Sleep Advances, 2024, **5**, zpae025
https://doi.org/10.1093/sleepadvances/zpae025
Advance access publication 10 May 2024
Living Legends in Sleep Research

Living Legends in Sleep Research

From pole to pole, life-long research of sleep in extreme environments

Alain G.C. Buguet*,[1]

[1]Invited Scientist (ret), Malaria Research Unit, UMR 5246 CNRS, Claude-Bernard Lyon-1 University, Villeurbanne, France

*Corresponding author. Alain G.C. Buguet, 21 rue de Champfranc, 38630 Les Avenières Veyrins-Thuellin, France. Email: a.buguet21@gmail.com.

Abstract

In November 1965, Michel Jouvet accepted me into his laboratory in Lyon as a medical student at a time when sleep research was an adventure. After 4 years of investigations in cats, I obtained my medical doctorate. Being a military physician, I was posted to Antarctica for wintering over and was initiated by Jean Rivolier into the psychology of small isolated human groups. I recorded 180 polysomnographic (PSG) nights in eight of my companions. This was my first contribution to research on human sleep under extreme environments and conditions. I then entered René Hénane's military thermophysiology laboratory, where I analyzed thermal exchanges during human sleep in the heat. Back to the cold, I spent 2 years in Canada and analyzed sleep during the Arctic winter under the direction of Manny W. Radomski, who headed the Defense and Civil Institute of Environmental Medicine and judged my PhD dissertation along with my first two mentors. Throughout my career, I worked in collaboration with Manny Radomski under the auspices of the Franco-Canadian Accord for Defence Research. We studied sleep and exercise, sleep deprivation, and recovery with and without chemical help. He also gave me support during several investigations in Africa. There, I studied normal sleep under various tropical climates (warm and dry in Niger, warm and humid in Côte d'Ivoire and Congo, temperate mid-mountain in Angola). I determined that human African trypanosomiasis, the ravaging sleeping sickness or tsetse disease, is not a hypersomnia, but a disorder of circadian rhythms, notably in the sleep–wake cycle.

This paper is part of the Living Legends in Sleep Research series, which is sponsored by Idorsia Pharmaceuticals and Jazz Pharmaceuticals.

Key words: (1) sleep in extreme environments: Antarctica; Arctic; Africa–(2) sleep in extreme conditions: Ramadan; exercise; sleep deprivation–(3) circadian rhythms: human African trypanosomiasis; intraocular pressure

I was born into a French military family, my father being a member of the French Air Force. At 5 years old, I experienced life on the central plateaus of Madagascar, where my father had been posted. After a 4-year sojourn in Dijon, we went to Algeria, where I passed the first part of the French high school diploma, followed by the second part in Toulon, France, 1 year later. My father's next posting was in Senegal. In 1962, I began my medical studies at the University of Dakar. I was particularly captivated by Professor Mazer's passion for physiology. While in Dakar, I was accepted as a graduate student into the French Forces Medical School (today's French acronym ESA-Lyon), and studied at the Rockefeller-Grange Blanche Faculty of Medicine of the University of Lyon.

My first professional assignment was as a medical officer in Adélie Land, Antarctica. Then, as a professional military scientist, I also had diverse overseas postings. This is how I had the opportunity to study human sleep under cold exposure in the Arctic winter. In Africa, either in long-term posting or in small-term and mid-term missions, I studied human sleep under diverse African climates. I also studied sleep in Ramadan intermittent fasting in Morocco, and the African sleeping sickness (human African trypanosomiasis, HAT) in Niger, Côte d'Ivoire, Angola, and Congo. Performing such research, I encountered biological rhythm constraints (sleeping sickness and intraocular pressure). When working on HAT, my colleagues and I developed the rat model of HAT to deepen our understanding of the pathophysiological pathways involved in the development of the disease (sleep, thermoregulatory, immunological, and NOergic processes). I also fulfilled more specific military commitments related to stressful military operations (exercise, heat tolerance, and sleep deprivation with and without chemical help). Progressively, our comprehension of the implicated phenomena and mechanisms led us to better understand the sleep and stress relationships. In recent years, we participated in alerting the neurological community about the potential neurological impact of the Covid-19 pandemic. Finally, the development of global warming exacerbated by extreme climatic events such as heatwaves, led us to integrate our findings into unified thoughts about how we will sleep when the Earth will be hotter. We also proposed physiological countermeasures for the deleterious effects of heat waves.

Submitted for publication: January 5, 2024; **Revised:** March 25, 2024

My early attachment to science and my curiosity have deeply impacted my personal and scientific working life. They led me to a life-long study of sleep as one of the main behaviors of human beings.

Initiation to Basic Sleep Research in Lyon

In November 1965, in my fourth year of medical studies, I was accepted by Professor Michel Jouvet, the renowned sleep researcher, as a sleep research trainee at his laboratory of Experimental Medicine, University of Lyon. Jouvet had recently described paradoxical sleep in the cat. By using polysomnographic recordings (EEG, EMG, ECG, respiration, and rectal temperature) [1], he determined that this sleep state with elevated awakening thresholds differed from synchronized sleep by tonic events (EEG activation with rhombencephalic 6–8 Hz spindles; skeletal muscle atonia) and phasic activities (rapid eye movements, REMs; extremity twitches; respiratory; and cardiovascular instability). Jouvet also established a parallel with the REMs described in humans by Dement and Kleitman [2] as corresponding to dreams. Jouvet considered paradoxical sleep or REM sleep (REM) [3] as the third state of the brain [4], as different from non-rapid eye movement sleep (NREM) [3] as NREM is from the awake state.

After 2 years of working with Bernard Roussel, a fellow graduate student, on the links between paradoxical sleep, the locus coeruleus, and noradrenergic brainstem networks [5], Jouvet assigned me to study the ponto-geniculo-occipital (PGO) waves of REM, which became 2 years later the participant of my medical doctorate dissertation [6]. Briefly, the PGO waves disappeared after the bilateral electrical coagulation of the pontine tegmentum nuclei (locus coeruleus, subcoeruleus, and parabrachialis medialis). In this area containing noradrenaline-containing neurons, in situ injections of 6-hydroxydopamine inhibited PGO waves and depleted noradrenaline content of the mesencephalon and geniculate nuclei [7]. This work ended my modest contribution to these REM-related events, as I had to fulfill my military duties.

Human Sleep Under Polar Environments

Conducting human sleep research in the field realities of Adélie Land, Antarctica

Preliminaries.

During my tenure with Jouvet, I had been indelibly marked by sleep research, which I deeply wished to pursue. I completed the 6-month military medicine courses at the Val-de-Grâce School of Medicine in Paris. There, I passionately followed Professor Jean Rivolier's presentation on the French Austral Territories (French acronym TAAF). Rivolier, a renowned specialist in the psychology of small isolated human groups, was the founder and director of the medical services of the French Polar Expeditions (French acronym EPF). He was interested in my university sleep research, and we agreed that I would apply for the 1971 polar expedition in Adélie Land, Antarctica. Before that, I had to follow the 6-month specialization course at the School of Tropical Medicine "Le Pharo" in Marseilles that included the final posting choice. As my first military posting, I chose that of medical officer of the 21st French Polar Expedition at Dumont d'Urville Station. In agreement with Rivolier, I would study sleep in relation to adaptation to isolation in a small human group.

Dumont d'Urville Station lies close to the South Polar Circle (66°39′47″ S; 104°00′10″ E), at a latitude that allows 4-hour daylight in July (midwinter). The station had been established on Petrel Island in the Point Geology Archipelago in 1953, after Port-Martin Station had burned down. Rivolier and three other men had established a cabin (Marret's Cabin, named after the group's chief) to study the emperor penguin rookery discovered during the preceding year. When the polar resupply ship, the *Tottan,* arrived to repatriate everybody to France, the four men and three others from Port-Martin decided they would winter over. Afterwards, Rivolier became a close collaborator of Paul-Émile Victor, renowned Franco-American Greenland explorer, and founder of EPF.

Before departing for Antarctica, the expeditionary members were subjected to a battery of psychometric tests and interviews dealing with the adaptation abilities to life in isolated small human groups; the tests had been developed by Rivolier and his group [8]. Having no official backing for my sleep studies, I found support from Professor Henri Félix, one of my former teachers at the medical school in Lyon and a Roche Laboratory manager. He loaned me an ALVAR Minihuit eight-channel polygraph equipped with two wiring heads for recording two persons simultaneously.

The polar ship *Thala Dan* left Hobart (Tasmania) with the expedition members (chief, M.D., and 13 scientific and 13 maintenance personnel), and landed at Dumont d'Urville Station on December 14, 1970 (Figure 1). One year later, the ship came back with the relief team, and departed Petrel Island on December 27, 1971 for Melbourne some 3000 km north.

Medical practice

My medical responsibilities consisted of consultations generally for minor injuries. Nevertheless, one team member concealed his hypertension condition during the selection process in Paris, compensating for his hypertension with medications. Shortly after arrival in Adélie Land, summer campaign staff officers referred him to me to identify why he avoided heavy work. I discovered his medical condition, and it was decided to repatriate him back to France on the next sailing, leaving the team with 28 members.

I happened to be the next medical casualty, due to a traumatic partial section of the right Achilles' tendon, which left me on crutches for 6 weeks. A month later, I was consulted by a patient complaining of frequent urination, slight perineal itch, and iterative pain in the right iliac fossa. Subsequently, he casually mentioned a year-old sojourn in West Africa. I microscopically diagnosed active urinary *Schistosoma haematobium* [9]. He was treated symptomatically until November 1971 when a US Navy Lockheed LC-130 Hercules plane landed on the continent to drop off a French glacial research team; along with the niridazole medication. Subsequent complete urinary tract exploration in Paris demonstrated that the symptomatic treatment had maintained bladder wall permeability, avoiding any sequelae.

