INVITED REVIEW

PHYSIOLOGY OF DREAMING

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Dreaming has been a subject of cogitation since remote Antiquity. In ancient Greece, Socrates, Plato and Aristotle discussed about the meaning of dreams, concluding that the prevailing mistic and mythic concepts about them were incorrect. Instead, they thought that dreams were not provoked by spirits, ghosts or gods, which took over the mind to express themselves through dreaming. Aristotle (ed. 1991), who had carefully observed several animal species while asleep, noticed that movements of several of their body parts were quite similar to those performed by humans during dreaming. Some of his statements, hereby reproduced in a simplified form from his book on sleep and dreams, briefly illustrate his contribution to the study of this subject:

"All creatures that have four limbs and are sanguine (mammals) *display signs that they dream while asleep. It seems that not only humans but also dogs, cows, sheep and goats and the entire family of four-legged viviparous animals do dream."*

"As to the oviparous creatures, it is obvious that they sleep but it is impossible to state that they dream. The same holds true for animals that live in water, such as fishes, molusks, crustacea and other similar animals; it is impossible to invoke as a proof that they do sleep the shutting of their eyes, inasmuch as they do not have eyelids but it is obvious that they periodically do rest, immobile, what perhaps does explain why at night their predators attack them heavily and devour them. When they sleep, fishes keep quiet, *with no apparent movements, and then they can be easily fished with a hand."*

"Insects are also creatures that do sleep, so much so that they can be seen resting with no movements whatsoever. This is specially true as to bees, that at night do interrupt their hum, "even if they are exposed to the light of a lantern".

"Dreams are not ghosts (phantasmata), since they are closely related to the events of the previous day."

In Greece dreams were called *oneiros*, a word that originated the adjective *oniric* but that meant not exactly what was dreamed about neither the dreaming process, which was not rated as something important, but the *phantasmata*, i.e. the apparitions. As a prevailing concept even today, dreams were considered premonitory, messages from the dead and mystical warnings. Herodotus, in his *Histories*, the first textbook on History ever written, tells that the Persian King Xerxes dreamed quite often about the war he was about to fight against Athens. He properly related such dreams to his concern with that important war. His personal oracle, however, disagreed and convinced him that his dreams were warnings from the gods. Xerxes, in fact, had discovered an important aspect of dreams but his oracle discarded such an explanation, in favor of the mystic one.

In the past, most civilizations boasted having wise people who could tell the meaning of dreams if conveniently paid for that, a fancy profession that still has its counterparts in modern nations. Psychoanalysis considers

dreams as an important window to the unconscious world, what makes dream interpretation a crucial factor in psychonalytic diagnosis and treatment. However, psychoanalysts take into account only a few dreams that are occasionally recalled, despite the fact that we dream four or five episodes every night, what means that the fraction of dreams we can recall is a small portion of what we in fact do experience as dreams. Psychoanalysis also considers dreams as the expression of repressed wishes; this is undoubtly true as to only a few dreams, whereas several studies reveal, instead, that most dreams are closely related to the events of the previous day, as Aristotle had already demonstrated.

Socrates, Plato, Aristotle and Xenophanes, nearly 2,400 years ago, were opposed to the prevailing view of the *phantastikon,* that is, mystic apparitions, and to the premonitory character of dreams as their main characteristics. However, they ignored that dreams were produced by the brain. Hippocrates and Alkmaeon, who discovered that the mind is in the brain, not in the heart, knew that dreams were originated in the brain. Later, the Roman writer Lucretius, the first popularizer of science, in his book *De Rerum Natura* (1978) credited these Greek philosophers for the discovery of the characteristics of sleep and dreams. Plato, despite his logical view of dreams, antecipated by 24 centuries one of the dogmas of psychoanalysis, stating that the dreams with a sexual background, mainly those with an incestuous content, and those in which the dreamer attacked or even killed someone, did, in fact, represent occult wishes that only could be fulfilled without punishment as an oniric experience. During the second century of the present era, Galen, a Greek physician who practiced Medicine in Rome and was a great anatomist and clinician, knew that temperature, heart rate and respiration exhibited cyclic changes at night, which he attributed to dreaming (Rothschuch, 1953).

During the medieval era in Spain, by then the very cultural center of Europe (probably of the entire world), and mainly in the 13th century, some Muslim Arabs and Jewish rabis, centered in Cordoba rediscovered the Greek literature, that had been concealed by early Christianism, and translated all that important work into Latin, Arabic and Hebraic. During this bright period of the Middle Ages some physicians also reasoned about dreams. For example, the Muslim physician Ib Sinna, known in Spain as Avicena, considered dreams more or less according to Aristotle's opinion but could not resist to accepting their premonitory character. The ancient Chinese scientific inquiry tried to understand dreaming but usually also considered them mistically.

During the nineteenth century several physiologists and neuropsychiatrists tried to understand the mechanisms and meaning of dreams. McNiss, in his book *Philosophy of Sleep*, published in 1854, agreed with Aristotle, regarding eye movements as a consequence of visual dreams, and Pinkerton, in *Sleep and its Phenomena*, also took the facial movements of

dogs and cats during sleep as a manifestation of dreams (De Sanctis, 1899; Gardner et al., 1975). An important contemporary of these authors, Charles Darwin, in his landmarking book *Emotions in Man and Animals*, published in 1872 and reedited several times in the twentieth century (Darwin, 1965), states that "*at least* birds and mammals do dream", a concept that still remains unchallenged, despite which most researchers that carry out studies on sleep still hold that dreaming is specifically human.

At the end of the 19th century several authors published on oniric activity. Esquirol, one of the French psychiatrists who started the revolution that changed the ancient (a cruel) view of the mental diseases, spent several hours at night observing how his patients behaved during sleep and concluded that their movements while asleep were related to their dreams, just as Aristotle had found long ago. The American psychologist Mary Whiton Calkins published in 1893 an important, although entirely unkwnown, article under the title *Statistics of Dreams*, wherein she introduced the technique of arousing people when they moved parts of the body during sleep and asking them to report their dreams (De Sanctis, 1899; Timo-Iaria, 1997). Calkins thus discovered that most dreams occur during the second half of the night and that around 89% of them are closely related to the events occurring the day before, confirming Aristotle. Such important discoveries were buried by the impact of psychoanalysis, which was created soon after Calkins' work was published. Weed

& Halam listed in 1896 (De Sanctis, 1899; Timo-Iaria, 1997) the proportion of several kinds of dreams as related to their sensory content. Their data do not depart from modern studies of the same kind.

De Sanctis, in 1899, in his book *I Sogni, Studi Clinici ed Psicologici di un Alienista* (*Dreams, Clinical and Psychological Studies of a Psychiatrist*), cites no less than 323 articles and books dealing with dreams, which proves that the objective study of dreams did not start during the middle of the 20th century, as is usually taken for granted. De Sanctis, whose main research on sleep was the incorporation of sensory stimulation into dreams, states in his book that "by measuring the pulse and observing the movements in humans and other animals during sleep it is possible to detect the occurrence of dreaming and sometimes even to guess the dream content". Inasmuch as all this relevant knowledge is entirely ignored, we hope the present review may help in rescuing it.

Around 1860, Kohlschütter, a young medical student in Germany, showed that the threshold to awake humans by auditory stimulation oscillates along the night (De Sanctis, 1899; Kluger, 1997). In 1867, Michelson, a physiologist who was a relative to Kohlschütter, replicated his study and obtained the curve shown in Figure 1 (De Sanctis, 1899; Kluger, 1997). The oscillation of the sleep depth as cycles, as is well known presently, is quite clear in this figure. The first oscillation lasts around two hours, when sleep attains its deepest level; the ensuing cycles last less and

their depth tends to decrease until arousal finally occurs, a sequence that recent research has fully confirmed.
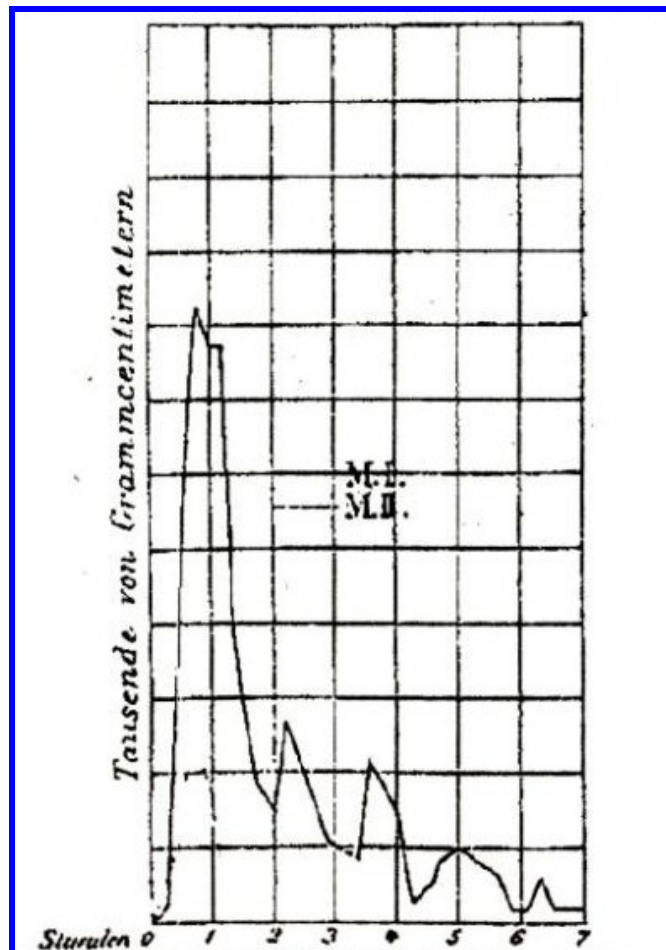

Figure 1 Depth of sleep, as originally expressed by Eduard Michelson in 1897 and evaluated through the intensity of sound able to produce an arousal. Sound was produced by a bang and measured as pressure exerted on a plate. In the ordinates, pressure in Kg *x* centimeter; in the abscissae, hours. (*Reproduced from Kluger 1997*).

During the first half of the twentieth century, despite the heavy influence of psychoanalysis, dreaming was again but sporadically studied scientifically. In 1926, for example, Denisova & Figurin (cit. Kleitman, 1963), recording heart and respiratory rate of sleeping children, found that both changed cyclically, what is presently known to occur as vegetative components of dreaming activity. In 1944 Obhlmeyer, Brilmayer & Uhlstrung (cit. Berlucchi, 1971) observed that in humans penile erection occurs during sleep at intervals of 85 minutes, which is the average duration of a sleep cycle. Penile erection, which also occurs in monkeys, is present

during *desynchronized* (*paradoxical* or *REM-sleep*) but it is not necessarily linked to erotic dreams. In rats penile erection in desynchronized sleep has also been detected and was found to cease after spinal transection; following mesencephalic transections that spare desynchronized sleep, penile erection was deeply reduced (Schmidt et al., 1999). However, reflex penile erection is facilitated after spinal transection whereas mesencephalic transections significantly increase the latency to its reflex induction, without affecting the percentage of tests eliciting an erectile event. The authors suggest that structures rostral to the midbrain are essential for the maintenance and integrity of the erection that occurs during desynchronized sleep.

It is well known that during desynchronized sleep the pupil undergoes an increase in diameter (midriasis), which is not produced by direct sympathetic activation but rather to parasympathetic inactivation, that overcomes the tonic pupillary constrictor activity of the parasympathetic system during synchronized sleep.

In 1936, Klaue (cit. Jouvet, 1986) described periods of sleep in cats characterized by high frequency electrocorticograms that he considered as a sign of deep sleep and in 1950 Passouant described a phase of *desynchronization* (a term coined by Adrian to label an increase in frequency with a decrease in voltage) of the EEG potentials in humans. Such periods were overlooked in the classic studies of Loomis and co-workers (1938), in which they identified the phases of *synchronized* (another term coined by Adrian but now to label slow waves, i.e., potentials with a low frequency and a high voltage) sleep. Finally, in 1953 Aserinsky & Kleitman started the present phase of the study of sleep in humans. They found that during the *desynchronized phase* there occur eye movements, the reason why such phase has been given the name of *REM-sleep*. Jouvet and colleagues (1959) soon identified the same phase in cats, naming it *paradoxical sleep*, inasmuch as the electrophysiological main pattern of this phase in humans resembles that of attentive wakefulness. Moruzzi's coined the name *desynchronized sleep*, which we prefer, because in humans desynchronization is the main electrophysiological marker of this phase. However, considering the high prevalence of dreams during this phase it should be more appropriately named *oniric phase of sleep*.

