A CONTRIBUTION TO THE PHYSIOLOGY OF SLEEP, BASED UPON PLETHYSMOGRAPHIC EXPERIMENTS.

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PLATE XXXI.

The primary object of these experiments was to determine the variations in volume of the arm as measured by a water plethysmograph during the entire period of normal sleep. The experiments were begun some years ago by Messrs. Bardeen and Nichols, who were at that time students in this laboratory. Their work gave them some very interesting curves, showing the sensitiveness of the vaso-motor centre to sensory stimuli not sufficiently strong to awake the subject experimented on, but they were unable to obtain a satisfactory plethysmographic record of an entire sleep period. This latter point I have endeavored to complete by experiments made upon myself at various times within the last few years. At first a large plethysmograph was used, measuring the changes in volume of nearly the entire arm; but this was afterwards abandoned, owing to the fact that the arrangements used to ensure immobility necessarily kept the arm in full extension, a position that quickly caused painful discomfort at the elbow joint and thus prevented normal sleep. The plethysmograph used in all the experiments here reported was much smaller, measuring the volume changes only in the hand and the lower part of the fore-arm, and allowing comfortable flexion and freedom of movement at the elbow. The apparatus employed was simple in character and can be sufficiently understood from a brief description.

DESCRIPTION OF APPARATUS.

The plethysmograph consisted of a glass cylinder of the usual form, 24 cm. in length and 10½ cm. in diameter, drawn out to a tube at the far end and having two tubulatures. In one of these latter a stopper was inserted carrying a thermometer to measure the temperature of the contained water, and a glass tube which ended within the plethysmograph just below the stopper and gave exit to the air when the plethysmograph was filled with water. The other tubulature, which was at the lower surface of the plethysmograph when this apparatus was arranged for an experiment, was used to fill and empty the instrument. A piece of stiff rubber tubing was connected with the distal end of the plethysmograph. This tubing passed to the recorder and transmitted the water that flowed into or out of the plethysmograph as the arm contracted or expanded. The recorder used was the Bowditch * form. It consisted essentially of a test tube swung by a spiral spring, which was so adjusted as to keep the surface of the water in the test tube always at exactly the same level, the test tube pulling the spiral out as water flowed into it, and the spiral pulling the test tube up as water flowed out. To prevent the rotation of the test tube that arises from the twisting of the spiral, the movements of the spring were transmitted to the test tube by unspun silk fibres passing over a delicate pulley. The large end of the plethysmograph carried a sleeve of band-rubber tubing which fitted snugly the rounded portion of the fore-arm.

To keep the hand immovable within the plethysmograph, a modification of the device used by Shields † was employed. A hinged collar of hard rubber fitted round the thumb between the first and second phalangeal articulations. This was connected by a rigid rod with a similar though larger hinged collar, which fitted loosely the rounded portion of the middle of the fore-arm. This latter ring had a shoulder that pressed against the rim of the plethysmograph when the arm was in position, and thus prevented a thrust of the arm into the plethysmograph. The rubber sleeve covered this collar and was in turn pressed firmly against it by a larger double ring of hard rubber. One portion of this outside collar clasped the rim of the plethysmograph, while the second ring, rigidly connected with the first, fitted snugly on

* Bowditch, *Proceedings of the American Academy*, May 14, 1879.

† Shields, *The Journal of Experimental Medicine*, i, p. 74, 1896.

the band tubing and held it firmly against the inner collar. In this way the pulling of the arm out of the plethysmograph was prevented. A further use of the outside rings, as described by Shields, was to prevent any parting of the rubber sleeve where it extended from the edge of the plethysmograph to the arm. This purpose they accomplished by nipping the sleeve close down to the arm. The plethysmograph was suspended from the ceiling, according to the well-known device of Mosso, so as to allow free swing of the arm. The elbow was, in addition, supported by a sling of thick velvet, which was attached by cord to the chain swinging the plethysmograph. This cord was adjustable, so that when the subject lay upon the bed ready for an experiment, a position of the elbow could be found that was easy and comfortable. With the plethysmograph arranged in this way, the arm could swing freely from the shoulder and elbow without altering the position of the hand in the plethysmograph or changing the volume of water. Movements of the fingers gave, of course, pressure waves which affected the test-tube recorder, but such movements were only temporary and caused no permanent alteration in volume.

In preparing for an experiment, the hand and fore-arm were first thoroughly greased with vaseline to prevent the imbibition of water by the skin during the long immersion. The hand was then placed in the plethysmograph and the rubber sleeve and the holders were properly adjusted. Through the lower tubulature of the glass cylinder the apparatus and the tube passing to the recorder were filled with water warmed to 34° C., care being taken to force all air bubbles out of the tubing. It was found that the arm would keep the water in the plethysmograph very nearly constantly at 34° C. during a night's experiment. If the temperature varied slightly, that is, from 0.5 to 1° C., the latter being about the maximum variation observed, the alteration in volume of the water thereby produced was found to be so small as not to influence perceptibly the quantitative value of the plethysmographic curve. The pen that marked the movements of the test-tube recorder was made to write upon the blackened surface of the drum of a kymographion which was moved slowly by clock-work, making one entire revolution in about twelve hours. In the same vertical line with the test-tube pen there was arranged an electric signal connected with a clock and marking intervals of fifteen seconds. After the apparatus had been filled with water, the pressure of water upon the arm was adjusted by moving the test-tube recorder so as to place the surface of the liquid in it at or near the level of the middle of the glass cylinder, the exact level varying slightly with the position of the arm in the plethysmograph. The result aimed at was to bring the middle of the arm as it lay in the plethysmograph to zero pressure. Since it is obviously impossible, in a water plethysmograph, to have the entire arm free from positive or negative pressure, it would seem to be most desirable, theoretically, to have the zero pressure as nearly as possible at the middle of the portion of the arm used. Under these circumstances the positive pressure of an inch or two of water upon the under portion of the arm is counteracted by a similar negative pressure upon the upper portion. As Shields has shown in his paper, this point is one of considerable practical importance. If the entire arm is under slight positive pressure, a distinct diminution in volume results, apparently from the effect of this pressure on the superficial veins, while a negative pressure has the opposite effect. Practically, it was found that the best results were obtained when the point of no pressure was at the middle of the portion of the arm immersed in the water.

This whole difficulty can be obviated by using an air instead of a water plethysmograph. In an air plethysmograph the changes in volume of the arm cause a flow of air out of or into the cylinder, and the quantity of air displaced can be measured conveniently by a delicate counterbalanced spirometer. An apparatus of this kind was used in several experiments, but was afterwards abandoned, since, naturally, its accuracy depends very largely upon keeping the temperature of the air constant, and in all-night experiments this was not practicable. Even in shorter experiments the records are vitiated from a quantitative standpoint by the fact that a congestion of the arm causes a greater radiation of heat from the skin and *vice versâ*.

When the various details described above had been properly arranged, the lights were lowered and the subject of the experiment, who lay upon a comfortable bed, attempted to go to sleep. During the entire experiment a watcher, who sat at a little distance, made copious notes of the movements of the sleeper and their effect upon the curve, and of any disturbing noises, from cabs in the street and the like, that seemed to affect in any way the record that was being taken.

I desire in this connection to express my great thanks to Dr. G. T. Kemp and Dr. Reid Hunt, who most kindly assumed this disagreeable task, and by their friendly interest in the work made possible what measure of success was eventually attained.

It was arranged between the sleeper and the watcher that if the former awoke at any time during the night he was to utter the word " awake," so that the fact might be indicated on the record. In some cases this indication was given satisfactorily, the sleeper remaining awake for a longer or shorter time in a drowsy condition, but finally falling asleep again, usually within a few minutes. In other cases, however, the return of consciousness on the part of the sleeper was not sufficiently complete to enable him to articulate the word " awake " satisfactorily. In some instances of this kind the sleeper subsequently remembered distinctly being awake and thought that he had given the signal agreed upon; but the notes of the watcher recorded only that the sleeper muttered unintelligibly. At other times the sleeper was conscious of being awake, but his mental condition was such that he considered it unnecessary to state the fact, or indeed felt an irritable objection to making an exertion to speak. This perverse condition was remembered afterward with regret upon full awaking, but at the time there seemed to be lacking on the part of the sleeper a full comprehension of his interest in the experiment. An interesting and rather unexpected fact with regard to these experiments was that in none of them did the sleeper have any conscious recollection of dreaming. The unusual and somewhat uncomfortable conditions of the experiments had led him to suppose that disagreeable dreams would trouble his slumbers.

