

# The 'scanning hypothesis' of rapid eye movements during REM sleep: a review of the evidence

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## ABSTRACT

*Rapid eye movements (REMs) and visual dreams are salient features of REM sleep. However, it is unclear whether the eyes scan dream images. Several lines of evidence oppose the scanning hypothesis: REMs persist in animals and humans without sight (pontine cats, foetus, neonates, born-blinds), some binocular REMs are not conjugated (no focus point), REMs occur in parallel (not in series) with the stimulation of the visual cortex by ponto-geniculo-occipital spikes, and visual dreams can be obtained in non REM sleep. Studies that retrospectively compared the direction of REMs to dream recall recorded after having awakened the sleeper yielded inconsistent results, with a concordance varying from 9 to 80%. However, this method was subject to methodological flaws, including the bias of retrospection and neck atonia that does not allow the determination of the exact direction of gaze. Using the model of RBD (in which patients are able to enact their dreams due to the absence of muscle atonia) in 56 patients, we directly determined if the eyes moved in the same directions as the head and limbs. When REMs accompanied goal-oriented motor behaviour during RBD (e.g., framing something, greeting with the hand, climbing a ladder), 90% were directed towards the action of the patient (same plane and direction). REMs were however absent in 38% of goal-oriented behaviours. This directional coherence between limbs, head and eye movements during RBD suggests that, when present, REMs imitate the scanning of the dream scene. Because REMs index and complexity were similar in patients with RBD and controls, this concordance can be extended to normal REM sleep. These results are consistent with the model of a brainstem generator activating simultaneously images, sounds, limbs movements and REMs in a coordinated parallel manner, as in a virtual reality.*

### Key words

*Rapid eye movements • REM sleep • Dream • REM sleep behaviour disorder • Sleep*

## History

The discovery of rapid eye movements during certain periods of sleep was a major step in sleep research (Gottesmann, 2009). In their same seminal work, Aserinsky and Kleitman noted that 80% of the awakenings during periods of sleep with ocular movements (and none during other sleep periods) were associated with dreams, in the sense of complex, image- and emotion-filled mental content (Aserinsky and Kleitman, 1953). This identification was so important that the new sleep stage, after it had been named

“emergent stage 1” (Dement and Kleitman, 1957; Dement and Kleitman, 1957) was ultimately named rapid eye movement (REM) sleep and the remaining periods of sleep were named, in contrast, non-REM sleep (Gottesmann, 2009). Soon after the work of Aserinsky and Kleitman, Michel Jouvet observed that markers of central nervous system activation (REMs, dream mentation, desynchronised EEG activity, theta activity within the hippocampus, and as shown more recently, marked perfusion of the temporal and occipital brain areas) contrasted with a generalised postural muscle atonia during REM sleep, a paradox that led

him to name this stage “paradoxical sleep” (Jouvet and Michel, 1959). Following his identification of the brainstem structures responsible for the postural atonia in REM sleep, Jouvet developed a cat model with REM sleep but without the atonia. He observed the simultaneous release of complex behaviours in these sleeping animals (called “oneiric behaviours”), which looked like enacted dreams (Jouvet, 1962). These initial tight links between a period of sleep with REMs, dreams, and dream enactment (when muscle atonia is suppressed) were so strong and appeared with such an internal logic that even now, some authors remain unconvinced that “true” dream mentations may also occur in non REM sleep (Nir and Tononi, 2010). The question whether the directional properties of REM sleep eye movements are related to shifts of gaze related to dream imagery (the “scanning hypothesis”) or are random markers of brainstem activation has fascinated sleep scientists since the discovery of REM sleep (Dement and Kleitman,

1957; Berger and Oswald, 1962; Jacobs et al., 1972). There were many advocates for and against the scanning hypothesis between the 1950s and the 1980s, all of whom proposed various lines of evidence to support their views. This evidence is summarised in Table 1 and will be discussed below.

In 1986, Carlos Schenck and Mark Mahowald identified patients with violent behaviours and absence of normal atonia during REM sleep (Schenck et al., 1986). This condition, named REM sleep behaviour disorder (RBD), was associated with dream reports congruent with the observed behaviour, and resembled the dreamlike behaviour in Jouvet’s cats. We recently used the RBD model to fuel the debate about the scanning hypothesis (Leclair-Visonneau et al., 2010) as we feel that RBD provides an attractive model with which to study the motor and cognitive activities during REM sleep without awakening the sleeper (De Cock et al., 2007). Throughout this review, we will restrict the term REMs to the rapid eye movements of REM sleep.

Table I. Summary of studies in support and against the REMs scanning hypothesis.	
Against Hypothesis	Supporting Hypothesis
<i>Mechanical properties of REMs</i>	
In cat, bursts of REMs are observed only in REM sleep and have no similarity with the eye movements of the animal observing a target in the awake state (Jeannerod et al., 1965)	Isolated and grouped REMs have a similar pattern and speed during REM sleep and during the awake state (Jeannerod et al., 1965)
Some binocular REMs are not conjugated: they lack a fixation point. It argues against the idea that REMs actually “track” dream images, unless each eye is watching its own dream (Zhou and King, 1997)	
<i>Neurophysiological properties of REMs</i>	
PGO waves (stimulating the visual brain areas) and REMs are simultaneously generated (in parallel, not in series) (Vanni-Mercier and Debilly, 1998)	
<i>Sight and REMs</i>	
Foetuses and neonates have REMs, although they have no sight. Pontine cats and cats without a visual cortex have REMs (Jouvet, 1962; Arnulf et al., 1998).	
Congenitally blind people have REMs, although they have no “visual” dreams (Kerr et al., 1982)	Congenital blind people have “visual” dreams (Bertolo et al., 2003)
Visual dreams are also reported in non REM sleep (Fosse et al., 2001)	
The absence of fixation point argues against the idea that REMs actually “track” dream images, unless each eye is watching its own dream (Zhou and King, 1997)	
<i>Retrospective correlation (after awakening the subject) between REMs direction and direction of gaze in the dream</i>	
Positive in 9-32% of awakenings (no higher than random) (Moskowitz and Berger, 1969; Jacobs et al., 1972).	Positive in 70-80% of awakenings (Dement and Kleitman, 1957; Roffwarg et al., 1962; Herman et al., 1984)
<i>Direct correlation between REMs direction and direction of limb action during RBD</i>	
REMs are absent during 38-42% of goal oriented actions that would require a visual control if performed awake (Leclair-Visonneau et al., 2010).	When present (58-62% of goal oriented actions), 90% of REMs are directed in the plane and side of the limb action (Leclair-Visonneau et al., 2010).

