mental reaction of lethargy and the weakened attention and "grasp"; Dr. Greenfield had shown that there might also be visible evidence of cortical cell degeneration. The mental changes could best be understood by utilizing the conception of "neural energy," and thinking of mental and nervous phenomena as evidences of orderly evolution and distribution of energy derived from the activity of the neurons at different levels in the nervous system. Head had observed that the decerebrate cats of Bazett and Penfold responded to stimuli reflexly and purposefully, so that a drop of water placed in the ear led to shaking of the head, while touching the ear with a finger produced a different but appropriate response. This purposeful adaptive character of reflex response to stimulation was only seen when the internal and external environment of the animal was good and the nervous system was said to be in a state of "vigilance"; it was abolished temporarily, for example, when the cat was given a little chloroform or suffered from sepsis. By considering what "vigilance" implied physiologically and applying that conception to high cortical levels, a close parallelism would appear between high vigilance in the cortex and high mental efficiency, with its heightened attention and ability to respond appropriately to whatever stimuli might arise in the changing environment of the individual. Attention implied in psychology largely what "vigilance" did in physiology—namely, that condition of the mind (nervous system) in which a selective response to a stimulus could be obtained at its optimum. It was these psychic characters which were impaired in mental disturbances of toxic and infective origin. Hence arose lethargy, defective power of concentration, loss of interest, and the inability to organize reactions according to social standards which characterized the child sufferer from encephalitis lethargica and head injury; possibly the same accounted for the asthenic syndrome described by Dr. Riddoch.

OPTIMAL RHYTHM IN THE MAMMALIAN HEART AND THE ACTION OF THE CARDIAC NERVES.*

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UNDER experimental conditions, with the influence of anaesthetics, etc., the mammalian heart muscle shows two distinct types of behaviour, in which the ventricular contraction force is very differently influenced by changes in the rate of beat, whether such changes owe their origin to local alterations in the normal pacemaker, to artificial or abnormal excitations, or to the influence of the cardiac nerves. In a communication to the International Physiological Congress in 1923, these types were designated I and II. Cats and rabbits were employed, anaesthetized with chloroform, ether, urethane, etc., or decerebrated during anaesthesia with chloroform and ether. Graphic records were made from auricles and ventricles by the Cushny myocardiograph or by an optical form. Intracardiac pressures, etc., were also registered in many experiments.

CHARACTERS OF TYPES.

In Type I, which is the normal, premature or much accelerated beats tend to be of diminished force, while delayed beats, as seen after a compensatory pause or during simple slowing of rhythm, usually tend to be stronger. Within limits, the longer the interval between beats the larger is the ensuing beat. The optimal interval is indefinitely long. In Type II, on the other hand, there is a certain range of interval which is approximately optimal as regards contraction force. Slowing leads to weakening, the degree of which stands in strikingly close relation to variation in the length of the intervals. Acceleration beyond the limits of the optimal rate is attended by reduced

size of beat. The optimal rate varies under different conditions; it may be very much higher than the ordinary heart rate of the animal—in the cat, with its normal 90 or 100 beats a minute, the optimal rate may be 200 to 240—about the maximum rate of the heart after section of the vagi.

Sudden changes between periods of optimal and sub-optimal rhythms are attended by sudden diminution or augmentation of the beats. Similarly, single beats following an optimal or suboptimal interval show immediate and striking differences in size, not depending on changes in blood pressure, but connoting a special metabolic condition of the ventricular muscle in which recovery after a contraction is rapid and is followed by early decline in contraction power, if another excitation does not occur after an interval of such duration as is suitable or optimal in the particular conditions of the muscle at the time. The behaviour of the contraction force is similar in ventricular beats due to excitatory impulses arriving from the auricles in normal fashion through the auriculo-ventricular bundle and in beats provoked by artificial stimulation of any part of the ventricular muscle.

The phenomena in question are related to what has been described as a "supernormal" phase in nerve and cardiac muscle of lower vertebrates under certain conditions. But the enlarged ventricular beats are not really supernormal; their increased size represents a return to or towards the normal from a subnormal size, which had been determined by the presence of a suboptimal rate of succession with intervals long enough to lead to a decline of contractile power below the optimum.

