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REM sleep and depression seen in an evolutionary perspective.

Endothermy, or "warmbloodedness" due to a high and relatively stable rate of metabolism, and a particular rather enigmatic state occurring periodically during sleep called REM (rapid eye movement) sleep are two physiological states that characterize all mammals.

This paper is an outline of an hypothesis (1) about a possible connection between these and another psycho-physiological state, the endogeneous depressive condition, based on evolutionary speculations.

Mammalian origins

A reptilian group named therapsides is the mammalian origin. Therapsides were among the first reptilian groups to emerge early in the Permian age nearly 300 million years ago. They were not only among the very first, but they also were among the most successful. They became the major reptilian group in the Permian age.

While the Carbonaceous age prior to the Permian had a warm, humid and stable climate, the latter was characterized by cold, dry and very changing weather conditions creating large differences in temperature between geographical zones, between day and night, and between seasons.

It was this climatic change that forced the development of terrestrial animals from aquatic-living amphibians, because it drastically reduced the living space available to the latter.

The drying up of the lakes and swamps, however, is only one aspect of this process. Permian climate meant still another reduction of living space, as massive as the drying up and thus as consequential in evolutionary terms.

Amphibians like all prior animals are ectothermic or "cold-blooded", as were the first reptiles being a sort of land dwelling amphibians.

Ectothermy means that the internal temperature of the animal is determined by the temperature of the environment, or very nearly. Thus the animal's rate of metabolism and the ensuing rate of activity are similarly related. Activity therefore must follow the spatial and temporal changes in external temperature.*

In a rather changeless climate like the warm Carbonian, this is no real restriction on activity. But the Permian weather confronted the ectothermic reptile with barriers of temperature no less physical and impenetrable than those of dry land. And as the latter reduced the living space of the amphibian, so the former reduced the living space of the ectothermic reptile.

Selective pressures solved the problem of dry land by creating a reptile capable of terrestrial life. A similar set of selective pressures also must have been at work forcing the development of an animal capable of breaking the barriers of low temperatures.

The answer to these pressures, of course, would be an endothermic or "warm-blooded" reptile capable of keeping its internal temperature and rate of metabolism independent of the change in external temperature, thereby widening the available life space considerably.

Paleontological evidence (3) credits the therapsid group with the beginning of this development. It was brought about by making the metabolic functions more efficient in several aspects and by furnishing the animal with an efficient insulation for the conservation of heat produced in the metabolic processes. Therapsids in all probability thus became the first endothermic animals.

The problem of therapsidian decline

According to common thinking, warm-bloodedness is one of the greatest evolutionary triumphs and the cause of mammalian supremacy. It is therefore disturbing to learn that the following geological period, the Triassic, saw the downfall of therapsides.

* New research (2) has shown that ectothermy is a less restricting condition than is commonly thought. Where the possibility of choice exists the ectotherme can choose areas favorable for the performing of its activity, that is areas of optimal temperature conditions.

Their reign was broken by another group of reptiles, the thecodonts, which for the next 100 million years were to dominate the animal kingdom in the form of dinosaurians.

Evolutionary logic now forces us to conclude that the thecodont or dinosaur was better equipped for the conditions of life than the endothermic therapsid.

This could be due either to advanced features in dinosaurian equipment, flaws in the therapsidian equipment, or both.

Dinosaurians have for a long time been considered ectothermic, which hardly can be seen as an evolutionary advancement. But objections have recently (4) been raised against this age-old belief. It has been said that animals built for speed like dinosaurians must have had an energy supply making speed possible, hence some sort of warmbloodedness.

The counter argument (5) goes that due to their size, dinosaurians with mammalian rates of metabolism would have required unobtainable amounts of food.

Both arguments make sense. One could speculate, however, that dinosaurs, unlike ordinary mammals, had developed the ability to alternate between the endothermic and the ectothermic condition according to need and situation. If this is physiologically feasible, it would not only solve the apparent contradiction between speed and size, but it would also mean that the dinosaurian energy regulation would circumvent certain problems that might have strained therapsidian endothermy. In that case the former would actually be an advancement in relation to the latter. This brings us to the possible flaws in therapsid-mammalian endothermy, the discussion of which is our main theme.*

The necessity of fitness to a particular environment

A major evolutionary rule is that animals must fit morphologically and functionally into their environment. Behavior is no exception to this rule; responding to it, animals show a close correspondence between activities and reactions and environmental conditions and events.

In sub-mammalian species this correspondence is most often extremely close. The animal almost seems to be built into the

* The question of dinosaurian temperature regulation has affinity to the question of avian temperature regulation, since birds most likely have a dinosaurian origin. If avian regulation does not differ from mammalian, the hypothesis stated here is seriously weakened.

environment. In a way one could say that the environment is the external "brain" of sub-mammalian species, orchestrating their behaviors.*

But in order to keep this vital correspondence between environmental variables and animal activities, the animal must stay within the boundaries of a particular - often very particular - environment. If the animal leaves its ecological niche, it parts with its external brain, so to speak, with well known dire consequences. This necessity of particularity is the reason behind speciation.

