Reading list

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What does a cat dream about?

Michel Jouvet

When the neural systems which are responsible for postural atonia during paradoxical sleep are destroyed, sleeping cats periodically display stereotyped motor activity, revealing a rich repertoire of non-goal-directed 'oneiric behaviour'.

In birds and mammals there exist two states of sleep: slow wave sleep and paradoxical sleep (or rapid eye movement – REM – sleep). Although it is possible that dreaming may sometimes occur in man during slow wave sleep, numerous studies have shown that a subject awakened during paradoxical sleep (PS) will almost always describe a vivid memory of a dream. This subjective experience is still the only way to explore the content of dreaming, although electro-oculographic methods have revealed in a few cases some striking correlations between the patterns of REM and the scenery of the dream. These findings led to the "looking at the picture" or the "scanning" hypothesis of REM sleep[10], which we shall consider below.

It is the field of experimental neurophysiology that has permitted us, through a detailed analysis of the neural mechanisms of PS, to open the door to the ethological study of dreaming or 'oneiric behaviour' in the cat.

Paradoxical sleep – polygraphic aspects in the cat

The polygraphic features of PS can be divided into two components: *tonic* phenomena, characterized by fast low voltage cortical and olfactory bulb activity and a total disappearance of the electromyogram (EMG) of the neck muscles, an indication of postural atonia; and *phasic* phenomena, represented by high voltage slow waves in the pons, the lateral geniculate nuclei, and the occipital cortex (hence the name 'ponto-geniculo-occipital activity' or 'PGO waves'). This activity is directly responsible for REM[1] and indirectly related to other phasic peripheral phenomena like the twitching of the whiskers or the ears. But whatever might be the intensity of these peripheral phasic events, postural atonia prevents gross body movements, and on most occasions a dreaming cat lies totally flat on the ground and it is impossible to guess whether these phasic events are randomly distributed or whether they are part of some more organized motor activity.

Some executive structures responsible for paradoxical sleep

The pontine reticular formation is responsible both for PGO activity and for postural atonia since these two major indices of PS still periodically occur in chronic pontile cats[6]. From coagulation or kainic acid lesions, and microelectrode recordings and anatomical studies it has been possible to differentiate the postural atonia and PGO systems in the dorsolateral part of the pontine tegmentum[11].

The system commanding postural atonia is located in a small bilateral cluster of neurones in the medial part of locus coeruleus α and its immediate vicinity. These neurones, in which activity is selectively tied to PS, are connected through a descending pathway with the *nucleus magnocellularis* in the medulla. This nucleus corresponds to the inhibitory reticular formation discovered by Magoun and Rhines[8], and is ultimately responsible for postural atonia by acting upon spinal motoneurones[9]. However, a possible direct pathway descending from the locus coeruleus α to the spinal cord might also be mediating some inhibitory influences.

The PGO 'generators' are located very near the postural atonia command system. Ascending PGO activity originates in the *nuclei laterodorsalis tegmenti* and *parabrachialis lateralis*, and relays, at least in part, in the so-called 'region X' of Sakai[11], dorsal to the *brachium conjunctivum*, before reaching the visual system. This system is also connected with numerous other structures including the extrapyramidal system as shown by the PGO modulation of their unit activities. REM are under the influences of a lateroventral extension of the PGO generator located in the region of the *nucleus Kolliker-Fuse*.

Oneiric behaviour

Oneiric behaviour (Fig. 1) occurs after a selective bilateral lesion of the locus coeruleus α or its descending pontine pathway[4,7,13,14]. This lesion does not induce any alteration in waking or slow wave sleep. However, at the time the cat would enter PS with postural atonia, it suddenly raises its head and moves it horizontally or vertically as if it were watching something. This is not waking. The pupils are myotic and covered by the nictitating membranes as during PS, and the cat does not follow moving objects placed in front of it. At this time, and during the entire behavioural sequence, the polygraphic recording looks like PS without atonia: the EMG of the neck is increased, but other polygraphic indices of PS are present, namely fast low voltage cortical and olfactory bulb activity, and PGO waves. After the orientation reaction which starts oneiric behaviour other behavioural sequences follow in a totally unpredictable way[14]. Sometimes a sudden vertical jerk occurs so violently that the cat may knock the ceiling of the observation cage and awaken. More frequently the cat will stand up and go around the cage as if it were pursuing some prey. It may stop as if watching, with one of its front legs raised in the typical felid specific watching stance. Predatory attack characterized with either play-like pawing or cuffing may fol-