Animal experimentation, by making it possible to implant electrodes in any part of the nervous system and to lesion and stimulate (electrically or chemically) also any nucleus or pathway, has been of the utmost relevance for the understanding of the mechanisms causing not only sleep but also the manifestations of dreaming. Unfortunately, despite the opinion of great scientists of the past, most researchers that deal with sleep and dreaming, probably moved by philosophical, religious prejudice and a faulty reasoning, do not accept the

idea that non-human animals do dream. With Darwin (1965), we are fully convinced that "*at least birds and mammals do dream*". As a matter of fact, manifestations of dreaming have been identified in many species, including chickens, chimpanzees, cats, rats and in some birds. While humans dream around 100 minutes every night, cats exhibit signs of dreaming during nearly 200 minutes per day. Desynchronized sleep has been identified in many mammals and birds (Klein et al., 1964) but below the birds only in crocodiles brief periods of an equivalent phase (eye movements, low voltage electro-oscillograms and cervical hypotonia) seem to occur (Peyrethon & Dusan-Peyrethon, 1969). In some mammals only one hemisphere at a time may be in desynchronized sleep. In cats, Thomas & Benoit (1967) have found oniric activity during synchronized sleep, similar to what we described in rats as *pre-paradoxical sleep* (Timo-Iaria et al., 1970; Gottesmann et al., 1984) as *intermediate phase*.

WHAT IS A DREAM

A dream is a conscious experience that occurs during sleep. Although it may happen in any sleep phase, it prevails during the desynchronized phase.

The very essence of dreams is, certainly, memorized information. As shown in Figure 2, information released (by some passive mechanism) or revoked from memory (through some active but entirely unknown mechanism) is combined by processes that may be equivalent to, but different from, those that produce thoughts during wakefulness (Timo-Iaria & Valle, 1995). As any neural information, it has to be analyzed, so that the nervous impulses, which carry it be decoded and integrated as a specific neural configuration, that contains all the information released (or revoked) from the mnemonic archives. Such a configuration is subsequently compared to memorized patterns and then, and only then, it can be identified by means of the conscious process. *The result of such conscious identification is a dream*. As any information consciously identified, a dream triggers a specific behavior, that we call an *oniric behavior*.
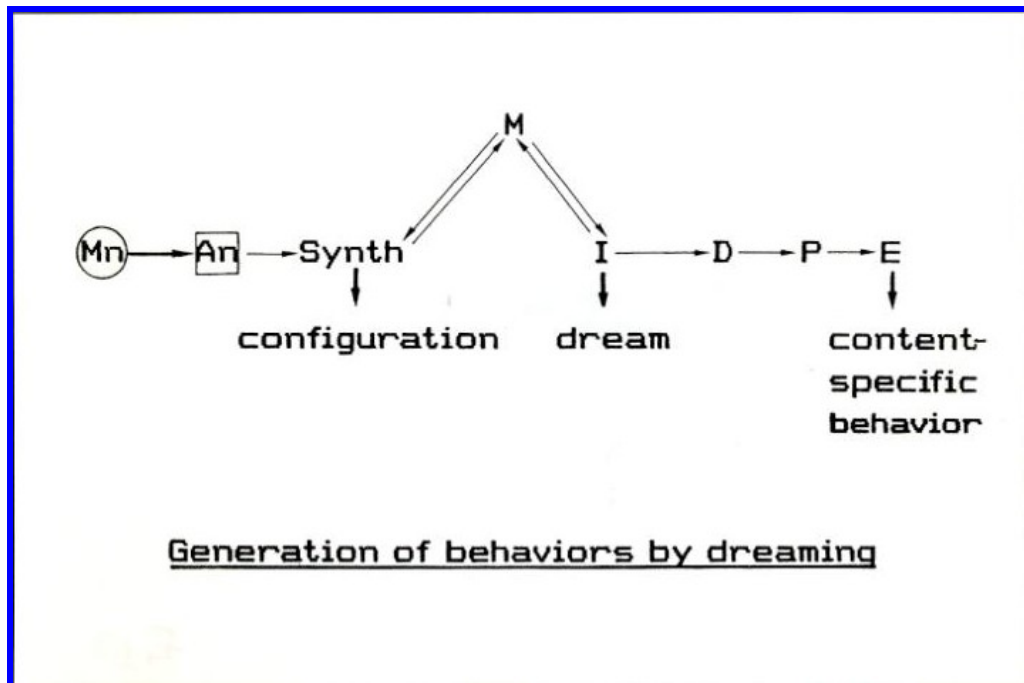
Figure 2. Flowchart of steps that probably generate a dream and the consequent oniric behaviors. *Mn*: memorized information in mnemonic archives. *An*: analysis of such information. *Synth*: specific synthesis as a neural configuration of the information released (or retrieved) from memory archives after it has been analyzed. *M*: memory (expressed as *M* instead of *Mn* to mean memorized patterns). *I*: identification of the synthetized pattern after its matching with memorized patterns, the result of such identification is the dream. *D*: decision. *P*: programming. *E*: execution of the oniric behavior. (*Modified from Timo-Iaria & Valle 1995*).

In humans a dream may be reported and its content can thus be analyzed. Recall of dreams is much greater and the report is much more detailed when one is awakened *during* desynchronized sleep and the stage I of synchronized sleep, right after alpha waves disappear and are replaced by a lower frequency and lower voltage electro-oscillographic pattern (Dement 1955; Dement and Kleitman, 1957; Vogel et al., 1972). A correlation has been proposed between the development of desynchronized sleep in children and their waking cognitive maturation (Foulkes, 1982). This author reported that dream production in human

subjects from 3 to 5 years of age was minimal and that the content of the dream reports generally consisted of "static imagery" in the absence of narrative context. Consequently, Foulkes concludes that they do not dream but this conclusion is probably incorrect, inasmuch as at this age children have a highly limited narrating capacity and their poor reports about dreams are certainly linked to such a limitation, not their absence. At the age between 7 and 9 years Foulkes' subjects produced much more consistent narrations of the dream content, as should be expected.

Researchers working on dream usually do not believe that dreaming may occur in non-

human animals, probably due to religious and philosophical reasons but also to a great mistake, i.e., that dreaming is a high level mental activity, such as doing mathematics, but it is not. It is most likely an elementary brain activity in homeotherms and thus, if dreaming has a function, it probably plays a similar role in the human brain and in non-human brains as well.

In non-human animals the report regarding dreams is obviously impossible but, fortunately, a dream can be detected in both humans and other species by analyzing its motor, vegetative and electrophysiological manifestations, as will be described below.

Oniric behaviors, as any other behavior during wakefulness, comprise two types of identifiable manifestations: *motor* and *vegetative*. The *motor components* are usually weak and poorly expressed movements during a dream, mainly if it occurs during desynchronized sleep; when a dream takes place during synchronized sleep phase I, near wakefulness, not only movements are more faithful to the dream content but also the latter is much more logic. The *vegetative components*, that are phasic increases of heart rate, blood pressure, respiration, pupillary diameter, and most probably metabolic adjustments as well, are expressed more consistently during a dream, as they are during attentive wakefulness. The reason for such vegetative adjustments is obviously that the nervous tissue is metabolically very demanding, so much so that 20% of the inspired oxygen goes

to the nervous system. Therefore, any neural event, be it running or just thinking, or dreaming, requires a large amount of oxygen, which is carried to the nervous system by the blood through powerful hemodynamic adjustments, such as increase in blood pressure, heart rate and central blood flow (Cravo et al., 1995; Decety et al., 1993; Timo-Iaria & Valle, 1995). When a dream is a nightmare, both motor and vegetative events may be very intense. In some animals, however, a reduction of heart rate and respiration may occur, what also happens during an attentive wakefulness if they are threatened. In such a condition, the brain produces a behavior that immobilizes the animal, in order to simulate it is dead and may thus become uninteresting to a predator, which is in search of fresh flesh.

Recordings of electrical activity of the brain, which we will refer to as *electro-oscillograms*, reveal specific patterns that express the phases of sleep in several central regions of the brain, including the phase during which most oniric activity takes place, the *desynchronized* or *paradoxical sleep*. Desynchronization is the rule, during this phase, in all cortical electro-oscillograms in humans and other primates. In cats, cortical electro-oscillograms are also desynchronized but in the hippocampus *theta waves* (that will be later described) predominate. In rats only the frontal cortex presents desynchronization whereas in all the remaining cortex, and in many subcortical

sites, the electro-oscillograms oscillate as theta waves.

Analysis of the electro-oscillograms yields extremely relevant information that can be correlated with movements and changes in heart rate, blood pressure and respiration. If, as an advantage, in humans such manifestations of dreams can be related to their reported content, in non-human animals it is possible to record with a high degree of accuracy not only the motor and the vegetative manifestations of dreaming but the electro-oscillograms of many central structures as well. Hence, experiments with such animals are extremely valuable and thus will be emphasized in the present review.