By talking about an environmental brain we have emphasized the necessity of animals fitting into their environment. In this respect the animal may be seen as a machine reacting to the changes in environmental conditions.

But animals are not machines; they are living entities. The direction of their action is determined by the environmental brain but the action itself is the animal's own. This side must also be considered, if we are to assess the problems of endothermy.

The motivational structure of vertebrates

On the molecular level animals are chemical structures of high complexity. Like any other complex chemical structure it must be broken down due to the forces expressed in the second thermodynamic law. If the animal is to live, it must counter the dissolution. This is done through metabolism, which is and must be a continuous process, at least under all but the most special circumstances.

To maintain metabolism the animal must secure energy and organic building materials; these are obtained from other animals or from plants. Metabolism thus requires food-getting, i.e., finding and eating. This is an outward process, while metabolism itself is an inward process.

Since it is necessary that the outward process be executed in accordance with the need of the inward process, all animals - at least of the vertebrate order - are designed in such a way

* With an external "brain" the need of an internal brain is small and species like insects seem to prove that tiny-brainedness and extreme fitness go hand in hand. Contrary growth of large internal brains could indicate adaptational problems.

that information about the metabolic state can reach the activity-executing centers. This is done by means of neuronal pathways from sensors registering the inner environment to the motor programmes of the brain.

Since the food-getting behavior in most species needs only be periodical in order to sustain the continuous metabolic process, the informational pathway from inner environment to motor programmes is so designed that it can accumulate the output from the sensors until this has reached a certain magnitude. This "pool" is then released, leading to food-getting activity.

The process from sensors registering metabolic state to the activity programmes is called drive. The activation of the animal is thus determined by a drive accumulation followed by a drive release. This leads to a cyclical process monitoring the continuous metabolic processes, insuring the necessary periodical food-getting activities.

The animal's activities and behaviors are thus determined from the inside as well as from the outside.* Most behavior is the composite result of the two influences: activity-production from the inside and activity-shaping from the outside.

The contradiction of endothermy

One variable of environment is the ambient light. The field of ambient light makes it possible for animals to detect or "see" objects and relations between objects at large distances. The visual capacity thus has been of importance for most species through the history of life.

The advent of terrestrial life gave this modality an even greater adaptational importance than seen before in aquatic and semi-aquatic life, because of the open terrestrial spaces.** Sight therefore surpassed smell and hearing in informational importance.

* Another important inner produced activity, the sexual, has not been mentioned here. Principally it functions similarly to the metabolic system. It is the amount of certain hormones the drive system here monitors instead of metabolic variables. The rise and fall in hormones is determined by environmental variables, e.g. light.

** An earlier terrestrial invasion, i.e. the insects, shows the close relationship between terrestrial life and the need of precise visual capacities.

Unlike most other environmental variables, light cannot be kept constant or nearly constant. It inevitably undergoes radical changes with the time of day no matter what ecological niche a terrestrial animal occupies.

In order to develop an efficiently adapted visual apparatus, the animal then must choose* a particular light condition; that is, a particular period of day.* Terrestrial life thus called for use of particular day zones, leaving other zones untouched, since fit could not efficiently be established in both. That the change of day and night can reverse adaptational advantages considerably is exemplified by the owl and the sparrows.

But since the exploitation of the world of light requires the limitation of activity to certain periods of the day, it also requires that animals be capable of avoiding other periods.

What determines the release of activity is the drive process following metabolic rates. Since the metabolic rate in the ectothermic animal follows external temperature, that is, the change of day, the ectothermic animal is superbly suited for the use of the informational potential in ambient light. Ectothermy is in this respect a great selective advantage, since ectothermy as shown in fig. 1 ties activity to a particular zone of day.***

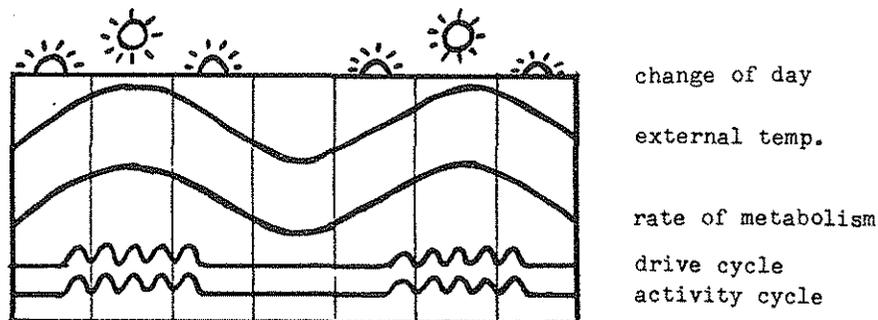


fig. 1. Ectotherme animal

* Anthropomorphic language is used throughout the paper for convenience. A more precise language could, of course, have been used.

** The problems of endothermy are in this paper exemplified by the environmental variable light. Other variables following the same logic might be found. So the case of light need not be paramount to the demonstration of the endothermic contradiction.