low; sometimes there may also be some biting without any goal (even if a dead or 'play' mouse is placed in front of it). Aggressive attack is accompanied by a greater intensity of foreleg movements, by downward position of the ears and opening of the mouth. Flight behaviour may also occur, with a typical semi-crouched posture. This can be followed by the most dramatic rage behaviour with arching of the back and piloerection. However, despite such emotional display, the pupils remain myotic. The other pattern of oneiric behaviour we have observed is grooming – either licking the forelegs or the floor of the cage (when the actions look like drinking). Grooming is also not goal-directed. If a piece of paper is fixed to the cat's fur, this will induce local goal-directed licking during waking, but whenever grooming occurs during PS, this objectivity does not occur.

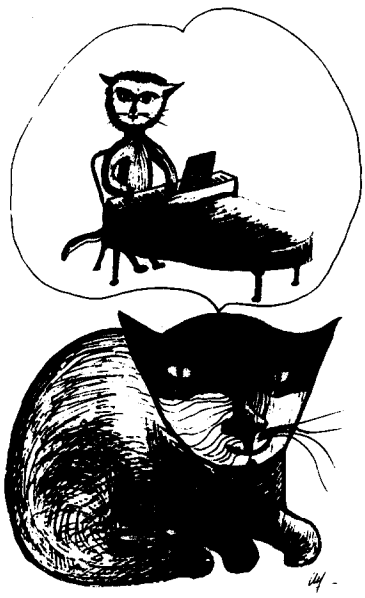
Each of these sequences may be followed by a short-lasting arousal and the cat returns to slow wave sleep. The succession of different sequences may last up to 5 min (which is the average duration of a PS episode).

We have never noticed, in more than 300 episodes registered on videotape, any sexual behaviour (erection in males or lordosis in non-oestrous females). Each cat seems to present a rather stable percentage of behaviours in its repertoire (on a weekly average). Some cats, however, which are always very friendly when awake, may have a high incidence of aggressive behaviour during PS.

Mechanisms of oneiric behaviour

Besides polygraphic recordings, other evidence indicates that oneiric behaviour occurs during atonia-suppressed PS. Indeed these activities can be suppressed by the same drugs which selectively suppress PS, such as monoamine oxidase inhibitors or chloramphenicol[13]. Thus it is most likely that the destruction of the system responsible for postural atonia has disinhibited a repertoire of motor activities which occur during PS, but are normally inhibited at the level of the spinal cord. Since these behaviours are not goal-directed, the main problem consists of delineating the internal mechanism which commands them. The PGO systems are good candidates for at least two reasons. First, there is a striking correlation between the bilateral PGO waves recorded in the pons, and the head and eye movements which follow them[13]. Secondly, destruction of the PGO generators in association with the locus coeruleus α decreases or suppresses PGO activity, and almost totally suppresses oneiric behaviour[13].

Considering the relationship between the PGO systems and oneiric behaviour, there are two possible hypotheses. The first one is germane to the "scanning" or "looking at the picture" hypothesis which was developed to explain the REM of dreaming in man, and may be summarized as follows. Ascending PGO activity impinging upon the visual system would be responsible for hallucinations (the visual scenery of dreaming) and the cat would react adaptively to these PGO-induced sensory events. Hence the name, 'pseudohallucinatory behaviour' which was first coined after the discovery of these episodes[7]. However this hypothesis must be rejected since the onset of REM recorded either in the oculomotor nucleus or in the lateral rectus muscle (during the orientation reaction at the begining of oneiric behaviour) *precedes* the onset of the PGO wave in the lateral geniculate by 20 ms[12]. Thus, eye movements cannot follow a putative visual hallucination elicited by ascending PGO activity. Moreover, it is well known that REM still occurs during PS in a pontile cat or after destruction of the ascending PGO pathway.



