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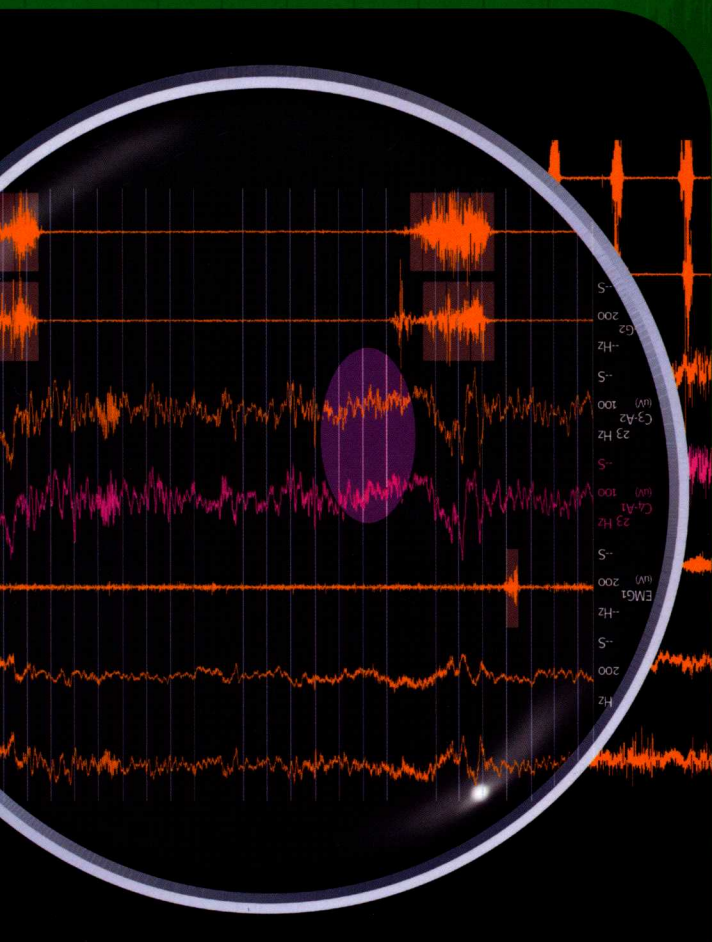
Series Editor

Sudhansu Chokroverty  
Luigi Ferini-Strambi

Edited by

# Sleep Disorders

Oxford Textbook of



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# Oxford Textbook of Sleep Disorders

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**Oxford Textbook of**

# **Sleep Disorders**

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# Preface

There have been rapid advances recently in basic science, technical, clinical, and therapeutic aspects of sleep medicine that have captivated sleep scientists and clinicians. Concomitantly, there has been a rapid increase in the number of individuals involved in clinical sleep medicine and sleep research, in addition to an explosive growth in the number of sleep centers, laboratories, and programs and an increasing number of sleep societies (national and international) and sleep medicine journals worldwide. There is an eagerness and increasing desire to absorb this evolving knowledge about sleep and its disorders. Therefore, there is a need for new books encompassing all this new knowledge. Despite the publication of a number of sleep-related books in the last few years, gaps remain in many areas. It is obvious that there is a distinct lack of adequate knowledge and awareness of sleep disorders within the neurological community, and thus sleep disorders are not dealt with adequately by most practicing neurologists. There are a few neurologically oriented short books available, but these do not give in-depth coverage of the topic. It is therefore an opportune moment to produce a volume in a succinct and lucid manner, covering the topic in a logical and orderly way and emphasizing the practical aspects with an underlying basic science component. Peter Stevenson, Senior Commissioning Editor of Medicine, Neurology, Neurosurgery, Psychiatry, and Oxford Medical Libraries at Oxford University Press (OUP), Oxford, United Kingdom contacted the Senior Editor (SC) to consider compiling such a book to fill these gaps, in collaboration with a co-editor from the European continent. Professor Luigi Ferini-Strambi from Milan, Italy agreed to be co-editor. We then proceeded to produce a comprehensive,

balanced, and easily readable book emphasizing sleep neurology as part of the Oxford Textbooks in Clinical Neurology (OTCN) series in conformity with the wishes of Professor Chris Kennard, editor of the new OTCN series.

Most of the recent advances in sleep medicine have been captured in this monograph, with special emphasis on sleep neurology. The volume is essentially a clinical compendium, but also provides a background to the underlying basic science and techniques. The book is divided into 12 sections and several subsections: (1) Basic science; (2) Laboratory evaluation; (3) Clinical science: general introduction; (4) Hypersomnias; (5) Insomnias; (6) Circadian rhythm disorders; (7) Sleep neurology; (8) Parasomnias; (9) Sleep and medical disorders; (10) Sleep and psychiatric disorders; (11) Sleep in children, older adults, and women; (12) Miscellaneous sleep-related topics.

This book is directed primarily at neurologists and senior trainees, as well as internists (especially those specializing in pulmonary, cardiovascular, gastrointestinal, renal, and endocrine medicine), general practitioners/family physicians, psychiatrists, psychologists, pediatricians, otolaryngologists, dentists, neurosurgeons, and neuroscientists, and others interested in understanding sleep (eg, technologists, nurses, and other healthcare professionals). The book should be useful to both beginners and those advanced in the field.

