

Michel Jouvét and his Importance for Brazilian Preclinical Sleep Research

Gabriel Natan Pires¹
Sergio Tufik¹
Monica Andersen¹

¹ Departamento de Psicobiologia –
Universidade Federal de São Paulo – São
Paulo, Brazil.

The world of sleep medicine received with great sorrow the sadly news of Michel Jouvét's death. He passed away on October 3rd 2017, in Villeurbanne, France, at the age of 91. Dr. Jouvét was one of the forefathers of sleep research, being responsible and involved in several of the main breakthroughs on the early years of sleep medicine.

Dr. Jouvét was initiated on the field of sleep research in Long Beach, California in 1954, by working on the laboratory of Horace Magoun (1907-1991), who have worked together with Giuseppe Moruzzi (1910-1986) on the identification of brain structures underlying sleep. Among his main research achievements are the description of muscle atonia during REM sleep, in 1959, which had been described only a few years before by Eugene Aserinsky (1921-1998) and Nathaniel Kleitman (1895-1999). Jouvét realized that both cats (main animal model for sleep research at that time) and humans presented an almost complete muscle atonia during REM sleep. The contrast of the lack of muscles tonus with intense electroencephalographic activity led to the term “paradoxical sleep”. He later worked on detailing the structures generating paradoxical sleep, reason why it was also referred to as “rhombencephalic sleep”, in opposition to the “telencephalic” (i.e. NREM) sleep. More recently he worked on the discovery and clinical usefulness of modafinil, used on the treatment of narcolepsy and overall excessive daytime sleepiness.

The work of Dr. Jouvét has greatly affected Brazilian preclinical sleep research. The noteworthy article of Timo-Iaria et al.¹ which for the first time described the sleep phases and stages of rats based on electroencephalographic parameters, was much based on previous descriptions by Jouvét about the neurophysiology of sleep states and previous polygraph recordings in rodents^{2,3}. The most impacting feature of Jouvét's scientific output to Brazilian sleep research might have been the description of the flower pot technique for paradoxical sleep deprivation in cats³. This method consisted in placing an animal on an inverted flower pot surrounded by water. The animal is able to sleep on this pot, but whenever it entered the REM sleep, it falls from the platform or touches its snout on the water due to the characteristic muscle atonia of this sleep stage, consequently awaking. Thus, this method leads to a specific deprivation of REM sleep, while NREM sleep is reasonably preserved. This method was adapted to rats after a few years (Cohen and Dement, 1965) and refined to reduce stress due to locomotion restraints⁴. Afterwards, Brazilian researchers have worked on further refinements, proposing the so-called modified multiple platform method⁵, as well as testing variations and new applications for this methods⁶⁻⁹. Much of the Brazilian preclinical output in sleep research has been derived from the platform methods. On a quick search on Scopus for preclinical articles using platform-derived sleep deprivation methods, limited to journal articles published on the last decade (2007-2016), Brazil is ranked first, being the country which has mostly used this methods on preclinical sleep research (130 out of 418 articles – Figure 1). Noteworthy, several research groups on the country uses these methods. The most prolific research group on the field has been the one headed by Tufik and Andersen, at the Federal University of São Paulo, accounting for 95 out of 418 articles (23.4%). It has also been employed by the groups of De Bruin^{10,11} (Federal University of Ceará), Suchecki^{7,8,12-15} (Federal University of São Paulo), Lima¹⁶⁻²⁰ (Federal University of Paraná), Hoshino^{9,21-24} (São Paulo State University) and many others. Finally, Sleep Science, the official journal of the Brazilian Association of Sleep, has published several articles based on platform-derived methods^{16,17,23-25}.

The impact of Jouvét's legacy on Brazilian preclinical sleep research is just one among several fields that have developed based on his achievements and discoveries. Undoubtedly, other fields, countries and individuals have grown based on his findings. As an example, the

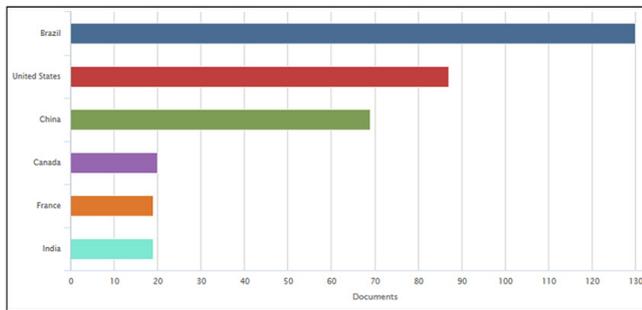


Figure 1. Research output or articles using platform-derived sleep deprivation methods during the last decade, ranked by country. Data extracted from Scopus, limited for journal articles published between 2007 and 2016, using the following search string: ((sleep AND (platform OR "flower pot" OR "rem sleep deprivation" OR "paradoxical sleep deprivation") AND (rat OR rats OR mice OR mouse OR murin* OR animal*) AND NOT rotating)).

clinical definition and all research about REM sleep behavior disorder only become possible due to Jouvett's observation of muscle atonia during paradoxical sleep in cats, as well as of oneiric behavior in animals²⁶. In any case, as basic sleep researchers, we must recognize much of what has been achieved in recent years were only possible due to Jouvett's seminal works, on the decades of 60 to 80.

All the Brazilian sleep research community and specially those involved in preclinical research will greatly miss Michel Jouvett's brilliance and remarkable scientific insights. His work remains alive though, in all those who work to unravel the neurobiological basis of REM sleep and to dissect the effects of paradoxical sleep deprivation.

