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·Review·

Perchance to dream? Primordial motor activity patterns in vertebrates from fish to mammals: their prenatal origin, postnatal persistence during sleep, and pathological re-emergence during REM sleep behavior disorder

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An overview is presented of the literature dealing with sleep-like motility and concomitant neuronal activity patterns throughout the life cycle in vertebrates, ectothermic as well as endothermic. Spontaneous, periodically modulated, neurogenic bursts of non-purposive movements are a universal feature of larval and prenatal behavior, which in endothermic animals (i.e. birds and mammals) continue to occur periodically throughout life. Since the entire body musculature is involved in ever-shifting combinations, it is proposed that these spontaneously active periods be designated as 'rapid-BODY-movement' (RBM) sleep. The term 'rapid-EYE-movement (REM) sleep', characterized by attenuated muscle contractions and reduced tonus, can then be reserved for sleep at later stages of development. Mature stages of development in which sustained muscle atonia is combined with 'paradoxical arousal' of cortical neuronal firing patterns indisputably represent the evolutionarily most recent aspect of REM sleep, but more research with ectothermic vertebrates, such as fish, amphibians and reptiles, is needed before it can be concluded (as many prematurely have) that RBM is absent in these species. Evidence suggests a link between RBM sleep in early development and the clinical condition known as 'REM sleep behavior disorder (RBD)', which is characterized by the resurgence of periodic bouts of quasi-fetal motility that closely resemble RBM sleep. Early developmental neuromotor risk factors for RBD in humans also point to a relationship between RBM sleep and RBD.

Keywords: sleep; development; evolution; spike-train analysis; spontaneous motility; neuronal networks; neuroplasticity; REM sleep behavior disorder

An earlier essay examined the physiology of periodic, apparently non-purposive, spontaneous movements in species ranging from phylogenetically primitive animals, such as coelenterates and nematodes, to endothermic vertebrates such as birds and mammals[1]. Together with 'wakefulness' (in its motorically quiet as well as its active form) and 'sleep', which hitherto had been considered to be an exclusively motorically quiescent state (e.g., Siegel 2008[2]), this defines a fourth class of behavior which is widely distributed throughout the animal kingdom[3]. A 2 x 2 matrix consisting of the axes, *active vs. quiet* and *wakefulness vs. sleep*, thus dictates the term 'active sleep' as the most appropriate appelation for this fourth broad category of behavior (see Corner 2013)[4].

Subsequently, the ontogeny of this striking phenomenon - which has been referred to as 'seismic' sleep[5] or, more generally, motorically '*active* sleep' (MAS) – was reviewed across a wide spectrum of

invertebrate phyla, classes and orders[4]. Although the so-called mature form of MAS (viz., *rapid eye movement* (REM) or 'paradoxical' sleep[5-7]) appears to have evolved independently in birds and mammals[2,8,9], many ectothermic vertebrates are also on record as showing repetitive, apparently non-purposive and often stereotyped, spontaneous muscular contractions during early ontogeny[3,10,11,12] (Fig. 1). The present paper reviews the evidence that MAS, with its defining multi-second spontaneous rhythms[13], far from being a phylogenetic 'end point' (e.g, Rattenborg[14]; Siegel[8]), in fact represents the persistence of a primordial developmental state that is characteristic for animal behavior from the very onset of multicellular animal evolution. More generally, sleep may well be a fundamental manifestation of many simple neuronal networks[1,15–17].

Prenatal Origins of Intrinsic Neurogenic Motility

Early prenatal development reveals a highly uniform picture which is consistent with the postulate of a primal neurological set of mechanisms being the starting point for behavioral evolution[1]. Thus, intermittent ('phasic') neurogenic muscle contractions, both local and generalized, are present from the time of initial innervation by motor nerves[18,19]. These develop rapidly into a complex oscillatory bursting pattern which gradually becomes the dominant feature of fetal behavior[10,12]. Deafferentation experiments *in situ* soon confirmed the intrinsic, non-reflexogenic, nature of motility in the chick embryo[20], while *in vitro* experiments led to the same conclusion for amphibian and mammalian neuromotor systems[15,21,22]. It could be relevant for the understanding of sleep-related movement and behavioral pathologies in later life[23] that stereotyped, well organized, muscular contractions are in fact present from the onset of spontaneous motility both ontogenetically[24-26] and phylogenetically[3,4]. REM sleep behavior disorder (RBD)[27] for instance, mimicks in many respects normal fetal and early postnatal motor movement patterns. RBD not only manifests with complex dream-enacting behaviors, but more often during video-polysomnographic monitoring demonstrates simple twitches and jerks, and an array of movements, including repetitive movements, that may not carry much clinical importance, but rather carries neurodevelopmental scientific importance, which is a focus of this paper.

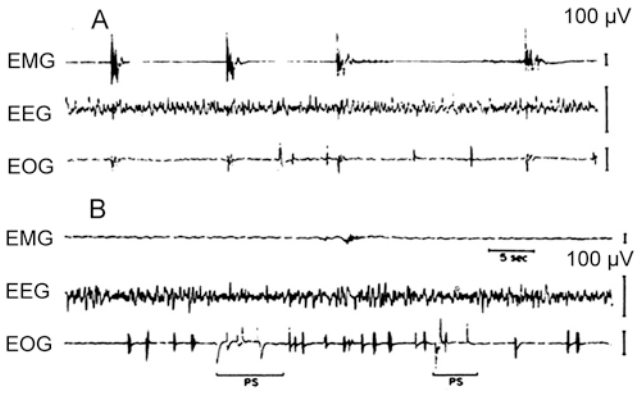

Fig. 1. Spontaneous body movements (EMG), eye movements (EOG) and cerebral EEG in a chick embryo (Gallus domesticus) on the day before hatching, during periods of (A) continuous slow-wave sleep and (B) sleep with intermittent brief 'paradoxical' EEG episodes (from Corner 1985[10]). [Note that stereotyped bursts of whole-body movements, as illustrated in trace A, are largely absent during sleep episodes when Paradoxical Sleep (PS) is frequent (trace B), the latter being rather short as is typical for birds].