Sudhansu Chokroverty  
Luigi Ferini-Strambi

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contents, making corrections, typing, and editing, in addition to her main function as editorial assistant to the journal. Since Ms. Bacala left, Ms. Jamie Winder, the current editorial assistant took care of these functions. Last but not least, the senior editor must express his love and gratitude to his wife, Manisha Chokroverty, MD for her unfailing and continued support, love, patience and tolerance throughout the long period of editing, writing, and proof-reading during the book's production.

Sudhansu Chokroverty  
Luigi Ferini-Strambi



# Abbreviations

5-HT	5-hydroxytryptamine (serotonin)	BIPN	bilateral isolated phrenic neuropathy
5-HT <sub>1</sub> , ...	serotonin receptors	BMI	body mass index
5-HTT	serotonin transporter	BP	blood pressure
A	adrenaline (epinephrine)	BPAP	bilevel positive airway pressure
AAP	American Academy of Pediatrics	BPSD	behavioral and psychological signs of dementia
AASM	American Academy of Sleep Medicine	BRS	baroreflex sensitivity
ABG	arterial blood gas	BSMI	benign sleep myoclonus of infancy
ACE	angiotensin-converting enzyme	BZD	benzodiazepine
ACh	acetylcholine	BZDRA	benzodiazepine receptor agonist
AChR	acetylcholine receptor	CA	central apnea
ACTH	corticotropin (adrenocorticotrophic hormone)	CA	confusional arousal
AD	Alzheimer disease	CAF	central activation failure
ADA	adenosine deaminase	CAP	cyclical alternating pattern
ADCADN	autosomal dominant cerebellar ataxia, deafness, and narcolepsy	CBF	cerebral blood flow
ADH	antidiuretic hormone	CBT	cognitive-behavioral therapy
ADHD	attention-deficit hyperactivity disorder	CBTI	cognitive-behavioral therapy for insomnia
ADL	Activities of Daily Living	CBZ	carbamazepine
ADNFLE	autosomal dominant nocturnal frontal lobe epilepsy	CCHS	congenital central alveolar hypoventilation syndrome
AED	antiepileptic drug	CDR	Clinical Dementia Rating
AHI	apnea-hypopnea index	CFS	chronic fatigue syndrome
AI	apnea index	CGI	clinical global impression
AI	atonia index	CGRP	calcitonin gene-related peptide
AIDS	acquired immunodeficiency syndrome	CHF	chronic heart failure
ALMA	alternating leg muscle activation	CHF	congestive heart failure
ALS	amyotrophic lateral sclerosis	CI	confidence interval
ALTE	apparent life-threatening event	CJD	Creutzfeldt-Jakob disease
AMD	acid maltase deficiency	CKD	chronic kidney disease
AMS	acute mountain sickness	CMD	congenital muscular dystrophy
ANS	autonomic nervous system	CMS	Centers Medicare and Medicaid Services
APAP	autotitrating continuous positive airway pressure	CMS	chronic mountain sickness
ARAS	ascending reticular activating system	CMS	congenital myasthenic syndrome
ArD	arousal disorder	CMT	Charcot-Marie-Tooth disease
ASD	autism spectrum disorder	CNS	central nervous system
ASPD	advanced sleep phase disorder	CNZ	clonazepam
ASV	adaptive servo-ventilation	COMT	catechol-O-methyltransferase
ASV	assisted support ventilation	COPD	chronic obstructive pulmonary disease
ASWPD	advanced sleep-wake phase disorder	CPAP	continuous positive airway pressure
BALM	Basic Language Morningness Scale	CPG	central pattern generator
BDNF	brain-derived neurotrophic factor	CRC	central respiratory chemoreceptor
BF	basal forebrain	CRH	corticotropin-releasing hormone
Bic	bicuculline	CRP	C-reactive protein
		CRSD	circadian rhythm sleep disorder