By the method thus briefly described some twenty sleeping experiments were made. Of these not more than four or five gave entirely satisfactory results, although many of the partially successful experiments gave interesting curves that confirmed some of the general conclusions drawn from the better experiments. The causes of failure were numerous, and some of them may be referred to here in a few words. One great difficulty at first was my inability to go to sleep under the unusual conditions of the experiment. If it had been possible to make a continuous series of experiments, it is probable that I would have become accustomed to the surroundings and this difficulty would have vanished. Owing to other duties, which need not be specified, a continuous series was impossible, and the experiments were made at intervals over a period of two years. In order to sleep easily under the unusual conditions I found it necessary to make myself very sleepy. This end was attained most satisfactorily by sitting up the greater part of the night previous to an experiment and taking a considerable, but not an excessive amount of out-door exercise on the day of the experiment. This procedure was usually effective in enabling me to fall asleep within ten or fifteen minutes after the beginning of an experiment. A second serious cause of trouble was the adjustment of the pressure of the rubber sleeve upon the arm. The sleeve must be sufficiently tight to prevent leakage of water, and yet must not compress the skin so as to lead to a passive congestion of the parts within the plethysmograph. Numerous experiments were spoiled for quantitative purposes by an excessive pressure of the rubber sleeve, although they gave some results that were of value. To obviate this difficulty, the arm, where the sleeve pressed upon it, was coated thickly with vaseline, and the sleeve itself was selected of such a size as just to prevent a leakage. This size was determined by actual trial. The test of success in this matter, which was regarded as the best under the circumstances, was the fact that at the end of the experiment, upon awaking from sleep, the arm returned quite, or approximately, to the size it had shown at the beginning of sleep. A third difficulty, of much less importance, lay in the fact that the experiments were conducted in a laboratory adjacent to a public street, the noise of cable cars and passing cabs probably being responsible for some of the smaller changes in the curves.

DESCRIPTION OF THE CURVES OBTAINED, SHOWING THE CHANGES IN VOLUME OF THE ARM DURING SLEEP.

Examples of these curves are given in Figures 1 and 2, Plate XXXI, which represent two of the successful experiments. The details concerning these experiments are given in the descriptive legends accompanying the figures, and only the general features common to these and other curves need be dwelt upon here. It will be seen that from the beginning of the experiment, which coincides with the moment the sleeper closed his eyes and attempted to go to sleep, the curve begins to fall, that is, the portions of the arm in the plethysmograph undergo dilatation. Somewhere upon the descent of the curve the condition of sleep comes on. The exact time it was of course impossible to mark, but in these two experiments, and in most of the others, it may be asserted safely that the subject was asleep within fifteen minutes at the most. After sleep appears, the curve continues to sink with fair regularity, reaching its lowest point at one to one and a half hours after the beginning of the experiment, at which time the dilatation of the arm attains practically its maximum extent. For the next hour or two the curve remains at this low level, with the exception of certain periodic and incidental alterations that will be referred to later. After this period the curve usually begins to show a steady rise, which, for the first hour or longer, is quite gradual, but during the last half-hour or so preceding the final conscious awaking becomes much more rapid, so that at the time of awaking the volume of the arm is nearly or in some cases quite the same as at the moment of going to sleep. The time intervals specified here apply to a sleep lasting only from four to four and a half hours. If the period of sleep had been longer there would doubtless have been a longer interval after the maximum fall of the curve had been reached, before the rise began, and probably a longer continuance of the slow constriction. In the two curves given, the moment of final awaking is indicated by the mark ×.

In addition to this general course of the curve, it will be noticed that numerous secondary variations are exhibited. These minor variations fall into two classes: sharp oscillations, lasting a comparatively brief time and very variable in extent, and longer, nearly periodic waves. The latter were present quite constantly in all the curves recorded. The waves had, roughly speaking, an hourly period, the extreme limits of duration varying perhaps between half an hour and an hour and a half. They constitute one of the most characteristic features of the plethysmographic curve. The sharper and briefer oscillations were found in the great majority of cases to be connected either with external stimuli, such as noises, or in some experiments, electrical stimulation; or with movements of the sleeping subject, such as sighs or movements of the arms, legs or head. An explanation of these two classes of variations in the curve will be suggested when the cause of the changes in volume of the arm is discussed. It should be added that the act of final, spontaneous awaking was always accompanied by a steep rise in the curve. The exact alteration in the volume of the arm varied greatly in the different experiments, although the portion of the arm measured was, in all cases, substantially the same. The precise amount of the volume changes was easily determined by calibrating the test-tube recorder. In the two curves reproduced in Figs. 1 and 2, the maximum dilatation was 18.5 cc. and 15.91 cc. respectively. In other experiments in which the conditions were equally favorable the dilatation was much less pronounced, being as small as 8 or 9 cc., while in two of the earlier experiments in which the conditions were not so good the maximum dilatation was 4½ and 5½ cc. respectively. Among the numerous experiments which were regarded as unsuccessful great variations were noticed. When the rubber sleeve pressed too tightly upon the arm or when the arm was under a negative pressure a steady dilatation ensued, owing apparently to a passive congestion of the arm. The dilatation in such cases was excessive and was not prevented by awaking, although before awaking there was a noticeable retardation of the dilatation, while at the moment of awaking the usual sudden constriction occurred, quickly followed, however, by a continuation of the slow dilatation.

EXPLANATION OF THE CHANGES IN VOLUME.

Mosso's* well-known plethysmographic experiments have shown conclusively that there is an enlargement of the limbs during sleep,

* Mosso, Ueber den Kreislauf des Blutes im menschlichen Gehirn, 1881; Die Temperatur des Gehirns, 1894.

an enlargement which he attributes to a vascular dilatation. He has also been able to show, from numerous very interesting observations upon individuals with defects in the skull wall, that there is, in general, a coincident diminution in the volume of the brain during sleep, and that upon awaking the volume of the brain increases, while the volume of the limb in the plethysmograph diminishes. So also in mental activity, such as takes place in solving problems in arithmetic, Mosso has shown that the variations in volume of the arm and the brain stand in reciprocal relationship to each other, the volume of the arm decreasing while that of the brain increases. So far as the effect of mental activity upon the volume of the limbs is concerned, this observation of Mosso's has been abundantly confirmed by others. In this laboratory we have obtained numerous beautiful examples of this effect in experiments made by Messrs. Bardeen and Nichols, and by Dr. Shields, the mental activity being aroused by sums in mental arithmetic, unexpected examinations in the case of students, or by discussions or arguments upon questions that interested the subject of experimentation. In his later works, Mosso is inclined to deny that there is an exact reciprocal relationship between the volume of the limbs and the volume of the brain, since he has made observations which convince him that the blood-vessels of the brain possess vasomotor nerves that are capable of altering independently the amount of blood flowing through this organ.

Experimental work on the lower animals, however, tends strongly to show that a definite relationship does exist between the circulation in the brain and general arterial pressure. The experiments of Gaertner and Wagner,* Roy and Sherrington,† Bayliss and Hill,‡ Reiner and Schnitzler,§ and others agree in showing by different methods that an increased flow of blood through the brain follows upon every rise of general arterial pressure and *vice versâ*. More than this, the results of recent careful work upon the brain circulation (see,

* Gaertner and Wagner, *Wiener med. Wochenschrift*, 1887.

† Roy and Sherrington, *Journal of Physiology*, xi, p. 85, 1890.

‡ Bayliss and Hill, *Journal of Physiology*, xviii, p. 334, 1895.