In all three of the above-mentioned vertebrate classes, spontaneous behavior takes the form of isolated twitching at shifting bodily locations, interspersed with brief bursts of coordinated non-purposive movements that follow one another at highly variable intervals[3,10,28,29,30]. Sometimes such 'phasic' motility occurs several times in rapid succession for a few seconds but, more often, several seconds of quiescence intervene between clusters of twitches. The latter can involve any part or parts of the musculature, or all of it more-or-less simultaneously. It must be emphasized here that spontaneous coordinated bursts of movement in all the species studied closely resemble the short-lived escape responses elicited by tactile stimulation anywhere on the body surface[11,12,31,32].

Quiescent periods on the order of 30 seconds to several minutes, as well as occasional silences on the order of a half an hour or even longer, are also ubiquitous prenatal occurrences in immature sleeping vertebrates[3]. Embryonic sleep thus presents rhythmicities corresponding closely to, on the one hand, motorically quiet *versus* active sleep (MAS), and on the other hand, phasic *versus* tonic MAS as seen in mature indviduals. A high point of motility

is reached at ca. two weeks of incubation in chickens[18,20,32], around the time of birth in rats[5,33], post-natal day 35 in ferrets[34], and at 6–7 months of gestation in humans[35,36]. At this point, variable bursts of spontaneous body movements follow one another in rapid succession, after which the amount of time occupied by such overt somatic muscle contractions begins to decrease. Motility cycles with periodicities similar to those in full-term neonates, viz. 30 and 80 seconds, become prominent in the last month of gestation in humans[35,36]. Beginning a few days prior to hatching, chick embryos generate minute-long trains of stereotyped short bursts of struggling movements, alternating with recognizable active sleep episodes (Fig. 1), indicating that built-in 'fixed action patterns'[12,37,38] are already an integral component of sleep behavior.

The vigor and extent of muscular activity and its widespread neurological substrate in prenatal animals[39-42] call for a distinctive terminology, such as *'rapid-BODY-movement'* (RBM) sleep, which would highlight the developmental continuity with what in later life is conventionally called *rapid-EYE-movement* (REM) sleep. A striking example of this continuity is the preservation throughout life of the stochastic and rhythmical nature of fetal spontaneous motility[10,43,44]. This implies that subliminal excitatory fluctuations may still be taking place within the spinal cord and medulla oblongata, needing now only to receive adequate stimulation from the pontine trigger zone[6,7,45] in order to once again reach threshold for effectively evoking motoneuron discharges, as has been nicely demonstrated in chick and mouse embryos[46,47].

Both in chick embryos and neonatal rats, RBM sleep is clearly a compound state, as illustrated, for instance, by the differential susceptibility of twitching and global bursting to pharmacological interventions[48]. Thus, while clomipramine selectively suppresses REM sleep in neonatal rats, it fails to eliminate coordinated bursting (i.e., type III embryonic motility of Hambuger[20]), but causes an almost total disappearance of spontaneous twitching (type I motility Hamburger[20]; Fig. 2). The sedative chloral hydrate, in contrast, selectively suppresses type III movements while sparing twitches and startles, thus suggesting that one or more components of the 'arousal' system underlying waking behavior is intermittently engaged even during sleep. This could be an important clue to the neurological abnormalities

Fig. 2. Spontaneous movements during sleep in a 3-day-old rat pup, *Rattus norvegicus*, showing (upper trace) all three basic components of fetal motility, viz., twitches, startles and whole-body quasi-struggling movements. Lower trace: selective elimination of twitching by the REM-sleep suppressant drug clomipramine (from Corner and Mirmiran[48]).

underlying the clinical condition of 'REM sleep behavior disorder' (RBD), in which coordinated body movements during sleep surface later in life[23,27]. Since spontaneous motility is reflected all the way up to the cerebral cortex level by virtue of proprioceptive feedback evoked by each movement[49,50], these could contribute to activity-dependent maturational processes at many levels of the developing central nervous system. It would be of great theoretical importance to find out what the relative contributions of these sleep-like behavior patterns (Fig. 2; [3,18]) are at each stage of development. Sleep and wakefulness might thus not be as distinct, physiologically speaking, at the brainstem level[30] as they appear to be when attention is directed towards forebrain control mechanisms.

Neonatal Persistence of Sleep-Like Motor Rhythms

Since mature mammalian REM sleep is a labile state which often fails to manifest itself if environmental conditions are not "just right"[5,8], and since, furthermore, it is conceivable that it disappears altogether in cold-blooded organisms prior to attaining adulthood, it is imperative in this field to work backwards in time in order to avoid potentially false negative conclusions about the presence or absence of REM/RBM sleep in a given species[51,52]. In other words, ectotherms may best be distinguishable one from the other not (as in endotherms) on the basis of adult RBM sleep percentages but, rather, by the length of time that any motorically active sleep (MAS) persists following emergence from the egg.