## Characteristics of REMs

### *Recording methods*

In human sleep studies (Aserinsky and Kleitman, 1953, 1955; Roffwarg et al., 1962; Vaughan, 1964), the electro-oculography (EOG) is the only way to continuously monitor eye movements when the eyelids are closed. Any routine sleep monitoring performed in human subjects, whether for research or clinical purposes contains, in addition to an EEG and chin surface electromyography, an EOG, that identifies the REMs characteristic of REM sleep. The conventional time constant for recording eye movements is 0.3 s (Rechtschaffen and Kales, 1968), but some animal and older human studies use a time constant of 0.1 s, which modifies the visual aspect of REMs. The EOG, however, is an indirect measure of eye position, because it depends on a corneo-retinal potential measured by surface electrodes placed around the eye, which exhibits a baseline drift. A more precise technique, using electromagnetic search-coils in cat and monkey studies, provides accurate horizontal and vertical binocular eye position records during natural sleep (Vanni-Mercier et al., 1994; Zhou and King, 1997). In blind subjects, where the corneo-retinal potential may be absent, the presence of eye movements can be assessed by placing a ceramic strain gauge on the eyelid (Gross et al., 1965). The direct observation of eye movements has been performed in a few cats (Jeannerod et al., 1965) and human volunteers who were able to sleep with their eyelids artificially fixed in the “open” position (Rechtschaffen and Foulkes, 1965).

### *Spatiotemporal features of REMs*

REMs are rapid saccades visible under the closed eyes of the sleeper, that are similar in humans to saccades in the awake state when visual inputs are absent but imagined or remembered (Herman et al., 1983; Sprenger et al., 2010). Yet some REM characteristics (round-shouldered appearance, looped trajectories, slow, oblique and torsional patterns) render these eye movements unlike any of those occurring during wakefulness (Fuchs and Ron, 1968; Jacobs et al., 1971). In the cat, REMs are more rapid than the eye movements when the animal observes a moving target in the awake state (Jeannerod et al., 1965), and have a slope of acceleration twice as high (Vanni-Mercier et al., 1994). In human, the eyeballs

rotate at a speed greater than 30° per second, with a mean speed of rotation of  $58.7 \pm 0.2^\circ/\text{s}$  (Takahashi and Atsumi, 1997). The mean amplitude of REMs is within the range of 4–15° (De Gennaro and Ferrara, 2000). REMs are different from the slow eye movements that herald sleep onset and persist during all other sleep stages, but cannot be differentiated from eye movements in the awake stage (Fig. 1).

### *Phylogenic and ontogenic development of REMs*

REMs are observed during paradoxical sleep (a synonymous for REM sleep) in all mammals, except in the mole, which is blind and has a degenerated visual system (Allison and Van Twyver, 1970). In human foetuses, rapid eye movements begin at 23 weeks of gestation and become more frequent between 24 and 35 weeks (Birnholtz, 1981). In human infants, the REMs frequency increases during the first six months of life, paralleling the development of the oculomotor system in the awake state (Lynch and Aserinsky, 1986). The frequency of REMs does not differ between young and elderly subjects; however, in the elderly, REMs tend to cluster into bursts and increase in frequency across sleep cycles decreases (Ficca et al., 1999).

### *Pattern and conjugation of REMs*

The REMs are either isolated or grouped in a series, or burst, during REM sleep. The isolated REMs have a slope slightly lower than the eye movements of an awake cat observing a target (Jeannerod et al., 1965). The other REMs are either grouped REMs with 2 to 4 successive movements without pause (such movements can also be observed during the awake state), or are bursts of 5 or more successive REMs (these bursts are specific to REM sleep and cannot be seen in the awake state). In cats, half of the movements are isolated or grouped in small series, and half of them are produced in bursts specific to the REM sleep phase. During pauses (quiescent REM sleep), the eyes are placed either in an intermediary position or with a tonic lateral deviation (Jeannerod et al., 1965). These pauses in a tonic posture can involve a single eye, which can then join, with a slow movement, the contralateral eye in a conjugated movement (Berlucchi et al., 1964). Direct observation of the eyes in cats (Berlucchi et al., 1964; Jeannerod et al., 1965) and the electromagnetic search-coils tech-