The same plane also conveyed one of the team members to McMurdo Station for immediate repatriation towards Paris. During the month preceding the plane landing, he had presented symptoms evoking potential medullary compression, which disappeared in Paris.

Medical and psychological research.

Every fortnight, I completed individual questionnaires on health, abnormal events, and eventual adaption difficulties for each team member. Based on my observations of each individual, I completed a 16-item assessment on mood (from "depressed" to "too happy'), oral communication, work quality, sleep quantity/quality, appetite, alcohol consumption, outside walk, companionship, domestic service, collective work and leisure, sociability

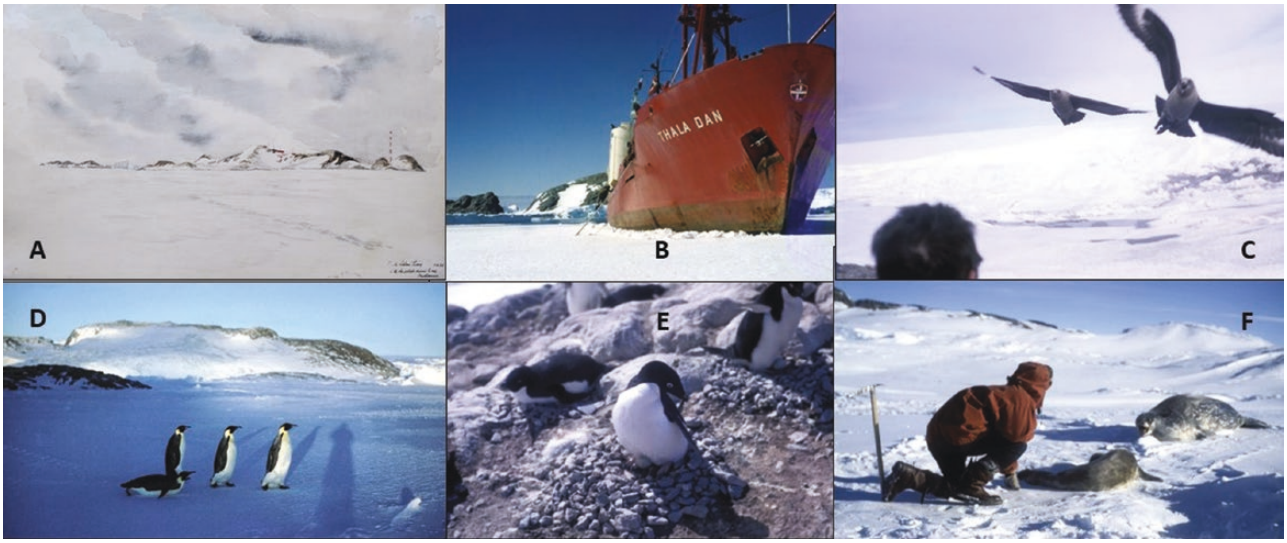

Figure 1. Dumont d'Urville Station's environment and neighbors. (A) Watercolor sketch of Petrel Island in Adelie Land, Antarctica, during the winterover, with permission by Pierre de Château-Thierry. Petrel Island (~800-m long and 400 m wide) culminates at 42 m above sea level. All buildings are situated on the northern upper plateau. (B) The Thala Dan ship is trapped in the ice in view of Petrel Island. The ladder was used to set foot in Adélie Land. (C) Skuas. (D) Emperor penguins in winter. (E) Adélie penguins in summer on their stone nest. (F) Wedell seals in the spring (photos A. Buguet).

(low or none to too much), attitude towards the chief or the M.D. (aggressive to flatterer), and role in the group or opposing the group (scapegoat to leader). This assessment was to follow individual and group adaptation capacity; it remained stable despite medical or familial incidents. The qualitative indirect evaluation indicated that predeparture interviews proved a better predictive value than the psychometric tests for individual adaptation to the life conditions at the station.

Radial pulse rate decreased in the field with the lowest values in midwinter. Blood pressure decreased, confirming cold-induced cardiovascular adaptation. Interestingly, from ECG monitoring during sleep, I later found a similar bradycardia in the Arctic winter [10].

Biological research consisted of collecting urine and blood samples that were shipped to Paris. Unfortunately, the maintenance of the cold chain was broken in France, and the samples were not analyzed!

Sleep research.

Eight of the twenty-three team members who claimed to be good sleepers were selected for the sleep investigation [11]. The purpose of the polysomnographic (PSG) sleep study in Antarctica was to verify whether adaptation processes differed with personality types.

The PSG recordings (EEG, EMG, and EOG) began in April, when the new building and its proper heating system became accessible (the "Old Base," a metal building dating back to the 1957–1958 International Geophysical Year, IGY). On 2 successive weekdays (Monday–Tuesday, Thursday–Friday), four pairs of volunteers were chosen for the geographical positioning of their bedrooms in the building allowing me to record two participants simultaneously. A total of 156-night recordings were analyzed following Rechtschaffen and Kales recommendations [12]. I had to contend with incidents such as power failures, displaced electrodes, paper printer blockages, or radio interference. To correct any paper blockages, I remained awake reading Teilhard de Chardin's books until the junction between the two paper blocks had passed. I then slept in a sleeping bag in the corridor separating the participants' bedrooms. PSG interpretations were performed either in the daytime or several months later in Paris.

I observed an increase in N3 (Figure 2), which I attributed to physical exercise during marches permitted even at the midwinter due to the proximity of the Polar Circle. REM remained at normal levels. The tentative hypothesis regarding a relationship with adaptation capacities to isolation in a small human group was not confirmed. Due to independent circumstances (health, academic competition, external posting to Canada and Africa), the related article was only published in 1987 [11]. The data were used in my Human Biology PhD dissertation, judged in Lyon by my mentors Michel Jouvet, Manny Radomski, and Jean Rivolier [13].

Once in France, I became aware of divergent findings obtained in studies on the so-called IGY polar insomnia [14]. In a preliminary investigation on two participants, US teams had recorded sleep during yearly summer campaigns at South Pole Amundsen-Scott Station (2804 m altitude, equivalent to 3350 m due to low barometric pressure) [15]. A lack of N3 and decreased REM were attributed to altitude. A subsequent observation, conducted at South Pole Station in four participants during summer and winter sessions confirmed the N3 decrement and slight decrease in REM during midwinter recordings, although total sleep time (TST) did not differ from baseline recordings obtained at Oklahoma City [16]. At the British Antarctic Survey Halley Bay II Station, Paterson [17] had recorded 38 nights in 10 participants between April and December 1971. The windowless station was located on the moving Brunt Ice Shelf (75°31′ S; 26°43′ W; 30-m altitude) and had been rebuilt several times, being buried below the snow surface. N3 decreased in August, October, November, and December and was attributed to permanent daylight and the lack of physical exercise.

When I returned to France, I was posted to Lyon and succeeded 1 year later in the academic examination to join the Physiology Department of the French Forces Medical Research Center at Lyon (French acronym CRSSA). My future research career was confirmed.

Sleeping in the cold in the Arctic

First sleep investigation in Arctic cold nights.

In 1974, I was posted to the Defence and Civil Institute of Environmental Medicine in Toronto, Canada (DCIEM) for 2 years

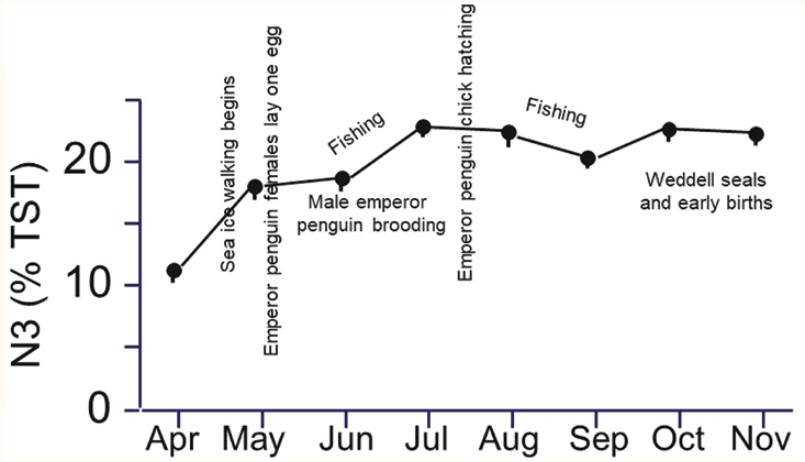

Figure 2. N3 sleep throughout the overwinter, as impacted by exercise due to diverse activities (walks on the sea ice, visits to the emperor penguin rookery, visits to the Astrolabe Glacier, visits to the continent, fishing, etc.).

as a NATO Exchange Officer under the Franco-Canadian Accord for defense research.

Soon after my arrival at DCIEM on Thanksgiving in October 1974, I asked my Director at DCIEM, Professor Manny Radomski, what he wished me to do; he replied by asking me what I would like to do. I replied "study sleep in the Arctic."

19 In February 1975, I participated in a preliminary study organized jointly by DCIEM and the British Army Personnel Establishment (Farnborough, Great Britain) at Fort-Churchill, Manitoba (58°46′51″ N; 94°11′13″ W), on Hudson Bay's shores. Out of the 24 Scottish Highland Royal Marine Commandos, two (19 and 22 years old) volunteered to sleep for 10 consecutive nights in an unheated tent adjacent to the laboratory building. The EEG equipment was located inside the building. Two thermoneutral baseline PSG recordings were performed inside the building on the participants sleeping in a liner at a dry bulb temperature (Tdb) of 19–21°C. Ten cold-exposure nights were then recorded on the participants sleeping in the cold in Canadian Forces sleeping ensembles (air-filled mattress, nine-Clo sleeping bags, liner, inner, and outer bags). This was followed by two thermoneutral recovery nights in the building. Participants performed regular military-type activities during the daytime. Tent Tdb varied between −28.2°C and −33.3°C. PSG traces were interpreted following conventional criteria [12]. Body temperatures were taken at 5-minute intervals from thermistors (rectal temperature, Tre; and seven skin-site thermistors); mean skin (*Tsk*) and mean body (Tb) temperatures were calculated using conventional formulas [18, 19].