Motor components of dreaming

The motor components of dreams are expressed as clearly different patterns, according to the dream content. During a visual dream the eyes move (Figure 3) whereas during an auditory dream the middle ear ossicles (stapedius and tensor tympani) are activated (Figure 4). When a dream has a verbal content the tongue, lips and other facial muscles do contract and if the dream is deambulatory several lower limb muscles do contract, expressing the behavior triggered by the imagined walking. Visual dreams provoke eye movements. Although such movements are not always obviously compatible with the dream content (Oswald, 1962), as should be expected (see below), as a rule they can be related to the dreams.
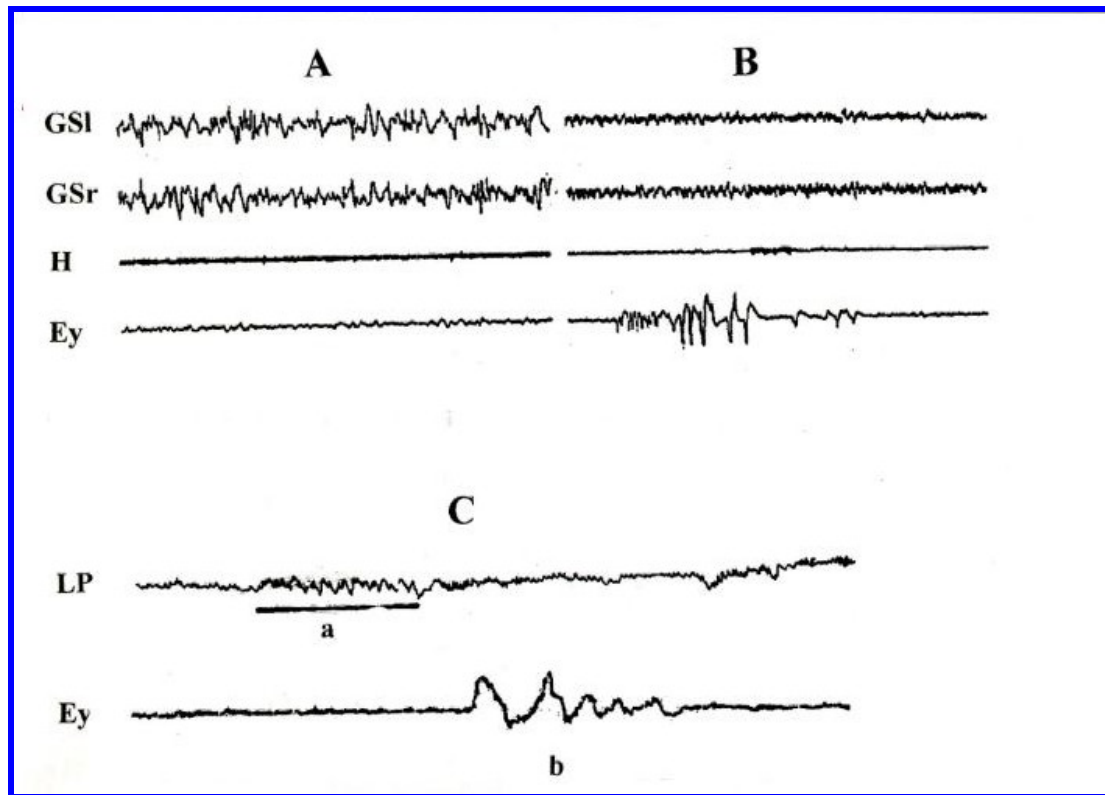
Figure 3. *A*: synchronized sleep of a cat. Notice spindling and delta waves that characterize phase SII and absence of movements. *B*: desynchronized sleep a few minutes after the previous phase, showing light motor activity of the neck muscles (trapezius) but intense eye movements. *C*: saw-thooth waves in the electroencephalogram from the right parietal cortex (human), followed by eye movements. *GSl*: left sigmoid girus. *GSr*: right sigmoid gyrus. *H*: electromyography of the trapezius muscles, expressing head movements. *EM*: eye movements.
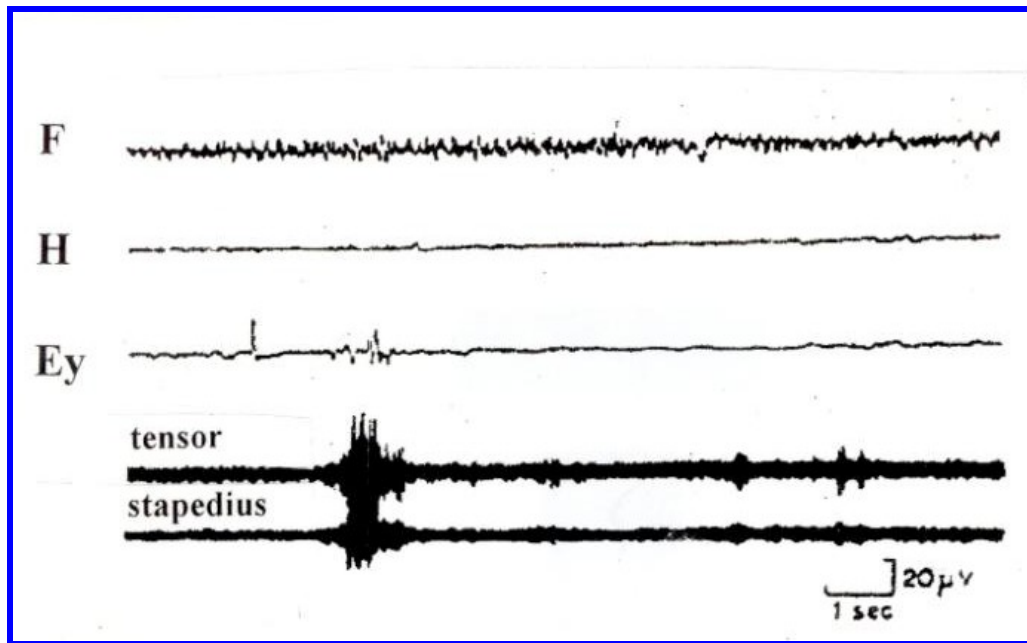
Figure 4. Episode of desynchronized sleep of a cat. The frontal electro-oscillogram (*F*) is desynchronized, the neck electromyogram (*H*), which expresses head movements, shows a very weak activity whereas eye movements (*Ey*) are intense. Concomitantly with the eye movements the tympanic muscles (tensor and stapedius) exhibit a powerful activity, which is suggestive of a dream with auditory components (*Baust, 1971*).

In 1937, Fenn & Bursh, recording the eye movements while their subjects closed and opened the eyes, found that the voltage (*V*) of the potentials that expressed the movements were proportional to the angle of rotation

$$V = k.2.sen\alpha$$

in which *V* is the voltage of the recorded potentials, *k* is a factor of proportionality and *a* is the angle of rotation. Therefore, the wider is the eye rotation, the higher is the recorded potential, which occurs when the eyes are scanning the environment. The narrower is the angle of rotation, the lower is the recorded potential, which happens when attention is being directed to a very small part of the object or when the object is very near. By measuring the voltage of the potential generated by the rotation it is possible to know if the object is near or far. Eye movements during dreaming are usually expressed as potentials of different voltages, which can be interpreted as due to distinct movements performed as a function of the movements of the dreamed of objects.

Vanni-Mercier and co-workers (1994) believe, however, that in cats eye movements during desynchronized sleep are in general asymmetric, that is, the eyes tend to move preferentially to one side of the visual field, what, according to these authors, disprove the hypothesis of the scanning character of eye movements during dreams. Our experience with eye movements

in rats (Valle et al., 1992; Timo-Iaria et al., 1990; Valle et al., 2002) and cats (Hernández-Peón et al., 1963) shows, however, that eye movements are sometimes asymmetric but in other occasions they tend to be of the scanning kind. The preferential eye movements direction may be related to the dream content and, perhaps, as such also to hemispheric dominance but it should always be taken into consideration that *any movement originated by a dream is always faulty, otherwise we would perform normal behaviors during a dream, what does not happen due to the inhibition of motoneurons*. If we dream we are walking, the electromyographic recordings from muscles involved in such behavior show quite clearly that they are not able to produce normal movements. In humans, Hansotia and colleagues (1990) found in humans, in accordance with our own observations in rats and cats, that oniric eye movements may be directed to one side or the other, not exclusively to one side, as stated by Vanni-Mercier and co-workers (1994).

Eye movements in humans predominate because vision is our main sensory channel and our visual memory is overwhelmingly predominant, resulting in preponderance of visual dreams. As will be shown below, in rats, that are macrosmatic animals, rostrum (snout) movements predominate during desynchronized sleep over eye movements (Timo-Iaria et al., 1990; Valle et al., 2002). Miyauchi and colleagues (1987) suggested the occurrence of two kinds of eye movements

during dreams, one associated to the very dream content, another of reflex nature, that may be involved in those occurring in children and in blind people but such a hypothesis is unlikely to be valid. Eye movements in born-blinds are probably due to a quite different reason. Vision is our predominant sensory channel, so much so that if we hear a sound we immediately convey the eyes to the source of the sound, trying to identify its origin, even if vision is absent. Similarly, in rats any kind of sensory stimulation does immediately mobilize sniffing and vibrissal scanning movements. No wonder that most dreams in humans have a visual component, explaining the reason why eye movements occur in any kind of dream, alone or as part of non-visual dreams. In nocturnal macrosmatic animals, olfaction is the predominant sensory channel and their vibrissae are usually very long, to detect the presence of objects at relatively large distances. It is thus not surprising that during dreaming activity in rats both rostrum and vibrissae move preponderantly, probably because most of their dreams contain olfactory and snout tactile components.

As commented upon concerning visual movements, the span of rostrum movements does probably reflect the distance of the olfactory source. If the animal is trying to identify the source of an odor that is located at a large distance, snout movements are expected to span wide angles at low frequencies, whereas when the source is near such movements are expected to span narrow

angles, at high frequencies, just as during wakefulness.

Roffwarg and co-workers (1973; see also Roffwarg et al., 1975) have recorded contraction of the tympanic muscles (stapedius and tensor tympani) during human sleep. Around 80 per cent of such motor activity was found to occur during desynchronized sleep, what points to its participation in dreaming activity. In blind people, whose auditory and somesthetic sensitivity is enhanced, auditory dreams predominate, as expected from their high auditory sensibility. In cats, tympanic muscles sometimes contract during desynchronized sleep (Baust, 1971), as shown in Figure 4. This may well reflect auditory dreams, as has been found in humans (Roffwarg et al., 1973; Roffwarg et al., 1975). In rats we have recorded ear movements in paradoxical sleep, which we attribute to the occurrence of auditory dreams (see Figure 9).

Head jerky movements may reflect vestibular dreams. Doneshka & Kehaiyov (1978) reported dreams with striking vestibular sensations. In normal humans they found that around 20% of the dreams contain a vestibular component (vertigo, sensation of head drop) but in people with a vestibular illness the proportion of such dreams increased to over 70%, as expected from the close relationship between dreams and the events occurring in the previous day.

Dreams in which walking occurs are very common (De Sanctis 1899; Gardner et al.,

1975) and coincide with limb movements, however faulty. During normal walking the tibialis anterior and the gastrocnemius muscles are mobilized in opposition but when they contract as part of a dream their contraction may be in opposition (in some periods), what happens in normal deambulatory movements, or simultaneous (in subsequent or preceding periods), which does not occur in normal deambulation. Such patterns mimic oniric eye movements, which may occur in functional coincidence or not with the visual scenes that are dreamed of.

The correlation between dream content and the oniric movements was first studied by Aristotle, who *identified lip, eye and limb movements and correctly related them to what was being dreamed of*. Many studies performed during the eighteenth century confirmed such statement (see De Sanctis, 1899 and Timo-Iaria, 1997). Several authors also quantified the kinds of dreams as related to their sensory content. In 1896 Weed & Halam (cit. De Sanctis, 1899) published the first quantification of dreams content. During the past two decades several authors also did quantify the kinds of dreams. Table I shows the results of some of such studies, including our data concerning nearly 2,000 dreaming episodes recorded from rats. Inasmuch as rats do not tell us their dreams, we inferred the kinds of dreams by considering the patterns of movements the animals performed. The data reported in table I reflect a close distribution of the dream content as related to their sensory content.

56

Its is noteworthy that Weed & Halam's data, published in 1896, are close to those reported by Rechtschaffen & Buchignani in 1992, which was calculated as the mean of the average of seven different studies published by other authors.

It should be recalled here that, comparing the dream content in humans with events of the previous day, Calkins found in 1876 that nearly 89% of the reported dreams were closely related to such events.

Table I. Proportion of the types of dream, as a fraction (percentage) of the total, according to their sensory (in humans) or motor (in rats) manifestations.

	Proportion of the dream patterns according to their sensory or motor content			
	Weed & Halam	McCarley & Hoffman	Rechtschaffen & Buchignani	Valle, Pellarin & Timo-Iaria
	(human, 1986)	(human, 1981)	(human, 1992)	(rat, 2002)
	mean%	mean%	mean% of the mean of 7 studies	mean%
Visual	84.4	100	100	18.3
Auditory	67	64	69	1.6
Tactile	10.8	1	11.5	---
Olfactory	---	1	1	48.8
Gustatory	6.7	1	<1	---
Thermal	---	4	---	---
Vestibular	---	8	---	1.1
Forelimb	---	---	---	3.1
Hindlimb	---	---	---	0.7

The reason why when we dream that we are walking we do not get out of the bed and really walk, or when we dream that we are talking to someone we do not really talk, is that neural circuits located in the neighborhood of locus coeruleus, in the pontine tegmentum, inhibit the motoneurons and do not allow the real movements to occur. However, we still do not know why most motor units are inactivated while a few ones are mobilized, *causing real but incoherent and non-efficient movements*. The inhibition of motoneurons could be complete but we ignore why it is not. Fortunately, thanks to this peculiar incomplete motoneuron inhibition we are able to record movements occurring in both humans and non-human animals and thus infer the presence of dreams. Unless we agree that such movements in human and in non-human animals are manifestations of dreaming activity, it is impossible to explain

the electro-oscillograms and the movements that both classes of animals exhibit during desynchronized sleep.

Plotting the amplitude of the Achillean reflex of cats during sleep Pompeiano (1967) found that while the animal coursed synchronized sleep, this stretch reflex was almost normal, only slightly reduced as compared to its intensity during wakefulness. However, during desynchronized sleep it was drastically reduced, being entirely inhibited for most of the time. A powerful defensive behavior, the withdrawal "reflex" (or *retraction behavior*, as we prefer to call it), is also completely inhibited during this phase of sleep. In humans, both reflex activities are also deeply inhibited during desynchronized sleep. Yet, it is well known since Kohlschütter and Michelson (see De Sanctis, 1899 and Kluger, 1997) that the threshold to awaken a human being during desynchronized sleep is much lower than the one to produce wakefulness during synchronized sleep. It seems that a systematic investigation regarding the threshold to different types of stimulation is still lacking and should be performed, in order to establish which kinds of stimulation and effective thresholds are able to awaken humans and non-humans during sleep. It is likely that even strong stimuli may be ineffective in producing an arousal during sleep if they are trivial, whereas light stimulation containing relevant information may be highly efficient. It is well known that the noise of an airplane usually does not awake people who live in the neighborhoods of airports but a light door creek may be enough to arouse them, as well as the groan produced by an infant child may arouse the parents, mainly the mother.