§ Reiner and Schnitzler, *Archiv für exp. Pathol. u. Pharmakol.*, xxxviii, p. 249, 1897.

especially, Bayliss and Hill) go to show that the brain vessels possess no vaso-motor fibres, and that the volume of circulation through them is regulated passively by variations in arterial pressure in the remainder of the body. A vaso-constriction of parts of the body outside the brain sufficient to cause a rise of general arterial pressure tends to drive a greater quantity of blood under higher pressure through the brain, while a local or general vaso-dilatation of the blood-vessels sufficient to cause a fall in general arterial pressure causes a lessened flow through the brain. To this means of regulating the flow of blood through the brain we must add the effect of the accelerator and inhibitory nerves upon the heart beat. Other conditions remaining the same, an augmented heart beat must increase the blood flow through the brain as well as through other parts of the circulation.

The volume changes described in the present experiments must be interpreted as meaning a vaso-dilatation in the arm vessels, and indeed from what we know of the vaso-motor supply of the muscles and skin respectively, it is altogether probable that the dilatation is due mainly to a relaxation of tone in the skin vessels.* There is every reason to believe that a similar dilatation occurs over the cutaneous surface generally. This belief is borne out by the well-known fact that the skin is flushed and of considerably higher temperature during sleep, and is indicated also by the fact that in Mosso's† plethysmographic experiments upon the foot this limb was found to vary under the influence of mental activity in a way similar to that described for the arm. The amount of dilatation of the hand and the part of the fore-arm used in my experiments varied, in round numbers, between 8 and 18 cc. If

*The substance of this paper was communicated at a meeting of the American Physiological Society, December, 1896. At that time Dr. Meltzer suggested that the dilatation might be due in part to a relaxation in the tonicity of the skeletal muscles during sleep. This possibility must be admitted, but it is not definitely known how variations in tonicity in the striated muscles affect the blood capacity, and in any case it is not probable that this factor could explain the increase in volume obtained, owing to the small muscular mass in the parts used, namely, the hand and the lower portion of the forearm.

† Mosso, Die Temperatur des Gehirns. Leipzig, 1894.

the dilatation in other parts of the skin is proportional in amount, it is probable that during sleep a very considerable fall of general arterial pressure takes place, and this conclusion is verified by the direct experiments made by Tarchanoff* on sleeping dogs. Tarchanoff observed that in young dogs in which sleep occurred while the animal's blood pressure was being recorded, there was a fall of general arterial pressure during sleep amounting to from 20 to 50 mm. of mercury, the pressure returning to normal when the animal awoke.

Taking these facts together, it seems highly probable that the plethysmographic curves described in this paper may be interpreted to mean, in general, that during sleep there is a diminished peripheral resistance in the skin area, and therefore a lower arterial pressure and a smaller blood flow through the brain. Or, assuming that the volume of the brain circulation stands in reciprocal relationship to the volume of the arm, the changes in the amount of blood circulating through the brain during sleep may be stated as follows: At the commencement of the period preparatory to sleep the blood flow through the brain begins to diminish in quantity, owing to the fall in arterial pressure, and for a period of an hour or more after sleep has appeared the blood flow grows less and less, following the continued diminution in arterial pressure. After reaching its minimum, the volume of the brain circulation remains practically constant, with the exception of the temporary variations which have been referred to previously, for one or two hours, or possibly longer, if the period of sleep lasts for a greater time than was obtained in these experiments. The blood flow through the brain begins then to increase gradually, following the rise in blood pressure produced by the slow constriction of the skin vessels, and this increase becomes much more rapid for the short period of one-half to three-quarters of an hour preceding spontaneous awaking. At the time of awaking, therefore, the volume of the blood flowing through the brain is approximately the same as at the time sleep appeared.

One may ask whether the dilatation of the blood-vessels during sleep affects the visceral organs as well as the superficies of the body.

* Tarchanoff, *Archives ital. de Biologie*, xxi, p. 318, 1894.

The question is a difficult one to answer satisfactorily, but it seems probable from the incomplete facts in our possession that the internal organs do not share in this dilatation; it is possible, on the contrary, that the volume of blood circulating through the internal organs is diminished rather than increased in quantity. Mosso, in his interesting experiments on the temperature of the brain, has shown that the temperature of the rectum falls slowly during sleep, following a curve nearly parallel to that of the brain. The temperature curves of the brain and the rectum, in fact, show a striking similarity to each other in their general features, and also to the curve of vascular dilatation of the arm during sleep obtained in my experiments, the minimum temperature agreeing closely in time with the maximum dilatation of the superficial vessels. It is, perhaps, permissible to suggest that the general relaxation of the skin vessels, with the consequent lowering of blood pressure, diverts blood not only from the brain, but also from the rectum, and thus causes the gradual fall of temperature. It is stated also by Roemer* that the temperature of the skin of the hand remains always during the day below the average and during the night above the average, while in the rectum the case is just the reverse. If the other parts of the alimentary canal behave similarly to the rectum in losing temperature during sleep, it would seem probable that less blood rather than more blood circulates through them during sleep. Upon awaking his subjects Mosso obtained a gradual and parallel rise of temperature in the rectum and in the brain, just as in awaking a subject with his arm in a plethysmograph there is a constriction of the vessels in the arm. As further evidence in the same direction, it may be recalled that the secretions and movements of the alimentary canal and the secretions of the kidney and the liver are said to be diminished during sleep, and these facts point to a lessened blood supply rather than to an increased blood supply during this period. Moreover, from the data that I have obtained of the actual increase in volume of the arm during sleep, and from the figures given by Mosso and others of the amount of constriction

* Roemer, quoted from Hermann's Handbuch der Physiologie, Bd. iv, ii, p. 385.

of the arm during mental activity, it is evident that if similar figures hold for the entire cutaneous surface, the variations in skin circulation under these conditions are far too great to justify the supposition that the large increase or decrease in blood capacity of the skin is compensated by changes in the volume of blood in the brain alone. Our best evidence, in fact, goes to show that the actual volume of blood in the brain can undergo only small variations at most, and the large changes in the amount of blood in the limbs during sleep or mental activity must be compensated by opposite variations in the volume of the circulation elsewhere. It seems possible, therefore, that simultaneously with the dilatation of the limbs during sleep there is a lessened volume of blood in the viscera, but experimental evidence is requisite before positive statements can be made on this point.

THE MINOR VARIATIONS IN THE PLETHYSMOGRAPHIC CURVE.

The slow, wave-like variations in the curve that have been spoken of on page 320 are well illustrated in the two curves printed as Figs. 1 and 2, Plate XXXI. These long oscillations, as has been said, were found in all my records and form a characteristic feature of the sleep curve. I do not know that this phenomenon has been noticed before. Mosso* speaks of spontaneous changes in the volume of the arm that do not depend upon external stimuli or respiratory movements, but these changes, if I understand his descriptions correctly, are of much briefer duration than those now under consideration. It can scarcely be doubted that these slow, nearly periodic constrictions and relaxations of the volume of the arm are due to a slowly developing vaso-constriction of the vessels in the arm followed by a gradual dilatation. The very gradual development of the waves, lasting in most cases for about one hour, makes it improbable that they are owing to the action of external stimuli or to internal stimuli, such as psychical processes in the cerebrum. While it is not possible to give any experimental proof of their causation, the general character of the curves suggests at once that they are caused by rhythmic changes in the

* Mosso, Ueber den Kreislauf des Blutes im menschlichen Gehirn, p. 95.

vaso-motor centre, and indeed, if the assumptions made as to the sleep curve in general are correct, to a rhythmic increase and relaxation of tone in that part of the vaso-constrictor centre controlling the vessels of the skin. The ultimate cause of this variation does not appear upon the surface, but rhythmic changes of this sort seem to be characteristic of the vaso-motor centre, as is seen, for instance, in the well-known Traube-Hering waves. In fact, the variations which we are discussing here resemble closely the Traube-Hering waves in their general character, with the exception that they are of much longer duration.