During the first third of the night of sleeping in the cold [20], apart from difficulties in falling asleep, the occurrence and succession of sleep stages were normal, with N3 and REM phases occurring at corresponding baseline times (Figure 3). Thereafter, NREM became scarce, and was interrupted by frequent body movements and shivering. REM occurred in a narcoleptic-like manner, starting directly from wake.

Second sleep investigation in Arctic cold nights.

One year later, a second investigation was organized by DCIEM at Fort Churchill within the Franco-Canadian Accord for Defence Research. The sleep study, consisting of 192 PSG recordings, was conducted with 11 volunteers (three French and eight Canadian commandos) [21]. They slept for 16 consecutive nights in unheated tents in previously described conditions wearing DCIEM "thermal underwear" (skin thermistors and rectal probe; Figure 4), preceded by 5 nights for habituation to the sleeping gear, and five thermoneutral baseline nights with PSG recordings. Nocturnal urine collections were conducted for hormone assays.

Our preliminary findings from the first trial were confirmed. The succession of sleep stages was undisturbed during the first half of the night, with normal N3 amounts, accompanied by a decrease in Tre to 35°C. Thereafter, NREM was interrupted by body movements and shivering. REM occurred with shorter phases than at thermoneutrality, provoking cold-level-related REM deprivation [21].

We also assessed the effectiveness of a pre-adaptation technique consisting of a series of cold-water immersions before transferring to the Arctic. The technique consisted of 2 weeks of daily immersions in cold water (15°C) for 20 to 60 minutes until the rectal temperature dropped to 35°C [22]. Three different volunteers had been preadapted three weeks before the field study [22]. The normal cold-induced diuresis disappeared along with a decrease in urinary norepinephrine and 17-hydroxycorticosteroids, indicative of a milder reaction to cold and adaptation to cold following preimmersions in cold water.

Sleep Under Warm and Hot Conditions

Laboratory thermoneutral and warm ambient temperatures in Lyon

When I returned to CRSSA from Antarctica (September 1973), I joined the Department of Physiology, headed by Professor René Hénane, a thermophysiologist. I became in charge of studying thermal exchanges during sleep in the climatic chamber at CRSSA. We measured radiative exchanges between the body and anodized aluminum black matte walls, and convective exchanges with the ambient air [23]. Evaporative heat loss from sweating was calculated from weight loss measured continuously on an electrical differential balance (accuracy, 3 ± 0.2 g/min). The participant wearing swimming trunks lay on a meshed bed and was equipped for PSG and body temperature measures. The effects of heat on thermal exchanges were assessed at chamber thermoneutral Tdb (30–34°C) and warm Tdb (35–39.5°C) temperatures.

At thermoneutrality, weight loss occurred rapidly from sleep onset, at a time when N3 was most abundant, and plateaued

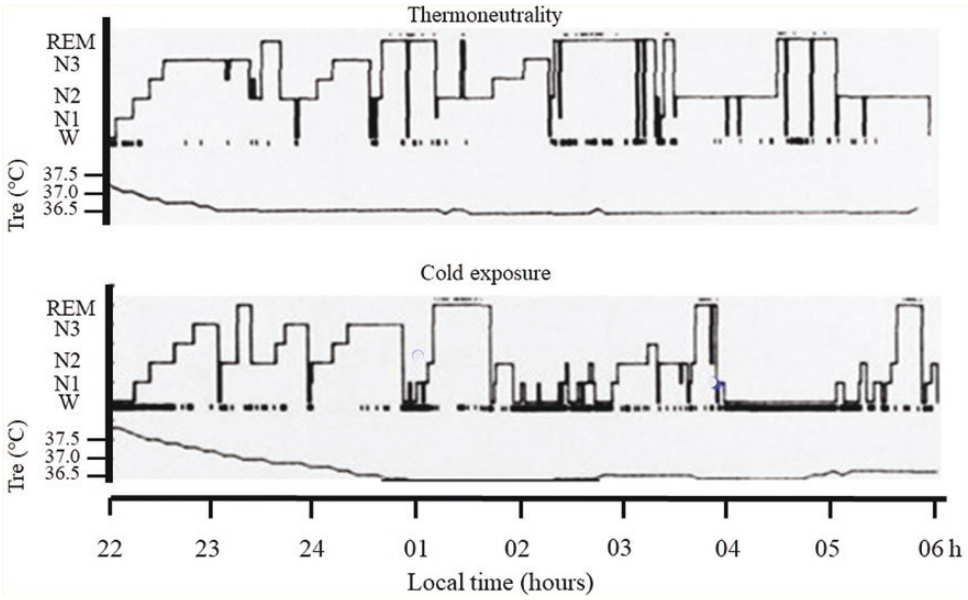

Figure 3. A representative example of the effects of cod exposure on sleep. Note the normal succession of sleep stages during the first half of the night along with the drop in Tre. Thereafter, sleep consisted of only N1 and N2 (no N3) and short phases of REM. Interestingly, shivering was inhibited, compared to the waking stage. Adapted from Buguet AGC, Livingstone SD, Reed LD, Limmer RE. Effects of cold on EEG patterns and body temperatures during sleep, DCIEM Technical Report No. 77X15, May 1977. (Accessible from https://apps.dtic.mil/sti/citations/ADA044286).

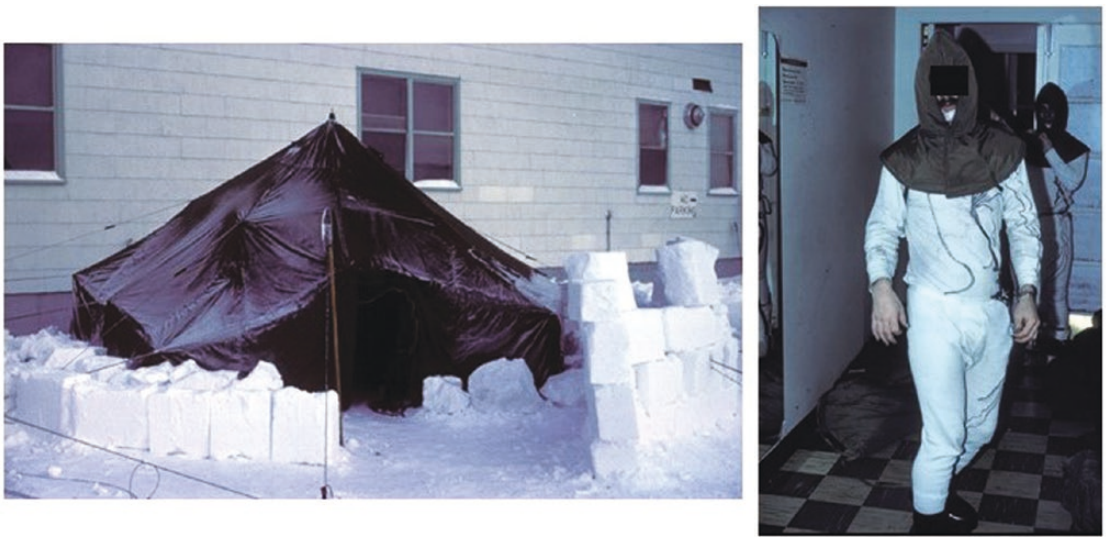

Figure 4. Sleep environment during the trial for the participants. Left: unheated 4-man tent outside the laboratory building. Right: a participant wearing the DCIEM "thermal underwear" (with skin thermistors and rectal probe).

during all REM phases [23, 24]. As the skin dried up with concomitant vasoconstriction [25], *Tsk* increased due to a decrease in sweat evaporation. Weight loss accelerated again and *Tsk* decreased during subsequent NREM phases, especially during N3. At a Tdb of > 35°C, sleep was more frequently interrupted by awakenings, resulting in a diminution of TST, and an increased sweat output. The opposite changes between NREM and REM may relate to a downshift of the hypothalamic setpoint for sweating [26], and serve to downregulate body temperature, thus preventing hyperthermia [27].

Anhidrotic ectodermal dysplasia.

A patient who did not sweat because of anhidrotic thermal dysplasia was submitted to 35°C Tdb. No changes in *Tsk* and evaporation were observed [28]. Weight loss was maintained at a constant 34.1 g/h rate throughout the night, compared to the 78.1-g/h weight loss of healthy participants in similar conditions [24]. On two occasions, Tre decreased by 0.3°C concomitantly with an N3 episode, without any variation in *Tsk*. These data confirm the pioneering work of Brebbia and Altshuler [29] who showed that oxygen consumption in sleeping humans is lowest during NREM.

Sleep under warm and hot climates in Africa

From 1981 to 2015.

In 1981, I was posted for eight years to the University of Niamey, Niger, to teach physiology. Thus began my life interest in studying sleep in Africa in healthy participants in their natural hot

habitats and in the vector-borne HAT, sleeping sickness, transmitted by Glossina (tsetse fly) bites. Initially, I studied sleep in healthy Africans in a sleep laboratory created in Niger. Thereafter, I launched field investigations on HAT and healthy volunteers in Côte d'Ivoire, Angola, and Congo, jointly with university professors Pascal Bogui (Abidjan), Teofilo Josenando (Luanda), and Gaston Muanga (Brazzaville). I also analyzed European expatriate's sleep in Niger and Côte d'Ivoire. Several investigations were also performed while I was at CRSSA-Grenoble and as Deputy Chief of the Pharo Institute of Tropical Medicine in Marseilles. I retired from the Armed Forces in November 2004. My friend Raymond Cespuglio, Jouvet's successor, invited me to Lyon University as an Invited Scientist. I then pursued laboratory studies on our rat model of HAT, and also field investigations in the Congo under WHO/TDR grants (2005–2009).