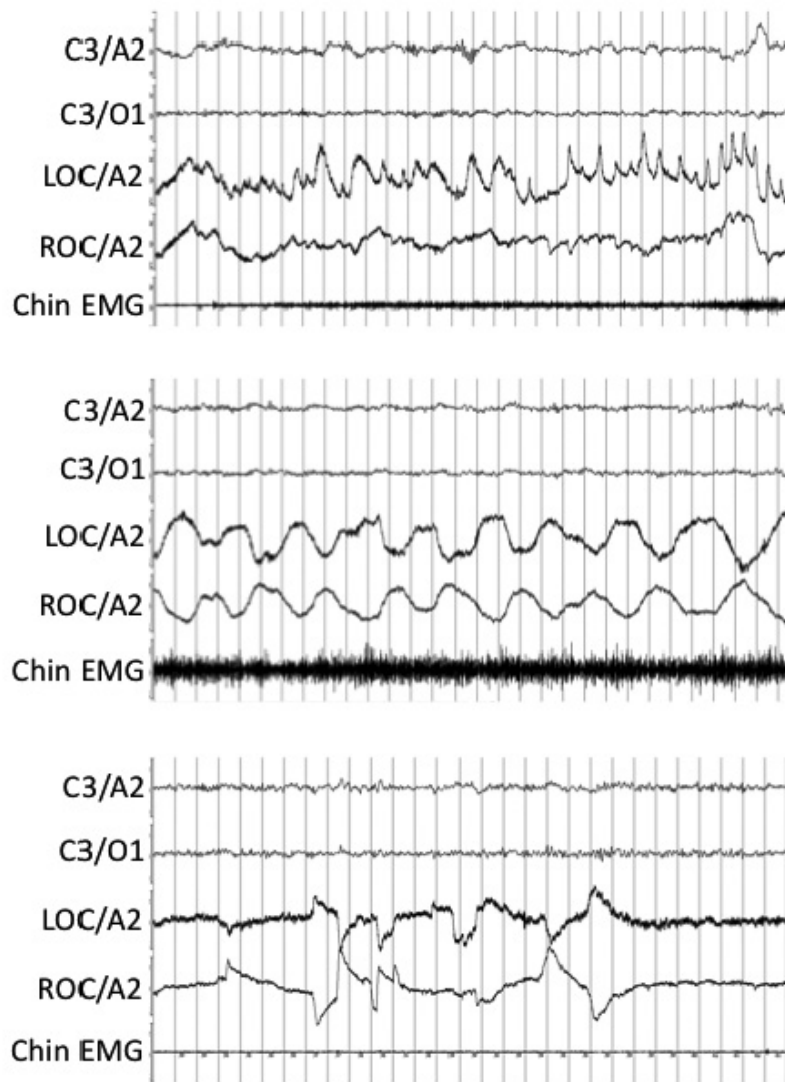


Fig. 1. - Eye movements recorded during 30 s of quiet wake (upper panel), sleep onset (middle panel) and REM sleep (lower panel) by conventional bipolar electro-oculography (left inferior external orbital canthus and right mastoid, LOC/A2, and right inferior external orbital canthus, ROC-A2), combined with central C3-A2 and C3-O1 EEG and chin muscle tone (EMG). During wakefulness, rapid eye movement recordings are artifacted by eyelid blinks, mostly visible on the LOC/A2 channel. Slow rolling eye movements (middle panel) are mainly observed at sleep onset but are also apparent with a lower amplitude throughout all sleep stages. In contrast, rapid eye movements (REMs, lower panel) with a sharp onset are observed only in REM sleep. They can occur as isolated movements or as bursts of REMs. There are no eyelid blinks, as the eyelid is closed.

nique in monkeys demonstrate that some binocular REMs are not coordinated (Zhou and King, 1997). This lack of conjugation suggests an absence of fixation point. The authors conclude that their data argue against the idea that REMs actually “track” dream images, unless each eye is watching its own dream.

#### *Frequency of REMs*

REMs are present during 14-27% of REM sleep (which means that, conversely, 73-86% of REM

sleep is devoid of REMs). The periods of REM sleep containing REMs are often designated as “phasic REM sleep”, as opposed to the periods with ocular quiescence, named “tonic REM sleep”. There is a mean of 15.9 REMs per minute of REM sleep and a range of 5 to 35 REMs per minute (Takahashi and Atsumi, 1997). In normal subjects, rapid eye movement activity peaks 5-10 min after the onset of a REM sleep period and then declines if the episode lasts longer (Fig. 2). The frequency of REMs

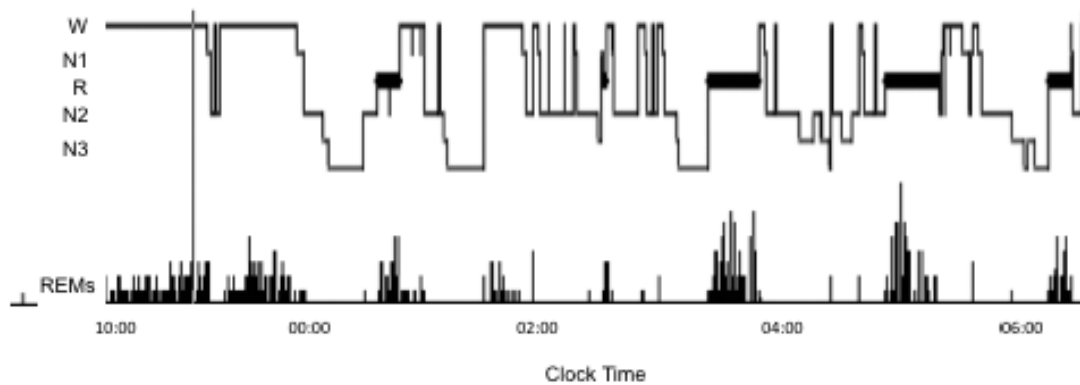


Fig. 2. - The sleep stages (W: wake, N1, N2, N3, 4: non REM sleep stages 1, 2, 3 and 4; R: REM sleep) are represented on the first track in a normal subject. The time of the night is represented on the x axis. The rapid eye movement activity (bottom trace, "REMs", the scale below the word REMs corresponding to 4 conjugated movements/min) is present during wakefulness. It peaks 5-10 min after the onset of an REM sleep period and then declines if the REM sleep episode lasts longer than 10 min. In a normal subject, it increases from early to late REM sleep periods across the night.

increases from early to late REM sleep periods (Aserinsky, 1971). The frequency and magnitude of REMs vary more among individuals than within individuals across successive nights (Takahashi and Atsumi, 1997). The frequency of REMs is increased in primary depression, compared to normal subjects (Foster et al., 1976).

## Mechanisms of REMs

### *Generators of REMs*

The ventromedial part of the caudal pontine tegmentum (VMCPT) is implicated in the generation of REMs bursts. It has a direct projection to the abducens nucleus, which, in turn, stimulates the contralateral oculomotor nucleus (Vanni-Mercier and Debilly, 1998). REMs (as well as ponto-geniculo-occipital [PGO] waves and muscle atonia) can be elicited by injections of carbachol (a muscarinic agonist) within the VMCPT. Conversely, their number is reduced (especially the REMs bursts) by injections of atropine (a muscarinic antagonist) within the VMCPT. These results suggest that, at least in the cat, the generation of REMs bursts can be activated by acetylcholine. In contrast, the isolated saccades in REM sleep are not affected by these injections. It is speculated that isolated saccades result from the release of the spontaneous activity of the abducens nucleus when the serotonergic and catecholaminergic inhibitory terminals on this nucleus

cease firing during REM sleep. The VMCPT also receives serotonergic and catecholaminergic inhibitory terminals. This observation is consistent with the general permissive role of the monoaminergic systems on REM sleep mechanisms. Also, from a clinical point of view, it can explain the occurrence of isolated REMs during non-REM sleep when monoaminergic systems are inhibited by antidepressants in patients (Schenck et al., 1992).

### *Brain functional imaging and MEG activity associated with REMs*

Motor-related brain activity before REMs during REM sleep is thought to differ from the mechanism that controls eye movement during wakefulness (Abe et al., 2008). While awake, the saccades are controlled by the frontal association areas (frontal eye field, supplementary eye field and dorsolateral prefrontal cortex), the precuneus prefrontal cortex, the supplementary motor area, posterior cingulate cortex and the posterior part of the superior parietal cortex (Johnston and Everling, 2008). Notably, the dorsolateral prefrontal cortex, which is hyperperfused during waking saccades in the dark, is hypo-perfused during REMs (Peigneux et al., 2001). These findings support the relative hypo-activity of associative prefrontal areas during REM sleep (Maquet et al., 1996). During REMs, activity is higher in the supplementary motor area and lower in the inferior parietal and precuneus cortex compared to the wakefulness with eyes closed. In a magneto-

encephalography study, the frontal eye fields and midpontine nuclei are activated during both waking and REM sleep saccades but display differences in timing, amplitude, time scale and sequence of activation. These results suggest that, during REMs, the midpontine nuclei drive eye movement and the frontal eye fields receive feedback from this activation (Ioannides et al., 2004).