Aquatic vertebrates (fish and amphibians) are generally altricial at the time of hatching and continue to exhibit variable, often highly periodic, trains of short (ca. 1 s on average) stereotyped total-body movement bursts[11,12,31] (Fig. 3). These are identical in appearance to the animals' coordinated escape responses to tactile stimulation anywhere on the body surface, a striking example of what in ethology is called behavior 'in vacuo' (never before reported for such early stages: Tinbergen[53], although vivid examples in salamanders, bullfrogs and crocodiles can be seen on the internet: personal obervations). Remarkably similar spontaneous motility rhythms, involving short bursts of coordinated swimming as well as isolated 'tail flicks' have also been reported for the larval stages of such a primitive chordate species as the ascidian, *Ciona intestinalis* ('sea cucumber'[54,55]), a putative early evolutionary forerunner of the vertebrates[56].

Once sustained swimming and goal-directed feeding commence, a global physiological state akin to waking in endothermic vertebrates[32] (Fig. 4) has evidently taken over the control of behavior. The period of development between this early stage of putative wakefulness and sleep in adults has hardly been looked into for ectotherms, but it can be surmised that a similar waning of overall sleep time as takes place in birds and mammals – and also in the cuttlefish, a highly evolved cephalopod mollusc[4,57] will be observed as these animals grow older. It will be of special interest to see if their sleep shows spontaneous bouts of

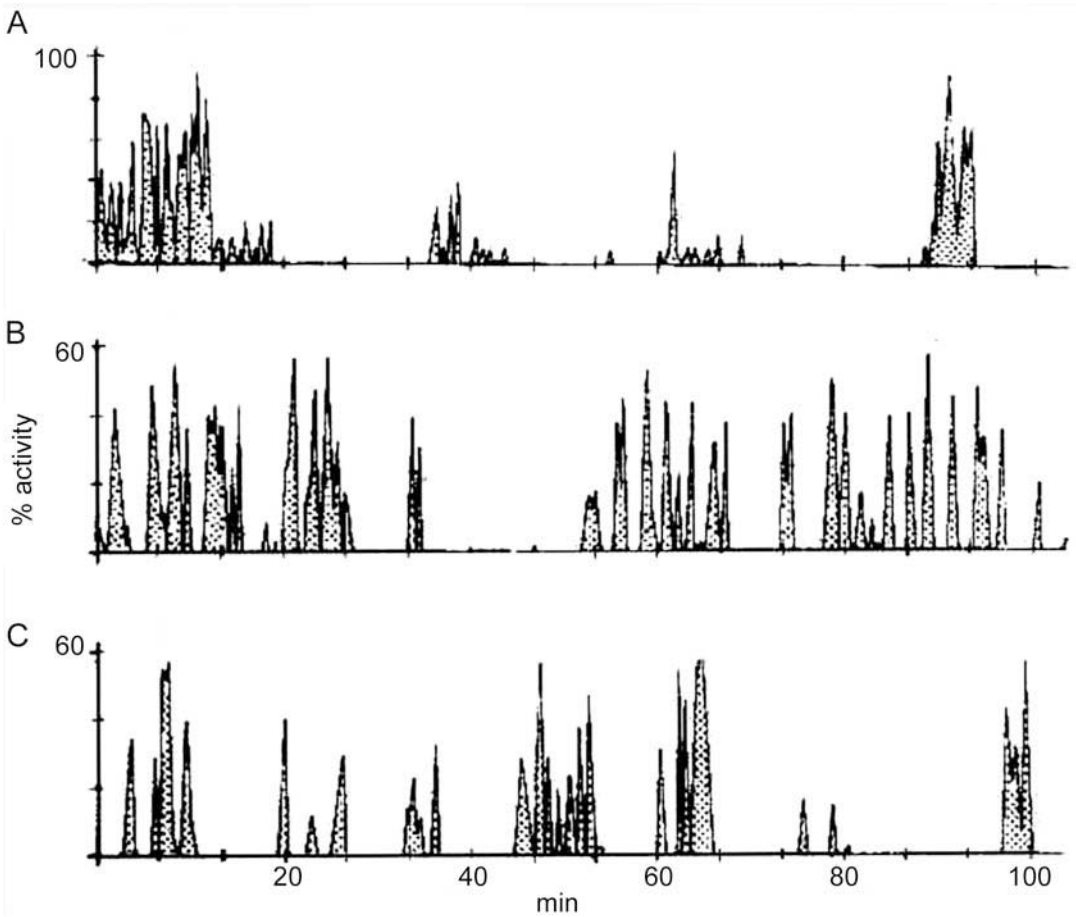

Fig. 3. Spontaneous motility in three specimens of an aquatic toad (*Xenopus laevis*) showing peaks of activity every few minutes as well as quiescent periods on the order of 10–20 min. Each peak consists of a train of short (ca. 1 s) bursts of vigorous wriggling movements. The ordinate gives the percentage of time spent moving in successive 1-min blocks (abscissa) (From Corner 1985[10]).