The tonic inhibition of motoneurons by circuits in the alpha-coeruleus nucleus during desynchronized sleep is mediated by hyperpolarization of their membrane (Pompeiano, 1967; 1976; see also Chase & Morales, 1990). This hyperpolarization is due to an increased motoneuronal membrane permeability to chloride ions, which suggests that glycine or γ-GABA are released on the motoneuronal membrane during desynchronized sleep (Kubin, Davies & Pack, 1998). In cats, during movements related to dreams such hyperpolarization is reinforced by presynaptic inhibition of afferents to motoneurons.

Afferent transmission in the somesthetic pathways is inhibited during desynchronized sleep (Baldissera, Cesa-Bianchi & Mancia, 1964; 1966; Baldissera & Broggi, 1967) and may be the main reason of the powerful inhibition of stretch reflexes in desynchronized sleep. In the somesthetic system inhibition occurs at the very first central neurons in the sensory pathway (both spinal and in the brain stem) and appears as a reduction of evoked potentials in the medial lemniscus when peripheral afferents are electrically stimulated (see Pompeiano, 1967). Accordingly, the H reflex, an equivalent to the Achillean reflex that is provoked not by stretching the gastrocnemius tendon but by applying electrical pulses to its

afferents in the sciatic nerve, is highly depressed during this phase of sleep (Hodes & Dement, 1964).

Muscle atonia during desynchronized sleep is, as stated above, generated in the alpha-coeruleus nucleus and involves both direct and indirect pathways that inhibit the motoneurons. A direct pathway arising in the region of the coeruleus complex that projects to the bulbar medial reticular formation was described by Magoun & Rhines (1946) and does heavily inhibit motoneurons. Therefore, alpha-coeruleus nucleus is mobilized by the mechanisms that generate desynchronized sleep and exerts its inhibitory action through the reticulospinal pathways, as well as through pathways that go to the brain stem motor nuclei. By lesioning the alpha-coeruleus nuclei such an inhibitory effect is prevented and during oniric activity the movements generated by the dream itself can be expressed, as was clearly demonstrated in Jouvet's Laboratory (see Sakai et al., 1979; Sakai, 1981) in cats; the animal suddenly gets up, walks, miews and strikes with the paws, as if the animal were awake.

Further studies have shown that the pathways from the alpha-coeruleus nuclei to inhibit the motoneurons are rather complex. Electrical stimulation of the nucleus reticularis pontis oralis evokes bilateral muscle atonia in decerebrate cats (Oka, Iwakiri & Mori, 1993). Neurons from the nucleus reticularis pontis oralis send fibers to nucleus reticularis gigantocellularis in the medulla, a part of which passes through the dorsal tegmental field of the pons, and electrical stimulation of both nuclei also produces inhibition of muscle tone (Mori, Shik & Yagonitsin, 1977; Takakusaki, Ohta & Mori, 1977). Axons from neurons of the nucleus reticularis gigantocellularis descend along the ventral and ventrolateral funiculi and connect with inhibitory interneurons in the spinal cord (Matsuyama et al., 1993; Mori et al., 1992). These interneurons inhibit motoneurons by means of glycinergic synapses (glycine is a powerful inhibitory neurotransmitter), as shown by Soja and collaborators (1991). Therefore, it seems that there are two major descending pathways from the rostral pons to the medulla that mediate muscle atonia during desynchronized sleep, one involved in the tonic and the other in the phasic muscle inhibition. Lesion of the alpha coeruleus nucleus impairs the tonic motor inhibition; lesion of the pedunculo-pontine tegmental nucleus impairs the phasic motor inhibition (Shiromani, Lay & Siegel, 1990; Kohyama, Shimomira & Iwakawa, 1994).

It is interesting to consider that while muscles all over the body are paralyzed during sleep, respiration is little affected, except that some muscles in the upper respiratory airways are inhibited during sleep (Kubin, Davies & Pack, 1998). Respiratory frequency decreases during the entire sleep cycle but is phasically activated during dreaming because it is a vegetative function

that has to be increased in any behavior, including the oniric ones.

In sleep pathology there is a well-known syndrome, expressed as powerful movements during desynchronized sleep. Such movements may take the sleeper to fall off the bed. Although it has not been shown that the alpha-coeruleus nuclei are lesioned in these patients, it is tempting to consider that their lesion underlies such sleep disturbance.

The motoneuron inhibition, responsible for the sleep atonia and abolition of movements, is not complete in infancy (Figure 5). Motoneuron inhibition is mild in the early post-birth days and increases according to a saturation curve (Kohyama, Shimohira & Iwakawa 1997). From a very weak inhibition in early infancy, it goes up rapidly up to 15 years of age, evolving asymptotically from this period on.
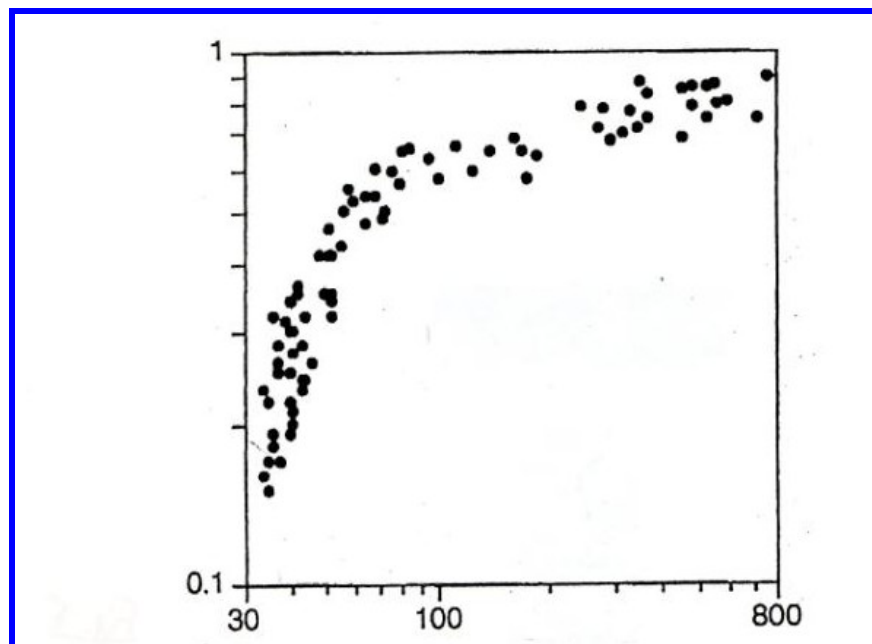

Figure 5. Relative degree of motor inhibiton during desynchronized sleep as a function of age. Maximal inhibition (which is not complete, thus allowing eye, limb, lips, tongue etc. movements to occur during dreaming) is reached around 15 years of age (*Kohyama, Shimomira & Iwaka 1997*).

Vegetative components

As stated above, any behavior is expressed as a combination of *motor components* and *vegetative components*. The latter are absolutely necessary for any neural activity to occur, inasmuch as the oxygen required by the nervous system amounts to 20% of the total oxygen consumption (near ten times as much as the average of the body as a whole). There are two kinds of vegetative components: *1.* Those that are common to all behaviors (increase in heart rate, blood

pressure, blood flow to the nervous system and muscles, ventilation, pupil diameter and palmar and plantar electrical conductance) and are intended to increase the supply of blood, oxygen, glucose etc. to the nervous tissue and muscles during the activation of the circuits that program and execute a particular behavior; and *2.* Those that are specific to certain behaviors. Salivary, gastric, enteric, pancreatic and billiary secretion and contraction of the smooth muscle of the gastrointestinal viscera are specific vegetative components of feeding behavior, as well as secretion of luteotropic hormone, increase in cavernous blood pressure and vaginal blood flow and several other endocrine adjustments are part and characteristic of sexual behavior.

Some authors have not been able to find changes in heart rate and respiration during desynchronized sleep (see Spreng et al., 1968) but there are striking demonstrations that blood pressure is reduced (Figure 6),

attaining values as low as 60 mmHg of systolic pressure; heart rate is also reduced and ventilation decreases (Candia et al., 1962; Baust, 1971). Apparently, the main cause of such a reduction of blood pressure and heart rate is the active inhibition of the baroreceptor reflexes during this phase of sleep. In cats, Guazzi, Baccelli & Zanchetti (1966) demonstrated that due to such a cardiovascular hypoactivity the sensory afferents from glomus carotideus and glomus aorticus, that carry information from chemoreceptors sensitive to a decrease in oxygen blood concentration, attain an overwhelming relevance, inasmuch as following the transection of such afferents blood pressure goes continuously down during desynchronized sleep, leading to death. It is not known if such a mechanism does exist in humans; if it exists, what is highly possible, we can reason that it is the activity of the chemoreceptor system that senses pO_2 that keeps us alive during desynchronized sleep.
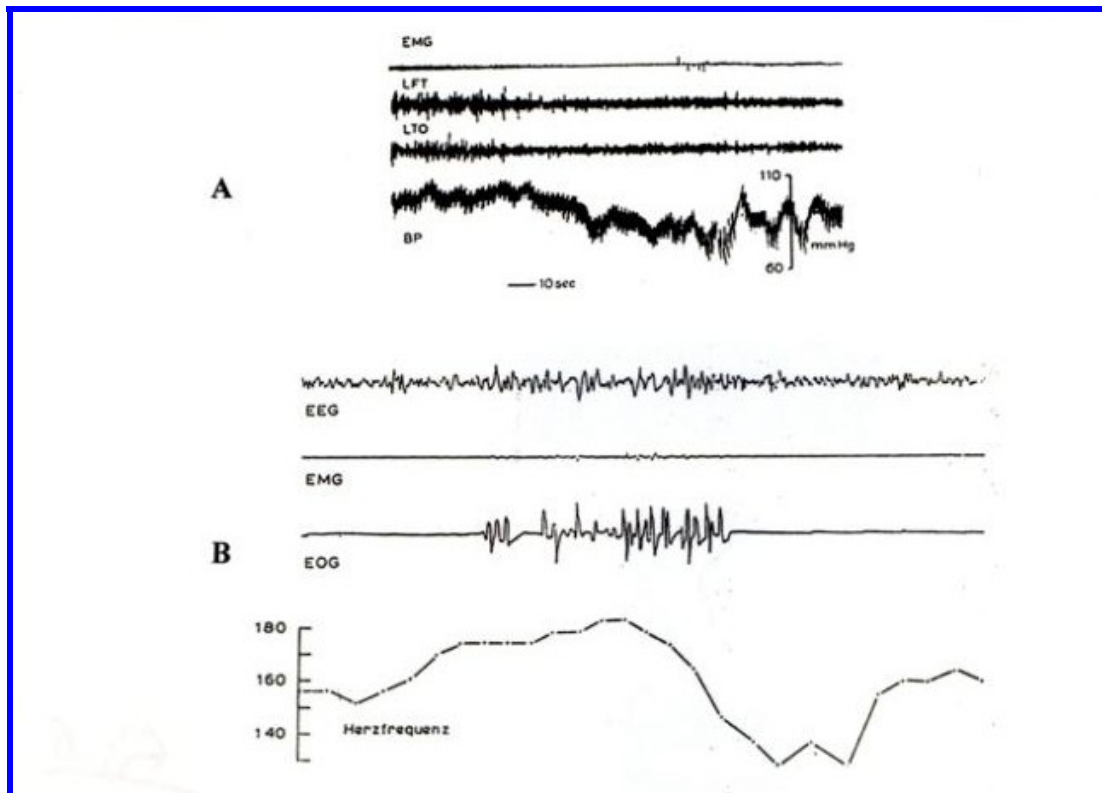
Figure 6. *A*: period of synchronized sleep of a cat (notice the slow waves in the left fronto-temporal lead, *LFT,* and in the left temporo-occipital lead, *LTO)* is followed by desynchronized sleep (low voltage, high frequency EEG), when blood pressure (*BP*) decreases steeply to very low levels (*Candia, et al., 1962*). *B*: desynchronized sleep (see desynchronized *EEG*), with mild movements of the head (*EMG*) but very active eye movements (*EOG*) while heart rate increases, attaining levels prevalent during wakefulness (*Baust, 1971*).