### *Factors controlling REMs*

In cats, REMs are decreased during REM sleep when the occipital cortex is removed; however, they are greatly enhanced (almost doubled) and much more complex (bursts containing more than 50 REMs without any pause are commonly observed) when the frontal cortex is removed (Jeannerod et al., 1965). These results suggest that structures within the frontal cortex block REMs in the normal state, whereas the occipital cortex promotes them.

### *The frequency, amplitude and direction of REMs are influenced by the previous waking experience*

It is interesting to note that modification of oculomotor activity in an awake subject influences the characteristics of REMs over the following nights in a reciprocal manner. For example, when monkeys are conditioned to lower their eye movement frequency when awake, their REMs frequency increases during REM sleep (Berger, 1968). Subjects who wear goggles that contain minification lenses curtailing their vision to a 5° field for 5 days have a decreased amplitude and frequency of their eye movements in the awake state, and a much greater amplitude in their REMs during subsequent nights (Herman and Roffwarg, 1983). An increase of rightward horizontal saccades during waking causes a decrease of rightward eye movements during the subsequent REM sleep (De Gennaro et al., 1995). The responsiveness of this phasic event system of REM sleep to waking oculomotor manipulations implies plastic capabilities within the system and an inverse physiological influence of waking experience on REM sleep. Similarly, increased stimulation of the auditory system during wakefulness results in a decreased frequency of middle-ear muscle activity (another phasic marker of REM sleep) during the following night (De Gennaro et al., 2000). However, the oculomotor findings are specific to the saccadic system, as a pre-

sleep optokinetic stimulation exerts no influence on REMs (De Gennaro and Ferrara, 2000).

## Neurophysiological correlates of REMs

### *REMs do not always correlate with other phasic activities in REM sleep*

During REM sleep, the pupilla is mostly in a tonic, narrow myosis, but it can suddenly turn towards a wide mydriasis, mostly during the REMs (Berlucchi et al., 1964; Jeannerod et al., 1965). On average, 66% of middle ear muscle activity occurs in concordance with eye movements, but they are not always simultaneous (Pessah and Roffwarg, 1972).

### *Ponto-geniculo-occipital activity*

In animals, a specific phasic activity, named ponto geniculo-occipital (PGO) activity occurs in REM sleep and is tightly associated with REMs. PGO spikes are generated in the pons (caudoventral pontine tegmentum), with an output to the lateral geniculate nucleus, the pulvinar, the nuclei centralis lateralis and intralaminaris of the thalamus, and then a projection to the occipital, parietal and temporal cortices (Datta et al., 1998). They are routinely recorded in the lateral geniculate nucleus in cats. They occur as isolated spikes at the end of slow wave sleep, shortly before REM sleep, and then as isolated, grouped in doublets, or longer bursts during REM sleep (Jeannerod and Kiyono, 1969). PGO activity and REMs occur in close conjunction during REM sleep (Fig. 3). Some PGO waves are however not associated with REMs (Morrison and Pompeiano, 1966). It is possible to suppress PGO activity without suppressing REMs activity via lesions of specific pontomesencephalic areas, including the locus coeruleus pars alpha, the nucleus laterodorsalis tegmenti, the lateral parabrachialis and the pedunculopontine tegmentum or X area (Hobson, 1965; Sakai et al., 1976; Datta and Hobson, 1995). Conversely, the suppression of REMs by curare does not affect PGO activity (Jouvet, 1972). PGO spikes are generated simultaneously with REMs but not before (Nelson et al., 1983). Collectively, these experiments demonstrate that PGO activity and REMs occur in parallel rather than in series, with a common generator in the ventromedial part of the caudal pontine tegmentum (Vanni-Mercier and Debilly, 1998). This VMCPT

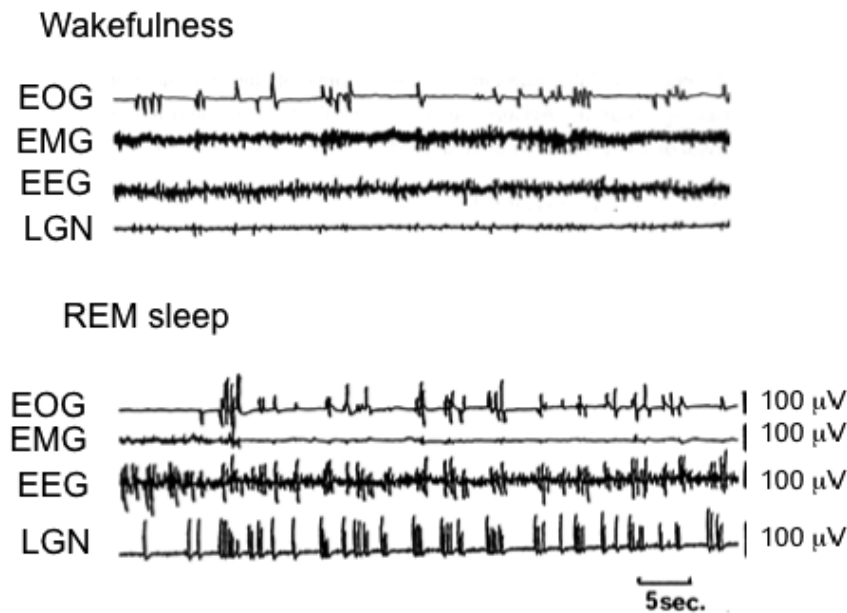


Fig. 3. - Polysomnography recordings in a cat, including eye movements via electro-oculography (EOG), neck electromyography (EMG), cortex activity (EEG) and deep brain recording of local field potentials within the lateral geniculate nucleus (LGN). In wakefulness (upper panel), eye movements occur without concomitant activity in the LGN, and muscle tone is high. During REM sleep (lower panel), REMs occur simultaneously with spikes in the LGN that represent ponto-geniculo-occipital (PGO) activity. Muscle tone is absent.

generator stimulates the saccade system, mostly via a decussated pathway (stimulating the contralateral eye nuclei). A schematic of the underlying connections is illustrated in Fig. 4.