*** This important advantage of ectothermy could be the reason behind the success of thecodonts over therapsids. But it is also evident that the type of combination we suggested to account for thecodont superiority would add the ectothermic advantage of close fit to the endothermic advantage of high activity. Such a system would portray the same relationships as shown in fig. 1.

While the ectotherme could meet the possibilities - which in evolution means necessities - of ambient light fully prepared, it was a completely different matter for the endotherme animal, as seen in fig. 2.

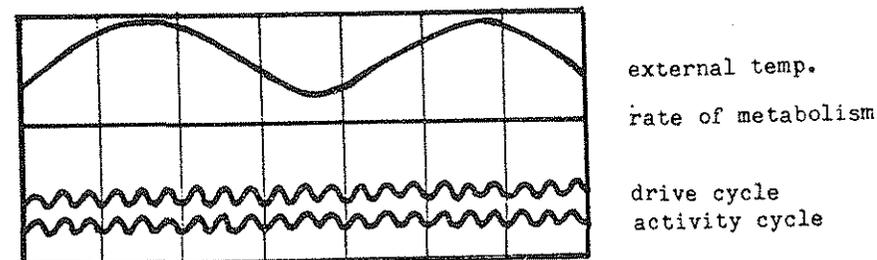


Fig. 2. Endotherme animal in principle

Since the endotherme has a constant high rate of metabolism, it also has - as can be seen - an unvarying drive cycle and its activity must be performed with regular intervals completely independent of the change of day. It is therefore not possible to develop an optimal adapted visual apparatus.

By following the evolutionary theme of endothermy in order to break the Permian restrictions on activity, the animal thus also broke the fine steering capabilities of ectothermy. The endotherme freed itself of the restrictions of temperature, and free indeed it became.

The rise of endotherme therapsids in the Permian age shows that it paid off to leave the possibility of utilizing the full potential of ambient light in favour of breaking the temperature restrictions on activity. The fall of the same animals in the following age shows that advantages had reversed.*

The use of the potential of visual perception could be one thing to account for the supremacy of the rising thecodonts, and we know that olfaction remained the dominant sense of the therapsids and thus of the first mammals.**

* The Triassic age meant a return to a more warm and stable climate, though still rather dry. The need of endothermy was thus less.

** When early mammalian types started to grow their famous brain, it was therefore built on the olfactory structures, and not on the visual. The necessity of bringing information from other modalities to the centers of smell then meant the enveloping of the olfactory structures by cortical layers. The Triassic shortcoming was thus the incubator of later triumph..

The endotherme contained a contradiction, because by being freed of the restrictions of temperature, the animal was simultaneously freed from important ties to the environment - the external "brain".* Since restriction and adaptation are nearly the same thing, the endotherme - by breaking temperature restrictions - also violated the rule of adaptational fitness.

In the Permian period, therapsides harvested the advantages, but in the Triassic they were confronted with the bill. Their lack of ability to utilize ambient light** had been a small problem until a competitor emerged who could utilize it. The flaws of endothermy materialized in the form of the superior thecodont. With this materialization the problem stemming from the lack of temporal specialization took on a new form.

The endotherme necessity

Adaptational restriction is at the same time protection. Outside the boundaries of an animal's environmental niche it is without protection. With the rise of thecodonts this became a major therapsidian problem. Having no temporal niche of their own in which they were well adapted, they fell prey to thecodonts in great numbers.

This problem had only one solution. The therapsides had to develop temporal specializations re-creating the broken temporal barriers. However, since the thecodonts were superior due to advanced vision and possibly also in speed, the therapsidian temporal specialization had to avoid the periods of day utilized by the thecodonts and instead exploit the periods of low activity of the thecodonts and their dinosaurian kin.

This was possible because thecodonts had specialized in the times of the day shown in fig. 1 in their attempt to use the environmental possibilities to the utmost, and therapsides were not hindered in utilizing low-temperature and low-light periods of the day because of their independence of external temperature.

* From this point on the theme of internal brain development is the therapsidian-mammalian theme, the first steps of which we are dealing with in this paper.

** Or any other environmental variable tied to the 24 hour cycle, and therefore demanding a temporal specialization.

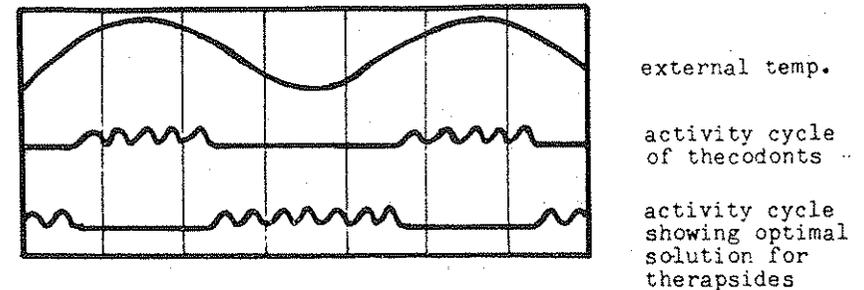


Fig. 3. The therapsidian necessity

This all means that therapsides facing thecodonts in the Triassic were forced to solve the problems inherent in the Permian developments. They had to restrict their periods of activity temporally in order to avoid extinction. Going back to ectothermy and thereby renewing the tie between metabolism and change of day, however, was not possible. They had to maintain a stable rate of metabolism, which rendered them independent of external temperature.