The investigations initially focused on extreme conditions [30, 31] and the geographical distribution of sleep in Africa [32]. In parallel, the occurrence of heat acclimatization was verified, and revealed no differences between African-born participants and Caucasian Expatriates, despite gender differences in each group [33].

Hereafter is the history of my research interest in human adaptation to warm and hot climatic conditions, and sleep in sleeping sickness.

In 2011, I accepted a 4-year medical clinic assignment in the Congo, returning to France at the end of 2014. At the invitation of Professor Stéphane Picot, I joined the Malaria Research Unit of the Biochemistry Department at Lyon 1 University. I was also invited to work with the Environmental Neurology Specialty Group of the World Federation of Neurology by Professors Jacques Reis (Strasbourg), Peter PS Spencer (Portland, Oregon), and Gustavo GC Román (Houston, Texas). We first alerted the neurology community on potential effects of the COVID-19 pandemic on the brain [34]. Recently, the data on acclimatization in warm and hot climates were reviewed in the context of "global warming" [35] and extreme events such as "heatwaves" [36], with a focus on adaptive and/or stress reactions, respectively. The stress reaction caused by heat waves may be countered by acclimation techniques [36].

Contrast between warm humid (forest) and warm semi-arid (Sahel) African climates.

The African forest zone climate is warm, with temperatures not exceeding daytime highs of 33–34°C Tdb with nighttime Tdb lows of 20–25°C. In Côte d'Ivoire, Angola, and Congo, we recorded 24-hour ambulatory PSGs on volunteers who slept spontaneously only at night.

Briefly, in the Côte d'Ivoire Forest zone, coastal Abidjan sleep patterns were similar in healthy Caucasians and Africans. Their sleep organization was also comparable with age-matched participants in Europe and Toronto (Canada), although sleep was slightly more fragmented in Africa. The Abidjan African participants' sleep was also comparable to that of villagers 400 km inland [37]. Both locations were similar climatologically, despite lower relative humidity in the villages (60% vs. 80%). Although TST did not differ between the two groups, the villagers had more N1 and less N3. These differences were attributed to multifactorial influences, among which was the lack of electrical power. Similar findings were obtained in Angola at an altitude slightly above 1100 m (Tdb 22–24°C), and on the shores of the Congo River at ~300 km north of Brazzaville (200 m altitude; Tdb 24–32°C).

On the other hand, sleeping during the dry season of the semi-arid tropical climate in Niger produced changes in sleep architecture. In the warmer months (April and May) daytime Tdb reached 41°C with 28–29°C at night. Compared to a temperate climate or a warm humid climate [32], the African and Caucasian Niger volunteers showed elevated amounts of N3 in the cooler season (January–February), with the warmer season being characterized by even higher amounts of N3 attaining ~30% of TST. The addition of an exercise-induced thermal load further augmented the levels of N3 in both cool and warm seasons in African and Caucasian participants. Compared to the distribution of N3 during the first half of the night under other climatic conditions, sleeping under the Sahelian climate was characterized by the occurrence of N3 in each of the successive NREM-REM sleep cycles. The level of REM remained stable in both seasons, at the upper limit of "normal" temperate values. REM was thought to be related to water preservation in a warm and dry climate [32].

Circadian Rhythms

African sleeping sickness, HAT

Epidemiological and clinical aspects.

Sleeping sickness or HAT is an endemic disease affecting 36 sub-Saharan countries, which is due to a trypanosome, *Trypanosoma brucei* (*T. b.*) *gambiense* (Western and Central Africa) or *T. b. rhodesiense* (East Africa) [38]. HAT evolves in two consecutive stages, the hemolymphatic stage 1 and the meningo-encephalitic stage 2. Stage 2 begins when trypanosomes and/or mononuclear inflammatory cells appear in the cerebrospinal fluid (CSF), marking the beginning of a central nervous system invasion. Among several neuropsychiatric symptoms, daytime sleepiness is almost consistently reported at stage 2. Untreated, HAT evolves towards death in weeks (Rhodesian form) or months (Gambian form). Medications that were used to treat successfully stage 1 do not cross the blood-brain barrier in sufficient amounts to affect central nervous system parasites. Stage 2 was treated with an arsenate, melarsoprol, which might cause severe encephalopathy. It was first replaced by eflornithine that had to be administered by repeated intravenous infusions. Today, far less toxic drugs, fexinidazole, and the new acoziborole, show promise in the elimination of the disease [39]. However, melarsoprol is still used to treat Rhodesian HAT.

Sleep in HAT.

Since the first 24-hour PSG recording in an HAT patient in Niamey, 243 patients were studied for a total of 435 24-hour PSG recordings over a 20-year period (1988–2009) [40]. To do so, we had to go to remote villages by road (Côte d'Ivoire, Angola) or by pirogue (African canoe in Congo) as patients were often found at the "end of the trail" (Figure 5).

Similar to the binary epidemiological and clinical aspects of HAT, sleep patterns were also affected in a binary way [40]. Figure 6 is an example of a polysomnography that shows that sleep is unaltered at stage 1 of HAT compared to healthy local controls. However, stage 2 patients were affected by what I termed the PSG syndrome of HAT (Figure 6).

I had submitted a proposal to use such a noninvasive technique to determine the stage of the disease and thus avoid the necessity of the lumbar punctures, but was unable to receive funding to implement this study.

Figure 5. Searching for patients at the end of the trail. Here on the Sangha River (Likouala District, Congo), with pirogues (A) carrying our equipment (B) to assess the population of the village (C) in search of eventual patients infected by Trypanosoma brucei gambiense.

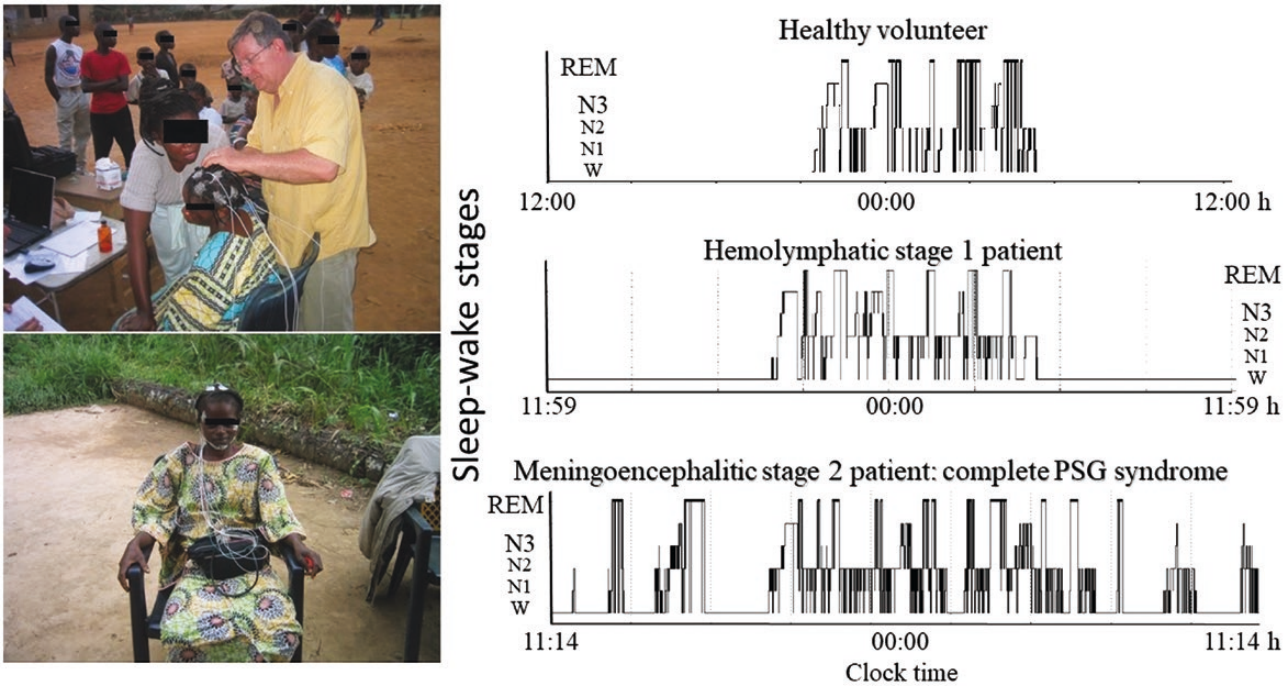

Figure 6. Polysomnography in the village Kombo Makambo (Likouala district, Cuvette department, Congo). Once the electrodes (EEG, EMG, and EOG) have been fixed, they are plugged into the recorder. The patient is free to wander in the village. The meningoencephalitic stage 2 PSG syndrome has two components: a circadian disruption of sleep–wake alternation with intense sleep fragmentation; and profound sleep structure alterations with Sleep Onset REM periods (SOREMP), REM occurring often in a narcoleptic-like manner directly after wake.

Endocrine rhythms in sleeping sickness.

The circadian disorder of sleep and wake distribution accompanied that of cortisol and prolactin [41], and plasma renin activity [42], although the intimate relationship between sleep stages and the endocrine response was preserved. This was especially the case for the N3-related growth hormone surge that occurs during each N3 episode [43]. One exception was plasma melatonin, which nevertheless demonstrated a 2-hour acrophase delay [44].

Our group at Grenoble CRSSA and Lyon University also developed the rat model of HAT. The sleep–wake circadian and structural alterations at stage 2 of the disease were confirmed [45, 46], and deep body temperature ceased to follow circadian rhythmicity as soon as the trypanosomes had invaded the brain [47].

The nitric oxide involvement was also specified at the periphery (blood) and in the brain [48, 49].