PGO spikes are suspected to generate dream images and other hallucinatory aspects of dreams because they project to visual and temporal sensory brain areas. The suppression of PGO spikes in kittens leads to morphological defects in the lateral geniculate nucleus, a visual area (Davenne and Adrien, 1984). Furthermore, in kittens with monocular deprivation, the monocular segment that is cut off from visual input in the lateral geniculate nucleus contains smaller cells; this effect is further amplified if the animals are also deprived of REM sleep (Oksenberg et al., 1996). These series of experiments suggest that external (vision) and internal stimulation of brain visual areas via PGO spikes during REM sleep exerts a synergistic, positive effect on the subsequent development of the visual system. Moreover, they demonstrate that there are certain internal sources of visual input during REM sleep.

During RBD in cats with brainstem lesions, the motor sequences begin with a unilateral PGO spike coupled to an ipsilateral single REM, as if the cat

were watching an invisible target as it moves his head and eye laterally (Sastre and Jouvet, 1979). Later, REMs and PGO spikes occur in bursts as the cat develops more complex behaviours. Furthermore, isolated high-amplitude REMs are related to orienting behaviour in cats, whereas REMs occur in bursts during generalised movements (jumping, attacks or phasic unorganised movements) and are absent during continuous slow body movements such as licking (Soh et al., 1992). Recently, event-related functional MRI analysis time-locked to the occurrence of REMs revealed that the pontine tegmentum, ventro-posterior thalamus, primary visual cortex, putamen and limbic areas were activated in association with REMs, providing evidence for the presence of PGO spikes in humans (Miyauchi et al., 2009).

### Other functions ascribed to REMs

In addition to the scanning hypothesis of REMs, detailed below, several authors suggested that the REMs may be used for lubricating the ocular surface (Murube, 2008), warming the brain (Wehr, 1992), stimulating and stabilising the circuits that have been

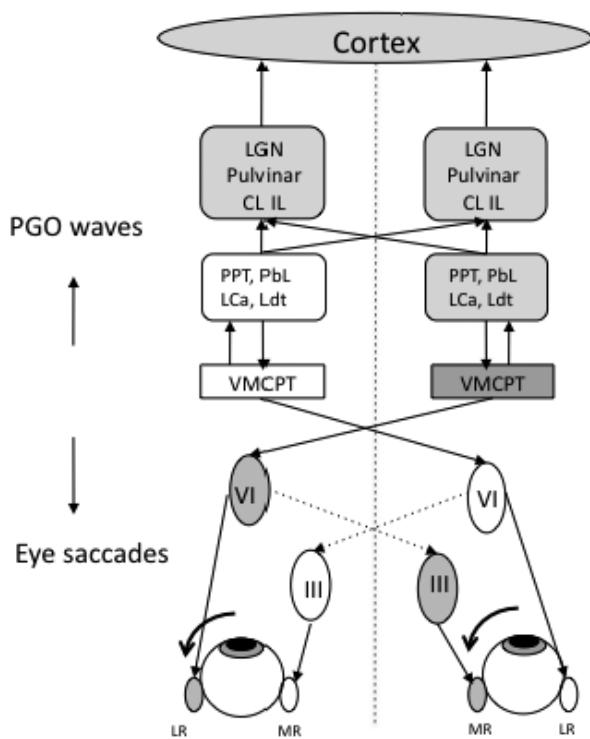


Fig. 4. - Schematic representation of the model linking the PGO and the REMs activity during REM sleep (adapted with permission from Vanni-Mercier and Debilly, *Neuroscience*, 86: 571-585, 1998). A common generator, the left ventromedial part of the caudal pontine tegmentum (VMCPT), has two simultaneous stimulating projections: (i) it projects to the right abducens nucleus (VI) of the opposite (right) side that induces lateral REMs by contraction of the lateral rectus (LR), which can be conjugated by projection to the left oculomotor nucleus (III) and contraction of the medial rectus (MR), as in wakefulness; (ii) The left VMCPT, projects simultaneously to several structures on the same (left) side, including the pedunculopontine tegmentum (PPT) or X area, the nucleus parabrachialis lateralis (PbL), the pars alpha of the locus coeruleus (LCa), and the laterodorsal tegmentum (Ldt). These "PGO-on" cells have bilateral projections to various thalamic nuclei (lateral geniculate nucleus, LGN, pulvinar, nucleus centralis lateralis of the thalamus, CL, and nucleus intralaminaris of the thalamus, IL), which in turn project to the temporal, parietal and occipital cortices. The III nucleus is represented at the bottom of the figure for clarity. This does not represent its anatomical location. Note that the inhibitory influences of serotonin neurons from the raphe nuclei and of noradrenergic neurons from the locus coeruleus onto the cholinergic neurons of the pontine tegmentum need to be first removed for the PGO and REMs to appear.

insufficiently activated during waking (Herman and Roffwarg, 1983), and affording intense endogenous stimulation to enhance the ontogenic development of the central nervous system (Roffwarg et al., 1966), or that REMs may serve no purpose at all and may

be simply random markers of brain activation. By analogy, penile erection during REM sleep mostly occurs in the absence of sexual dreams (Schenck et al., 2007); hence, it may serve a proper goal (possibly rehearsing the sexual function and keeping the reproduction system healthy, which is mandatory for human species to survive) independently of the dream (and brain) content.

## Cognitive correlates of REMs

### *Correlation between visual dreams and REMs frequency*

If one hypothesises that REMs and visual dreams are related, the more there is to "see" in a dream, the more eye movements there should be. In a single subject (to rule out inter-subjects differences), there is a strong correlation (0.76 to 0.82) between the amount of visual imagery in dreams and the number of REMs when they are counted during the four minutes preceding the awakening (Hong et al., 1997). However, visual imagery can occur in the absence of REMs. An early work by Molinari and Foulkes reported more visual imagery in conjunction with REMs than in tonic REM sleep without REMs (Molinari and Foulkes, 1969), but the same team failed to reproduce this result in a larger sample size (Foulkes and Pope, 1973). In addition, there were no differences in the frequency of dreams, mood and dream content in 11 subjects awakened during phasic versus tonic REM sleep (Hodoba et al., 2008). However, healthy volunteers report more active dreams when awakened during bursts of REMs (Berger and Oswald, 1962). Dream mentations obtained during non REM sleep also contain visual imagery, especially if they are collected in the early morning (Fosse et al., 2001). There are however more hallucinations (whether visual, auditory or tactile) during REM sleep than during non-REM sleep mentations.