In other words, the therapsides had to maintain the endotherme rate of metabolism and at the same time restrict their periods of activity. The tie between rate of metabolism and activity had to be severed, and it could happen in only two ways.

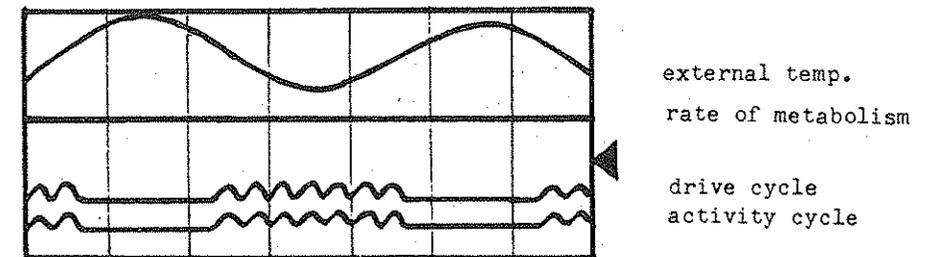


Fig. 4. Solution no. 1

The first way is shown in fig. 4. It consists of cutting the tie between rate of metabolism and the drive cycle. This would lead to the necessary temporalizing of the cycle of activity. Or more precisely, it would allow other steering mechanisms to control the activity cycle according to the time of day by temporalizing the drive cycle.

The second way is shown in fig. 5. It consists of cutting the tie between drive cycle and activity cycle. This would also allow the necessary temporal restrictions or adaptations.

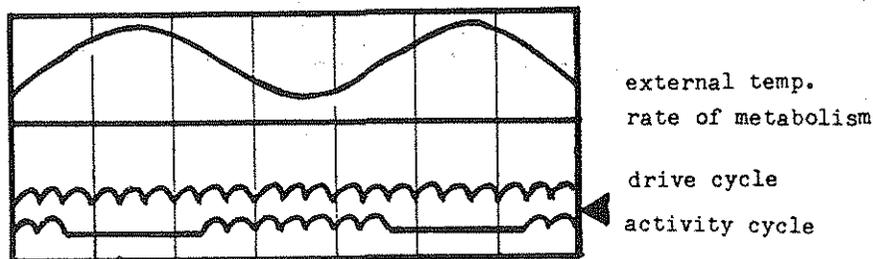


Fig. 5. Solution no. 2

Both solutions seem impossible, since the ties among metabolism, drive and activity are as old as vertebrates themselves, and thus must constitute the genetic core of these animals' behavior systems.

But since we must choose, as Nature must have chosen, the second solution is perhaps the more likely, since the activity side of the system is more plastic than the inner energetics. Since prevention of unwanted activity is the object of the change, interference with the activity system also seems the more direct approach.

According to our logic, endothermy negates the tie between external temperature and behavior. Thus, sooner or later, it must be followed by a negation subverting or undoing the disadvantageous aspects of the first negation. The cut between external temperature and rate of metabolism eventually becomes intolerable and must be followed by a cut between drive cycle and activity cycle restoring the connection between the latter and temporal environmental changes. The fit must be re-established.

Endothermy is the first negation. The hypothesis put forward in this paper is that the REM sleep phenomenon is the second negation separating drive cycles and activity cycles, and that REM sleep is part of a temporal adaptation linking the therapsid or mammal to a certain period of day, thus protecting it against superior competitors or predators from the thecodontian stock.

Let us assess the REM sleep phenomenon in light of this hypothesis.

REM sleep

The answer to the necessity of restricting the periods of activity facing the therapsides* in the Triassic is ordinary sleep. Sleep can very likely be seen as a temporal adaptation keeping the animal out of circulation and saving energy in non-favourable times of day. Thus we think that therapsides developed into more or less nocturnal animals due to the competition from diurnal competitors.

Lying idle for longer periods of time through sleeping is, however, impossible due to the structure and function of the inner activity determining processes, unless something is done to prevent the cyclical drive release leading to overt activity with frequent intervals, thus destroying the purpose of sleeping.

Sleeping thus presupposes solution no. 2 as depicted in fig. 5. That is, the separation of the activity cycle from the drive cycle making longer periods of inactivity possible despite the unhindered rolling on of the drive cycle.

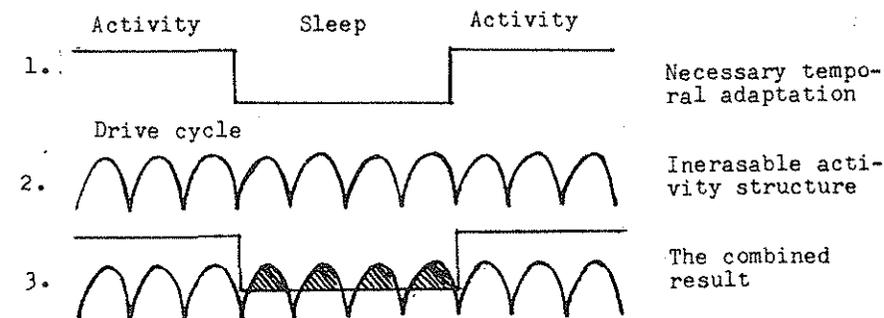


Fig. 6

This situation is reformulated in fig. 6, showing the necessary conflict between activity and drive release that the temporal adaptation of sleep would mean for the endotherme with a high and stable metabolic rate and drive cycle.