The circadian rhythm of intraocular pressure

While in Niger in 1989, I met a French patient who complained of ocular pain during sleep between 4:00 and 6:00 hours [50]. Professor Abdoua Moussa Kabo gave the patient a complete ophthalmologic checkup. Then, I recorded the patient during three PSG nights and found unusually high levels of REM (25.8% to 27.4% of TST) and N3 (29.7% to 46% of TST), with N3 equally distributed in all NREM-REM cycles as already noted in Niger.

Back in Grenoble, I contacted Professor Jean-Paul Romanet, head of the ophthalmology ward at the University Hospital. A 15-year cooperation was established. He was very interested in my observation and we decided to study the eventual relationship between intraocular pressure (IOP) and sleep, and established a 24-hour protocol with hourly IOP measures using electronic tonometers. During nocturnal sleep, the participants were awoken for less than 1 minute every hour for measurement of IOP [51]. We found that IOP follows a circadian rhythm with a nocturnal acrophase and a daytime batyphase. IOP levels varied with the sleep stages, being higher when awoken in N3 and lowest during REM.

An investigation was also organized in Niger on 16 healthy volunteers and 11 open-angle glaucoma patients. They were encouraged to have afternoon naps and night sleep. Night sleep patterns were similar in both groups. The IOP rhythm was reversed in the glaucoma patients with an acrophase in the afternoon, although the IOP-sleep stage relationship was maintained [52]. This may be related to a disturbance of the eye's glymphatic system evidenced by Maiden Nedergaard's group [53].

Sleep in Ramadan, a time delay story

In 1997, I was contacted by Rachida Roky, a former student of Michel Jouvet and James Kruger living in Morocco. Professor Farid Hakkou and her had been funded by the King Hassan II Foundation for Scientific and Medical Research on Ramadan. A joint protocol was first presented at the second International Congress on "Health and Ramadan" in Istanbul, on December 1–3, 1997. The investigation was then organized to study the impact on human sleep during the Ramadan daytime intermittent fasting period and late evening meals [54]. Eight Muslim males (20–28 years old) reported to the Pharmacology unit of the Casablanca University on four occasions: before Ramadan (December 1997) for baseline measures (outside Tdb 9–17°C); on the 11th and 25th days of Ramadan (beginning and end of Ramadan; January 1998, Ta 10–18°C); and 2 weeks after Ramadan (February 1998, Tdb 10–18°C). The participants were instrumented for ambulatory PSG (Oxford Medilog MR-9000 II), and 24-hour Tre measures.

Compared to baseline, Ramadan provoked a slight weight loss (2–3 kg), along with slightly decreased skinfold thicknesses. More specifically, bedding downtime was delayed by ~45 minutes, and returned to baseline values after Ramadan. Sleep latency increased by ~40 minutes, inducing an accordingly proportional decrease in TST, although wake-after-sleep onset did not vary. A REM decrement occurred throughout the fasting period, along with slight decreases in N3. The delay in sleep onset was synchronous with the decrease in Tre, which itself was delayed by 2 hours during Ramadan compared to baseline data (Figure 7).

In reexamining the data, I found that in any given participant, sleep occurred only when Tre had decreased to a given value, e.g. 36.8°C [56, see pages 34–37], suggesting the existence of a thermopreferendum [55] for core temperature that might be a signal of a gate to sleep.

Human Sleep and Military Operations

Exercise effects on sleep and thermoregulation

In October 1976, I returned to CRSSA-Lyon to pursue academic competitions. A new Franco-Canadian Accord investigation was launched to study sleep reactions after physical exercise [56]. Twenty-six Ski Commandos (~21 years old) from the fourth Chasseur Regiment at La Valbonne (~28 km north of Lyon) marched 36 km daily from 9:00 to 17:00 hours on the Dombes plateau at cool November temperatures (Tdb 3.6 ± 2.0°C SD, relative humidity 94 ± 8%). Walking energy expenditure averaged 384.4 kcal/h, and was adjusted individually at 40% of maximal oxygen

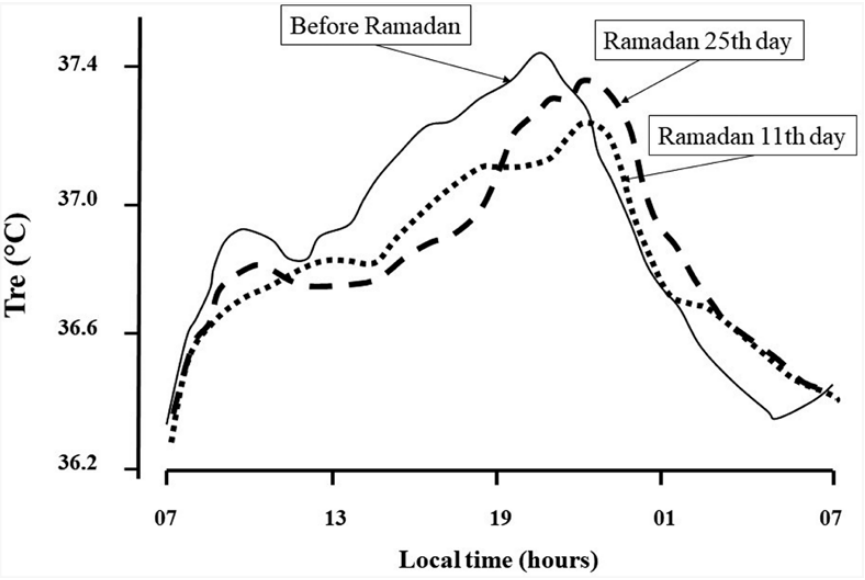

Figure 7. Changes in the acrophase of rectal temperature (Tre, °C) during Ramadan, with a 2-hour delay compared to baseline data. Adapted from Roky et al. [54].

consumption through backpack loads. Body temperatures were recorded telemetrically using specially designed equipment [57].

Six volunteers (~20 years old) participated in nocturnal PSG recordings during baseline (5 nights), post-exercise (6 nights), and recovery periods (5 nights). Urines were collected during the march and at night (22:00–06:00 hours) for creatinine and 17-OHCS assays to evaluate HPA activity.

The main result concerned N3 variations in relation to HPA activity (Figure 7). An individual approach was therefore adopted and participants were ranked according to their sleep and 17-OHCS excretion patterns (Figure 8).

Cardiovascular changes during sleep after exercise.

From the ECG traces of the PSG recordings, heart rates from four of the participants were counted manually [58]. Heart rates increased during the nights following daytime exercise, compared to baseline and recovery nights. Heart rates and heart rate variability were higher during REM compared to preceding NREM, especially N3.

Exercise-induced heat acclimation.

Eight Ski Commandos were also tested in the CRSSA climatic chamber before and after the field exercise trial for heat adaptation [59]. Tympanic (Tty) and mean skin temperatures were taken throughout the 120-minute sweat test, with a target Tty of 38°C. Tdb and wet bulb (Twb) ambient temperatures were thereafter maintained for one hour and sweat output was measured. In the post-trial test, the sweating threshold was delayed and sweat output increased. The moderate prolonged exercise performed in a cool environment and repeated daily for 6 days improved heat acclimation in these young fit men, without any change in maximal aerobic power.

Recovery sleep after 64-hour sleep deprivation, pharmacological help

Under the Franco-Canadian Accord, two investigations on sleep deprivation with continuous activity and under pharmacological help, specifically modafinil, were conducted at DCIEM. On that occasion, I was delighted to work with Paul Naitoh, sleep and performance expert in the U.S. Navy. The DCIEM 64-hour continuous work model with a 15-minute break every two hours was used to analyze mental performance and recovery [60]. Figure 9 shows the effects of modafinil on mental performance.

Modafinil, versus amphetamine or placebo, allowed for sleep to occur rapidly, decreased spontaneous sleep duration, and permitted recovery of sleep debt in N3 and REM during the first recovery night (Figure 10) [61].

Key Findings of My Research

Sleep and thermoregulation

REM and N3 act in opposite manners in their thermoregulatory behavior. N3 is an active thermoregulatory stage that aims at decreasing body heat content. It favors heat loss through sweat evaporation and radiative skin vessel vasodilation, and simultaneously decreases metabolic heat gain. It may therefore be involved in energy conservation [29].

Conversely, REM decreases sweating in the heat, jeopardizing evaporative heat loss, and is accompanied by vasoconstriction of skin blood vessels and increases in skin temperature. It also inhibits cold-induced shivering, as it may hamper the sensitivity of the thermoregulatory function in a poikilothermic-like manner [62]. In any case, REM is an active energy-demanding state [63] that also occurs in a cooler brain [64].

Sleep and stress, a temporal relationship

From our findings, we are convinced that the sleep states, especially N3 and REM, are dually and temporally (diachronic/synchronic [65]) related to the strain/stress relationship. When daytime strain does not elicit a stress reaction, N3 is enhanced at night (diachronic). This represents a neurogenic treatment of strain; the brain does not recruit the HPA [65]. When daytime strain triggers a stress reaction, N3 is decreased (diachronic) the following night, calling on the HPA reaction (somatic strain treatment). When the stress reaction persists during the night (synchronic), REM is also affected.