The shorter, more numerous and more irregular oscillations of the sleep curve are perhaps more easily explained. These changes, as may be seen from the records published, are very variable in extent. Many of them were clearly traceable to external stimuli, such as noises or, in one series, to electrical stimulation of the skin. Some of them were not, so far as could be determined, connected with any obvious cause; they were apparently spontaneous and possibly, as Mosso suggests, in what I consider similar cases, were owing to psychical processes of an unconscious or, at least, of an unremembered character. But most of the changes in question were undoubtedly connected with deep respirations, as in sighing, or with movements of other parts of the body, such as the head, feet or other arm. It may be asserted safely, I believe, that these movements did not affect the plethysmographic record by causing actual movements of the arm into and out of the glass cylinder, nor were the changes in question produced by simultaneous movements of the parts of the arm within the apparatus. In the first place, the arm was so fastened in the swinging and freely movable plethysmograph that movements into and out of the cylinder were practically prevented; and, secondly, if a retraction or thrust of the fore-arm had been possible to a slight extent, the character of the change in the plethysmographic record would have been entirely different. The same remark holds true for movements of the fingers within the plethysmograph. In either case the effect upon the plethysmograph curves would be sharp and sudden. Movements of the fingers, for instance, would cause the pen of the recording test tube to move rapidly up and down, producing upon the slowly moving drum, which required twelve hours for a complete revolution, only a sharp up-and-down stroke. This effect was not infrequently observed during the course of an experiment, and an example may be seen in the curve shown in Fig. 1, Plate XXXI.

The changes which we are describing were, on the contrary, characterized by a fairly rapid rise of the curve, that is, a constriction of the arm, which was followed by a relatively gradual return to the original level. Indeed, even the comparatively rapid rise when observed with the eye was nothing like so sharp as that caused by movements of parts within the plethysmograph. The pen mounted slowly to its maximum and dropped back much more slowly. In fact, the waves in the record made by movements of muscles in other parts of the body resembled in every respect those caused by electrical or sound stimuli. These latter are unquestionably vaso-motor changes, and we must suppose that the waves produced by muscular movements are also due to reactions upon the vaso-motor centre. The physiological mechanism by means of which the movements of the foot, for example, may cause a vascular constriction in the skin of the fore-arm and hand is not easily understood. It is possible, of course, that the effect may be owing to a sensory reflex of a pressor character, originating from an irritation of sensory fibres in the part moved, but this explanation does not seem probable, particularly as it has been shown that stimulation of muscular nerves produces usually a depressor effect, that is, a vascular dilatation.* It seems possible to the author that discharges from the motor cortex, like other forms of cerebral activity, affect directly the vaso-motor centre and bring about a constriction that is more or less marked, according to the condition of the vaso-motor centre, being especially pronounced, perhaps, during sleep, when a part of the vaso-motor centre is in a condition of relaxed tone. This suggestion is supported, to some extent, by the experiments of Stricker† and of Danilewský‡ upon the effect of stimulating

* See Hunt, *Journal of Physiology*, xviii, p. 381, 1895.

† Stricker, quoted from Hermann and Schwalbe's *Jahresberichte*, xv, p. 44, 1886.

‡ Danilewsky, Pflüger's *Archiv fur die gesammte Physiologie*, xi, p. 136.

the motor area in dogs. According to these observers, stimulation of the cortex, in certain parts at least of the motor areas, is accompanied by a rise of blood pressure. It may be interesting to add that in many of the sleep experiments the oscillations of the curve became more pronounced toward the end of the sleep, particularly during the half-hour or so preceding awaking, when the constrictor centre was rapidly regaining its normal tone.

RELATION OF THE PLETHYSMOGRAPHIC CURVE OF SLEEP TO THE CURVES OF INTENSITY OF SLEEP.

The intensity of sleep in the adult during normal slumber has been measured by Kohlschütter,* by Mönninghoff and Piesbergen,† and by Michelson.‡ The method used was substantially the same in all of these investigations; that is, the depth of unconsciousness was measured in terms of the intensity or energy of the sound necessary to awake the sleeper. In Kohlschütter's curve it appears that immediately upon going to sleep the intensity of unconsciousness increased rapidly to a maximum, which was reached at the end of the first hour. The curve then fell very rapidly during the next half-hour, and more gradually in the succeeding hour, so that two and a half hours after the beginning of sleep the curve was nearly at the base line, or, in other words, only slight stimuli were necessary to awake the sleeper. From this point to about the eighth hour the arm gradually approached the base line, and during this entire period the depth of unconsciousness was but slightly below the threshold. The curve obtained by Mönninghoff and Piesbergen is, in its general features, similar to that obtained by Kohlschütter, with the exception that the maximum intensity was reached one and three-quarters of an hour after the beginning of sleep, and a second much lower rise of intensity was noticed between the fifth and sixth hours. In detail their curve shows that during the first hour the intensity was so slight as to be scarcely measurable by

* Kohlschütter, *Zeit. f. rat. Med. 3te Reihe*, xvii, p. 209, 1863. Also xxxiv, p. 42, 1869.

† Mönninghoff and Piesbergen, *Zeitschrift für Biologie*, xix, p. 114, 1883.

‡ Michelson, quoted from Wundt's Physiologische Psychologie, 4th ed. 1893.

their method, but that beginning at an hour and a quarter after sleep the intensity rose very rapidly, reached its maximum at an hour and three-quarters, and then sank as rapidly during the next half-hour. From two and a quarter to four and a quarter hours the curve fell more gradually, then showed a slight rise, reaching its maximum at five and a half hours, and subsequently dropped slowly to the base line.

The plethysmographic curve described in this paper shows no resemblance to either of these curves except during the first period. Upon the interpretation of the plethysmographic curve given by me, it may be said that during the period of rapidly increasing intensity of sleep, especially as illustrated in the curve by Kohlschütter, there is a corresponding diminution in the volume of blood flow through the brain, and the maximum of intensity of sleep corresponds apparently with the minimum flow of blood through the brain. But from this point onward the intensity curve and the plethysmographic curve show no resemblance to each other. While the irritability of the brain cortex rapidly approaches the normal, and after the second to the third hour lies almost at the threshold, the anæmic condition of the brain remains practically as it was during the period of deepest sleep. During this period the circulatory conditions in the brain are apparently not connected with the depth of unconsciousness of the sleeper. Some interesting conclusions that may be drawn from this comparison of the two curves will be referred to in the subsequent section discussing the causation of sleep.

It seemed to the writer that in view of the discrepancy between the two curves and the fact that the curves published by Kohlschütter and by Mönninghoff and Piesbergen represent results obtained from a very limited number of individuals, it was advisable to test his own curve of intensity to ascertain whether it conformed to the types described by the authors named. Experiments were accordingly made in this direction, the results of which, although not sufficiently complete for the publication of details, showed clearly that in the writer the normal intensity of sleep follows in general the curve described by Kohlschütter, in that the maximum is reached within the first hour or so after the beginning of sleep, and that from this point the curve drops at first rapidly and then more slowly to the base line, although it does not approach so nearly to the base line in the second to the third hour and subsequently as in Kohlschütter's curves. It would seem, therefore, that the want of parallelism between the intensity and the plethysmographic curves mentioned above is probably a normal occurrence. It may be well to add that in my experiments upon the intensity of sleep I adopted a new method. The intensity of sleep was measured by the strength of the current from an induction coil necessary to awake the sleeper. The amount of the induced current was measured directly in scale deflections of a new dynamometer devised by Professor Rowland of this University. A description of this new and useful piece of apparatus will be published shortly. The stimulating electrodes were placed upon the forehead and were of a special pattern, being so constructed as to remain moistened with glycerine during the entire period. It is hoped in the near future to carry out a complete series of determinations with this apparatus, using a number of individuals, and when this is done, a more careful description of the method will be published. The matter is referred to here only incidentally for the purpose of showing that the author's sleep curve belongs apparently to the general type described by Kohlschütter, however much it may be found to vary in details.

THE CAUSE OF SLEEP.