P.G.O. Programming?! Those stupid scientists will never guess that I dream about playing cat-chat-Turian.

According to the second hypothesis, the PGO generators would be responsible for the motor programming of oneiric behaviour. This being so, the following problems need to be solved. What are the mechanisms of this motor programming? Does a sensory processing also occur? What is the 'programmer'?

We do not yet know the structures involved in the execution of oneiric behaviour. They are unlikely to be situated only in the lower brainstem since, during PS without atonia, a chronic pontile cat will execute only walking or running movements[6], but will remain on its side during these movements, not presenting any orientating behaviour. Thus the oneiric behaviour of a pontile cat still exists, but is very primitive. In the normal cat, the PGO generators probably instruct only eye and head movements, and that more complex species-specific 'innate' behaviours are selected from a predetermined set of neural circuits involving suprapontine structures which are now under investigations.

It is more difficult to know if sensory or perceptual programming occurs during oneiric behaviours. The unitary activity of some neurones located in the amygdala, which respond only to the mewing of a cat during waking, increases selectively during PS[5]. Is it related to ascending PGO activity? Or does it relate to non-goal-directed

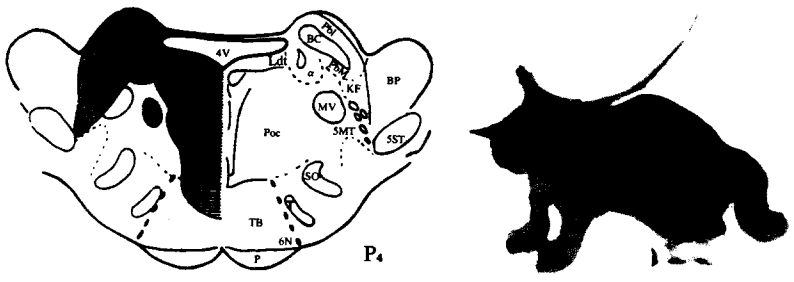


Fig. 1. Left. Frontal section of the pons of the cat in the Horsley-Clarke coordinate P4. The solid areas indicate the localization of the lesions which suppress postural atonia during paradoxical sleep. These lesions coincide with the locus coeruleus α (α) or its descending pathway. The horizontal hatching corresponds to lesions which do not suppress postural atonia. Right. Oneiric flight behaviour during paradoxical sleep three weeks after bilateral destruction of locus coeruleus α. Pbl: n. parabrachialis lateralis; Ldt: n. lateralis tegmenti dorsalis; PbM: n. parabrachialis medialis; KF: n. Kolliker-Fuse; Poc: n. pontis caudalis; BP: brachium pontis; 5MT: *motor nucleus of trigeminal nerve*; 5ST: *sensory nucleus of trigeminal nerve*; BC: brachium conjunctivum; 4V: *fourth ventricle.*

hallucinations? Finally, what is the putative 'code' of PGO activity? Does it relate to previous epigenetic events or is it related to genetic factors? There is some indirect evidence for both: on the one hand, some data favour a genetic coding of the PGO generator in mice, the only 'dreaming animal' in which genetic experiments can be easily performed. Indeed, the pattern of REM during PS (which depends directly upon PGO activity) is strikingly different in the C57BR and BALB/C strains provided that they are kept for a long time in isolation in the same environment[3]. On the other hand, recent events may also interfere with the patterning of phasic phenomena of PS, since deprivation of food or water slightly alters the patterns of tongue movements in mice[3].

The ethological description of the repertoire of oneiric behaviour in other species, such as the primates, would certainly help us to understand its significance and its possible diachronic modification during different processes of learning.

Whatever the function of oneiric behaviour (which is intimately linked with the function of PS), we have to accept this newly discovered class of behaviour among the growing list of innate behaviours that have been described by ethologists and which are not explicable by the stimulus-response paradigm of the Behaviourist School.

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[redacted]

During the last year various aspects of the controversy concerning the vesicular hypothesis have been aired in the columns of *Trends in NeuroSciences*. To bring this debate to a close, this month we are publishing a Commentary from H. Zimmermann (replying in the main to points put forward by Dunant and Israël in our April issue this year), an Overview from B. Collier, placing various experiments and views into an overall perspective, and a Review from P. Baker and D. Knight bringing in another aspect, namely the role of calcium in exocytosis, which has received little consideration to date.