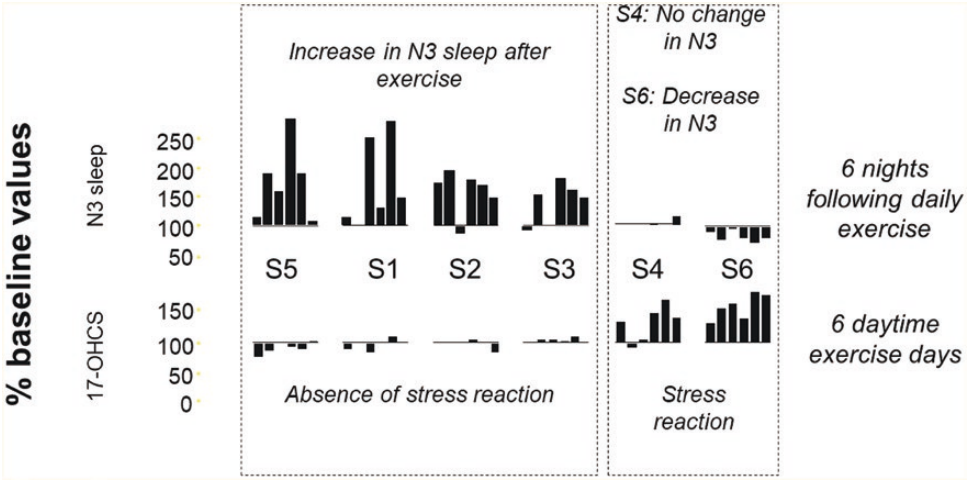

Figure 8. Post-exercise effects, expressed as percent of baseline values, on human sleep (N3) at night, and stress hormone urinary excretion (17-OHCS) during the march, in the six participants (S1-S6) classed after their sleep and stress reaction. In four participants, daytime HPA activity decreased or did not vary, and N3 increased. The other two participants either did not change or decreased N3 in relation to the amplitude of increased HPA activity during the daytime. In one of the latter participants, HPA activity increased also during the night. He was the only participant with a decrease in REM. Adapted from Buguet A. Sleep recovery from physical exercise: A new understanding of brain responses to stress. In: RTO Meeting Proceedings 42. The effects of prolonged military activities in man, physiological and biochemical changes, possible means of rapid recuperation. RTO/NATO 2001;5.1-5.12. (Accessible from ISBN 92-837-1054-1, and https://apps.dtic.mil/ sti/citations/ADA044286).

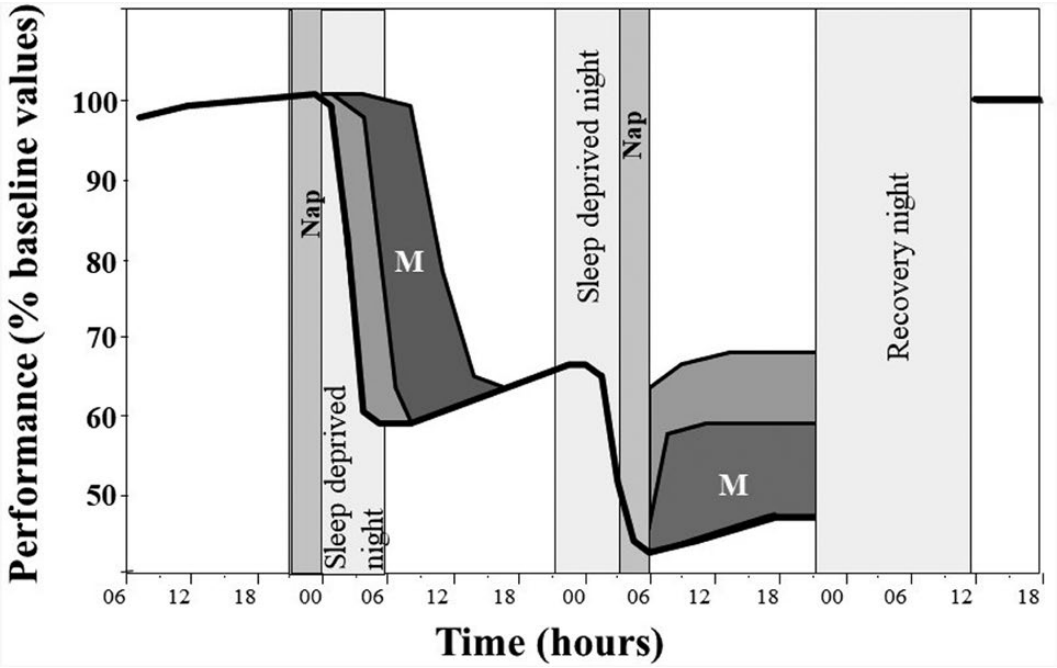

Figure 9. Mental performance recovery after modafinil administration compared to naps during the 64-hour continuous work. Modafinil, amphetamine, or placebo were administered at 23:30 hours on the first night (at the end of the first prophylactic nap), at 05:30 hours on the second night (at the end of the second nap), and at 15:30 hours on the third day of continuous work (to verify the impact of the drug on recovery sleep). Sleep was allowed at 20:00 hours after 64 hours of sleep deprivation [60]. Modafinil was more effective in maintaining alertness than a prophylactic nap during 36–40 hours of continuous operations; for longer operations, a prophylactic nap was recommended.

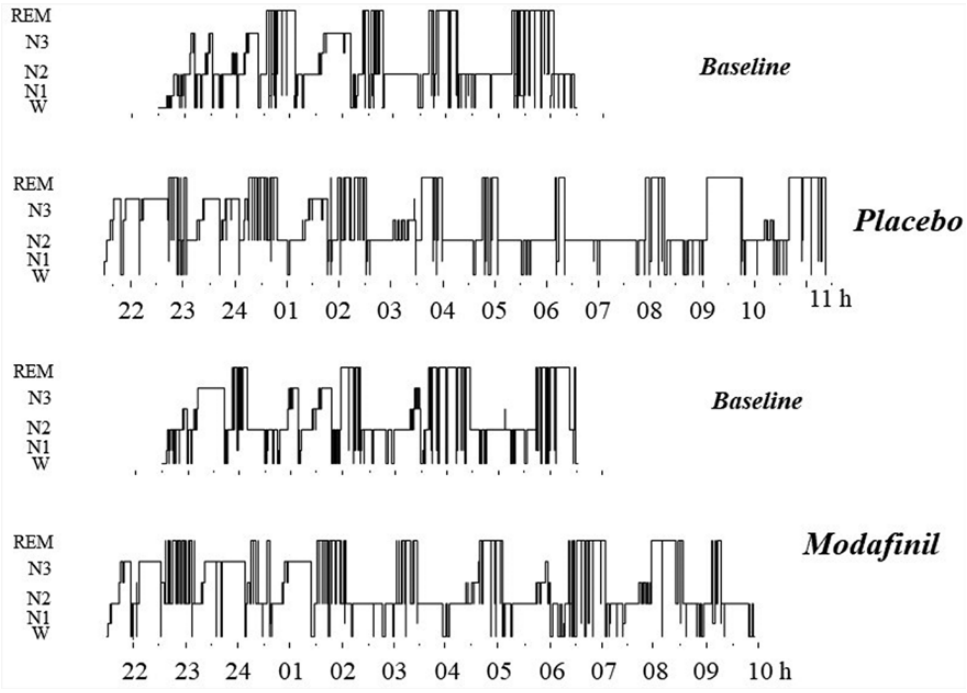

Figure 10. Sleep recovery after the 64-hour continuous work under placebo or modafinil compared to baseline data. Modafinil allowed for sleep to occur, shortened the duration of recovery sleep thus limiting the sleep need, and allowed the recovery in N3 and REM. Adapted from Buguet and collaborators [61].

Such findings have obvious applications in day-to-day life. Regardless of the obvious adaptation of exercise effort to individual capacities that can be helped by training, it is best to avoid heavy exercise in the evening. Regarding the deleterious effects of extreme events in the global warming context, the use of acclimation techniques such as exercise training and/or hot baths has been proposed, particularly in vulnerable persons (children, elderly, patients, etc.) [36].

Increases in overnight N3 sleep as an adaptive mechanism to protect the brain from global warming

In a recent paper focusing on global warming [35], our group concluded that "healthy humans may be well armed physiologically to face the ongoing climate change." The N3 distribution throughout the night of sleep in a hot climate is thought to allow iterative brain cooling that protects and permits the occurrence of the high energy-consuming and hypermetabolic REM [29]. This would preserve several key behavioral and psychological functions related to REM [66]. It may also ease the implication of growth hormone in body restorative processes, as demonstrated in sleeping sickness patients [43]. It may also play a key role in brain amyloid-ß, tau, and α-synuclein waste washing through the glymphatic system, which is more active in NREM, and especially N3 [67], and may protect the brain from degenerative evolution and dementia [68].

Conclusion

I have been fortunate to be affiliated with biomedical research. Throughout my life, I have considered scientific research as an intellectual adventure, which for me is parented to that of explorers. Working in geographically or intellectually isolated conditions encouraged me to look for collaborations. I was fortunate to be able to work in Africa, a continent that has fascinated me since my youth, being present in my early souvenirs. I have been fortunate to be inclined to human medicine, and ended up in Lyon where I was lucky to meet and train with Michel Jouvet, a great scientist in sleep research. I was fortunate to meet Jean Rivolier, who launched my research on extreme environments and conditions. I was fortunate to meet Manny Radomski, who taught me strict principles of biological research, such as the work is not finished until the paperwork is done, and you should measure variables only if you think that they will help in solving your hypotheses. All my life, I have been fascinated by the fact that research is endless, and always challenging, as hypotheses are never proven fully correct. Investigations have always led to new questions that may be investigated through new protocols. I enjoyed serving in the Armed Forces at a time when the freedom of imagination and creativity were respected. Above all, I have been fortunate that my research may serve our understanding of how the human body may cope with ongoing climate changes.

Disclosure Statement

This manuscript did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The author has not submitted this work to any preprint repositories.

Data Availability

No new data were generated in support of this paper, which is essentially a review article.

Acknowledgments

The author is thankful to Dr. Manny Radomski, Professor Emeritus at the University of Toronto, for his valuable comments, suggestions and advice on the manuscript, and his English language proofreading of the text. He is also indebted to Dr. Jacques Reis, Associate Professor at the University of Strasbourg, for his wise suggestions on the manuscript.