### *REMs in the absence of sight*

If REMs are directly related to looking around in dreams, they should disappear in the absence of sight. As we mentioned before, REMs are absent during paradoxical sleep in the mole, which is devoid of visual system (Allison and Van Twyver, 1970). In contrast, REMs persist in cats after lesion-



ing the visual cortex (Jouvet, 1962) and in pontine preparations (Arnulf et al., 1998), whereas they disappear during the awake state. The number of REMs is reduced by two-thirds, and their complexity is changed (most of them are isolated and lateral) in pontine preparations (Jeannerod et al., 1965). Despite their lack of vision, feline foetuses display abundant REMs during agitated sleep (a precursor of REM sleep), ten days before they open the eyes and are able to display eye movements while awake (Jouvet, 1962). This is also the case in human foetuses and neonates. Subjects who have been blind since birth display REMs during REM sleep (Gross et al., 1965). Whether they also have a kind of visual experience during their dreams is a matter of controversy. Although Kerr et al. earlier reported that two congenitally blind subjects (and those who lose their sight before the age of 5 to 7) had dreams without visual content (Kerr et al., 1982), Bertolo et al. recently challenged this result and demonstrated that the congenitally blind may have visual content in their dreams and are able to draw this content (Bertolo et al., 2003). In these instances (except for surgical preparations), the absence of visual perception does not imply an absence of visual imagery.

#### *Retrospective correlation between observed REMs direction and direction of gaze in the dream*

The possibility remains that there are central commands for eye movements related to dream imagery. In 1962, Roffwarg et al. made detailed observations of the relationship between the polygraphically represented patterning of REMs in REM sleep and the gaze alterations that were dreamed in the short intervals of time just preceding the experimental awakenings (Roffwarg et al., 1962). In all studies performed in normal humans, subjects were awakened during REM sleep (while their eye movements were monitored) and reported their dreams. Scenes requiring a determining control of gaze were selected. This approach required a relatively rapid arousal and rapid recollection of dream mentation, followed by the *post-hoc* assessment of eye movement-dream imagery correspondence, i.e., the temporal alignment of connected events in the dream narrative and the eye-movement recordings. Using this technique, some authors found a 70-80% correspondence (Dement and Wolpert, 1958; Roffwarg et al., 1962;

Herman et al., 1984). A demonstrative example was a sleeper looking up and down during REM sleep; followed by his report that he dreamed of climbing up a series of ladders looking up and down as he climbed (Dement and Kleitman, 1957). In contrast, others found only a 9-32% correlation (Moskowitz and Berger, 1969; Jacobs et al., 1972). One subject, for example, stated that she was looking at vertical rows of buttons from a distance of about 2 feet. She specified that she was looking vertically in her dream, but the EOG record was almost entirely horizontal before awakening (Moskowitz and Berger, 1969). However, determining the correspondence between eye movements and dream imagery is challenging due to the use of varying and subjective methodologies, as well as amnesia and a lack of clarity in dream recall. Furthermore, in the awake state, the eyes and head work in concert to produce gaze (Herman et al., 1984). Only with the summation of head and eye activity does an isomorphism between gaze and target become apparent. In normal REM sleep, the atonia spares the extraocular muscles but not the neck muscle so that the head cannot move, rendering the parallel between observed eye movements and the subject's description of gaze (in the dream) uncertain. Based on these numerous methodological problems, it was later concluded that the scanning hypothesis could not firmly be tested using the retrospective correlation between the observed REMs direction and the recalled direction of action and gaze in the dream (Herman et al., 1984).

## The REM sleep behaviour disorder

### *A model to access dream content*

One way to circumvent these methodological problems (recall bias, retrograde assessment, dissociation between the neck and eye movements) in humans is to study subjects with RBD. This recently-described parasomnia is characterised by dream enactment during REM sleep (Schenck et al., 1986). Patients yell, kick, slap or catch invisible objects, with incomplete atonia during REM sleep. REM sleep behaviour disorder affects subjects without any other disease (idiopathic RBD) or in association with various neurological and neurodegenerative diseases, mainly synucleinopathies (Boeve et al., 2007). Using video and sleep monitoring (Oudiette

et al., 2009) we observed several complex, non-violent dreams, enacted during REM sleep, including an ex-smoker mimicking the quiet gesture of smoking a fictive cigarette during REM sleep (Fig. 5 and Supplemental Video 1). We suspect that as he turns his head rightward and downward to scratch his cigarette in an ashtray, eye and head movements are coordinated towards the fictive cigarette in his hand. We therefore sought to determine how eye and head movements matched the suspected dream target in a series of patients with RBD.

### REMs in RBD

We monitored REMs by EOG in four directions (right, left, up and down), after having calibrated them with a target during wakefulness, and syn-

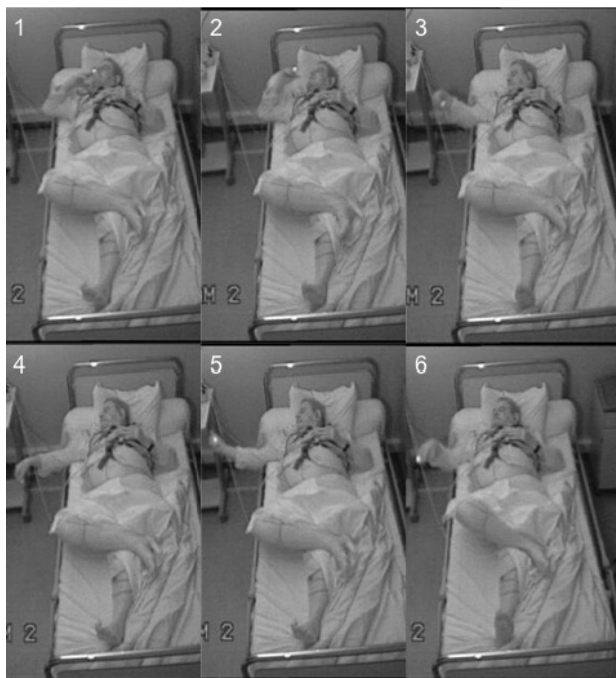


Fig. 5. - A narcoleptic patient is in REM sleep and displays complex sleep behaviour (the images are extracted from the video clip). He mimics the gesture of smoking a fictive cigarette (the oximeter on his right finger glows in infrared light). While the patient's eyes are closed, it appears that he first inhales the cigarette (images 1 and 2), extends the arm to shake off the ash (image 3) and then scratches the cigarette in a fictive ashtray (images 4 and 5). As he does so, his head turns toward his fingers, as he would do awake to reach the ashtray. Eventually, after he extinguishes the cigarette, he throws it away while turning his head in the opposite direction (image 6). The whole behaviour is compatible with a complex coordination of the gaze (via the head and eye coordinated motor system) toward the action in dream.

