears to be affected and proprioceptive impulses are not interfered with, a motionless state results, the muscular system not being thrown out of equilibrium. But when larger doses of the drug are given its effect extends to subcortical areas of the brain—still selecting the sensory elements, so that proprioceptive centres are interfered with, the subcortical motor centres no longer receive complete information, as it were, about the position of different parts of the body, and so exhibit disordered activity in purposeless, mechanical movements, or sudden violent efforts. This at least seems to be a possible interpretation of the action of bulbocapnine as suggested by the experimental work of de Jong and Baruk.

The fact that bulbocapnine in still larger doses causes convulsions ('epilepsy') does not necessarily belie these conclusions, for many different kinds of drugs in large enough doses can produce convulsions, through a disorganisation of the nervous system and of the body generally.