Biography

Alain, Georges, Christian Buguet, MD, PhD, is Professor (ret) of the Val-de-Grâce School (Paris), academic institution of French Forces medical officers. He retired from the Medical Services as a General Officer in 2004. His doctoral degrees were obtained under the supervision of Professor Michel Jouvet (Lyon University), with whom he discovered sleep research and the ambition to pursue this area of research throughout his career and beyond. He was deeply influenced by the African continent, discovered at 5 years old in Madagascar (1949). His father's postings took him also to Algiers and Senegal. He began studying medicine at Dakar University, but soon moved to the French Forces Medical School of Lyon. As a medical officer, he applied to serve in Adélie Land, Antarctica. During the 13-month winterover, in addition to his medical commitments, he obtained the loan of an EEG machine from Roche Laboratory, and studied the expeditioners' polysomnographic (PSG) sleep. As a result, in September 1973, he obtained academic degrees in physiological research from the French Forces Medical Research Center (CRSSA). Key findings regarding the relationship between human sleep and thermal exchanges in the heat revealed that sweating and vasodilation were inhibited during REM and exacerbated in N3; metabolic heat production decreased in N3. These relationships were studied in the Arctic cold in Canada, during his 2-year posting as NATO Exchange Officer to the Defence and Civil Institute of Environmental Medicine (DCIEM, Toronto): N3 was related to body cooling at the beginning of the night; REM was deprived, and shivering inhibited during REM. CRSSA-DCIEM collaborated in a physical exercise investigation on sleep and thermoregulation: sleep was affected by stress in a time-of-day manner. In 1981, Dr. Buguet was posted to the Medical Faculty of Niamey University, Niger. He taught physiology and created a laboratory. During sleep in African and Caucasian volunteers, N3 was enhanced during the hot season of the Sahelian climate, and further increased after exercise; N3 was present in all NREM-REM cycles. Professor of Niamey University, he acquired a similar Val-de-Grâce School rank in 1985. Human African trypanosomiasis (HAT), sleeping sickness, was encountered in a migrant patient in 1988, marking the beginning of a considerable body of work on sleep in HAT: a "PSG syndrome" (circadian alteration of the sleep–wake cycle, sleep fragmentation, sleep onset REM episodes) occurs at the meningoencephalitic stage 2 of the disease. Several hundred HAT patients were recorded in Côte d'Ivoire, Angola, and Congo, along with healthy controls. DCIEM collaboration established that stage 2 HAT patients developed dysrhythmia in endocrine and immune variables. In parallel, the operational use of modafinil as a sleep and mental performance helper was specified. In 2004, Dr. Buguet (ret) became an Invited Scientist at Lyon University and worked with Dr. Raymond Cespuglio, Jouvet's successor, on the rat model of HAT. The key role of nitric oxide (NO) in HAT pathophysiology was revealed. After a 4-year sojourn in Congo, Dr. Buguet returned to Lyon in 2015. He then collaborated with the Environmental Neurology Specialty Group of the World Federation of Neurology, alerting the neurologists about potential COVID-19-induced brain disorders. Recently, he used his previous African findings to foresee the sleep impact of climate change, regarding adaptive capacities toward global warming and the management of heatwave-induced stress reactions. Despite his remote postings,

he managed to publish numerous French and English professional papers and book chapters, and wrote nine books on sleep as affected by the operational activities or sleeping sickness. Dr. Buguet belonged to various scientific societies, and the centennial Exotic Pathological Society, created by Alphonse Laveran, Nobel Price.

References

1. Jouvet M, Michel F, Coujon J. Sur un stade d'activité électrique cérébrale rapide au cours du sommeil physiologique. *C. R. Soc Biol.* 1959;**153**:1024–1028. Google Scholar.
2. Dement W, Kleitman N. The relation of eye movements during sleep to dream activity: an objective method for the study of dreaming. *J Exptl Psychol*. 1957;**53**:339–346. doi: 10.1037/h0048189
3. Dewson JH, Dement WC, Simmons FB. Middle ear muscle activity in cats during sleep. *Exp Neurol.* 1965;**12**:1–8. doi: 10.1016/0014-4886(65)90094-4
4. Jouvet M. *Le sommeil et le rêve*. Paris: Editions Odile Jacob. 1992. ISBN: 2-7381-0154-2.
5. Roussel B, Buguet A, Bobillier P, Jouvet M. Locus cœruleus, sommeil paradoxal et noradrénaline cérébrale. *C. R. Soc Biol.* 1967;**161**:2537–2541.
6. Buguet A. *Monoamines et sommeils V. Étude des relations entre les structures monoaminergiques du pont et les pointes ponto-géniculo-occipitales du sommeil paradoxal*. Lyon: Tixier & Fils, 1969.
7. Buguet A, Petitjean F, Jouvet M. Suppression des pointes ponto-géniculo-occipitales du sommeil par lésion ou injection *in situ* de 6-hydroxy-dopamine au niveau du tegmentum pontique. *C. R. Soc Biol.* 1970;**164**:2293–2298.
8. McCormick LA, Taylor AJW, Rivolier J, Cazes G. A psychometric study of stress and coping during the International Biomedical Expedition to the Antarctic (IBEA). *J Hum Stress*. 1985;**11**:150–156. doi: 10.1080/0097840X.1985.9936752
9. Buguet A. *Schistosoma haematobium bilharziasis* during winter-over in Adelie Land: a tale of Antarctic medicine. *Health Risk Analysis*. 2022;**1**:101–105. doi: 10.21668/health.risk/2022.1.10
10. Buguet AGC. Cold-induced bradycardia in man during sleep in Arctic winter nights. *Int J Biometeorol.* 1987;**31**:21–31. doi: 10.1007/BF02192832
11. Buguet A, Rivolier J, Jouvet M. Human sleep patterns in Antarctica. *Sleep.* 1987;**10**:374–382. doi: 10.1093/sleep/10.4.374
12. Rechtschaffen A, Kales A. *A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects*. Washington, DC: Public Health Service, US Govt. PO; 1968.
13. Buguet A. *Le sommeil de l'homme placé dans des environnements ou situations agressifs. Étude au cours d'un hivernage en Antarctique, au cours de l'hiver dans l'Arctique, et après un exercice physique sous-maximal prolongé*. dactyl.: Thèse de doctorat d'état en biologie humaine, Lyon. 1984. Pp. 446.
14. Taylor IM. Medical experiences at McMurdo Sound. In: Horvath S, ed. *Cold injury*. NY: Josiah Macy Jr. Foundation. New York 1960: 117–140.
15. Joern AT, Shurley JT, Brooks RE, Guenter CA, Pierce CM. Short-term changes in sleep patterns on arrival at the South Polar Plateau. *Arch Intern Med*. 1970;**125**:649–654.
16. Natani K, Shurley JT, Pierce CM, Brooks RE. Long-term changes in sleep patterns in men on the South Polar Plateau. *Arch Intern Med*. 1970;**125**:655–659.
17. Paterson RAH. Seasonal reduction of slow-wave sleep at an Antarctic coastal station. *Lancet*. 1975;**305**:468–469. doi: 10.1016/s0140-6736(75)91552-4
18. Hardy JD, DuBois EF. Basal metabolism, radiation, convection and vaporization at temperatures of 22-25°C. *J Nutr.* 1938;**15**:477–497. doi: 10.1093/jn/15.5.477
19. Burton AC. Human calorimetry II. The average temperatures of the tissues of the body. *J Nutr.* 1935;**9**:261–280. doi: 10.1093/jn/9.3.261
20. Buguet AGC, Livingstone SD, Reed LD, Limmer RE. EEG patterns and body temperatures in man during sleep in Arctic winter nights. *Int J Biometeorol*. 1976;**20**:61–69. doi: 10.1007/bf01553173
21. Buguet AGC, Roussel BHE, Watson WJ, Radomski MW. Cold-induced diminution of paradoxical sleep in man. *Electroencephalogr Clin Neurophysiol.* 1979;**46**:29–32. doi: 10.1016/0013-4694(79)90046-4
22. Radomski MW, Boutelier C. Hormone response of normal and intermittent cold-preadapted humans to continuous cold. *J Appl Physiol*. 1982;**53**:610–616. doi: 10.1152/jappl.1982.53.3.610
23. Hénane R, Buguet A, Bittel J, Roussel B. Thermal rhythms and sleep in man. Approach to thermal comfort during sleep. In: Durand J, Raynaud J, ed. *Thermal Comfort/Confort Thermique. Les Editions de l'I.N.S.E.R.M., Vol. 75*. Paris: INSERM. 1977;**75**:195–234. ISBN: 2-85598-180-8.
24. Hénane R, Buguet A, Roussel B, Bittel J. Variations in evaporation and body temperatures during sleep in man. *J Appl Physiol.* 1977;**42**:50–55. doi: 10.1152/jappl.1977.42.1.50
25. Kobayashi R, Koike Y, Hirayama M, Ito H, Sobue Z. Skin sympathetic nerve function during sleep - a study with effector responses. *Auton Neurosci.* 2003;**103**:121–126. doi: 10.1016/s1566-0702(02)00261-8
26. Sagot JC, Amoros C, Candas V, *et al*. Sweating responses and body temperatures during nocturnal sleep in humans. *Am J Physiol.* 1987;**252**:R462–R470. doi: 10.1152/ajpregu.1987.252.3.R462
27. Bach V, Telliez F, Libert JP. The interaction between sleep and thermoregulation in adults and neonates. *Sleep Med Rev.* 2002;**6**:481–492. doi: 10.1053/smrv.2001.0177
28. Buguet A, Bittel J, Gati R, Marrot F, Livecchi-Gonnot G, Hanniquet AM. Thermal exchanges during sleep in anhidrotic ectodermal dysplasia. *Eur J Appl Physiol Occup Physiol.* 1990;**59**:454–459. doi: 10.1007/BF02388628
29. Brebbia DR, Altshuler KZ. .Oxygen consumption rate and electroencephalographic stage of sleep. *Science.* 1965;**150**:1621–1623. doi: 10.1126/science.150.3703.1621
30. Buguet A, Cespuglio R, Radomski MW. Sleep and stress in man: an approach through exercise and exposure to extreme environments. *Can J Physiol Pharmacol.* 1998;**76**:553–561. doi: 10.1139/cjpp-76-5-553
31. Buguet A. Sleep under extreme environments: effects of heat and cold exposure, altitude, hyperbaric pressure and microgravity in space. *J Neurol Sci.* 2007;**262**:145–152. doi: 10.1016/j.jns.2007.06.040
32. Buguet A, Gati Ouonkoye R, Bogui P, Cespuglio R. Geoclimatology and sleep in Africa: a mini-review. *Rev Neurol (Paris)*. 2019;**175**:581–592. doi: 10.1016/j.neurol.2019.06.001
33. Buguet A, Gati R, Soubiran G, Straboni JP, Hanniquet AM, Livecchi-Gonnot G, Bittel J. Seasonal changes in circadian rhythms of body temperatures in humans living in a dry tropical climate. *Eur J Appl Physiol.* 1988;**58**:334–339. doi: 10.1007/bf00417272
34. Román GC, Reis J, Spencer PS, *et al*. World Federation of Neurology Environmental Neurology Specialty Group. Coronavirus disease 2019 (COVID-19) international neurological registries. *Lancet Neurol.* 2020;**19**:484–485. doi: 10.1016/S1474-4422(20)30148-4