chronised these recordings with video and sleep monitoring (Leclair-Visonneau et al., 2010). The studied population included 56 patients with RBD of various origin (idiopathic RBD,  $n = 25$ ; idiopathic Parkinson's disease,  $n = 14$ ; multiple systemic atrophy,  $n = 10$ ; dementia with Lewy bodies,  $n = 5$ ; and idiopathic narcolepsy,  $n = 2$ ) and 17 healthy controls matched for age and sex. The participants were monitored during one or two consecutive nights. RBD-associated behaviours occurred 2.1 times more frequently during REM sleep with REMs than during REM sleep without REMs. This was the case for all categories of behaviours, from mild jerk of an arm to scenic, nearly subtitled complex behaviours. This result supports an association between the phasic generators of REMs and body movements. When behaviours were associated with REMs, eye movements were isolated ( $48.1 \pm 13.8\%$ ), clustered ( $37.3 \pm 10.3\%$ ), or bursting ( $14.6 \pm 12.6\%$ ). With regards to the temporal link between REMs and behaviours, we reported that  $43.5 \pm 8.2\%$  of REMs were concomitant with the behaviours. We observed that  $35.2 \pm 8\%$  of REMs preceded the behaviours and  $21.4 \pm 5.7\%$  of REMs followed the behaviours. However,  $78.3\%$  of REMs were not associated with body movements in the patients with RBD. In such cases, it is possible that the dreamers were passively "watching" moving pictures as a part of their dream without taking part in the action. Alternatively, the system that blocks muscle tone could be partially present during these periods. The hypothesis that some active dreams are transiently blocked by the REM sleep atonia is supported by the observation that only  $9\%$  of REM sleep time was associated with visible behaviours in these patients with RBD, suggesting that we only accessed a small, albeit interesting, part of the 'iceberg' of dream content (assuming, as was partially demonstrated by Dement and Wolpert in 1958, that dreaming takes place throughout REM sleep). If one compares the dream scene to a play, an absence of visible behaviour may either mean that there is no action at this moment in the play, or that the curtain is transiently closed. Conversely, body movements were also observed without REMs. In these cases, the control of vision could be unnecessary during this part of the inner scenario; for example the dreamer could be watching something at a distance or just staring at an object. In line with this hypothesis, Dement

and Kleitman showed that subjects awakened after periods of ocular quiescence during REM sleep were mostly watching distant objects (Dement and Kleitman, 1957).

REM density (% of REM sleep with REMs), index (frequency/min of REM sleep) and complexity (when classified as isolated, grouped or bursts, as in Jeannerod et al, (1965) did not differ between patients with RBD and controls.

#### *Gaze direction during targeted behaviours in RBD*

There were 19 goal-oriented behaviours in 9 patients. Patient 1 was attacked by lions and glanced at his aggressor while escaping. Patient 2 ordered an employee on his right-hand side (i), pulled a fictive object down (ii), waved to someone on his right side (iii), and lifted up an imaginary object, seemed to frame something with his hands (Fig. 6) then put it on his right side (iv). Patient 3 called someone on his right side (i), strangled an attacker just below him (ii), and challenged someone on his left (iii). Patient 4 was attacked on his left then on his right side (i), and started a fight on his left side (ii). Patient 5 grabbed an object below him (i), and grabbed something on



Fig. 6. - A patient with RBD associated with narcolepsy mimics the quiet gesture of framing (using a fictive camera) during REM sleep. In this patient, the eye movements (measured with an EOG under the closed eyes) are exactly within the frame formed by the hands during the whole behaviour.

his far left side (ii). Patient 6 talked to someone on his right side. Patient 7 kissed a fictive friend standing on her right side. Patient 8 kicked and challenged an aggressor on his left side. Patient 9 grabbed an object above him and then climbed a ladder (Fig. 7 and Supplemental Video 2) (i), grabbed something below him (ii), pushed someone on his left-hand side (iii), and grabbed an object on his left side (iv). The mean duration of the goal-oriented behaviours was  $14.2 \pm 7.1$  seconds.

Among the REMs that accompanied goal-oriented motor behaviour during RBD, 82% were directed towards the action of the patient (example in Fig. 7). When restricted to determinant REMs, the level of concordance increased to 90%. These results indicate that the limbs, hands, head and eyes move together in a coherent, directional manner during RBD. The final gaze is placed in the direction and plane of the fictive target. However, REMs were absent during 38 to 42% of behaviours. The main advancement of this study over preceding experiments testing the scanning hypothesis (based on dream-recall and *a posteriori* correlation) is the presence of an external, dreamer-independent, 'on-line' check of the dream scenario. This check is key in order to avoid the numerous biases associated with the *a posteriori* recall method (total or partial amnesia, censure, reconstruction of a scenario, clarity of recall, simplicity of the narrative, interference by the investigators).

This directional coherence between limb, head and eye movements during RBD suggests that, when present, REMs imitate the scanning of the dream scene. Because the REMs are similar in subjects with and without RBD, we suggest the extension of this concordance to normal REM sleep.

#### **REM sleep as a dynamic movie experience: an attempt to reconcile the results**

Collectively, the results from the sleep studies suggest a parallel organisation of the oculomotor, PGO and behavioural systems. This model has already been suggested by Vanni-Mercier and Debilly in 1998 for the parallelism of REMs and PGO. This type of organisation implies that REMs, PGO waves and movements are generated simultaneously, as