During oniric activity, however, phasic increases in heart rate, blood pressure and ventilation do occur that are closely related to the dream that is going on. Usually such increases in blood pressure are not enough to lead it to attain normal levels but during a nightmare blood pressure may go up to 200 mmHg. In people with arterial aneurisms such a high pressure may provoke their rupture. In cats, Baust (1971) recorded tachycardia starting 1 or 2 seconds before eye movements appear. Figure 6 shows an increase in heart rate from 150 bpm to 180 bpm (the latter is the normal heart rate during resting wakefulness in this species), coinciding with the peak of eye movements. Heart rate decreases down to nearly 150 bpm 1 or 2 seconds following the cessation of eye movements. The lag between tachycardia and eye movements may be related to all the neural processes that are involved in the phases preceding and succeeding the oniric behavior, including the very identification of the dream content.

In rats, heart rate is clearly accelerated during the periods of oniric activity,

expressed as rostrum+vibrissae, eye, head, ear and limb movements. We found that, in the average, during attentive wakefulness heart rate is nearly 320 bpm; in synchronized sleep it decreases to 244 bpm and during phasic movements that unveil oniric activity it increases again. When the rat moves the head, for example (which may indicate a vestibular dream), heart rate goes up and may be as high as 330 bpm, similar to that occurring during attentive behavior.

Despite such facts, some physiologists do not agree that heart rate and blood pressure decrease during desynchronized sleep. During dreaming, however, it is well known that both heart rate and blood pressure undergo short duration increases (as related to the decreased values), which are most likely linked to the oniric behavior. Candia and collaborators (1962) clearly demonstrated that in the cat blood diastolic pressure falls deeply to around 60 mmHg, beginning as soon as the electrocorticogram starts to desynchronize. The pressure also exhibits a series of bumps that may be related to dreaming activity (Figure 6). Our data with rats are quite consistent as to the variation of blood pressure and heart rate during oniric activity. Baust's data regarding the cat are also evident (Baust, 1971).

Thermoregulation is impaired in desynchronized sleep (Schmidek et al., 1972) but it is unlikely that body temperature changes due to dreaming activity, inasmuch as variations of temperature are slow while dreaming is a fast pace phenomenon. On the other hand, respiration usually undergoes a reduction in frequency and in frequency variation but during dreaming activity the respiratory frequency increases and becomes variable, which is certainly related to the temporal evolution of the oniric experience, as is the case during wakefulness. The hyperventilation that results from hypoxia is diminished during desynchronized sleep (Douglas, 1985), but there are no reports regarding changes in blood oxygenation while dreaming activity is occurring.

ELECTROPHYSIOLOGICAL CHARACTERIZATION

In humans the electro-oscillograms during desynchronized sleep are expressed as overall cortical desynchronization, whence the adequacy of the name created by Moruzzi, *desynchronized sleep*. Generally, in humans oniric activity is expressed as eye movements, what is obviously linked to vision as the main human sensory channel. Often eye movements are preceded in the electroencephalogram by small sawthoot-waves that superimpose on desynchronized potentials (Figure 3). However, human oniric behaviors are also expressed as lips, tongue and facial movements, as well as fingers, toes and whole limbs jerks, as described above.

In cats and monkeys eye movements are accompanied by monophasic spiky potentials in the occipital cortex, in the lateral geniculate body and in the pontine tegmentum (Brooks & Bizzi, 1963; Jouvet, 1967; Perachio, 1973; McCarley, Nelson &

Hobson, 1978). Accordingly, they are known as PGO (*p*ontine, *o*ccipital cortex and lateral *g*eniculate nucleus) potentials. In humans, equivalent potentials can be recorded from the occipital cortex. In rats we found similar potentials in the amygdala as related to olfactory dreams, expressed as rostrum movements (Timo-Iaria et al., 1990). No PGO potentials have been found in rats (Stern, Forbes & Morgane, 1974). Interestingly, bilateral ablation of the frontal lobes in cats leads to deep changes of the PGO potentials in the VI cranial nerves and in the mobilization of the lateral rectus muscles during desynchronized sleep (Gadea-Ciria, 1976). The number of PGO potentials undergoes a high increase after the frontal ablation, which is suggestive of a tonic inhibition of these potentials by the frontal cortex.

It is usually taken for granted that PGO potentials are essential manifestations for the electrophysiological identification of dreaming activity but such view is not well founded. Essential manifestations of dreaming are the conscious experience, the electrophysiological, the motor and the vegetative expression of oniric behaviors in humans as well as in other animals. The PGO potentials are correlates of dreams. Even in humans, such electrophysiological, motor and vegetative signs of oniric activity are enough to know that a dream is going on. Considering that most dreams in rats (Timo-Iaria et al.,

1990; Valle, Pellarin & Timo-Iaria, 2002) are related to olfaction, not to vision, potentials that resemble PGOs in the amygdala of this animal species should also be taken as signs of dreaming rather than PGOs.

In cats desynchronized sleep appears also as tonic cortical desynchronization (Figure 3) but in the hippocampus, septal area and amygdala theta waves predominate, as in rats and rabbits. Theta waves, discovered by Jung and Kornmüller in 1938, were extensively studied by Green & Arduini (1954), who proved they are related to arousal. Later, theta waves were also found in rats during both attentive wakefulness and desynchronized sleep (Roldan & Weiss, 1962; Timo-Iaria et al., 1970; Vertes, 1984; Gottesmann, 1992; Valle et al., 1992; Valle, Pellarin & Timo-Iaria 2002). Recently, the frequency of theta waves was shown in our Laboratory to be linearly related to the speed of learning in rats, as evaluated by the time necessary to learn operant conditioning tasks (Santos et al., 2002 submitted).

Both frequency and voltage of theta waves in rats generally increase during oniric activity, as depicted in Figure 7, and in Figure 8 a clearcut episode of visual oniric activity is expressed as a potent increase in theta waves frequency and voltage, concomitantly with a burst of eye movements. Figure 9 illustrates an episode of olfactory and vibrissal movements.
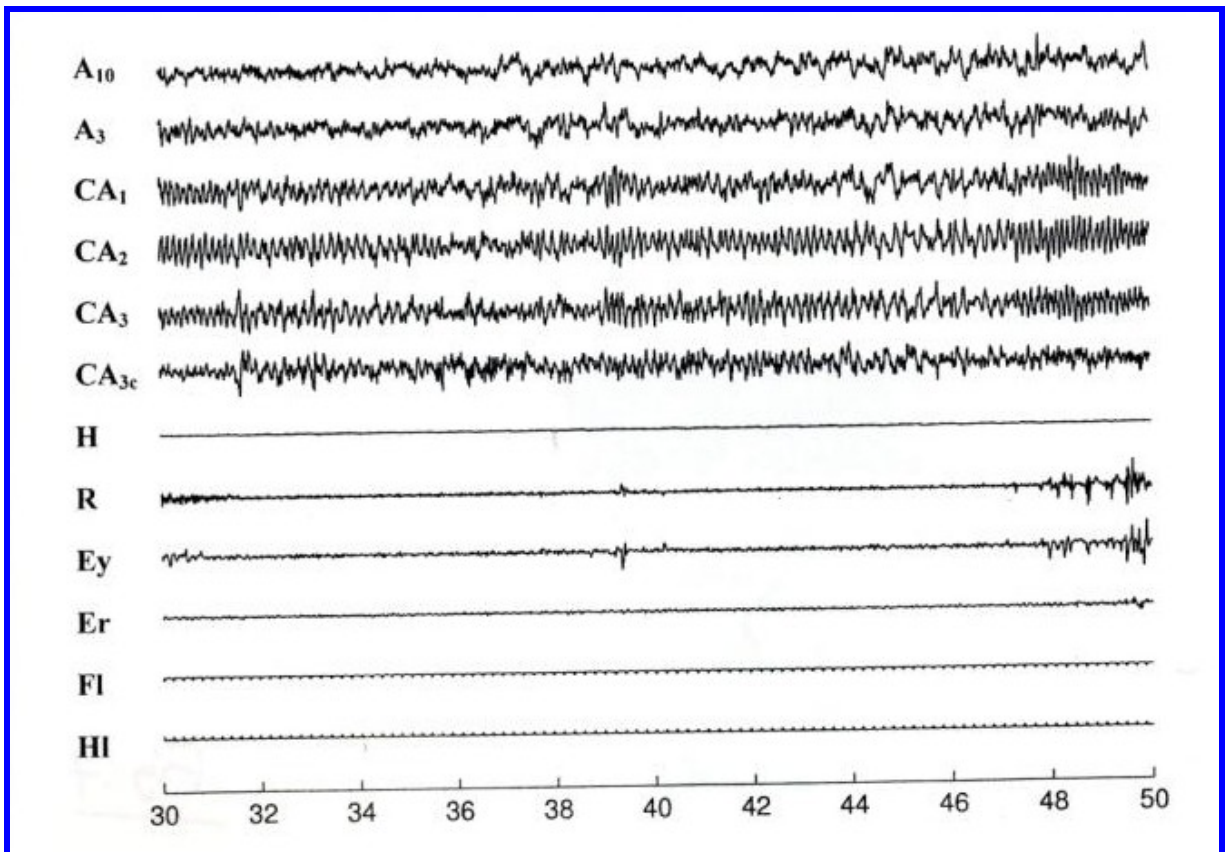
Figure 7. Desynchronized sleep and oniric activity of a rat. This is a typical figure in which a correlation between theta waves and oniric movements is quite clear. During the first episode the oniric activity, expressed as rostrum (*R*) and eye (*Ey*) movements, occurs when theta waves oscillate at a high frequency (8 Hz). It is then followed by a period in which theta frequency decreases to 5.7 Hz and no movements are detected in the recording. In the middle, a short burst of rostrum and eye movements do occur in coincidence with a short duration increase in voltage and frequency of theta waves. Finally, theta waves are again highly activated and rostrum, eye and ear movements occur, revealing oniric activity. Preceding the last episode theta waves frequency suddenly increases from 6.1 Hz to 9 Hz and then oniric activity starts again. A_{10}, frontal area 10. A_3, fronto-parietal area 3. CA_1, CA_2, CA_3 and CA_{3c}, corresponding hippocampal fields. *H*, head movements. *R*, rostrum+vibrissae movements. *Ey*, eye movements. *Er*, ear movements. *Fl*, forelimb movements. *Hl*, hindlimb movements. Time in seconds.
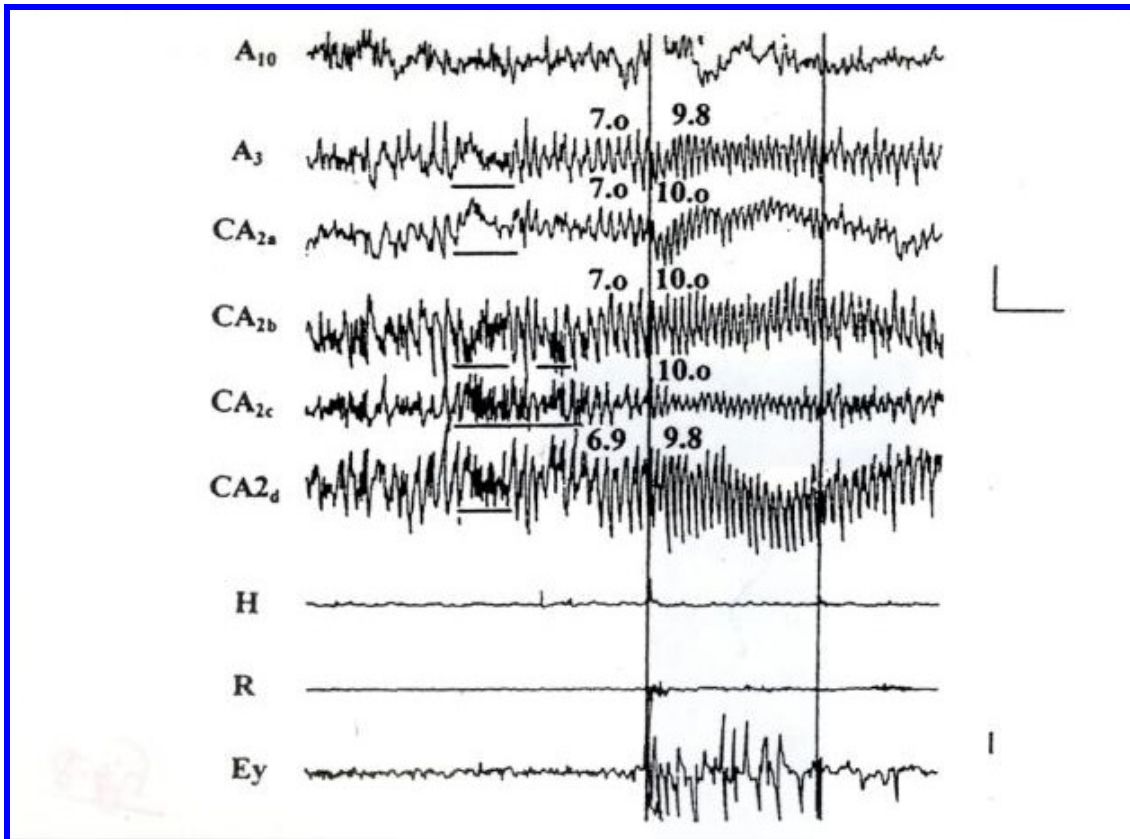
Figure 8. An oniric episode in a rat, expressed as very intense eye movements and a large increment in theta waves frequency (frequencies, in Hz, are indicated above the electro-oscillograms), brief head and rostrum movements are present only during the earliest 300 milliseconds of the oniric episode. During the first half of the figure synchronized sleep suddenly becomes desynchronized sleep and a short period of intense desynchronization lasting nearly one second breaks through synchronization. Such a period may correspond to a brief but intense arousal or to a brief but intense dreaming activity, in both cases without any detectable movement. A_{10}, frontal area 4. A_3, fronto-parietal area 3. CA_{2a}, CA_{2b}, CA_{2c} and CA_{2d}, four sites within hippocampal field 2. H, head movements. R, rostrum+vibrissae movements. Ey, eye movements.
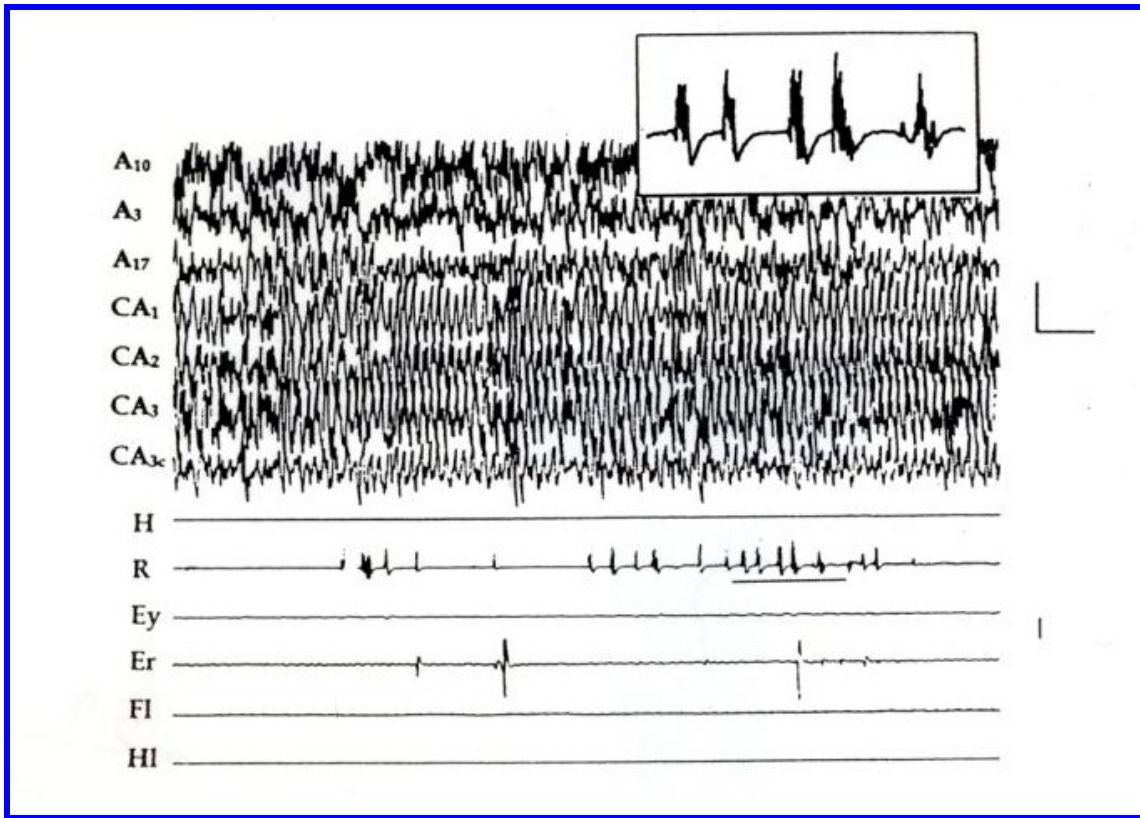
Figure 9. Oniric episode expressed as intense rostrum+vibrissae and ear movements, whereas eye movements are very weak. The underlined portion in *R* (rostrum+vibrissae lead) is magnified in the inset. The high frequency (around 7 Hz) of the *R* movements points to the prevalence of vibrissae mobilization, similar to what occurs during wakefulness when the rat is exploring the environment with its vibrissae. Ear movements are common as twitches of the ear. A_{10}, frontal area 4. A_3, fronto-parietal area 3. A_{17}, area 17 in the occipital cortex. CA_1, CA_2, CA_3 and CA_{3c}, corresponding hippocampal fields. *H, R, Ey, Er, Fl* and *Hl*, head, rostrum+vibrissae, eye, ear, forelimb and hindlimb movements, respectively. Calibration: 100 μV and 1 second.