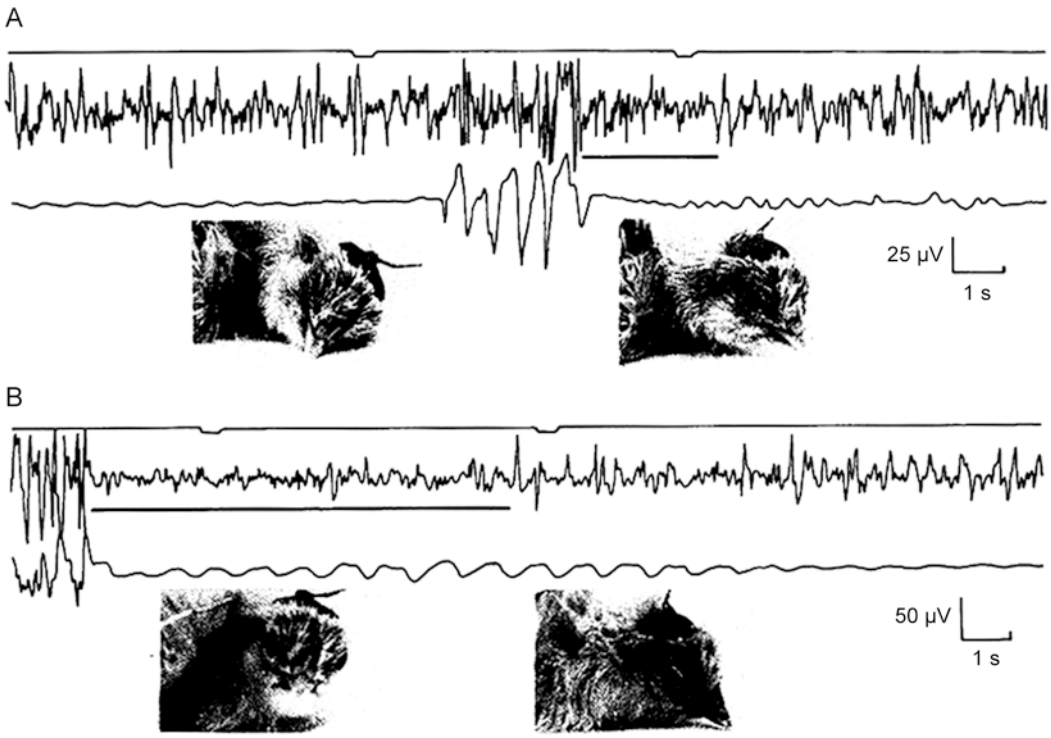

Fig. 4. Newly hatched domestic chicken at (A) immediately and (B) several hours after hatching, showing typical cerebral EEG flattening (indicated by the bar under the EEG) associated with behavioral arousal, triggered by a spontaneous struggling burst during sleep wth slow-waves (from Corner and Bot 1967[32]). [Trace A: immediately after hatching. Trace B: several hours after hatching].

stereotyped movements, since these have been reported recently in sensescent cuttlefish[58].

The domestic chicken begins postnatal existence with an enhancement of fetal struggling bursts, such that these now continue indefinitely at several second intervals until the shell cap breaks open and the head is able to elevate itself (Fig. 4). From that point on each burst of spontaneous struggling is transformed into an attempt to stand erect, which lasts longer and longer in the succeeding hours and is accompanied by a clear-cut flattening ('desynchronization') of the cerebral electroencephalogram. This abrupt transition to a qualitatively novel form of behavior (i.e., wakefulness) thus requires there to be sufficient proprioceptive sensory input at the head and neck level. In addition, there needs to be an intact reciprocal connection between the lower brainstem and the anterior hypothalamus[10].

It is not sufficiently appreciated that, if immobilized in a fetal position, chicks during the first week of life fall into an ongoing sleep state from which it is virtually impossible to arouse them while thus restrained[10], and during which they display a striking form of repetitive MAS bursting (Fig. 5). In other words, there is a regression to peri-hatching behavior that becomes less and less pronounced in the following days as waking mechanisms increase in potency. These bursts are modulated by temperature-dependent oscillations in the minute-order range, often closely mimicking the spontaneous motility rhythms of ectothermic vertebrates (Fig. 3). While not unexpected in view of their taxonomic proximity to the avian lineage[8,9], it is interesting from an evolutionary point of view that a monotreme mammal, the duckbill platypus, can be seen in a recent BBC Nature program (personal observation) to show a strikingly similar type of episodic struggling behavior in the course of hatching (http://www.bbc.co.uk/nature/life/Platypus#p004j5rl). Still another monotreme - the echidna – demonstrates in another BBC documentary (personal observation) that, as in birds, as soon as the head lifts itself out of the shell during a bout of struggling, hatching behavior (i.e., putative sleep) becomes dramatically transformed into crawling (unmistakable wakefulness) in a