Numerous theories of sleep have been proposed in modern as in ancient times. Among recent theories, those published by Cajal* and Duval† have, at least, the advantage of novelty. According to the former, the neuroglia cells in the molecular layer of the cortex expand between the communicating processes of the cell units and act as an insulating medium to interrupt physiological conductivity and bring on the unconsciousness of sleep. Duval advances the simpler theory that conductivity is broken by the withdrawal of the cell processes from each other by amœbiform contraction, conductivity being

* Ramon y Cajal, *Archiv f. Anat. (u. Physiol.)*, 1895, p. 375.
† Duval, *Comptes rendus de la soc. de Biol.*, Feb., 1895.

re-established upon awaking, or because of sensory stimulation, by the processes again elongating and intermingling. Theories of this kind are merely immediate speculative applications of anatomical facts. They can scarcely command serious attention unless supported by observations that indicate the possibility of such movements occurring. One may ask, for instance, whether conductivity is interrupted in the retina, the cord and the peripheral ganglia in the same way.

The general conception underlying most of the recent physiological theories of sleep seems to be that it is owing primarily to a fatigue of the elements of the central nervous system, and efforts have been directed toward explaining the immediate cause of this fatigue and the means by which the irritable condition of the nerve tissue is restored. Obersteiner,* for example, supposed that in the brain, as in the muscular tissue, functional activity is accompanied by the production of acid, which is not removed by the blood as rapidly as it is formed, and therefore accumulates and finally brings on fatigue, that is, lack of irritability, which is apparent to us as the condition of sleepiness. If the amount of acid is sufficient, sleep may occur involuntarily. Preyer† advocates a similar theory and specifies the lactic acid produced in muscular and nervous activity as the immediate cause of the occurrence of sleepiness, and its removal as the underlying fact of the recuperative effects of sleep. Pflüger‡ seeks the cause of fatigue in a different factor, namely, in the consumption of the supply of intra-molecular O stored in the nerve substance. During waking hours continuous functional activity is accompanied by katabolisms in which the O appears in the form of CO_2. The steady consumption of the stored O is not compensated by an equivalent absorption of O, and as a consequence the irritability of the nerve tissue runs down. Sleepiness is the result, and upon the withdrawal of external stimuli this passes normally into sleep, that is, the katabolisms in the brain cells cease, or, at any rate, sink below the level necessary to arouse consciousness. The very long rest which

* Obersteiner, *Allgemeine Zeitsch. für Psychiatrie*, xxix, p. 224, 1872–3.

† Preyer, *Centralblatt f. d. med. Wiss.*, xiii, p. 577, 1875.

‡ Pflüger, *Archiv f. die gesammt. Physiol.*, x, p. 468, 1875.

ensues, the period of normal sleep, would seem to be longer than is necessary to restore the adequate amount of combined oxygen, and Pflüger accounts for this delay upon the assumption of an inertia in the molecules of the nerve substance that must be overcome to start again the decompositions of functional activity; but once the molecules are set into vibration, each molecular explosion acts as a favoring condition to successive explosions.

None of these theories have been accepted as entirely adequate. They are difficult of experimental verification, and, so far as the attempt has been made, the results are not favorable to the theories. Preyer attempted to show that injection or ingestion of lactates produces the phenomena of sleepiness, but was obliged to admit that the results are variable with different individuals. The same experiment in the hands of others has given such uncertain results as to make it probable that sleep cannot be explained solely by an accumulation of lactic acid or lactates in the central nervous system. With regard to Pflüger's theory, Hill and Nabarro* have shown that the gaseous exchange in the brain is slight compared with that in the muscular tissue, and while this fact does not disprove the view that in the brain the oxygen consumption outruns the oxygen absorption, it at least tends to throw some doubt upon such an assumption. The exchange is not so great, normally, as to seriously alter the oxygen capacity of the blood streaming through the brain.

In normal sleep, moreover, we have to consider a phenomenon that appears with more or less suddenness and involves more or less completely and nearly simultaneously all the parts of the organ of consciousness quite independently of the degree to which these parts have been worked during the waking period. To take a concrete example, there can be no doubt that an individual who had passed an entire day without excitation of the centres of taste or smell might enjoy a sound sleep in which these centres would share. Normally, these centres are in activity only for short periods, yet during sleep they participate in the general loss of irritability of the cortex, perhaps to an even greater extent than the rest of the cortex, as it is an

* Hill and Nabarro, *Journal of Physiology*, xviii, p. 218, 1895.

interesting fact that dreams involving sensations of taste or smell are very unusual. It can hardly be supposed that these centres are fatigued from local production of acid or consumption of oxygen, and to account for their sleep upon the theories under discussion it would be necessary to assume that they had been robbed of their oxygen to supply other parts, or that the acid formed in other tissues had been transported to them. Neither of these theories seems to explain satisfactorily the common and nearly simultaneous loss of consciousness in all parts of the cortex.

A second group of theories has attempted to prove a relationship between the supply of blood to the brain and sleep. There has been an increasing amount of evidence within recent years to show that there is a lessened flow of blood through the brain during sleep. This has been shown by direct observations upon the exposed brain (Durham) or upon animals with a glass window in the skull (Donders, Durham), by the observations of Mosso and others, which have shown a diminution in volume of the brain during sleep in patients with defects in the skull, by observations upon the retinal circulation during sleep; and lastly, it follows apparently as a logical conclusion from recent experimental work on lower animals and plethysmographic observations on man, the tendency of which has been to show that a fall of blood pressure occurs during sleep. This fact, indeed, seems to be safely established. Whether there is really a lessened volume of blood in the brain or only a lessened blood flow need not be discussed here. The main point is, that the volume of blood circulating through the brain in a unit of time is lessened; there is a condition of cerebral anæmia. By some authors the anæmia has been regarded as a causal factor in the production of sleep, but in most cases it has been explained as a result of sleep, the cessation of functional activity being followed by a diminished blood supply.

The explanation which the author has been led to give to the plethysmographic curves, described in this paper, has suggested to him a theory of sleep that, in some of its features at least, is new. This theory may be stated briefly as follows: The immediate cause of normal sleep lies in a vascular dilatation (of the skin) that causes a fall of blood pressure in the arteries at the base of the brain, and thereby produces an anæmic condition in the cortex cerebri. This condition of anæmia, in connection with the withdrawal of external stimuli, causes a depression of the psychical processes in the brain cells below the threshold of consciousness. The fall of blood pressure is due, in the first place, to a relaxation of tone in that portion of the vaso-motor centre controlling the skin vessels. The immediate cause of normal awaking, on the contrary, is found in the augmented flow of blood to the brain that follows upon the gradual constriction of the skin vessels as the vaso-motor centre recovers its tone. The periodicity of sleep is therefore directly connected with a rhythmic loss and resumption of tone in the vaso-motor centre. Throughout the waking period the vaso-motor centre is under continual stimulation, and is therefore in continual activity. Sensory impulses, especially from the skin and the cutaneous sense organs, are at all times falling into the central nervous system in greater or less quantities, and through a reflex pressor action on the vaso-motor centre these sensory impulses keep up a constant activity of the centre, particularly of that part controlling the skin vessels, as is indicated by the striking effect of such stimuli upon the volume of a limb when measured plethysmographically. Mental activity in all its forms is accompanied by a similar pressor effect upon the vaso-motor centre, which is likewise known to affect the skin circulation. During the waking hours, therefore, the vaso-motor centre is in uninterrupted activity, and the result must be the production of a condition of fatigue in this centre proportionate to the amount of stimulation. If the fatigue is sufficiently pronounced, the centre will relax and sleep ensue in spite of even strong sensory or mental stimuli. If the fatigue is less marked, as is normally the case at the end of a waking period, adequate relaxation takes place only after the withdrawal of sensory and mental stimuli, and our voluntary preparations for sleep consist essentially in devices to minimize these stimuli. That the vaso-motor centre is susceptible to fatigue, the author has shown to his own satisfaction by experiments consisting in the continuous stimulation of sensory nerves (sciatic), in curarized and narcotized animals. The great rise of blood pressure that results from such stimulation soon passes off more or less completely, and that this result is owing to fatigue of the centre rather than to fatigue of the muscles in the walls of the blood-vessels is indicated by the fact that the blood-vessels in the ear of a rabbit may be kept in a condition of strong contraction for a long period (over an hour at least) by constant tetanic stimulation of the peripheral end of the cervical sympathetic nerve.