By visually examining the amplitude of theta waves in these examples it seems they vary at random but when the instant variation of voltage is plotted as a function of time, a regular variation appears during the phasic movements (Figure 10). A regular oscillation modulates the amplitude of the potentials. Frequency clearly increases and becomes regular, as compared with the trend before oniric activity. Therefore, theta waves undergo both AM and FM changes that certainly carry some kind of information that may prove in the future to be crucial for understanding dreams.
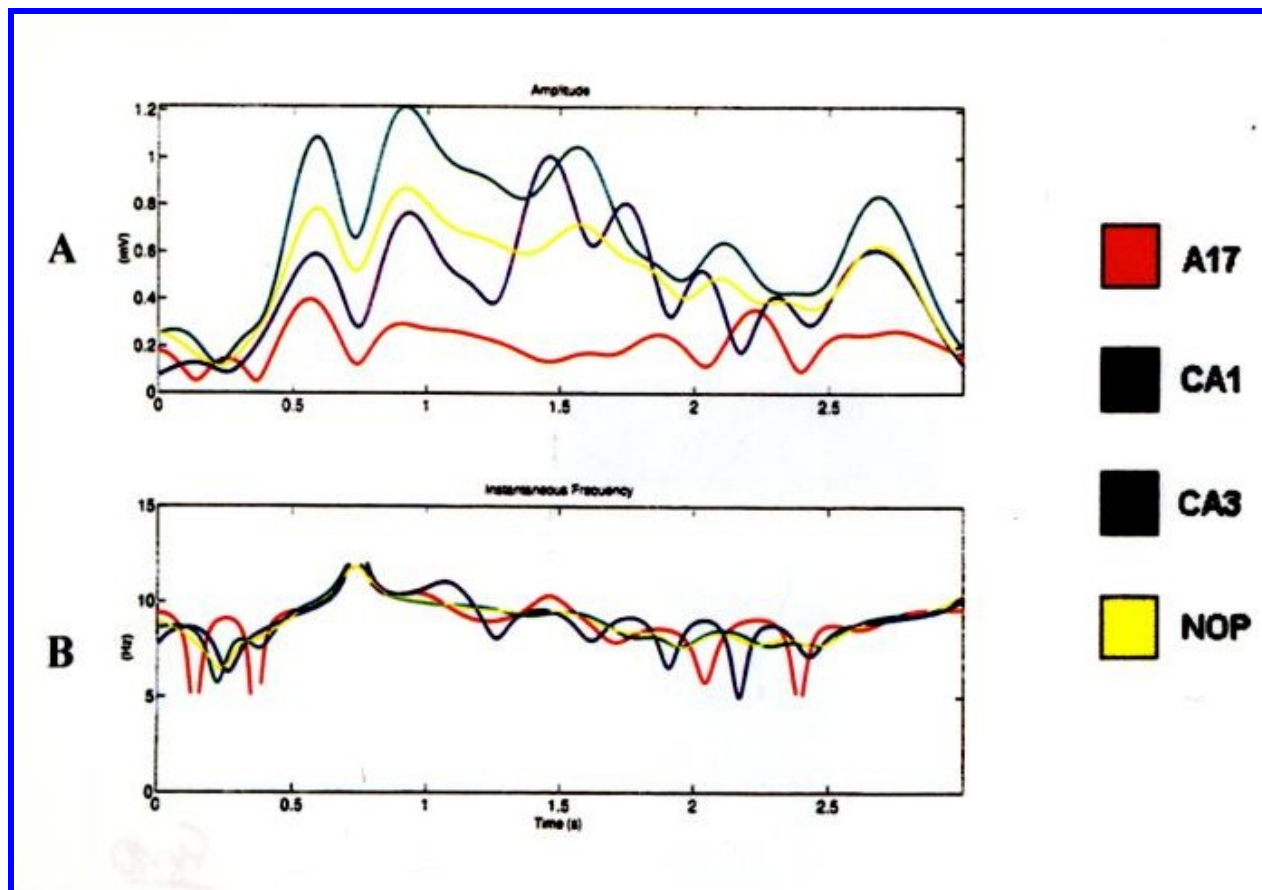
Figure 10. *A*: time course of the change in peak voltage of theta waves occurring in area 17, in *CA₁* and *CA₃* hippocampal fields and in nucleus reticularis pontis oralis (*NOP*) of a rat during a brief oniric episode. At right, colors correspond to the different curves. When the oniric episode begins, voltage of the theta potentials starts to oscillate regularly. *B*: frequency of the same potentials in *A*. It is very interesting that during a mere 0.5 period theta frequency went up quite steeply and in phase in all sites and then started to occur at a different rate in each site. Time: seconds.

Another change of the electro-oscillograms we disclosed in rats by carefully analyzing their time-course while a dream is on (as well as during attentive wakefulness) is the presence of short periods of desynchronization that interrupt or superimpose on theta waves. Considering that desynchronization is predominant all over the cortex in humans and in the frontal cortex of both cats and rats, we consider it to be a phylogenetically more recent functional acquisition. Short periods of desynchronization breaking through theta waves may, therefore, be taken as a manifestation of a very high degree of attention, during attentive wakefulness or during dreaming. In fact, it does frequently occur when movements are expressed as high frequency potentials. During wakefulness such periods in rats are concomitant with short but complete immobilization, which is well known to occur when a high degree of

55

attention is being directed to some external object. In humans it has been shown that not only EEG desynchronization but also increase in vegetative functions, such as heart rate and ventilation (Decety et al., 1993), accompany mental activity.

We hypothetize that theta waves are commanding signals that recruit in due sequence the circuits that generate wakefulness and desynchronized sleep and their components; their frequency and voltage generally increase in parallel with heart rate and intensity of movements (Valle & Timo-Iaria, unpublished results).

The command character of theta waves is probably the reason why such potentials occur almost simultaneously in different brain structures. In fact, when the voltage of each theta wave in one site is compared with the voltage in another site it is possible to assess the degree of coincidence or phase shift between the two sites. For instance, during desynchronized sleep theta waves, in rats, are highly coherent in nucleus reticularis pontis oralis and in the fronto-parietal cortex, as well as with the hippocampus (Simões, Valle & Timo-Iaria, 1996). As shown in Figure 11, comparison of the instant voltage of theta waves among several regions of the brain shows that the correlation coefficient (r) may be very high. The value of r is as high as 0.9618 when theta waves in the hippocampal CA_1 field of one side are matched with those in the nucleus reticularis pontis oralis, what points to a close temporal relationship between theta waves in hippocampus and in the nucleus reticularis pontis oralis. Also, correlation is high when theta waves in the thalamic reticular nucleus are matched to those occurring in the nucleus reticularis pontis oralis. Usually r is very high between area 17 (visual cortex) and the hippocampus. Such high values of r may mean that theta waves arrive in such areas almost synchronously, coming from some other sites in the central nervous system. Nucleus reticularis pontis oralis is thought to contain the generator of theta rhythm (Simões, Valle & Timo-Iaria 1996; Vertes & Kocsis, 1997) and is known to send direct efferents to the hippocampus and the cerebellar cortex, where we found theta waves that correlate closely with those in the hippocampus (Valle, Kubo, Iwamoto & Timo-Iaria, unpublished data).