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On the vesicle hypothesis

The first volume of *Trends in NeuroSciences* devoted considerable commentary space to the discussion of the validity of the vesicle hypothesis of neurotransmitter storage and release. Recently another commentary appeared in the same journal by Dunant and Israël[2] which criticizes further the vesicle hypothesis as well as the work of our group. I feel, therefore, that it is necessary to subject the experimental evidence which leads to a rejection of the vesicle hypothesis to a critical analysis; furthermore, I should like to present the readers with the experimental evidence which has encouraged us to support the notion of vesicular heterogeneity and which (in our opinion) has not been adequately referred to by either Marchbanks or Dunant and Israël.

Definition of the 'cytoplasmic' acetylcholine compartment

Subcellular fractionation has been used to determine the subcellular compartment from which acetylcholine (ACh) is being released. The synthesizing enzyme, choline

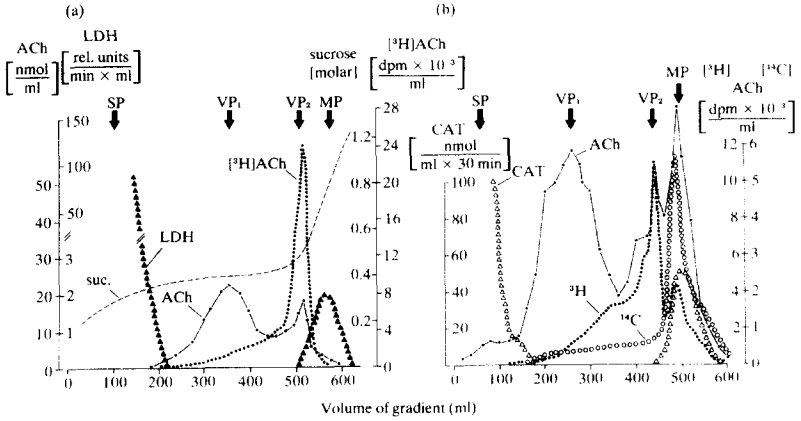

Fig. 1. Separation of two vesicle fractions with different turnover of ACh. (a) *Isolation of synaptic vesicles on a sucrose* (suc) *gradient (– –) after previous perfusion of electric tissue with [³H]acetate and stimulation (1800 pulses, 0.1 Hz). There appears a second, denser peak of ACh (not present in unstimulated controls where all vesicles sediment in the first vesicle fraction, equivalent to a density of 0.4 M sucrose) which contains the newly synthesized ACh (. . .). The enzyme marker for occluded cytoplasm, lactate dehydrogenase (LDH; ▲), is enriched in the membrane fraction and not in the second peak of ACh. Activity of cholinesterases and CAT (not shown) is also enriched in the membrane fraction. Using [³H]adenosine as a precursor, it can be shown by the same technique that the denser peak (VP₂) also contains the newly synthesized ATP[9].* (b) *Zonal separation of mixed parent fractions for the isolation of synaptic vesicles (containing [³H]ACh; . . .) and synaptosomes (containing [¹⁴C]ACh; ○○○). Two blocks of tissue derived from the same electric organ were perfused in parallel and labelled with [³H]acetate and [¹⁴C]acetate respectively. Stimulation was as for* (a). *There appears a third peak of ACh coinciding with the membrane peak which is enriched in the [¹⁴C]labelled ACh and the marker for presynaptic cytoplasm, CAT (△). The [³H]ACh is clearly enriched in a less dense part of the gradient and not together with the activity of CAT. Thus, this gradient separates the denser vesicles from particles containing presynaptic cytoplasm (and possibly cytoplasmic ACh).* SP: *supernatant peak;* VP₁ *vesicle fraction 1 which contains larger vesicles and little newly synthesized ACh;* VP₂: *vesicle fraction 2 which contains smaller vesicles and a newly synthesized ACh;* MP: *membrane peak containing membrane fragments as well as particles with included cytoplasm. The values for ATP are not given in this figure, but are contained in the article[11] from which these data are derived.*