DISTRIBUTION AND CHANGE OF TYPES.

Type II has been seen only in the ventricles, where in a long series of experiments extending over many years it has been found to be about as common as Type I in cats. In rabbits, on the other hand, under similar experimental conditions, Type I was always recognized. The auricles of all the animals examined (cats, rabbits, etc.) always showed Type I. Repeated changes of type were often observed in the course of a single experiment. Type I is frequently altered to Type II after a phase of asphyxia or intravenous injection of adrenaline, alone or after a depressing dose of potassium, etc. Type II is often replaced by Type I after the administration of pilocarpine, acetylcholine, and other drugs. The alterations in size of beat shown by the recording lever are not dependent on altered physical conditions—for example, blood pressure, or filling of heart.

RELATION TO ACTION OF CARDIAC NERVES.

Since slowing may *per se* cause weakening of the ventricular beats in Type II and acceleration may give marked augmentation, the question arises as to how far the effects of stimulation and section of the vagus and sympathetic nerves may be conditioned by simple rate changes in the heart under experimental conditions.

The Vagus.

The records show that pronounced ventricular weakening during vagus stimulation is sometimes capable of being accounted for solely by the associated slowing of rhythm resulting from the action of the nerve upon the pacemaker. During the period of slowed weakened beats a contraction excited at the optimal interval is of full size, in contrast to the greatly weakened preceding and following beats which have come after an unduly long (non-optimal) interval. But, on the other hand, there is frequently evidence of a direct weakening influence also being exercised by the vagus—the reduction in force being specially at the earlier part of the vagus period—out of proportion to the degree of slowing. There is thus a combination of rate effect and direct force-depressing vagus influence.

In Type I the vagus can show marked weakening effects in the ventricles (as well as the auricles). Here, though associated with slowing of rhythm, the weakening is not directly due to the slowing. Simple slowing, from vagus influence on the pacemaker, apart from a direct force-depressing influence of the nerve, usually leads to enlargement of the slowed beats. When weakening is marked it bears no constant relation to the length of intervals

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between the beats. During vagus standstill or slowing and weakening a rhythmical series of artificial excitations calls forth beats showing a progressive increase in size (staircase); this indicates an influence inimical to the force-depressing power of the vagus on the ventricular muscle. The actual effect of the vagus on contraction force depends on an interaction between the influences of rate changes and the direct force-depressing power of the nerve. In opposition to the current view that the vagus has no direct effect on the contraction force of the mammalian ventricles the present investigation affords abundant evidence of strong weakening effects, in exceptional instances more extensive than those seen in the auricles. The weakening action of the vagus on the ventricles differs in certain important respects from what holds good in the auricles, being differently conditioned by rates of beat, etc. In the auricles vagus weakening may occur without any change of rate, and acceleration (by artificial excitations) of slowed and weakened auricles does not produce the augmenting effects seen in the ventricles.

The Cardiac Sympathetic.

As regards sympathetic action it is clear that the acceleration induced may, in Type II, determine marked augmentation in the ventricles. But it is plain that such is not the sole mode of action of the nerve, for the augmentation may be much greater than results from simply bringing the heart rate to the optimum frequency level. And large augmentation may be obtained by sympathetic stimulation while Type I is present in both ventricles and auricles. Hence rate change is only a possible contributory factor in the ventricles in Type II. There is a further specific influence beyond the direct effects of rate changes, in the case of stimulation or section of either the cardiac augmentor or the inhibitory nerves, and operative on both the auricular and the ventricular contraction force.

THE MECHANISM OF VOLUNTARY MUSCULAR FATIGUE.*

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THE present inquiry deals with two forms of fatigue in man: (1) that induced by a series of voluntary contractions of the flexor digitorum sublimis, recorded by a Mosso's ergograph; (2) static contraction of the same muscle maintaining weights at certain levels and registered in the same way. Animal experiments (under anaesthesia) were also performed, the tibialis anticus of the rabbit and cat being used; contraction against an elastic resistance was registered graphically under different conditions. The relations of experimental ischaemia to the incidence and characters of fatigue were examined both in the human subject and in animals.