In addition to the effect of the cerebral anæmia, an accessory favoring condition to the production of sleep may be found in a certain degree of fatigue of the parts of the brain mediating psychical processes. Portions of the sensory and the association areas of the cortex, using Flechsig's nomenclature, must be active during the greater part of the waking period, and probably, therefore, lose their irritability to a greater or less extent. Upon the withdrawal of the normal blood supply, their irritability will tend to fall more quickly below the threshold of consciousness in consequence of this fatigue. We might, therefore, say that three factors combine to produce normal sleep: 1. A diminution of irritability, caused by fatigue, of large portions of the cortical area. 2. Voluntary withdrawal of sensory and mental stimuli involved in the preparations for sleep. 3. A diminished blood supply to the brain, owing to a relaxation of tone in the vasomotor centre and the fall of general arterial pressure thereby produced. The last factor is the immediate cause of sleep and explains its comparatively sudden and nearly simultaneous occurrence over the entire cortex. The relative importance of these three factors will vary, naturally, with attending circumstances. It would seem that the third condition must always precede sleep, and that, under normal relations, it is the determining element in the production of the unconsciousness of sleep. A combination of the 2nd and 3rd factors is probably adequate to cause sleep without preceding fatigue of the central nervous system. This probability is indicated by many facts in ordinary experience, such, for example, as the sleepiness felt when quietly resting after a heavy meal—the fall of blood pressure in this case following upon a dilatation in the splanchnic area. Perhaps a better instance is the often-quoted case of Strümpell's. In this case a boy whose only avenues of sensory communication with the outside world were the right eye and the left ear could be sent to sleep at any time by bandaging the eye and stopping up the ear. On the contrary, the normal condition of sleepiness that makes itself distinctly felt to the individual and that follows upon healthy active exertion of body and mind is most probably connected with a genuine fatigue of the vaso-motor centre, particularly, I believe, of the part controlling the skin vessels. When in this condition, only strong sensory or mental stimuli are adequate to keep the centre in tone and prevent a fall of blood pressure, and if the fatigue is excessive, even such means fail and sleep ensues quite against the will.

The probability of a relationship between the supply of blood to the brain and the condition of sleep is indicated also by the phenomena preceding normal awaking. For some time before awaking the arm undergoes a gradual constriction, and in the half-hour or so just preceding awaking this constriction becomes comparatively rapid, bringing the arm at the time of awaking nearly or completely to its normal volume. Upon the explanation of the plethysmographic curve that has been adopted in this paper, these changes would mean that after a certain period of relaxation the vaso-motor centre gradually regains its tone, the resumption being more rapid shortly before awaking. The result of this process is to force a greater and greater supply of blood through the rested brain until finally the threshold of consciousness is overstepped and spontaneous awaking occurs. It is probable that under ordinary conditions awaking is almost always accelerated by the effect of some accidental external or internal stimulus. At the same time it must be admitted that if such stimuli were removed spontaneous wakening would eventually follow the gradually increasing vascular tone. It is an interesting fact that in the plethysmographic curves taken by the author there was always a marked constriction of the arm at the moment of final awaking. As the subject awoke he could see the pen rising rapidly upon the kymograph. The effect in this case seemed to be analogous to that caused by mental activity. The sudden increase in mental processes coincident with the access of full consciousness acted as a stimulus to the vaso-motor centre, and the constriction produced was sudden and marked. Subsequently the pen again sank a certain distance, remaining finally at a level approximately the same as that shown at the time of going to sleep.

It frequently happened that during these experiments the subject awoke one or more times during the night. When the awaking was of the kind that brings full consciousness, it was accompanied by a marked constriction of the arm. In some cases, however, the awaking, although simultaneous with a sharp constriction of variable extent, was not followed by a permanent rise of the curve, the arm remained dilated to a much greater extent than was the case at the final awaking. Usually, if not always, in such cases the awaking was of the character that leaves the subject still drowsy; the eyes were kept closed and sleep soon returned. The incomplete extent of the return of consciousness in these cases is indicated by the facts mentioned on page 317. The subject, although awake and conscious of his surroundings, was certainly not fully awake, as he was mentally incapable, apparently, of recognizing distinctly his obligations to inform the watcher of his condition. This state of incomplete return of consciousness occurring during sleep is more or less familiar to every one. The effect upon blood pressure varies—in some cases it may apparently be slight or absent altogether—and this doubtless explains the quick relapse into the sleeping condition that usually follows. That consciousness may return temporarily without apparently any permanent increase in the flow of blood to the brain is an interesting fact that seems at first sight to be opposed to the views of the causation of sleep adopted in this paper, although the contradiction is only apparent. The usual relationship between the amount of blood flow and the intensity of the conscious processes does not at all exclude the possibility that changes sufficient to arouse consciousness may be produced in the brain cells by stimuli other than those implied in an augmented flow of blood. The phenomenon under consideration occurred usually after the intensity of sleep had passed its maximum and when the irritability of the nerve cells might be supposed to have returned nearly to the normal condition. Under these circumstances it may be conceived that the metabolic processes within the cells might be increased by internal causes of some kind and thus pass the threshold of consciousness, or that temporary sensory stimuli from without might produce a similar effect by direct effect on the cortical cells, and the conscious processes thus evoked might persist longer than the corresponding vaso-motor change. The point which the author is seeking to emphasize in his views upon the causation of sleep is that when internal or external causes, that in themselves are capable of exciting consciousness in the rested brain cells, are excluded, an augmented flow of blood to the brain may alone be sufficient to raise metabolism over the threshold of consciousness, and that this change is in fact the normal means provided to restore consciousness to the sleeping brain.

Some interesting suggestions arise from a comparison of the curve of intensity of sleep with the plethysmographic curve, assuming that the latter has been correctly interpreted in its bearings upon the circulation in the brain. This comparison has been made on page 328. One striking fact is, that during the period of increasing intensity of sleep there is a corresponding increase in the anæmic condition of the brain, the two conditions reaching their maxima apparently about the same time. If the normal appearance of the unconsciousness of sleep is owing immediately to the anæmic condition of the cortex, we can understand why the intensity of sleep should grow rapidly deeper after the threshold is passed, since the condition of anæmia becomes more pronounced in correspondence with the slow relaxation of tone in the vaso-motor centre. This increase in the intensity of sleep is not easily understood upon the theories of Obersteiner or Pflüger, and perhaps is more difficult of explanation upon the histological theories of Cajal and of Duval. It is impossible to say whether the maximum intensity of sleep corresponds exactly with the maximum anæmia of the brain. All that can be asserted is that during the first hour or so of sleep the two curves run a parallel course, as does also the curve of fall in temperature of the brain determined by Mosso. In their subsequent course, however, the plethysmographic curve and the intensity curve diverge widely. While the intensity curve returns rapidly toward the threshold, the anæmia of the brain remains practically maximal during several hours, and gives place finally to a gradual increase in the blood flow as the vaso-motor centre recovers its tone. It thus happens that between the second and third hours after the beginning of sleep the intensity of sleep (according to Kohlschütter's curve) is but slightly below the threshold, while the anæmia of the brain is still maximal or nearly so. This divergence in the two curves may be explained, perhaps, on the assumption that the cells of the cortex regain their normal irritability more rapidly than those of the vasomotor centre, being less fatigued or possessing a more active metabolism. At the time mentioned the brain cells are practically in a condition to awake, but their metabolism is kept below the threshold solely, perhaps, by the anæmic condition of the brain.

Attention has often been called to the fact that the curve of intensity of sleep does not explain the greater recuperative effect of a long slumber as compared with a short one. According to the intensity curve, the brain should be nearly completely rested after a sleep of three hours, whereas our experience seemingly proves the reverse. This apparent difficulty is explained by the plethysmographic curve; for after a sleep of three hours the vaso-motor centre is still in a condition of depressed irritability, and if awaking occurs at that time, this centre is stimulated to activity while still in a condition of fatigue. The usual long duration of sleep may be referred then to a slow recovery from fatigue on the part of the vaso-motor centre. We may suppose, indeed, that the actual beginning of sleep, its duration and normal awaking are directly connected, under ordinary circumstances, with the condition of the vaso-motor centre. Were it not for the long relaxation of this centre the cortical cells would probably enter into activity at a much earlier period than normally occurs, and would therefore be deprived of the benefit of a long rest. According to this view, the normal periodicity of sleep, which is its most characteristic phenomenon and the one most difficult of explanation upon previous theories, is to be referred finally to the characteristics of the vaso-motor centre.