In view of this, it is very interesting to learn** that a cyclical process is actually taking place during normal sleep.

* We use the name "therapsides" for the whole development of endotherme reptiles from the Permian beginnings to the advent of true mammals. This is, of course, taxonomically incorrect.

** It need not be said that the road of discovery is different from the road of presentation. The latter for reasons of clarity evidently overdoes the deductive character of the argument. In reality it was REM sleep that led to the argument and not the argument that led to REM sleep.

This results in the continuous interruption of normal sleep in all mammals - and mammals alone - by a distinct physiological state very different from that of normal sleep. This state is called rapid eye movement sleep because it is accompanied by spurts of rapid eye movements. But eye movements are not the only difference between REM sleep and normal sleep.

While normal sleep shows a very docile pattern for breathing, pulse and blood pressure, REM sleep shows rather wild patterns for the same features, and the EEG in REMS is desynchronized resembling that of a highly aroused animal in overt activity.

Despite its resemblance to the waking condition, the REMS is no light sleep. In no other sleep phase is it more difficult to waken the animal than in REMS despite its aroused condition. This contradiction is the reason behind the alternative and perhaps better name Paradoxical Sleep.

Both the agitated character and the cyclical nature of the REMS phenomenon point to that drive cycle which, according to figures 5 and 6, must underlie any state of inactivity.

That the REMS cycle actually is the drive cycle is further indicated by the close relationship between frequency of REMS and rate of metabolism in different mammalian species (6). The higher the rate of metabolism - hence, the higher frequency of drive release - the higher the frequency of REMS. The cycle length of a rat is 10-13 minutes, while it is 120 minutes for an elephant. Man has a cycle length of 90 minutes.* This accords closely to their respective rates of metabolism.**

An elegant demonstration of the relationship between rate of metabolism and REMS has been made by Jouvet (7). In a cat, surgically isolated from its centres of temperature regulation so that it functioned as an ectothermic animal closely following

* Rats have a higher metabolic rate than elephants due to their higher surface to bulk of body ratio. Man of course is in between.

** A particular cycle reflecting a periodic variation between rest and activity throughout the 24 hours has been found in all mammals. This basic rest activity cycle (BRAC) must reflect or be the drive cycle. The frequency of BRAC is precisely the same as the frequency of REMS, though the latter is seen only during sleep. This strengthens the view that REMS is the work of the drive cycle.

the temperature of external environment the REMS frequency varied accordingly. At low temperatures - low rate of metabolism - it was equally low.* At high temperatures the opposite.

Frequency is one way to measure REMS. Magnitude, the time spent in REMS in percent of total sleep time, is another.** While frequency points to the metabolic rate, magnitude points to the amount of drive accumulated in the drive pool. This is specific for different species, depending on the type of food-getting in which they have specialized. Animals with easy access to food need only small drive amounts, while animals who must perform more strenuous deeds to acquire their food need larger pools of drive.

According to this argument the magnitude of REMS should be larger in carnivorous species and smaller in herbivorous, with omnivores in between. This is precisely the relationship we find (8). Feline predators have twenty times the magnitude of REMS than have ruminating sheep.

Another indication of the close relationship between REMS and drive comes from that part of contemporary sleep research which deals with the deprivation of REMS. Deprivation of REMS, that is preventing people and animals from having REMS during sleep by wakening them, has been a particular interest of sleep researchers. The reason behind this is the fact that REMS episodes and periods of dreaming coincide; the interest was in what happened if dreaming were prevented.

Two results from this research are of interest to us. The first is that REMS behaves like a physical quantity. When prevented from being released, it accumulates, making further hindrance of release increasingly difficult (9). After deprivation was ended the following sleep periods showed a surplus of REMS activity precisely equal to that "lost" (10).

This course of events and what might be called the "indestructibility" of REMS accords closely with the idea that REMS should

* And this, of course, is also a demonstration of the close correspondence between drive cycle and external temperature in ectothermic animals shown in fig. 1.

** It should be noted that two animals with exactly the same cycle frequency can have very different magnitudes. F.ex. if a period starts every 60 minutes during sleep, but it lasts 10 minutes in one specie before return to normal sleep, while it lasts 25 minutes in another, the two species have the same REMS frequency but different REMS magnitudes.

be an expression of the workings of the drive mechanism: production, accumulation, and release.