Not only theta waves do occur in the cerebellar cortex during desynchronized sleep but also spindles and delta waves are found in this organ in synchronized sleep, just as in neocortical areas. In fact, all the phases of wakefulness and sleep, including desynchronized sleep, occur in the cerebellar cortex. Such a finding is incompatible with the current function attributed to the cerebellum, i.e., only correction of movements. Our hypothesis is that the cerebellum is involved in overall corrections of the components of all kinds of behavior, including sleep. Such hypothesis is grounded on the following steps. When any part of the brain programs a behavior it sends the program to the cerebellum. This organ

receives information from the entire body, including the baroreceptors, as shown by Moruzzi (1938). By comparing the program with the peripheral information, that tells it how the behavior is evolving, the cerebellum produces corrections, so that the execution can match the program. If this hypothesis is correct, it is no surprise that the phases of wakefulness and sleep are expressed in the cerebellar cortex by means of electrophysiological potentials.

From the spinal cord Marini (1997) recorded slow (delta) regularly oscillating waves during desynchronized sleep, which may be related to activation of spinal neurons during dreaming. In the 60's, Evarts (1964) had also recorded from monkeys high frequency bursts of impulses in the pyramidal tract axons, which may be related to activation of muscles intervening in oniric behaviors expressed as movements. However, interruption of the pyramidal tract hardly affects the appearance of muscular twitches during desyncronized sleep (Gassel, Marchiafava & Pompeiano, 1965) but the reticulospinal tract seems to be involved in such twitches (Vertes, 1990) whereas the associaton cortex does not appear to be activated (Noda & Adey, 1970).

By recording potentials from large ensembles of rat hippocampal neurons related to the body position in space (*place cells*) during behavioral tasks, Wilson & McNaughton (1994) found that neurons that fired together when the animals occupied particular locations in the environment (hence the name *place cells*) also exhibited an increased tendency to fire together during subsequent sleep, in comparison to sleep episodes *preceding* the behavioral tasks. On the other hand, cells that were silent during the behavioral task did not show the increase in frequency. The authors concluded that the correlation they found was probably involved in memory consolidation but such coincidence may indicate that during dreaming memorized information is being revoked to integrate a given dreaming pattern. Vertes & Eastman (2000) argue against memory consolidation during sleep, what is in opposition to Wilson & McNaughton's hypothesis. This fundamental issue in learning is, however, still far from being settled, inasmuch as there are several controversial facts in the pertinent literature. It may be more appropriate to explain the latter authors' results by reasoning that dreams are originated in memorized information and are, accordingly, closely related to events occurring before sleep.
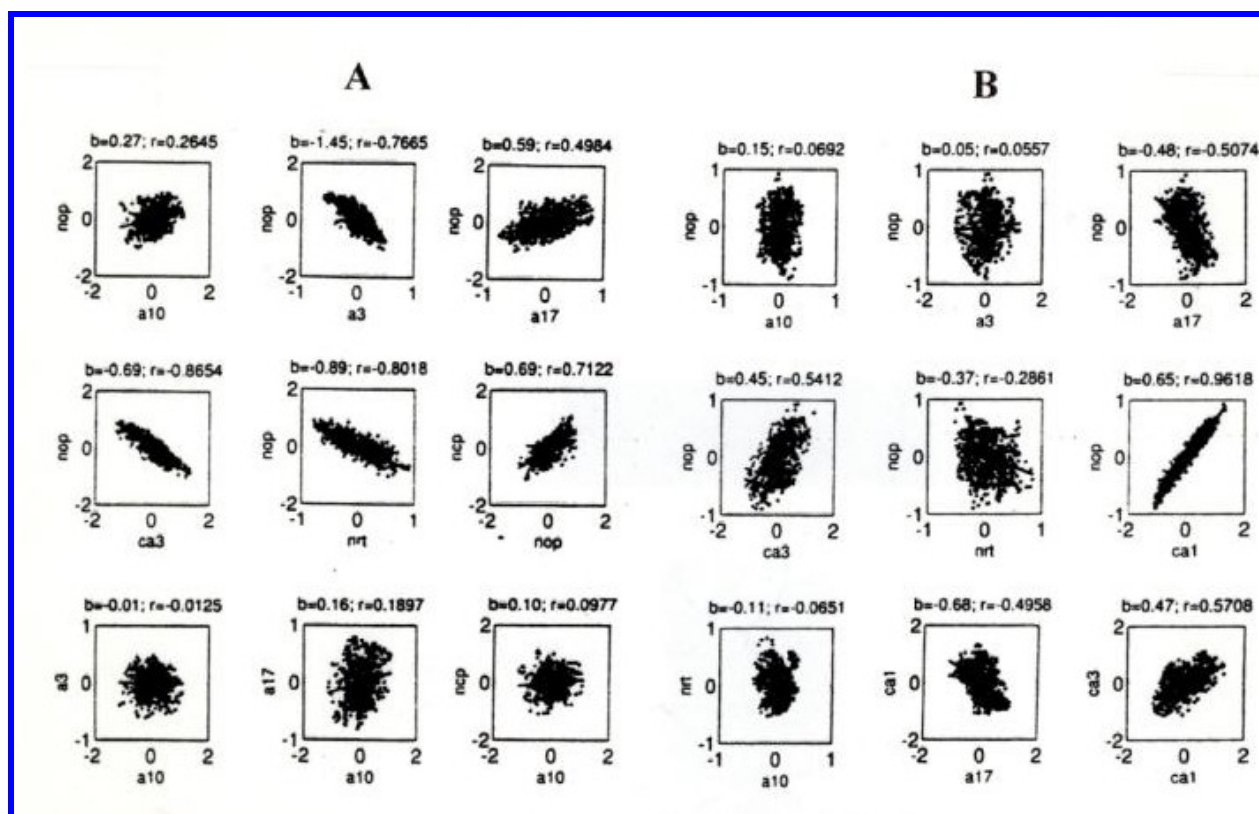
Figure 11. Scatter diagram displaying the correlation between concomitant theta waves voltage in several sites of the central nervous system during two periods (*A* and *B*) of desynchronized sleep of a rat. Each dot represents the peak voltage (expressed in mV), in a given instant, of concomitant theta waves in two sites and measured each 3.9 milliseconds. $n=768$ measurements, *r*: coefficient of correlation, *b*, slope of the regression line. The slope leaning to one side or the other is not relevant, inasmuch as it depends on the polarity of the potentials input in the amplification system. The sites of recording are indicated in the *x* and y axis. *NRPO*: nucleus reticularis pontis oralis. *NRT*: nucleus reticularis pontis caudalis. *CA₃* and *CA₁*: hippocampal fields. *A₁₀*, *A₃* and *A₁₇* correspond to cortical areas 10, 3 and 17, respectively (*Simões, Valle & Timo-Iaria, 1996*).

GENESIS OF DREAMING

Generation of sleep is reasonably well known but not that of dreaming. In 1963 we found (Hernández-Peón et al., 1963) that cholinergic stimulation of a descending pathway (within Nauta's *limbic-mesencephalic system*) causes sleep. The caudalmost portion of this system (then labeled *descending hypnogenic cholinergic*) comprises the ventral and dorsal Gudden's nuclei, whose stimulation with carbachol triggered sleep in nearly 20 seconds. The previous station of these nuclei is the interpeduncular nucleus, whose stimulation with carbachol caused sleep within nearly 30 seconds. In both instances sleep evolved according to the phases of synchronized and then of desynchronized sleep, during which eye movements always occurred. In more

recent years several approaches confirmed these findings (Hobson, 1992).

After transection of the brain stem at the pontomesencephalic transition, rostrally to locus coeruleus, desynchronized sleep still occurs below the transection (Berlucchi, 1971; Jouvet, 1972; Moruzzi, 1963; 1969; 1972). Desynchronized sleep can be provoked by carbachol infusion in the pontine reticular formation (Bourgin et al., 1995). Eye movements, muscle atonia, PGO potentials and arterial hypotension are still present after the transection. Above the transection, synchronized and desynchronized sleep keep occurring but without eye movements. In this preparation body temperature is not regulated anymore and the animal has to be artificially warmed at nearly 37 ^{o}C. Interestingly enough, if body temperature in cats subjected to pontomesencephalic transection is lowered, the amount of desynchronized sleep increases. At 36 ^{o}C, for instance, desynchronized sleep spans to about 10% of time, at 23 ^{o}C it occupies nearly 80% of the time, what has not been explained so far.

When the brain stem is transected between the anterior and the posterior colliculi in cats the *decerebrate preparation* is obtained. The main purpose of experimental decerebration is to study the mechanisms of the *fundamental posture*, that is, the standing posture. It has, however, been utilized with a great success in sleep studies. In decerebrate cats eye movements do occur and are integrated below the midbrain (Jouvet, 1967; Villablanca, 1966). Pompeiano and his group produced important knowledge in this field (Pompeiano, 1967; 1976), showing that the muscle contractions that produce the motor component of oniric behaviors, such as eye and limb movements, need that the pontine gigantocellularis nucleus be intact and activated. Reticulospinal and reticulobulbar tracts are involved in conveying to the motoneurons the impulses that cause oniric movements. Such movements occur while motoneurons are being inhibited through hyperpolarization of their membrane (Pompeiano, 1967; Vertes, 1984). The gamma-alpha loop has been shown to play no role in producing the movements that characterize dreaming. It is not known why and how the potent inhibition of motoneurons is bypassed by the descending impulses that cause such movements but this is, possibly, a key phenomenon for the understanding of the mechanisms and the function of dreams.

Eye movements that occur during desynchronized sleep are equivalent to limb and face twitches occurring during the same phase of sleep and seem to have the same functional meaning. There is experimental evidence that eye movements are generated near the nucleus of the abducent nerve but Pompeiano (1967) does not agree with this view (Berlucchi, 1971). Electrical potentials recorded from the medial vestibular nuclei precede eye movements by 20 to 30 milliseconds, which points to these nuclei as

the last synaptic stations in the pathway that produces eye movements during desynchronized sleep. Such electrophysiological studies demonstrate that the abovementioned sites in the central nervous system are involved in the oniric movements but they do not prove that such structures generate them. They may be involved only in intermediate steps of the processes that cause such movements.

Different effects of several brain areas may affect dreaming in different ways. In an extensive review on this subject, Solms (2000) describes a complete cessation of dreaming in patients with posterior cortical or deep bilateral frontal lesions. The posterior areas affected in this syndrome are the visual areas V3, V3a and V4 (Doricchi & Violani, 1992). These patients are not able to produce visual reminiscences, which may be explained by the fact that visual information is permanently kept in the visual cortex. Since evoking visual reminiscences during wakefulness and the building up of dreams with visual information are dependent on the visual cortex, both facts can be correlated.

THE MEANING OF DREAMS

This is for sure the most enigmatic issue about dreaming. There are many hypotheses to account for the existence of dreams but it is still a matter of debate why and what for we dream. In fact, we ignore almost completely why we dream. Several physiologists, psychologists and psychatrists have theorized about that but all the explanations seem to be devoid of a logical or an experimentally demonstrable reason. Some presently available explanations seem science fiction, rather than true science.

To discuss this issue we will concentrate only on a few hypotheses. As mentioned above, Plato, preceding by twenty four centuries one of the dogmas of psychoanalysis, believed that "forbidden" dreams, such as incestuous or criminal dreams, were only a way of doing incestual sex or killing someone without punishment. As such, this explanation may be interpreted as a way of doing something that we should never be allowed to do without paying for it. Dreams are still taken by a majority of the human kind as premonitory, ascribing them the function of telling us that something important will happen.