In conclusion it should be stated that although the above-described theory of sleep was arrived at independently by the author from a consideration of the results of his experiments, a survey of the literature shows that the same general idea has been suggested at various times by other investigators. Mosso* speaks of having at one time believed in a mechanical theory of sleep, according to which awaking was caused by blood being forced from the extremities toward the brain. His subsequent extensive and most interesting work caused him to abandon this theory as superficial and insufficient. Certainly no one is better qualified from wide experience with the subject to speak authoritatively upon the physiology of sleep, but after a careful study of Mosso's published works, so far as they have been accessible to me, I fail to find any convincing facts that oppose the vaso-motor theory. Mosso holds to the view of an independent regulation of the brain circulation through intrinsic vaso-motor fibres, a theory that is quite opposed to recent experimental work on lower animals. It seems also to the author that this distinguished investigator, particularly in his work on the temperature of the brain, looked for a sudden change of some character to mark the moments of sleep and awaking, whereas the passing of the threshold of consciousness in either direction may obviously occur without sudden circulatory or temperature changes, although such changes are apparent enough if considered in relation to the entire period of normal sleep.

De Boeck and Verhoogen† speak of a theory by Heger, according to which a necessary condition of sleep is a depression of vascular tone. If I understand the authors correctly, this theory was announced in Professor Heger's lecture, and not in a published communication. It is coupled with a suggestive reference to the differences in the circulation in the cortex and the base of the brain depending upon the different resistances on the two paths. This point is elaborated in the paper by De Boeck and Verhoogen. They state that the arterial branches from the circle of Willis supplying the basal ganglia are numerous, generally arise at a right angle, and are large and short, while those

* Ueber den Kreislauf des Blutes im menschlichen Gehirn, p. 75, 1881.

† De Boeck and Verhoogen, Contribution à l'étude de la circulation cérébrale. *Journal de Médecine de la Société royale de Bruxelles*, 1890.

destined for the cortex are smaller, longer and more tortuous. For this reason, under any given pressure in the circle of Willis, more blood will take the shorter, less resistant path to the basal ganglia. When, therefore, blood pressure is lowered, the anæmia of the cortex will be relatively greater than in the basal portions of the brain, and it may be supposed that with a certain low pressure the flow through the cortex may cease, while in the basal portion a circulation still persists. This idea is valuable in indicating a means by which the irritability of the cortex may be suspended by a moderate fall of arterial pressure, while that of the medullary centres, for example, may remain. In how far the basal portions of the brain are affected by sleep has not been demonstrated as yet. Some incomplete observations by Tarchanoff indicate that the spinal cord, when severed from the brain, shows as rapid a reaction time during sleep as in the waking hours. So, too, the familiar instances of individuals walking in their sleep show that the power of muscular co-ordination and locomotion may be associated with the unconsciousness of sleep.

In a work recently published by Hill,* that has appeared since my researches were completed, he advocates the theory that sleep depends on an anæmia of the brain brought about by relaxation in tone of the splanchnic area. The anæmia is produced, he believes, both by a fall in general arterial pressure and by a corresponding rise in general venous pressure, the latter factor tending to retard the flow of blood through the brain. Hill sums up his opinions in the metaphorical statement that "The vaso-motor centre is the hub round which turns the wheel of a man's active mental life." From my own observations and from those of Mosso, I cannot help believing that Hill is in error in supposing that the fall of arterial pressure occurring during sleep is primarily owing to a relaxation of tone in the splanchnic area. (The reasons for this conclusion have been stated on page 324 and need not be repeated here.) It is difficult to obtain positive evidence of the condition of the splanchnic circulation during normal sleep. So far as the author knows, no such evidence is in our pos-

* Hill, The Physiology and Pathology of the Cerebral Circulation. London, 1896.

session at present. On the contrary, our evidence as regards the condition in the skin seems to be decisive and capable of easy demonstration. When vascular dilatation does occur in the splanchnic area, it should lower blood pressure unless compensated by vascular constriction elsewhere; and in so far as it lowers blood pressure, should facilitate the production of sleep. The well-known sleepiness arising after a heavy meal, when the digestive organs are in functional dilatation, is an example of this effect. Dilatation in either the skin area or splanchnic area, or both, would suffice to fulfill the mechanical conditions of blood flow necessary to sleep; it is simply a question of where this dilatation takes place in normal sleep.

In the theory of sleep proposed in this paper it is assumed that the quantity of blood flowing through the brain in some way controls the amount of psychical activity. This idea seems to be at variance with accepted physiological conceptions of the relations between blood flow and functional activity in other organs of the body. With regard to the skeletal muscles, and many of the glands whose metabolism is directly controlled by peripheral nerves, it has been shown that mere increase of blood supply is not alone sufficient to arouse functional activity, and that under appropriate stimulation these tissues may continue to exhibit functional activity for a certain time after the blood supply is entirely cut off. It must be borne in mind, however, that all the tissues do not behave alike in this respect. In the kidney, for example, we have an organ that, unlike the sweat glands, the cilia or the skeletal muscles, is extremely sensitive to variations in the blood supply. When the volume of blood flowing through this organ falls below a certain level, secretory activity is suspended and, within limits, the amount of functional activity varies with the quantity of blood. The precise way in which the augmented blood flow increases the secretory activity is not known, but there can be little doubt that the effect is in the nature of a direct stimulus to the functional metabolism of the secretory cells.

In the brain the conditions are much more complex, and our knowledge of the effects of varying conditions is much less direct. The cells of the cortex cerebri are in manifold connections with other parts of the nervous system, and are therefore under frequent stimulation from impulses falling into them from without. But in addition to this factor, the evidence we possess seems to show that the irritability of these cells is directly influenced by the amount of the blood supply. When the latter falls below a certain level the irritability of the cells is correspondingly diminished, and external stimuli from other nerve units must be proportionately increased to arouse psychical activity. If the volume of blood is diminished to a still greater extent, even the strongest external stimulation fails to arouse functional activity. Unconsciousness is known to follow almost immediately in man from compression of the carotids, from failure of the heart beat, or from other conditions causing a sudden diminution in the blood supply to the brain. In some recent experiments made by Broca and Richet,* in which the excitability of the cortex (in the dog) was determined by direct stimulation of the motor region, it is stated that the excitability disappeared completely within thirty seconds after shutting off the circulation to the brain by clamping the arteries. The unconsciousness thus produced is not, of course, normal sleep, but its occurrence under the conditions described indicates that the great diminution in blood supply to the brain that does happen during sleep is one of the essential factors in the causation of the more or less pronounced unconsciousness of sleep. Whether the relation of the blood supply to the functional activity of the cortical nerve cells depends upon some single factor, such as the supply of oxygen or the removal of carbon dioxide, or whether it is much more complex, involving other nutritive changes and perhaps conditions of pressure, cannot be discussed profitably at present, owing to the lack of experimental data.

DESCRIPTION OF PLATE XXXI.