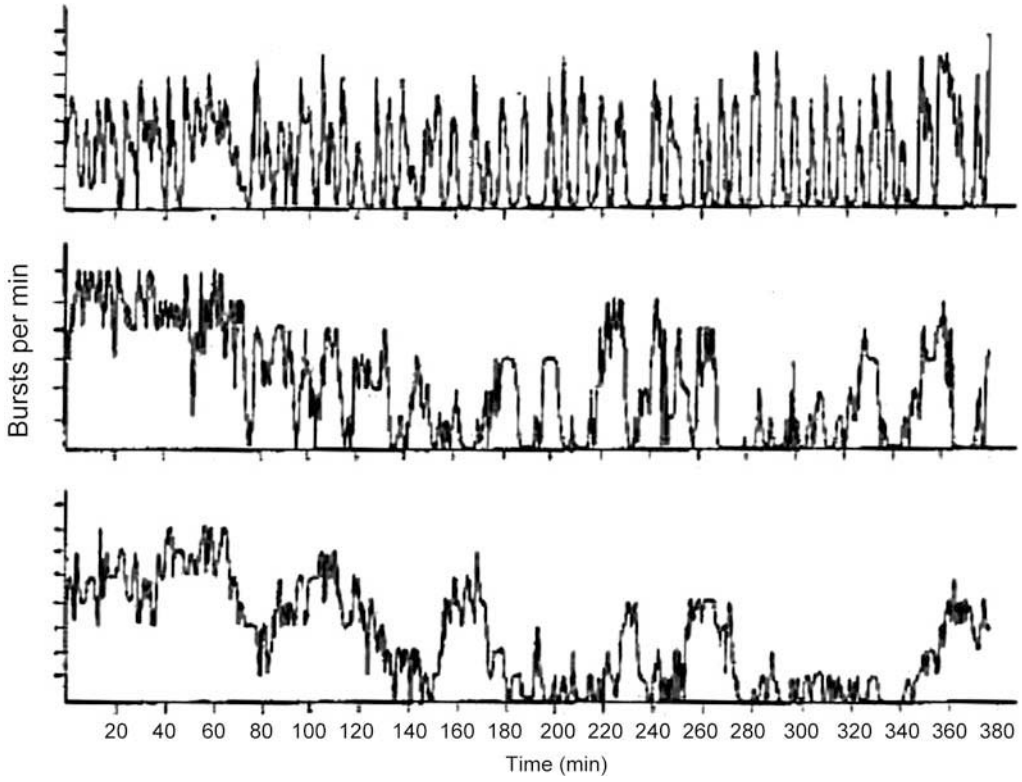

Fig. 5. Representative tachograms of stereotyped (ca. 1 s) burst trains in ca. 1-week-old chicks held at different temperatures in fetal position so as to prevent them from hatching. (top: 40 °C; middle: 36 °C; bottom: 32 °C; from Corner 1985[10]).

clear attempt to emerge from the confines of the eggshell (https://www.youtube.com/watch?v=K5Y2h5zjpWU).

During the second postnatal week in rats, before the cerebrum has begun to display the low voltage, fast-frequency electrical (EEG) activity characteristic of brain 'arousal' (Fig. 6; and see Fig. 4 for an illustration of the analogous phenomenon in chickens), the intensity of spontaneous muscle contractions becomes drastically reduced. This results in a state of weak twitching against a persistent background of muscle atonia[59] that can be considered to mark the beginning of 'REM' sleep in the conventional sense, with the prior RBM stage (which has been relegated by several authors to the semantic limbo of 'primitive, undifferentiated, or even proto-sleep'[5,34,60])

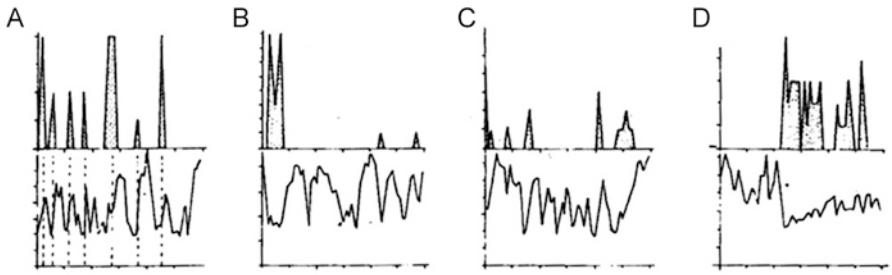

Fig. 6. Continuous sleep over 1h (10 min/div on the abscissa) in four randomly selected infant rats restrained in fetal position at 3 weeks of age, showing the incidence of quasi-struggling bursts per minute (top traces: A–D) together with an inversely correlated 5–10 min fluctuation in mean EEG delta-wave amplitudes (bottom traces: A–D). Each motility peak consists of a train of bursts (comparable in appearance to those illustrated earlier for the pre-hatch chicken). Modified from Corner and Kwee 1976[61].

representing a primordial form of MAS (c.q., active sleep). Amazingly, when restrained in a fetal position, rat pups up to at least three weeks of age display the same sort of struggling behavior as do hatching chickens[61]. Their ca. 1 s bursts of stereotyped movements come in trains lasting up to several minutes, separated by highly variable quiescent episodes, and are usually preferentially associated with periods of relatively low amplitude cortical delta wave activity (Fig. 6).

Brain Developmental Rhythmicity and Homeostasis

The irregular alternation between high and low periods of EEG power, as illustrated in Figure 6, appears to be an intrinsic property of developing cortical networks[15,32,62-65] (Fig. 7). Dispersed neuronal cell cultures typically display repetitive trains of synchronous bursts of neuronal firing lasting for variable periods depending on the availability of cellular energy (ATP). Especially striking in the illustrated example is the constancy of both the 'slow' rhythm (<1 Hz) governing the episodic nature of the short synchronized bursts, regardless of how long each epoch of bursting continues, and the constancy of the 'infra-slow' rhythm dictating epochs of activity and quiescence over periods of several minutes, regardless of how high the overall incidence of spontanous bursting is. Intermediate dosages produced intermediate effects. Such dependence on ATP utilization means that levels and patterns of bioelectric activity will be susceptible to abnormalities even at stages which may be critical for activity-dependent further maturation. The balance between excitatory and inhibitory synaptic drive in developing cortex cultures varies homeostatically with the overall activity level[66], but, conversely, exerts a profound influence on spontaneous network dynamics[67]. Such non-linear feedback mechanisms pose severe challenges to experimental analysis, making the ontogenetic establishment of homeostatic regulatory mechanisms in later life[68,69] one of the most puzzling unanswered questions in developmental neurobiology. Nevertheless, endogenously generated neural activity in general, and motor discharges in particular, contribute in an important but still poorly understood way to brain development[65,70,71].