35. Buguet A, Reis J, Radomski MW. Sleep and global warming: How will we sleep when the Earth is hotter? *J Neurol Sci.* 2023;**454**:120859. doi: 10.1016/j.jns.2023.120859
36. Buguet A, Radomski MW, Reis J, Spencer PS. Heatwaves and human sleep: Stress response versus adaptation. *J Neurol Sci.* 2023;**454**:120862. doi: 10.1016/j.jns.2023.120862
37. Buguet A, Bogui P, Picot S, Cespuglio R. Sleep patterns in villagers and urban African volunteers in a humid tropical climate: Influence of accessibility to electric light? *J Neurol Sci.* 2017;**376**:44–48. doi: 10.1016/j.jns.2017.02.064
38. Bouteille B, Buguet A. The detection and treatment of human African trypanosomiasis. *Res Rep Trop Med*. 2012;**3**:35–45. doi: 10.2147/RRTM.S24751
39. Dickie EA, Giordani F, Gould MK, *et al*. New drugs for human African trypanosomiasis: a twenty-first century success story. *Trop Med Infect Dis*. 2020;**5**:29. doi: 10.3390/tropicalmed5010029
40. Buguet A, Chapotot F, Ngampo S, Bouteille B, Cespuglio R. Management of African trypanosomisasis of the CNS: Polysomnography as a noninvasive staging tool. *Future Neurol*. 2012;**7**:453–472. doi: 10.2217/FNL.12.41
41. Radomski MW, Buguet A, Montmayeur A, *et al*. 24-hour plasma cortisol and prolactin in human African trypanosomiasis patients and healthy African controls. *Am J Trop Med Hyg.* 1995;**52**:281–286. doi: 10.4269/ajtmh.1995.52.281
42. Brandenberger G, Buguet A, Spiegel K, *et al*. Disruption of endocrine rhythms in sleeping sickness with preserved relationship between hormonal pulsatility and the REM-NREM sleep cycles. *J Biol Rhythms*. 1996;**11**:258–267. doi: 10.1177/074873049601100307
43. Radomski MW, Buguet A, Doua F, Bogui P, Tapie P. Relationship of plasma growth hormone to slow-wave sleep in African sleeping sickness. *Neuroendocrinology.* 1996;**63**:393–396. doi: 10.1159/000126980
44. Claustrat B, Buguet A, Geoffriau M, *et al*. Plasma melatonin rhythm is maintained in human African trypanosomiasis. *Neuroendocrinology.* 1998;**68**:64–70. doi: 10.1159/000054351
45. Montmayeur A, Buguet A. Time-related changes in the sleep-wake cycle of rats infested with *Trypanosoma brucei brucei*. *Neurosci Lett.* 1994;**168**:172–174. doi: 10.1016/0304-3940(94)90443-x
46. Darsaud A, Bourdon L, Mercier S, *et al*. Twenty-four hour disruption of the sleep-wake cycle and sleep-onset REM-like episodes in a rat model of African trypanosomiasis. *Sleep.* 2004;**27**:42–46. doi: 10.1093/sleep/27.1.42
47. Chevrier C, Canini F, Darsaud A, Cespuglio R, Buguet A, Bourdon L. Clinical assessment of the entry into neurological state in rat experimental African trypanosomiasis. *Acta Trop.* 2005;**95**:33–39. doi: 10.1016/j.actatropica.2005.04.011
48. Amrouni D, Gautier-Sauvigné S, Meiller A, *et al*. Cerebral and peripheral changes occurring in nitric oxide (NO) synthesis in a rat model of sleeping sickness: identification of brain iNOS expressing cells. *PLoS One*. 2010;**5**(3):e9211. doi: 10.1371/journal.pone.0009211
49. Amrouni D, Meiller A, Gautier-Sauvigné S, *et al*. Cerebral changes occurring in arginase and dimethylarginine dimethylaminohydrolase (DDAH) in a rat model of sleeping sickness. *PLoS One*. 2011;**6**(3):e16891. doi: 10.1371/journal.pone.0016891
50. Buguet A, Gati R, Kabo AM. Oculalgie transitoire pendant le sommeil. *J Fr Ophtalmol*. 1990;**13**:57–61.
51. Buguet A, Py P, Romanet JP. 24-hour (nychthemeral) and sleep-related variations in intraocular pressure in healthy Caucasians. *Am J Ophthalmol*. 1994;**117**:342–347. doi: 10.1016/s0002-9394(14)73143-5
52. Noël C, Kabo AM, Romanet JP, Montmayeur A, Buguet A. Twenty-four-hour time course of intraocular pressure in healthy and glaucomatous Africans: relation to sleep patterns. *Ophthalmology.* 2001;**108**:139–144. doi: 10.1016/s0161-6420(00)00411-5
53. Wang X, Lou N, Eberhardt A, *et al*. An ocular glymphatic clearance system removes β-amyloid from the rodent eye. *Sci Transl Med*. 2020;**12**(536):eaaw3210. doi: 10.1126/scitranslmed.aaw3210
54. Roky R, Chapotot F, Hakkou F, Taoudi-Benchekroun M, Buguet A. Sleep during Ramadan intermittent fasting. *J Sleep Res.* 2001;**10**:319–327. doi: 10.1046/j.1365-2869.2001.00269.x
55. Bligh J, Johnson KG. Glossary of terms for thermal physiology. *J Appl Physiol.* 1973;**35**:941–961. doi: 10.1152/jappl.1973.35.6.941
56. Buguet A, Roussel B, Angus R, Sabiston B, Radomski M. Human sleep and adrenal individual reactions to exercise. *Electroencephalogr Clin Neurophysiol.* 1980;**49**:515–523. doi: 10.1016/0013-4694(80)90394-6
57. Higgins R, Buguet A, Kuehn L. Measurement of skin temperatures of active subjects by wireless telemetry. *Aviat Space Environ Med.* 1978;**49**:1352–1354.
58. Roussel B, Buguet A. Changes in human heart rate during sleep following daily physical exercise. *Eur J Appl Physiol Occup Physiol.* 1982;**49**:409–416. doi: 10.1007/BF00441302
59. Bittel JHM, Buguet AGC. Improved response to heat after moderate physical training in man. *Experientia.* 1980;**36**:560–562. doi: 10.1007/BF01965800
60. Pigeau R, Naitoh P, Buguet A, *et al*. Modafinil, d-amphetamine and placebo during 64 hours of sustained mental work. I: effects on mood, fatigue, cognitive performance and body temperature. *J Sleep Res.* 1995;**4**:212–228. doi: 10.1111/j.1365-2869.1995.tb00172.x
61. Buguet A, Montmayeur A, Pigeau R, Naitoh P. Modafinil, d-amphetamine and placebo during 64 hours of sustained mental work. II: effects on two recovery nights of recovery sleep. *J Sleep Res.* 1995;**4**:229–241. doi: 10.1111/j.1365-2869.1995.tb00173.x
62. Dewasmes G, Bothorel B, Candas V, Libert JP. A short-term poikilothermic period occurs just after paradoxical sleep onset in humans: characterization changes in sweating effector activity. *J Sleep Res.* 1997;**6**:252–258. doi: 10.1111/j.1365-2869.1997.00252.x
63. Faradji H, Rousset C, Debilly G, Vergnes M, Cespuglio R. Sleep and epilepsy: a key role for nitric oxide. *Epilepsia.* 2000;**41**:794–801. doi: 10.1111/j.1528-1157.2000.tb00245.x
64. Jouvet M, Buda C, Debilly G, Dittmar A, Sastre JP. La température centrale est le facteur principal de régulation du sommeil paradoxal chez le chat pontique. *C R Acad Sci Paris Série 3.* 1988;**306**:69–73Corpus ID: 78842557, Google Scholar.
65. Buguet A. *Le sommeil raconté par un médecin itinérant. Des climats tempérés à la brousse africaine et aux pôles*. Paris: L'Harmattan. 2020. ISBN 978-2-343-20164-1.
66. Löhmus M. Possible biological mechanisms linking mental health and heat – a contemplative review. *Int J Environ Res Public Health.* 2018;**15**:1515. doi: 10.3390/ijerph15071515
67. Chong PLH, Garic D, Shen MD, Lundgaard I, Schwichtenberg AJ. Sleep, cerebrospinal fluid, and the glymphatic system: a systematic review. *Sleep Med Rev.* 2022;**61**:101572. doi: 10.1016/j.smrv.2021.101572
68. Nedergaard M, Godman SA. Glymphatic failure as a final common pathway to dementia. *Science.* 2020;**370**:50–56. doi: 10.1126/science.abb8739