REFERENCES

1. Timo-Iaria C, Negrão N, Schmidek WR, Hoshino K, Lobato de Menezes CE, Leme da Rocha T. Phases and states of sleep in the rat. *Physiol Behav.* 1970;5(9):1057-62.
2. Jouvett D, Valatx JI, Jouvett M. [Polygraphic study of sleep in the kitten]. *C R Seances Soc Biol Fil.* 1961;155:1660-4. French.
3. Jouvett D, Vimont P, Delorme F. [Study of selective deprivation of the paradoxal phase of sleep in the cat]. *J Physiol (Paris).* 1964;56:381. French.
4. van Hulzen ZJ, Coenen AM. Paradoxical sleep deprivation and locomotor activity in rats. *Physiol Behav.* 1981;27(4):741-4.
5. Nunes GP Jr., Tufik S. Validation of the modified multiple platform method (MMP) of paradoxical sleep deprivation in rats. *Sleep Res.* 1994;22(Suppl):339.
6. Machado RB, Hipólido DC, Benedito-Silva AA, Tufik S. Sleep deprivation induced by the modified multiple platform technique: quantification of sleep loss and recovery. *Brain Res.* 2004;1004(1-2):45-51.
7. Machado RB, Suchecki D, Tufik S. Sleep homeostasis in rats assessed by a long-term intermittent paradoxical sleep deprivation protocol. *Behav Brain Res.* 2005;160(2):356-64.
8. Suchecki D, Tufik S. Social stability attenuates the stress in the modified multiple platform method for paradoxical sleep deprivation in the rat. *Physiol Behav.* 2000;68(3):309-16.
9. Medeiros R, Lenneberg-Hoshino C, Hoshino K, Tufik S. Neuroethologic differences in sleep deprivation induced by the single- and multiple-platform methods. *Braz J Med Biol Res.* 1998;31(5):675-80.
10. Daniele TMD, de Bruin PFC, Rios ERV, de Bruin VMS. Effects of exercise on depressive behavior and striatal levels of norepinephrine, serotonin and their metabolites in sleep-deprived mice. *Behav Brain Res.* 2017;332:16-22.
11. de Oliveira RA, Cunha GM, Borges KD, de Bruin GS, dos Santos-Filho EA, Viana GS, et al. The effect of venlafaxine on behaviour, body weight and striatal monoamine levels on sleep-deprived female rats. *Pharmacol Biochem Behav.* 2004;79(3):499-506.
12. Machado RB, Suchecki D, Tufik S. Comparison of the sleep pattern throughout a protocol of chronic sleep restriction induced by two methods of paradoxical sleep deprivation. *Brain Res Bull.* 2006;70(3):213-20.
13. Suchecki D, Lobo LL, Hipólido DC, Tufik S. Increased ACTH and corticosterone secretion induced by different methods of paradoxical sleep deprivation. *J Sleep Res.* 1998;7(4):276-81.
14. Suchecki D, Tiba PA, Tufik S. Hormonal and behavioural responses of paradoxical sleep-deprived rats to the elevated plus maze. *J Neuroendocrinol.* 2002;14(7):549-54.
15. Suchecki D, Machado RB, Tiba P. Stress-induced sleep rebound: adaptive behavior and possible mechanisms. *Sleep Sci.* 2009;2(3):151-60.
16. Aurich MF, Rodrigues LS, Targa ADS, Noseda ACD, Cunha FDW, Lima MMS. Olfactory impairment is related to REM sleep deprivation in rotenone model of Parkinson's disease. *Sleep Sci.* 2017;10(1):47-54.
17. Noseda AC, Targa AD, Rodrigues LS, Aurich MF, Lima MM. REM sleep deprivation promotes a dopaminergic influence in the striatal MT2 anxiolytic-like effects. *Sleep Sci.* 2016;9(1):47-54.
18. Lima MM, Andersen ML, Reksidler AB, Silva A, Zager A, Zanata SM, et al. Blockage of dopaminergic D(2) receptors produces decrease of REM but not of slow wave sleep in rats after REM sleep deprivation. *Behav Brain Res.* 2008;188(2):406-11.
19. Lima MM, Andersen ML, Reksidler AB, Ferraz AC, Vital MA, Tufik S. Paradoxical sleep deprivation modulates tyrosine hydroxylase expression in the nigrostriatal pathway and attenuates motor deficits induced by dopaminergic depletion. *CNS Neurol Disord Drug Targets.* 2012;11(4):359-68.
20. Targa ADS, Noseda ACD, Rodrigues LS, Aurich MF, Lima MMS. REM sleep deprivation and dopaminergic D2 receptors modulation increase recognition memory in an animal model of Parkinson's disease. *Behav Brain Res.* 2018;339:239-48.
21. de Paula HM, Hoshino K. Correlation between the fighting rates of REM sleep-deprived rats and susceptibility to the 'wild running' of audiogenic seizures. *Brain Res.* 2002;926(1-2):80-5.
22. Furlan FA, Hoshino K. Fighting by sleep-deprived rats as a possible manifestation of panic: effects of sodium lactate. *Braz J Med Biol Res.* 2001;34(3):359-66.
23. Nunes HC, Pezzato FA, Hoshino K. Self-grooming, experimental anxiety and paradoxical sleep deprivation in rats. *Sleep Sci.* 2012;5(1):19-23.
24. Pezzato FA, Silveira DTL, Novais DB, Hoshino K. Assessment of impulsivity in REM-sleep deprived rats. *Sleep Sci.* 2012;5(3):79-83.
25. Pires GN, Tufik S, Andersen ML. Correlation of maternal and aggressive behaviors in normal and sleep-restricted lactating rats. *Sleep Sci.* 2013;6(2):80-4.
26. Sastre JP, Jouvett M. [Oneiric behavior in cats]. *Physiol Behav.* 1979;22(5):979-89. French.