Parallel with the shrinking of the neurological substrate for generating spontaneous movements during sleep, the percentage of sleep time taken up by RBM also declines progressively[5,33,72,73] largely due to the maturation of GABAergic inhibition within the caudal brainstem[45,74-77]. As development proceeds, this motorically active phase comes to occupy less and less of total sleep time, eventually falling to a species-specific mean value which in some species accounts for only a few percent of total sleep time[2,52]. That this inhibition is an active process is dramatically demonstrated by the phenomenon of "REM sleep without atonia", whereby localized pontine lesions in adult cats[5,78] or juvenile rats[79,80] can release vigorous motoric activity suggestive of 'oneiric' (dreamlike) behavior, to use Jouvet's evocative terminology[5].

Rats – especially middle-aged males – which have been subjected shortly after birth to prolonged pharmacological suppression of REM-sleep typically show exaggerated phasic motility and brain activity during active sleep[72], suggesting that some forms of motoric sleep disorders in humans (viz. RBD) could have their origin in early developmental disturbances of sleep regulation. It is fascinating that in the experiments in rats just described above, it is the middle-aged males that showed the most exaggerated motility--a finding mirrored in human RBD in which it is predominantly middle-aged and older males who demonstrate RBD (Fig. 8). The procedural difficulties involved in carrying out extensive clinical and epidemiological studies in humans[81], however, mean that there is a dearth of information concerning possible clinical sequelae of early interference with spontaneous motility, as found with infant rats[80]. A variety of genetic factors is known to be involved in the regulation of brainstem rhythm control circuits, but their implications for understanding the mechanisms of activity-dependent sleep ontogeny appear not to have been investigated[82]. Nevertheless, as emphasized above, the establishment and maintenance of appropriate homeostatic set-points for guaranteeing lifelong adaptive physiological responses is one of the important unexplored areas of developmental biology[65,68], and would undoubtedly benefit from systematic research into intrinsic brain rhythms and their relationship to the maturation of sleep and wakefulness.

Evidence Supporting Early Developmental Neuromotor Risk Factors for RBD in Humans

The most compelling and carefully documented cases in

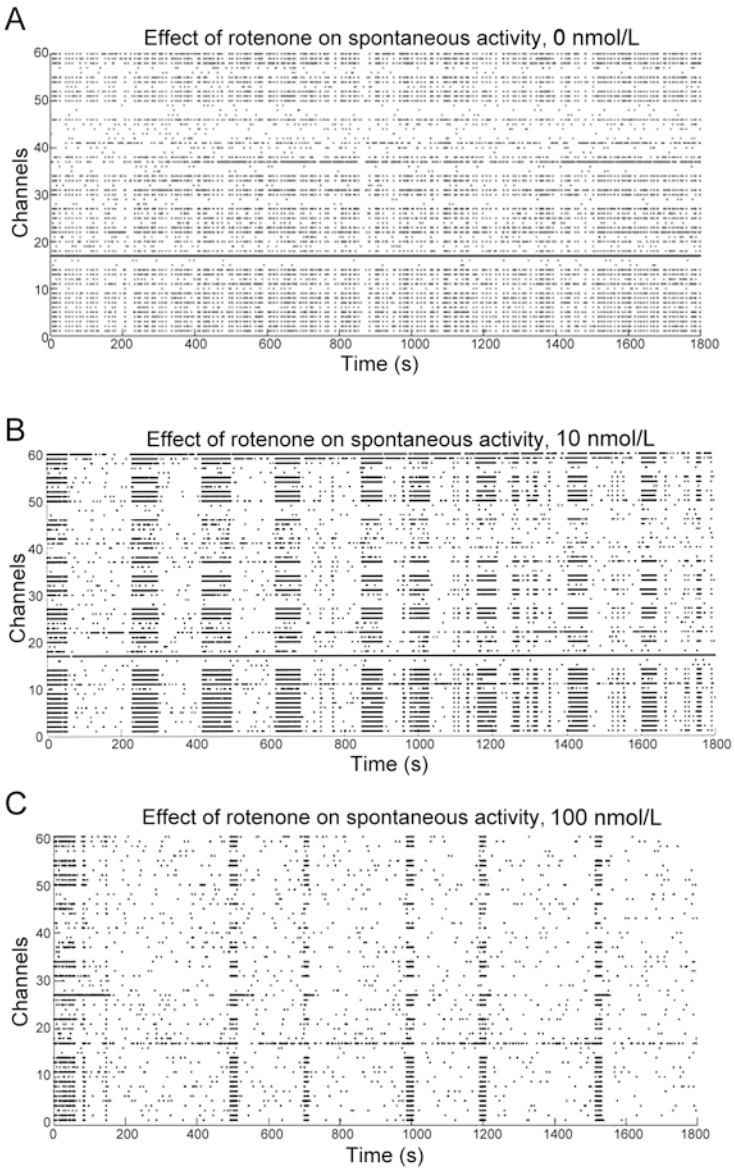

Fig. 7. Progressive reduction in the incidence of synchronized neuronal discharges in a neocortical cell culture shortly after exposure to different doses of the ATP inhibitor rotenone (Wong E. Energy metabolism and spontaneous neuronal activity in cultured cortical networks. Master's dissertation, Biomedical Sciences/Neurosciences, University of Antwerp, Belgium, Department of Biomedical Sciences. Available upon request: emma.emelinewong@gmail.com.): (A) 0 nmol/L; (B) 10 nmol/L; (C) 100 nmol/L. The dots indicate spontaneous spiking in successive time bins at one or more of 60 recording sites in a multiple electrode culture dish over a 30-min period. Especially striking is the persistence of the 'slow' rhythm (<1 Hz) governing episodes of short synchronized bursts, regardless of the incidence and duration of intervening quiescent periods ('infra-slow' rhythmicity, here on the order of a few minutes). Intermediate dosages produced intermediate effects.

the human RBD literature will now be presented.