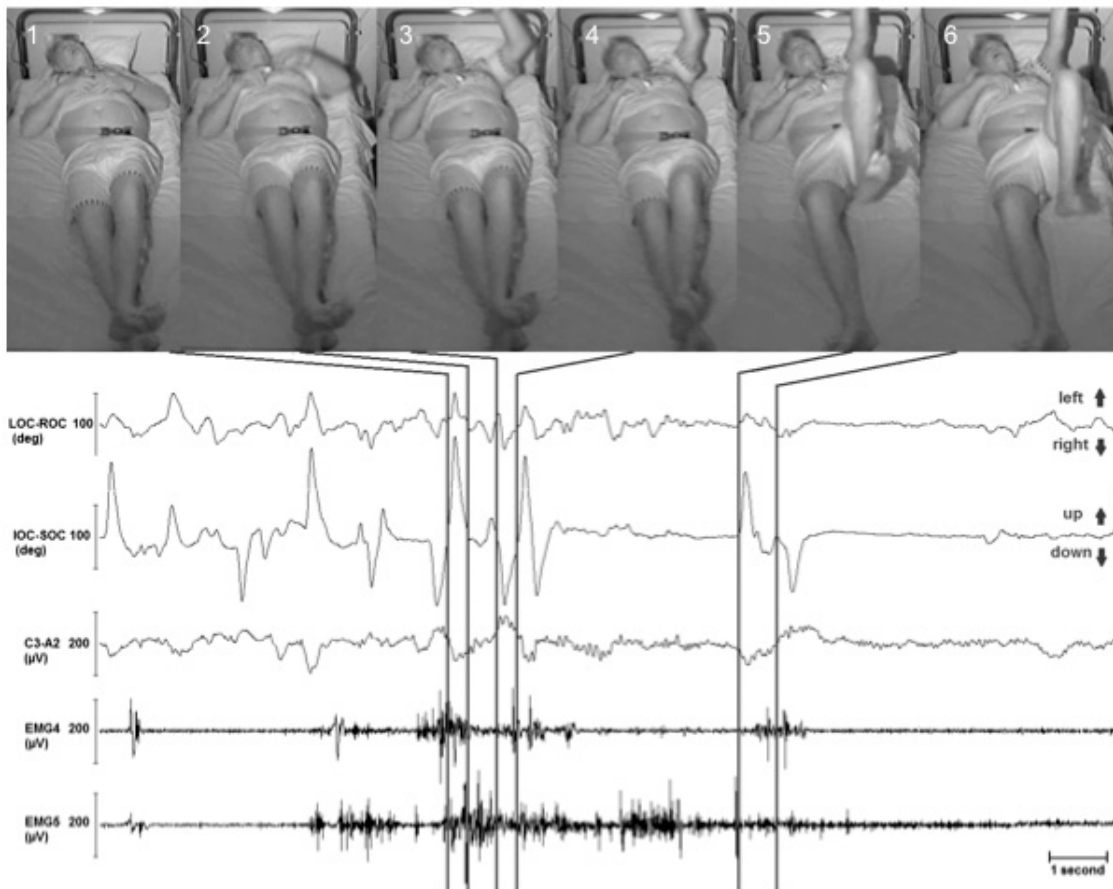


Fig. 7. - Example of REMs (lower panel) and synchronous RBD-behaviour (upper panel) when the patient (with Parkinson's disease) dreams that he is climbing on a ladder. The traces at the bottom represent a 20-second epoch of REM sleep with RBD. The two electro-oculography channels monitor (in degrees) the horizontal movements between LOC (left external canthus) and ROC (right external canthus) and the vertical movements between SOC (left supra-orbital canthus) and IOC (left infra-orbital canthus). C3-A2 is the EEG channel, and EMG channels monitor the muscle activity of the right (EMG4) and left (EMG5) extensor carpi. The vertical lines refer to the corresponding frames shown in the upper part of the figure (for full video, see supplemental Video 2): (1) The patient is resting, a leftward and upward gaze begins; (2) The head is directed towards the top and left part of the space, the left arm is raised, and REMs have just ended; (3) The head is still directed towards the top and left, the left arm is up, and the REMs begin to move rightwards and downwards; (4) The head is more directed to the bottom and the right, and the REMs are over; (5) The patient raises his left leg to climb on a ladder, while the REMs start to move upwards; (6) The head is more directed upwards (the patient trying to climb higher). Figure reproduced with permission of from (Leclair-Visonneau et al., 2010).

three corollary outputs of a common generator. Signals sent to the visual, parietal and temporal centres would represent a copy of the discharges sent simultaneously to oculomotor centres (mainly the abducens nucleus) and limb motor centres (probably the motor cortex), and vice-versa. This model allows a temporal link between images (supposedly generated by PGO), REMs and limb movements because they occur simultaneously, but it does not imply a causal relationship among these events. Therefore, it does not require that REMs are directed by the visual content of dreams, as it is the case during wakeful-

ness with open eyes, or during mental recollection of visual scenes with closed eyes. The only correspondence between visual, oculomotor and behavioural centres would be ensured by the similarity of neuronal discharges impinging on the three systems. One may imagine that these discharges have some kind of side and plane representation, such that any PGO projected to the left visual cortex (possibly generating an image) would be associated, through corollary discharges, with REMs and limb movements directed toward the left side. Stimulation of the auditory cortex, through ponto-geniculo-temporal spikes,

would be similarly associated to middle-ear muscle activity. This parallel organisation would function without feedback from the real visual world and from internally generated visual scenes. It would account for the complete dissociation between the PGO and the REMs systems in foetus or pontine cats, or for the occasional absence of conjugation between the eye movements. This model resembles a moppet, or the dynamic movie experience that can be found at some fairs (called the 4D Cinema Movie Theatre System) in which a spectator looks at a movie that is entirely shot from the first person perspective (as if the spectator were carrying the video camera). He is placed in a special motion chair, which moves simultaneously and rapidly in various positions in order to mimic the action at the screen (e.g., as if the spectator was turning when the car turns, or falls, swings depending on the action at the screen). In these instances, a common system coordinates the movements of the chair and the images on the screen. This type of outflow model fits the more general concept that the brain “innervates” itself during REM sleep. This type of model does not explain why this system exists or the origins of dreams, but it may shed some light onto a system of virtual reality driven by the brainstem every night.

## Summary

Rapid eye movements (REMs) and visual dreams are salient features of REM sleep. However, it is unclear whether the eyes scan dream images. Several lines of evidence oppose the scanning hypothesis: REMs persist in animals and humans without sight (pontine cats, foetus, neonates, born-blinds), some binocular REMs are not conjugated (no focus point), REMs occur in parallel (not in series) with the stimulation of the visual cortex by ponto-geniculo-occipital spikes, and visual dreams can be obtained in non REM sleep. Studies that retrospectively compared the direction of REMs to dream recall recorded after having awakened the sleeper yielded inconsistent results, with a concordance varying from 9 to 80%. However, this method was subject to methodological limitations, including the bias of retrospection and neck muscle atonia that does not allow the determination of the exact direction of gaze. Using the model of RBD (in which patients are able to enact their dreams due to the

absence of muscle atonia) in 56 patients, we directly determined if the eyes moved in the same directions as the head and limbs. When REMs accompanied goal-oriented motor behaviour during RBD (e.g., framing something, greeting with the hand, climbing a ladder), 90% were directed towards the action of the patient (same plane and direction). REMs were however absent in 38% of goal-oriented behaviours. This directional coherence between limbs, head and eye movements during RBD suggests that, when present, REMs imitate the scanning of the dream scene. Because REMs index and complexity were similar in patients with RBD and controls, this concordance can be extended to normal REM sleep. These results are consistent with the model of a brainstem generator activating simultaneously images, sounds, limbs movements and REMs in a coordinated parallel manner, as in a virtual reality.

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