The second result are the behavioral patterns stemming from REMS deprivation. To cite one of the pioneers of this research, Dement*: "In summary, the effects of prolonged REM sleep produce a characteristic behavioral change which appears to reflect an alteration in drive state or emotion, or in more objective terms, an increased probability that the animal will emit a stereotyped "drive-oriented" response in the presence of the appropriate stimulus, or even without." (11)

In other words, the results from REMS deprivation can be seen as increasing drive accumulation in the deprived animal or person, because the release of this drive is prevented by the prevention of REMS.

This should establish the probability that REMS is not only tied to the drive cycle, but also is an expression of drive release.

We should not be surprised, though, since we have shown in fig. 5 and 6 that the drive cycle is and must be a continuous phenomenon 24 hours a day and that it also must continue through periods of inactivity like sleep.

This leads us back to the therapside problem. The drive cycle must continue, but it must not lead to overt activity in the "forbidden" periods of the day. The problem is evidently solved in sleep, where the REMS-drive release does not lead the sleeping animal into overt action. How is it done?

The negation of the negation

REMS is differing from normal sleep in one more aspect, but this time it is also differing from the waking condition. From the onset of REMS and throughout the REMS episode the person or animal suffers a radical drop in the muscle tone of the large skeletal muscles.

The result of this tonal fall-out is, that the animal or person becomes quite flaccid, and animals which are able to stand

* Many strange conceptions of the rationale of REMS have been presented through the last decades. Dement has constructed a few himself, but he has also presented the view that REMS is outlet of drive (12). It makes Dement the predecessor of this hypothesis, which was first formulated in 1975.

erect while sleeping must lie down during REMS.

In other words, the apparatus of movement and action is completely blocked during REMS, which efficiently deprives the animal or person of the ability to perform activity, despite the release of drive into the motor programmes of the brain.

Had it not been for the motor blockade through tonal fall-out, the drive release would have meant open activity. Jouvett (13) demonstrated this in another fine experiment, where the inhibitory centers responsible for the drop of muscle tone in a rat were destroyed. During sleep this rat initiated rage-like activity on the commencement of REMS. It ran around in the laboratory demonstrating a wild and determined behavior unseen in the waking condition. On the cessation of the REMS episode it lay down again continuing the sleep. At no point in the whole session was it awake.

So it seems that the separation of the drive cycle and the activity cycle so necessary for therapsides when meeting a temporal adapted competitor is caused by a blockade of the motor apparatus through muscle tone drop out. The physiological results of the drive release are demonstrated throughout the nervous system, but the actual behavior is efficiently prevented.

This enabled the therapside-mammal to become truly nocturnal. It had negated the negation and through the processes of motor blockade and drive-valving it could re-establish its temporal adaptation and still keep the potentials of unvarying endothermy.

They had escaped extinction and were ready to reemerge into the world of light, when the dinosaurs met their mysterious fate in the Cretaceous age.

The double-purposed system*

The original necessity of the system letting drive be released

* Still another purpose deserves mentioning, though it is not appropriate to the arguments of this paper. It has been shown (14) that fetuses in the last weeks of pregnancy besides having frequencies of REMS according to their high metabolic rates also have the highest magnitudes seen of all. This means that they spend more time in the REMS state than in any other state. This seems puzzling, unless we see that the foetus in placental animals is dependent upon another organism with a much lower rate of metabolism. The foetus therefore registers low metabolic values which in the last stages of pregnancy should lead it into overt activity through the actions of the drive system. This most likely would be disruptive unless hindered in some way: the drive release and motor blockade of REMS. The transition from egg-laying mammals to placental could hardly have happened without the aid of the REMS system.

but preventing overt activity was to re-establish the tie between temporal variables of external environment and behavior, which had been a biological rule until broken by endothermy.

But this necessity became manifest with the rise of the dinosaurian competitor and the dinosaurian predator in particular. The necessity for temporal adaptation therefore took the form of a defensive need.

The "drive-valve/motor-blockade" system thus had a double-faced character being at the same time an adaptation to temporal aspects of environment and a defensive measure. While the implications of the temporal adaptational side are clearly demonstrated in the REMS phenomenon, the defensive side is less clear. We will try to probe into it.

It was the thecodonts, superior in speed and vision, that forced the development of the blockade system according to our logic. Their advanced use of visual information widened their field of detection considerably, and their rapid mobility made the exploitation of this enlarged space possible. Further, their behavioral programming was so tied to the visual information that the latter functioned as an external "brain." Such an environmental fit meant that when information of a moving victim reached the predatory thecodont the hunt was pursued to its fatal end with the efficiency of a machine. Only other thecodonts had the chance of escaping such a hunter due to capabilities they had in common, capabilities that therapsides definitely did not have.

The thecodontian hunting programmes were built upon the fact that victims flee when pursued by a predator; all they needed was to have the visual pattern of the fleeing victim fed to them in order to put the thecodont on its deadly tracks.*

The only way inferior therapsides could escape their fate would be not to feed the thecodontian programmes the fatal information. That is, not to flee in face of the predator, but rather becoming immobile. For all the thecodont would know the immobilized therapside had disappeared.

In order to apply such an extraordinary strategy turning the thecodont's environmental "brain" against itself, the therapside would have to negate the compulsory inner urge - old as time itself - to flee.