A theory that has many followers is the one that connects dreams, in particular, desynchronized sleep in general, with memory consolidation. Despite several demonstrations that this hypothesis is correct, a few argue against such a view. Vertes & Eastman (2000), for instance, believe that the stressful conditions in experiments intended to demonstrate a role of desynchronized sleep and dreaming in consolidation of memory spoil the results. These authors argue that despite the marked suppression of desynchronized sleep provoked by tricyclic antidepressants neither selective serotonine reuptake inhibitors and mono-amino-oxydase nor learning and memory are disrupted.

Recently a more acceptable evidence in favor of the consolidation hypothesis arises from the study of a gene involved in neuronal activation. This gene protein, zif-268 (Milbrandt, 1987), binds to a specific DNA molecule present in the promoters of a variety of genes expressed in the nervous system (Christy & Nathans, 1989) and its up-regulation is thought to initiate a program of gene regulation leading to neuronal plasticity (Chaudhuri, 1997). For instance, zif-268 has been shown to induce the expression of a synapse-specific protein, synapsin II (Petersohn et al., 1995), and has been linked to the induction of hippocampal long-term potentiation (Cole et al., 1989; Roberts et al., 1996) and other plasticity phenomena. In addition, zif-268 is up-regulated in several novelty or learning behavioral paradigms, including two-way active avoidance (Nikolaev et al., 1992), brightness discrimination (Grimm & Tischmeyer, 1997), and enriched environment exposure (Wallace et al., 1995). Fos-like immunoreactivity was also found in association with cholinergically induced REM sleep (Shiromani et al., 1995; 1996). In 1999, Ribeiro and colleagues, assaying zif-268 expression in control rats and in rats subjected to a rich environment training, found that in control animals this gene protein generally decreased, mainly in the cerebral cortex, from wakefulness to synchronized sleep and from synchronized to desynchronized sleep. However, in the animals subjected to a rich-environment zif-268 increased significantly from synchronized to desynchronized sleep but decreased from wakefulness to synchronized sleep. Such activation of zif-268, which is likely to be correlated with the effect of learning on desynchronized sleep, was larger in the frontal and hippocampal cortices, where memorization is well known to occur.

Foulkes (1982) considered that dreams are so easily forgotten because the brain in desynchronized sleep is in a "reflective state". We suppose, instead, inasmuch as dreams are forgotten if we are not aroused while dreaming or within ten to fifteen minutes immediately after the dream has ceased, that it may well be that dreams are forgotten because the reticular activating system is highly deactivated during desynchronized sleep and thus the memory of the dreams cannot be consolidated.

Electrophysiologically, it has been shown (Wilson & McNaughton, 1994) that the same type of hippocampal cells that are activated during training in a radial maze are also endogenously reactivated during sleep, which accounts for memory consolidation and for a close correlation between dreams and events preceding sleep.

The hypothesis has been recently put forward by Revonsuo (2000) that the function of dreaming is to simulate threatening events, and to rehearse threat perception and threat avoidance. This seems to be a highly improbable conception, among other reasons because, as dreaming is concerned, threatening events are as dangerous to the organism as bad news we hear and as crossing

a street or watching a movie full of violence. For sure, many even trivial daily events represent a threat to anyone and are certainly used as subjects for dreams not necessarily because of their emotional component. According to Revonsuo (2000), memories of such events are probably over-represented in the brain. Since memorized information is the basic material to build up dreams, it is understandable that many (but not all) dreams are threatening and emotionally highly charged.

It is interesting that the representation of animals in dreams of infants is quite conspicuous. It decreases, apparently exponentially as a function of age, from 60% at 4 to 30% at 7-8 and to 10% at 18 years of age (Van de Castle, 1970). This may be related to the presence of pet animals in most families in the Western countries and consequently this "subject" probably becomes the main thought of children. Later, school and work dominate the mental field and the main features in dreams also change accordingly, supporting this hypothesis.

Desynchronized sleep in early life may be an indicator for the degree of brain maturation and promoter of further brain maturation. Deprivation of desynchronized sleep during early development not only retards brain maturation but also inhibits the growth response to the brain environmental stimulation later in life (Mirmiran & van Someren, 1993). In rats subjected to early desynchronized sleep deprivation, ejaculation was deeply reduced in adulthood

(Mirmiran, 1995; Mirmiran, van Dungen & Uylings, 1982), what is a profound impairment of a very important instinctive behavior. The authors suggest that such a disturbance of reproduction occurs because desynchronized sleep (and consequently dreaming) was prevented to occur normally in infancy but the functional meaning of this interesting phenomenon.

Another hypothesis to account for desynchronized sleep function is that this phase of sleep is programmed to occur when central temperature is low and that it has a thermoregulatory function. Therefore, desynchronized sleep should be ascribed a homeothermic function (Wehr, 1992). Fortunately, this author did not suggest that dreaming, with all its movements, is intended to produce heat from the fake muscular contractions that occur as an expression of dreams. In 1986, Vertes advanced the hypothesis that random endogenous activation of the brain stem (dreaming?) during desynchronized sleep prevents sustained brain inactivity, which might occur during sleep.

A related point of view was put forward by Krueger & Obal (1993), who proposed that, on the basis of use-dependent synaptic stabilization, the neuronal assembly not activated during wakefulness will be activated during sleep, to prevent it from atrophy.

Another fancy hypothesis is the one that proposes that we dream to forget, in order to delete "unwanted" information by reverse

learning or unlearning (Crick & Mitchison, 1983). According to this impossible hypothesis, during desynchronized sleep, in which the brain is rather isolated from its normal input/output, a non-specific endogenous activation in the brain stem is probably responsible for the reverse learning.

Jouvet (1986; 1978), one of the most important researchers on sleep, suggests that dreaming is "a guardian and programmer of the hereditary part of our personality" and as such it plays a role in our general behavior. Thanks to the extraordinary possibilities of functional connections that take place in the brain when the "basic circuitries of our personality are programmed", dreams do contribute to shape new solutions for new problems. Jouvet believes that dreaming activity plays a key role during the earliest years of life and thus may be involved in continuously programming some of the most subtle reactions of our consciousness during wakefulness.

Whereas Freud was convinced that dream forgetting was an active function of repression, Hobson, Pace-Schott & Stickgold (2000) attribute the failure to recall a dream to a state-dependent amnesia caused by aminergic demodulation of the sleeping brain. The waking level of aminergic modulation falls to 50% during synchronized sleep and to nearly zero in desynchronized sleep (Steriade & McCarley, 1990; Kahn, Pace-Schott & Hobson, 1997). It would appear that the intense activation of desynchronized sleep must overcome this demodulation and persist into subsequent waking, in order for very vivid dreams to be remembered.

It has been proposed (Hobson, Pace-Schott & Stickgold, 2000; Rados & Cartwright, 1982; Roussy et al., 1996) that presleep mentation is infrequently incorporated in top dreams and that "naturalistic" day time events rarely enter dream content, but several authors correlated dream content to the previous day events, starting with Aristotle 2,400 years ago and with Calkins in 1893. Hobson, Pace-Schott & Stickgold (2000) do not take into consideration that a single object or a brief key fact or image occurring in the day preceding a given dream may be enough to trigger an entire dreamed "story" related to it. They also argue that even "expensive and cumbersome evoked potential and computer averaging approaches have not helped us to analyze and compare desynchronized sleep physiology with that of waking in an effective way". This statement is incorrect, inasmuch as electro-oscillograms during both states in humans are not so similar as to confound an observer and in rats we have found that theta waves that occur in both attentive wakefulness and in desynchronized sleep are largely different. During wakefulness theta waves consistently exhibit a lesser voltage and are less regular than during desynchronized sleep, what makes it easy to tell wakefulness from desynchronized sleep from the shear inspection of the electro-oscillograms (Timo-Iaria & Valle, 1995; Valle,

1995; Valle et al., 1992; Valle, Pellarin & Timo-Iaria, 2002).

In rats bilateral lesion of the midbrain reticular formation is followed by a long lasting state of synchronized sleep, with predominance of phase III (Timo-Iaria, Assumpção & Bernardi, unpublished observations). If the animal is kept alive by forced feeding and is kept warm, in six days frontal desynchronization and theta waves in the other cortical areas reappear and then not only wakefulness is fully recovered but also desynchronized sleep, including oniric activity. Such a recovery means that other mechanisms are put into action, which are able to generate not only wakefulness but desynchronized sleep as well. When only one side of the reticular formation is also destroyed, the same pattern of recovery does occur; if the other side of the reticular formation is also destroyed after two or three weeks, recovery of wakefulness and desynchronized sleep is even faster than when both sides are lesioned at the same time. This is an additional fact to point to the activation of other mechanisms capable of producing wakefulness and desynchronized sleep, including dreaming.

According to Hobson, Pace-Schotter & Stickgold (2000), since image studies show activation of "limbic" and "paralimbic" structures of the forebrain during desynchronized sleep, as compared to wakefulness (Braun et al., 1997; Maquet et al., 1996; Nofzinger et al., 1996), emotion may be a primary shaper of dream plots,

rather than playing a secondary role plot instigation. However, we all know that many dreams are not emotional at all.

Braun and colleagues (1997) found during desynchronized sleep a consistent activation of the pons, midbrain, anterior hypothalamus, caudate and medial prefrontal, caudal orbital, anterior cingulate, parahippocampal and inferior temporal cortices. These findings do not necessarily mean that such areas are involved in generating dreaming. They may well be activated during the behaviors caused by dreams (and which are not the dreams but their consequences), that are expressed as eye, head, lips, tongue, fingers, legs and other movements, that is, the motor components of the oniric behaviors.

Selective deactivation of the dorsolateral prefrontal cortex has been found in desynchronized sleep. Maquet and co-workers (1996) and Braun and colleagues (1997), in their PET studies, found a significant deactivation, in desynchronized sleep, of a large portion of the dorsolateral prefrontal cortex, what was found also by Madsen and collaborators (1991) and Lovblad and colleagues (1999). No wonder that dream recall is impaired in brain-damaged patients (Doricchi & Violani, 1992). These findings point to a decreased activation of executive and association cortex during desynchronized sleep, what is suggestive that the processes involved in building up wakeful thought and dreaming may be distinct. Despite such discrepancies, however, during synchronized

sleep PRT studies reveal a decrease in global cerebral energy metabolism relative to both waking and desynchronized sleep. Metabolism during desynchronized sleep tends, in fact, to be equal to or even larger than that of waking (Buchsbaum et al., 1989; Heiss et al., 1985). In addition, blood flow velocity in the middle cerebral artery decreases during synchronized sleep whereas in desynchronized sleep it is similar to that occurring in waking (Kuboyama et al., 1997).

Winson (1990) believes that dreams "reflect an individual strategy for survival. The subjects of dreams are broad-ranging and complex, incorporating self-image, fears, insecurities, strengths, grandiose ideas, sexual orientation, desire, jealousy and love". According to this author, in children at the age of two, when the hippocampus, which is still in the process of development at birth, becomes functional, REM sleep takes on its interpretive memory function.

According to Mancia (1995), the brain "produces dreams" as "a symbolic process of elaborating, interpreting and reorganizing in narrative sequences all the material accumulated in the memory during waking hours". This author "thus proposes a psychoanalytical model of dreaming, in which dreams constitute a way of representing the individual's inner world with internal objects related with one another and with the self".

Considering dreams as hallucinations, Hernández-Peón (1966) theorized that they are possible because the system responsible for wakefulness is inactivated during sleep,

releasing memory tracings which are brought to consciousness. Although related to the information fluxogram displayed in Figure 2 of the present review, Hernandez-Péon's process involves the function of participating in "adaptive waking behavior", which does not seem to have a real meaning.

The meaning of dreams is therefore still an unsolved problem. Many hypotheses have been advanced but so far they do not explain why and what for we do dream. Despite the fact that many studies have found that mental activity during wakefulness differs from that during dreaming, the mechanisms involved in both may differ as to the degree of control over the release and combination of memorized information in wakefulness and in desynchronized sleep.

Inasmuch as dreaming seems to occur in most birds and mammals, it is unlikely that it has no function in the animal organism. Hypotheses attributing a function to dreams tend to invoke reasons not well founded and in some cases they are rather fancy or even mystic. Much experimental work is needed before a convincing function can be ascribed to the fascinating physiological phenomenon that is dreaming.

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