Idiopathic RBD has been documented in a series of four children[83]. Clinical history and video-polysomnography (vPSG) confirmed the diagnosis of RBD in the four children, who had a mean age of 9 years; gender was not reported. They had histories of complex sleep behaviors accompanied by vivid dreaming and nightmares. Developmental neuromotor risk factors for RBD need to

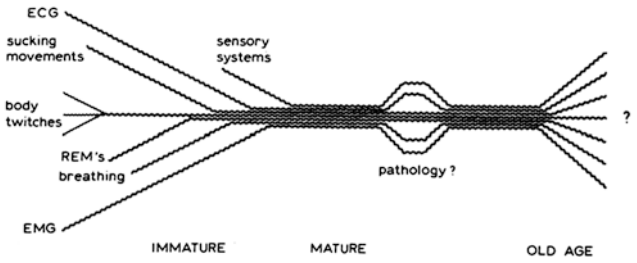

Fig. 8. A 'rope' analogy illustrating the multi-stranded nature of mammalian sleep: its diverse manifestations are initially present as more or less distinct rhythms, which then gradually coalesce into a definable, i,e. reproducible set of identifiable 'state' parameters (modified from Corner 1985[10]).

be considered in these childhood idiopathic RBD cases (i.e. spontaneous RBD cases not associated with any neurological or medical disorder).

iRBD has been reported in a 35 year-old female with prominent RBD behaviors that affected her husband's sleep and greatly stressed their marriage[84]. She was healthy, but had a notable childhood-onset sleep history that included sleeptalking, episodic screaming, and nightmares. During adolescence, a sibling observed recurrent episodes of bilateral arm waving during sleep associated with sleeptalking and shouting, which always occurred several hours after sleep onset and never within the first hour of sleep, which is highly suggestive of a REM

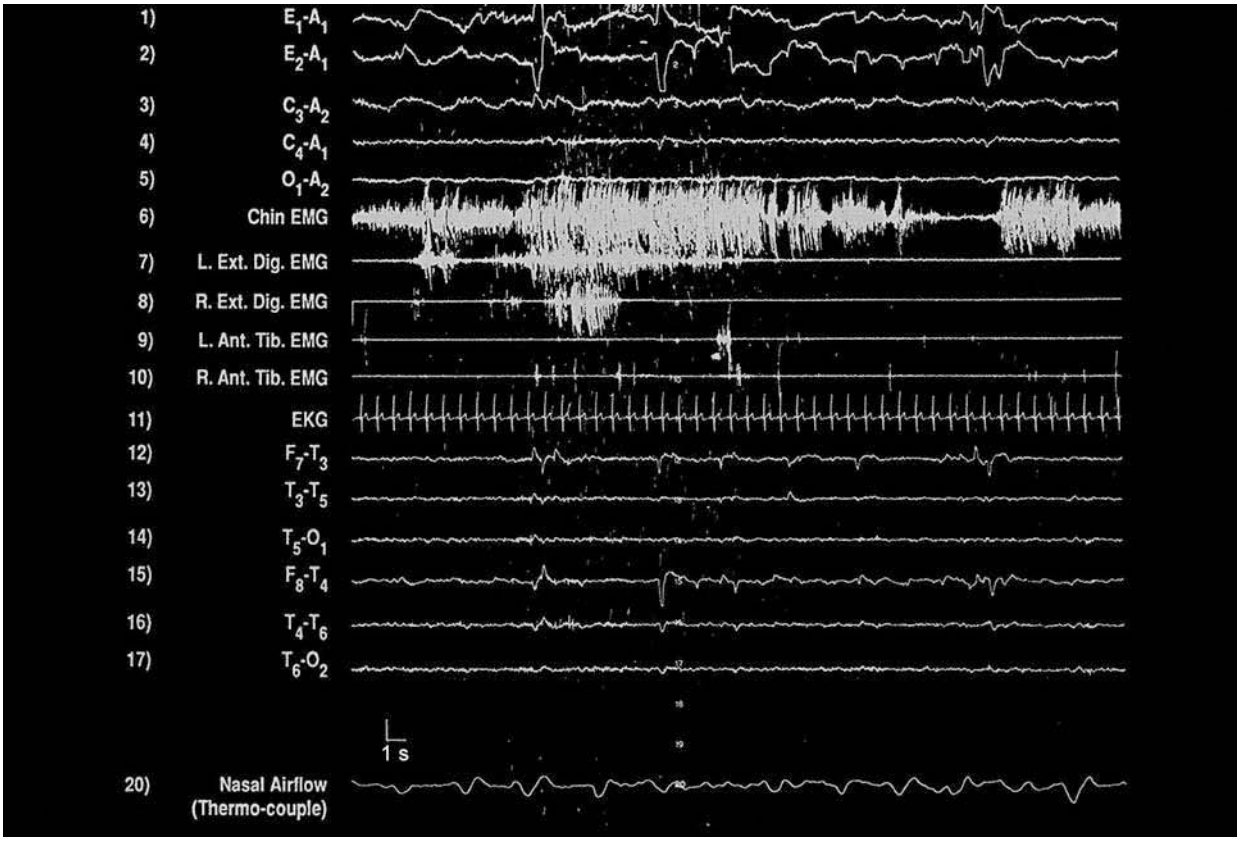

Fig. 9. Polysomnogram (PSG) during REM sleep in a patient with REM sleep behavior disorder. There is continuous "REM-without-atonia" (with one interruption near the end of the tracing that demonstrates normal REM-atonia), as reflected by the high-voltage, tonic and phasic electromyographic (EMG) activity in the submental (chin) EMG (channel 6). Dense REM activity is present in the electrooculogram (channels 1–2). The EEG (channels 3–5; 12–17) shows the characteristic low-voltage, fast frequency activity of REM sleep. Time-synchronized video-PSG monitoring revealed minor movements of the digits with phasic activation of the left/right extensor digitorum EMGs (channels 7–8). The legs show no movement during this tracing, with minimal twitching of the left/right anterior tibialis EMGs (channels 9–10). The electrocardiogram (EKG; channel 11) shows a constant rate, and there is no respiratory disturbance (channel 20).