* Perhaps analogous to contemporary birds of prey.

Here we recognize the theme of the necessary temporal adaptation making inactivity possible in spite of the inner urge of drive release. We suggest that the drive release/motor blockade system developed to serve the double purpose of limiting activity to a certain time of day and of escaping predators through non-activity.

Narcolepsy

Some people suffer from a condition of irresistible sleep attacks. At any time of day, they can suddenly be overwhelmed by an violent urge to sleep, and in more severe cases simply fall to the floor and sleep. This condition is called narcolepsy and was a medical enigma until it was shown (15) to be episodes of REMS taking place more or less fully outside of normal sleeping, with instant dreaming and often with muscle tone collapse as well.

REMS not in actual sleeping, of course, points to the other purpose of the drive-valve/motor-blockade system, namely defensive protection.* That the narcoleptic attack and the cataleptic muscle tone fall out are often instigated by surprise and fright support this view.

Narcolepsy may be seen as a rare occurrence** of an old mammalian defensive response, no longer current. It ties both purposes of the drive-valve/motor-blockade system together since its purpose most probably is defensive, while its functional mechanism is that of REMS, the temporal adaptation.

Depression

Though it is not widely recognized, narcoleptic conditions seem to play some role in depressive disorders diagnosed as endogenous.

* Due to the non-transparency of what constitutes threats to people in complex psycho-social contexts, it is very difficult to prove that conditions otherwise seen as diseases due to faulty inner workings should actually be meaningful psychological responses. The argument of this paper creates a context from which narcolepsy can be seen as a more molar phenomenon than physiological or chemical malfunction.

** After the extinction of the dinosaurians, when mammalian predators became efficient hunters and a threat to their own kind, the defensive system of immobilization in most cases - the exception possibly being very young animals unable to outrun any predator - became a hazard instead of an advantage. But at this turn of evolution the system had already been part of the therapside-mammalian repertoire for many million years and thus maybe unremovable from the genotype.

Kraines (16) in a summary of endogeneous* depression as a process lists symptoms of hypersomnia, excessive sleep, as a characteristic of the preliminary phases of depression. In later phases it changes to hyposomnia, the frequently reported sleep difficulties of depressives.

A reduction of sleeping does not necessarily point to diminished REMS outlet, if the latter takes more time than before. It is very interesting that Hartmann (17) was able to show that depressives despite their sleeping difficulties had significantly higher REMS magnitudes than did normals. In addition to higher magnitude the onset of the first REMS episode during sleep occurred nearly immediately after having fallen asleep. This characterizes persons deprived of REMS and persons suffering from narcolepsy, but not normals.

I have been able to confirm this connection between early depression and narcoleptic-like conditions from my own experience with depression (18) and I further made the observation that many of the symptoms of early depression and of persons being experimentally deprived of REM sleep are the same.**

There seems to be an apparent contradiction in depressives showing excessive REMS and at the same time showing symptoms of REMS deprivation. This contradiction can be easily solved if we recognize that both conditions could apply to a situation in which the need of REMS release exceeds the capacity of the REMS system. In this case release of REMS above normal values and symptoms of accumulated need of REMS would show at the same time.

One could say that early depression may be a sort of narcoleptic attack which was arrested and prolonged. This would make the depressive reaction a case of defensive reaction akin to the narcoleptic attack as a defense and to our archaic therapside-mammalian drive-valve/motor-blockade function. This accords, of course, with psychopathological theories seeing depression as

* Endogeneous depression is here used as a descriptive and not an aetiological term, since the causes of this phenomenon are neither agreed upon nor known. The term "depression" is further used as if it covered a single disorder. This need not be the case. One should, however, follow the rule of parsimony and see how far this will go before splitting depression up into different kinds. The latter procedure is not optimal for finding the causes behind the phenomenon, because it gets too easily stuck at surface variations that does not touch the core.

** The only exception to this is very important. Depressives lack the symptom of enhanced drive that characterizes the person deprived of REMS.

a defensive withdrawal reaction.

If the amounts of drive released through REMS is radically raised in depression, or in its early stages, it must mean that the REMS system is cutting into the amounts of drive necessary to sustain normal activity unless the organismic drive production is also raised. This does not seem to be the case. The raising of REMS activity is therefore followed by a corresponding drop in behavioral drive. This drive-drop is the fundamental symptom of depression common to all known types.

A new experimental and clinical route to the alleviation of depression strengthens this idea of a shift between outlet of drive into overt action and outlet of drive through REMS in depression. Since it is a common feature of depression that the person feels worst in the morning after waking, attempts were made to prevent people from waking simply by preventing them from sleeping during the night. The results of such sleep deprivation were in many cases rather amazing since people felt increasingly better the longer they were deprived (19). For a time - until they slept again - they actually began to feel normal.*

This strange recovery which has no equal in medication or any other remedy fits into our scheme of thinking, if we see REMS deprivation as the important aspect of the sleep deprivation. In that case we interpret the situation as follows. The deprivation prevents the drive release of the REMS system. This means that the amount of drive available for behavioral purposes will approach normal levels and in the case of prolonged deprivation will reach super normal levels, as in the case of Dement's cats.