Fatigue from Serial Voluntary Contractions.

When fatigue results from a series of voluntary contractions the failure of effective muscular response is primarily "central"—that is, it is primarily due to defective outgoing motor impulses from the central nervous system. This is shown by the fact that further muscular response can still be obtained from electrical stimulation of the median nerve or of the muscle directly by single induction shocks or by faradic currents at rates of 40 to 200 per second. But though the fatigue is primarily central it is not always wholly so; there is evidence of marked depression of contractility in the muscle itself, at least when fatigue is induced by a very rapid series (for example, 120 to 160 per minute) of voluntary contractions, especially when the weight raised is considerable—for example,

2 kilos. Here there is an overlapping of central and peripheral changes. On the other hand, when a slow series (40 to 80 per minute) of voluntary contractions is employed to produce fatigue the muscular response to direct electrical stimulation may be practically unimpaired at the point of time when voluntary effort fails to raise the weight; the failure is distinctively central in this case.

The comparative effects of electrical excitation of the nerve trunk and of the muscle directly do not afford evidence of any marked selective influence of fatigue on the field of conjunction of nerve and muscle—the myoneural junction. The power of the contractile response obtained from (a) the nerve trunk, and (b) the muscle directly stimulated shows little difference even in advanced fatigue involving a great diminution of the available muscular energy. For example, in a rabbit's limb with intact circulation there was only a slightly greater response from (b) after about 50,000 contractions (pulling against an elastic resistance) had been executed in a period of four and a half hours, with reduction of the excursions to less than one-tenth of their original size. Such results are opposed to the hypothesis that comparatively early failure of transmission through the junctional region between nerve and muscle plays an important part in the genesis of voluntary fatigue.

Some previous observers have stated that after fatigue has been induced by direct electrical stimulation, voluntary effort can still cause effective contraction. In the present inquiry it has been found that after thorough fatigue has been induced by local stimulation voluntary impulses fail to elicit any marked further contraction.

Fatigue in the Ischaemic Condition.

In the ischaemic arm muscular fatigue from a series of voluntary contractions occurs much more rapidly than in the normal limb—for example, in two to three minutes, as compared with fifteen to twenty minutes. The direct depressant effects of the bloodless condition of the working muscle might be supposed to account for this, but it is found that local excitation (median nerve or body of muscle) still gives a marked, though reduced, contractile response. The fatigue is primarily in the central nervous system in this case also; weakening of the muscle develops as well, though much more slowly than the voluntary failure.

Why should central failure occur much more readily here than in the limb with normal circulation, since the central nervous system is far removed from the ischaemic area and beyond the reach of chemical agents, metabolites, etc., transmitted from the ischaemic limb? It is evidently contingent on afferent nervous impulses from the working muscle, depending on conditions set up in it by repeated strong contractions—conditions (chemical, etc.) naturally accentuated in the bloodless muscle setting up painful afferent impulses much more rapidly than in the normal arm.

Ischaemia *per se* cannot be regarded as the cause, for with quiescent muscle ischaemia up to a duration of fifteen minutes produces no discomfort and has no appreciable influence on the power of voluntary contraction. From the much earlier failure of response to voluntary effort during ischaemia it is evident that local conditions in the working muscle form part of the mechanism of fatigue. But the central nervous system is also involved, since further contractile response is given to local stimulation after voluntary effort has failed. The "central" failure is not simply a primary or direct one affecting some part of the central nervous mechanism concerned in voluntary motor discharge, but is largely a reflex effect of afferent impulses from the working muscle—no doubt protective against excessive prolongation of activity and undue development of fatigue in the muscle.

Thus the conditions of developing fatigue, arising primarily in the working muscle, do not directly induce the depression of contractile power shown in the ergographic records. Their influence is exercised in reflex fashion by afferent impulses concerned in producing the "central" failure which determines the ineffectiveness of voluntary effort (in both normal and ischaemic limbs).