Fig. 1.—Plethysmographic record of hand and lower part of fore-arm, on the right side, taken on the night of July 25th, 1895. The watcher was Dr. G. T. Kemp. A fall in the curve indicates dilatation of the arm, and a rise, constriction. On the previous night only about three hours of sleep had been obtained, owing to an unsuccessful attempt at a similar experiment. On the day of the experiment (July 25th) had taken a long journey, partly

* Broca and Richet, *Comptes rendus de la Soc. de Biol.*, Feb. 12, 1897.

by water and partly by rail. As nearly as could be determined, was asleep about 1 A. M. A fall of 1 mm. in the record corresponds to an increase of 0.37 cc. in the volume of the arm. At 2.45 A. M., two hours after the beginning of the experiment, the dilatation of the arm was equal to 18.5 cc. The subject of the experiment awoke finally, shortly after 5.30, the moment being marked on the record by a ×. The arm contracted rapidly and subsequently fell slowly. The subject remained in the apparatus for another half-hour, talking with the watcher, the arm retaining a fairly constant volume which was greater than that at the moment of going to sleep. The sharp upstroke at the end of the experiment was purposely made by moving the hand in the plethysmograph, with the object of ascertaining the position of the time pen with regard to the pen of the plethysmograph recorder. From 2.57 to 3.07 the notes of the watcher record that the sleeper was probably awake, was uneasy, shifting his position frequently and sighing. The series of sharp oscillations at this period are probably accounted for by these movements. The sharp rise at 1.17 was coincident with a jerk of one of the feet and a change in position; the rise just beyond 1.45 was coincident with a change of position, a deep sigh and a movement of the plethysmograph arm; at 2.33 the notes record several twitches of foot, several deep sighs, drawing up of both feet; the large rise just after 4 A. M. occurred while the watcher was out of the room; at 4.24 the notes record " uneasy, sighs, nothing to account for the great rise of the curve "; at 4.38, " shifts position, sighs, great rise in curve "; at 5.10, " sighs, shifts position, curve drops and then rises rapidly." The character of the record here is such as to indicate a movement of the hand within the plethysmograph, thus accounting for the first sudden drop of the curve; at 5.22, " has been perfectly quiet, breathing regularly but not deeply, two abrupt and considerable rises have occurred on the curve "; at 5.35, " sighs, shifts position, rubs his eyes but does not open them "; at 5.37, " awakes suddenly and asks the time," this is the point marked ×. Throughout the record there are numerous notes of changes in position, sighs, noises happening simultaneously with the oscillations in the curve. The parts of the notes reproduced above refer to the most noticeable of these oscillations.

Fig. 2.—Plethysmographic record of hand and lower part of fore-arm, on the right side, taken on the night of September 17, 1895. The watcher was Dr. Reid Hunt. A fall in the curve indicates dilatation of the arm, and a rise, constriction. On the previous night the subject of the experiment had sat up until 3 A. M. and slept from 3 to 6 A. M. As nearly as could be determined, was asleep by 1.37. A fall of 1 mm. in the curve indicates an increase in the volume of the arm of 0.37 cc. At 2.12, 50 minutes after the beginning of the experiment, the dilatation of the arm was equal to 15.91 cc. At 5.45 the sleeper awoke suddenly, at the point on the curve marked ×. After the sharp constriction of the arm, which was observed by the subject of the experiment while it was taking place, there was a slow dilatation, which was followed by a second permanent rise to a level corresponding to that near the beginning of the experiment before sleep appeared. At 4.18 and at 4.59, according to the notes of the watcher, the subject awoke and gave the signal agreed upon, the work " awake "; at each point there is a sharp rise of the curve. The period of consciousness was very brief, sleep soon coming on. The notes of the watcher in this case are brief and may be given entire.

1.22, lights lowered, experiment begun. 1.30, large rise in curve, coincident with sneeze on the part of the watcher. 1.31, movements of sleeper. 1.35, loud talking and disturbance in the street. 1.48, sighs, 1.50, sighs. 1.58, deep breath. 2.09, deep breath. 2.12, kicks the foot. 2.20, movement of free hand toward plethysmograph, legs drawn up, simultaneously the large rise on the curve just before the mark 2.22. 2.36, movements of the legs, large rise in the curve. 2.42, cab drove by. 2.50, movements of legs. 3.03, movements of legs. 3.12, slight movement. 3.20, deep breath, movements. 3.25 and 3.34, movements. 3.38 and 3.45, movements of legs. 3.52, very quiet. 3.54, cab in the street. 4.02, 4.13 and 4.16, movements of the legs. 4.18, sleeper calls out "awake." 4.37, very quiet. 4.59, sleeper spoke. 5.06, sleeper moved and rubbed his eyes. 5.15, moved and rubbed his eyes. 5.18, moved and rubbed his eyes. (The sleeper after the experiment could not recall being conscious at these times.) 5.45, awoke and began to converse.

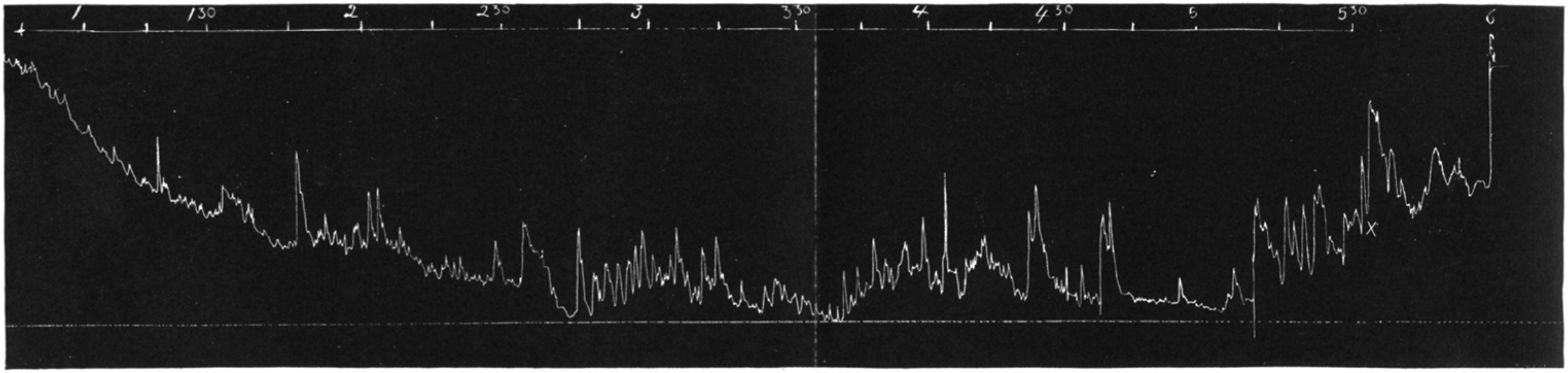
1
130
2
230
3
330
4
430
5
530
6
×

Fig. 1.

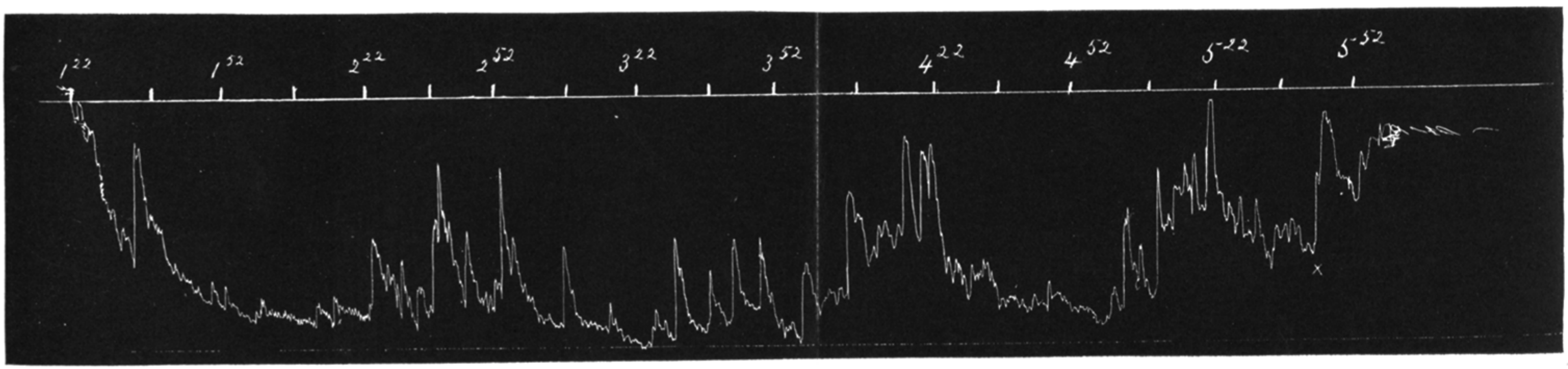
1 22
1 52
2 22
2 52
3 22
3 52
4 22
4 52
5-22
5-52
×

Fig. 2.