All this points to the conclusion that depression is a shift in the ratio between drive released for behavioral purposes and drive released through the drive-valve system, that is REMS. This is exactly the same that happens in the narcoleptic attack; that is, the archaic defense reaction in the face of otherwise unavoidable danger, only that the narcoleptic attack is a pure form of this old therapside-mammalian response, while depression is an arrested and more complex variation.

* Unfortunately people felt drive ridden again after sleep, as they should according to our logic, and this was such a "depressive" experience after having felt normal for a while that the method was thought rather questionable. After all, it was not possible to postpone sleep indefinitely and thus the restoration of the drive "stealing" of the REMS system.

This should not be surprising, though, since more than 300 million years have gone since the Triassic problem presented itself, and these years have not passed without changing the therapsid-mammal.

From a rather primitive creature controlled solely by the environmental "brain" and the internal metabolic rhythms an animal developed with considerable self controlling capabilities. This process of development, reflected in the development of the limbic lobes and the cortex, eventually took over the determination of overt activities and reduced the drive cycle to the status of a sort of guiding rhythm or clock, now recognized as the BRAC.

From here on, activities and behaviors are no longer under strict environmental control, nor under rigid control of the drive release system, but are directed according to the computations of higher brain centres.

Most probably it is these higher brain centres in general and the limbic system in particular that interfere with the old defense mechanisms and thus create the characteristics of depression.

The arrest of the narcoleptic attack allows other mechanisms to play a role in the determination of depression. It is a well known fact that any receptor can change its firing in relation to stimulation according to messages from the CNS. This is also true for the need registering receptors.

This means that the CNS can control the amount of drive produced in relation to a constant degree of need. The biological advantage of this is obvious. In summer and fall when foods are plentiful, drive levels above those keeping the animal in a metabolic balance between need and expenditure would bring about the building up of food stores - either externally, as in squirrels, or internally - meaning building up of fat reserves that the animal can use during winter. In this period it would be a saving of energy if the drive level were kept as low as possible. Such a controlled drive level would mean that drive had a seasonal rhythm tuned to the necessities and possibilities of the animal under changing environmental conditions.

Another way of controlling the drive level would be to keep it in relation to behavioral expenditures. If more drive were produced than was used in behavioral activities, it would be economical to reduce the drive level. One way to read the ratio

between produced drive and used drive would be to monitor the ratio between produced drive expended through behavior and drive expended through REMS. Were the latter to reach too high a level, the drive production of the need registering receptors would be lowered. Both controlling methods are acceptable as adaptations, since both are advantageous for animals.

But if such a regulatory system existed, it would be activated by the arrested narcoleptic attack in depression. This would make depression a double phenomenon. First, the depressive reaction would be activated by some threat to the organism or person. This would lead to prolonged narcoleptic conditions with the symptoms of REMS deprivation, since it is a change in the drive ratio between behavior and REMS. After awhile, however, this situation would lead to a genuine drop in the drive production of the organism because the unbalanced ratio between behavior and REMS would be read as an over production of drive. The regulatory drive drop then would bring depression into a different phase.

The first phase is psychological in its purpose, namely the avoidance of a threat; the second phase is purely physiological. Since it is the second phase which has the worse consequences, it is this phase which brings the person to the clinician, who therefore is "justified" in seeing the disorder solely as a physiological phenomenon.

The course of an endogeneous depression could easily be read as a result of this double process, and it would further explain why some depressions seem to be tied to a seasonal rhythm. If a major component of an endogeneous depression is a regulatory drive fall instigated by a distorted behavior to REMS ratio, and if such drive regulations normally - at least in mammalian history - are associated with the change of seasons, through some effect of external determinants on the CNS, the course of the depression could very likely be seasonal, too.

Summary

It was argued that the uniform endothermy characteristic of mammals violated an important tie to environment and thus had to be followed by a re-establishment of this tie. But this would mean that behavior and the drive system somehow had to be separated, something not seen before in evolution.

Since sleep is one adaptation, which according to our logic would be impossible without this separation, it was argued that the rhythmic REMS phenomenon was a product of the separation.

REMS then showed that the separation was brought about by allowing drive to be released, but blocking the accompanying motor activity through a muscle tone drop out.

It was also argued that since the separation became a manifest necessity due to the threat of superior dinosaurians, it also had to serve a defensive function. This defensive function was identified in the phenomenon of narcolepsy, which also is REMS outside actual sleeping.

It was further argued that the depressive reaction, too, is a defensive reaction of the above mentioned type, and that it actually might be an arrested and prolonged case of narcolepsy.

But this would lead to the activation of another feature, namely the reduction of the organismic drive level according to the ratio between behavior and REMS. This could explain depression as a double phenomenon, where the first phase - the psychological defensive reaction of narcolepsy - is quite different from the second - the physiological drive lowering.

All this is, of course, speculation, though the hypothesis seems to fit most of the empirical facts. Whether it sticks or not, however, there seems to be a common context for sleep, narcolepsy and depression which should be found.

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