sleep motor-behavioral disorder rather than a non-REM sleep parasomnia such as confusional arousals or sleep terrors. There was no history of sleepwalking. During a vPSG study (after stopping medications for 1 month), she demonstrated tonic and phasic electromyographic (EMG) abnormalities during REM sleep, and she had 3 behavioral episodes during REM sleep with frequent bilateral arm waving, leg movements and brief vocalizations. This case may reflect an early developmental sleep motor dysregulation as a contributor to her RBD; in fact, she may have had congenital RBD or very early childhood-onset RBD. A distinctive prodrome for RBD was found in 25% of a consecutive series of 96 patients with video-PSG documented RBD, with the prodrome often being prolonged and lasting up to 48 years in some cases[85]. This prodrome manifested with sleeptalking and yelling, limb twitching and limb jerking that often progressed in frequency and intensity until the eventual frank emergence of RBD. Early sleep neuromotor system dysregulation may thus have played an instrumental role in generating the long RBD prodrome leading up to the eventual emergence of clinical RBD.

Parasomnia Overlap Disorder (POD) involves generalized motor-behavioral dyscontrol across REM and NREM sleep, manifesting as RBD and a Disorder of Arousal from NREM sleep (sleepwalking, sleep terrors) in the same patient[86]. In the first reported series of POD, involving 33 patients[86], 22 patients (15 males) had idiopathic (i.e. spontaneous) POD, with mean age of onset of 8.8 years (range, 1–28 years) that was substantially younger than the 11 patients with symptomatic POD (i.e. secondary to a neurologic or other clinical disorder) who had a mean age of POD onset of 27.3 years (range, 5–66 years). Also, in a retrospective study of a series of RBD cases, idiopathic (i.e. spontaneous) POD was diagnosed in 15 of 91 (16.5%) RBD cases[87]. However, in RBD diagnosed before age 50 years, 65% (13/20) of patients with idiopathic RBD also had sleepwalking, and thus idiopathic POD. In contrast, in RBD emerging after age 50 years, only 6.1% (2/33) of patients with idiopathic RBD also had sleepwalking/POD. These findings with idiopathic POD raise the question of early sleep neuromotor developmental dysregulation promoting future linked REM sleep without atonia/RBD/NREM sleep parasomnias.

In support of a major thesis in this paper that ontogenetically and phylogenetically early neuromotor activity patterns during RBM and REM sleep can resurface in stereotypical or quasi-stereotypical fashion with simple movements and complex behaviors found with human RBD, the following study on “a motor signature of REM sleep behavior disorder” will be described[88]. This study sought to determine if there was a common pattern in movements during RBD across three RBD clinical subgroups: idiopathic (i.e. spontaneous) RBD; narcolepsy with RBD; and Parkinson’s disease with RBD. Video clips of movements during RBD, and during wakefulness in the sleep lab, were blindly analyzed. The scorers accurately guessed the sleep/wake stage for 94% of the video clips. Compared with wakeful movements, RBD movements were faster and more often repeated, jerky, and pseudo-hallucinatory, and rarely involved the environment in an appropriate manner. The same characteristics of the movements in REM sleep were found in all three RBD-related conditions (idiopathic RBD, Parkinson’s disease-RBD, and narcolepsy-RBD), thus delineating a common motor signature of RBD, which underlines a major thesis of this paper.

Furthermore, the appearance of paroxysmal release of behaviors in bursts during REM sleep associated with REMs (i.e. “phasic REM sleep”) against a background of simple jerking in REM sleep without REMs (i.e. “tonic REM sleep”) has also been observed in studies using detailed video analysis of REM sleep behaviors in human RBD[89,90]. The close correspondence between the paroxysmal motor-behavioral activity in human RBD and RBM activity in early phylogeny and early ontogeny is striking and calls further attention to a major hypothesis in this review. Also, in the two studies just cited[89,90], there were a very large number and a great variety of motor events during REM sleep in RBD, with most of the motor events lasting <2 s. These findings are also in keeping with the hypothesis of early phylogenetic/ontogenetic release of RBM sleep in human RBD. Fig. 9 illustrates an example of various types of tonic/phasic electromyographic (EMG) abnormalities found during REM sleep in human RBD. Minor movements of the digits (reflected by the EMG in channels 7–8) occur during phasic REM sleep, along with dense REM activity (channels 1–2), against a background of continuous muscle tonus (as reflected by the submental [chin] EMG).

In conclusion, both on the basis of basic research and

on documented clinical and vPSG findings in humans, there is reason to believe that dysregulation of the developing sleep neuromotor system can be expected to have adverse long-term effects, with behavioral and dream disturbances emerging during sleep as RBD later in life in humans, and also in dogs and cats[27]. Furthermore, early developmental sleep neuromotor dysregulation may also predispose to the later emergence of a spectrum of other abnormal dissociated sleep-wake motor-behavioral states emerging as parasomnias, apart from RBD[91,92].

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