CRSWD	circadian rhythm sleep–wake disorder	FOSQ	Functional Outcomes of Sleep Questionnaire
CSB	Cheyne–Stokes breathing	FOT	forced oscillation technique
CSF	cerebrospinal fluid	FRC	functional residual capacity
CSWS	electrical status epilepticus during slow-wave sleep (continuous spike and wave during slow-wave sleep)	FRSD	free-running (non-24-hour) sleep disorder
CTb	cholera toxin b subunit	FSH	follicle-stimulating hormone
CV	cardiovascular	FSHD	facioscapulohumeral muscular dystrophy
CVD	cardiovascular disease	FTD	frontotemporal dementia
CWP	chronic widespread pain	FVC	forced vital capacity
D <sub>1</sub> , ...	dopamine receptors	GABA	γ-aminobutyric acid
DA	disorder of arousal	GAD	glutamate decarboxylase
DA	dopamine	GBP	gabapentin
DAT	dopamine transporter	GBS	Guillain–Barré syndrome
dDpMe	dorsal deep mesencephalic reticular nucleus	GER	gastroesophageal reflux
DHE	dihydroergotamine	GERD	gastro-esophageal reflux disease
DLB	dementia with Lewy bodies	GH	growth hormone
DLCO	diffusion capacity of carbon monoxide	GHRH	growth hormone-releasing hormone
DLMO	dim light melatonin onset	GI	gastrointestinal
DM	dermatomyositis	Gia	alpha gigantocellular nucleus
DM	myotonic dystrophy (dystrophia myotonica)	GiV	ventral gigantocellular nucleus
DMD	Duchenne muscular dystrophy	Glu	glutamate
DORA	dual orexin receptor antagonist	Gly	glycine
DPGi	dorsal paragigantocellular nucleus	GnRH	gonadotropin-releasing hormone
DPS	diaphragm pacing stimulation	GTCS	generalized tonic–clonic seizure
DR	dorsal raphe	HA	histamine
DRG	dorsal respiratory group	HACE	high-altitude cerebral edema
DSM	Diagnostic and Statistical Manual of Mental Disorders	HAPE	high-altitude pulmonary edema
DSPD	delayed sleep phase disorder	HAPH	high-altitude pulmonary hypertension
DSPS	delayed sleep phase syndrome	Hcrt, hcrt	hypocretin (orexin)
DSWPD	delayed sleep–wake phase disorder	HCSB	Hunter–Cheyne–Stokes breathing
DU	duodenal ulcer	HD	hemodialysis
DZ	dizygotic	HD	Huntington disease
EA	epileptic activity	HF	high-frequency
EAE	experimental autoimmune encephalomyelitis	HFLM	high-frequency leg movements
EDS	excessive daytime sleepiness	HFpEF	heart failure with preserved ejection fraction
EDSS	Expanded Disability Status Scale	HFT	hypnagogic foot tremor
EEG	electroencephalography	HH	hypnagogic hallucination
EFM	excessive fragmentary myoclonus	HHV	human herpesvirus
EHS	exploding head syndrome	HIV	human immunodeficiency virus
EMG	electromyography	HLA	human leukocyte antigen
EOG	electrooculography	HMSN	hereditary motor and sensory neuropathy
EPAP	expiratory positive airway pressure	HPA	hypothalamic–pituitary–adrenal
EPSP	excitatory postsynaptic potential	HPS	hypothalamic–pituitary–somatotrophic
EQS	excessive quantity of sleep	HR	hazard ratio
ERP	event-related potential	HR	heart rate
ESES	electrical status epilepticus during sleep	HRQoL	health-related quality of life
ESRD	end-stage renal disease	HRV	heart rate variability
ESS	Epworth Sleepiness Scale	HUTT	head-up tilt test
FAP	fixed action pattern	HV	hippocampal volume
FASPD	familial advanced sleep disorder	IBS	irritable bowel syndrome
FASPS	familial advanced sleep phase syndrome	ICD	International Classification of Diseases
FCD	focal cortical dysplasia	ICHD	International Classification of Headache Disorders
FDG	[ <sup>18</sup> F]fluorodeoxyglucose	ICSD	International Classification of Sleep Disorders
FFI	fatal familial insomnia	ICU	intensive care unit
FiO <sub>2</sub>	fraction of inspired oxygen	IED	interictal epileptiform discharge
FLEPS	Frontal Lobe Epilepsy and Parasomnias Scale	IFN	interferon
fMRI	functional magnetic resonance imaging	Ig	immunoglobulin
		IH	idiopathic hypersomnia
		IL	interleukin
		ILD	interstitial lung disease

IPAP	inspiratory positive airway pressure	NDRI	norepinephrine (noradrenaline)–dopamine reuptake inhibitor
IPN	isolated phrenic neuropathy	NFLE	nocturnal frontal lobe epilepsy
ipRGC	intrinsically photoreceptive ganglion cell	NIV	noninvasive positive pressure ventilation
IPSP	inhibitory postsynaptic potential	NLP	no conscious light perception
iRBD	idiopathic REM sleep behavior disorder	NM	nucleus basalis of Meynert
IRLSSG	International Restless Leg Syndrome Study Group	NMDA	<i>N</i> -methyl- <i>D</i> -aspartate
ISI	Insomnia Severity Index	NMO	neuromyelitis optica
ISWRD	irregular sleep–wake rhythm disorder	NMS	non-motor symptoms
IVIg	intravenous immunoglobulin	NMSQuest	Non-Motor Symptoms Questionnaire
JLD	jet lag disorder	NMSS	Non-Motor Symptoms Scale
JME	juvenile myoclonic epilepsy	NO	nitric oxide
KLS	Kleine–Levin syndrome	NOA	number of awakenings
KSS	Karolinska Sleepiness Scale	NOS	not otherwise specified
LC	locus coeruleus	NPARM	non-polyalanine repeat mutation
LDT	laterodorsal tegmental nucleus	NPs	nasal prongs
LEMS	Lambert–Eaton myasthenic syndrome	NREM	non-rapid-eye-movement
LES	lower esophageal sphincter	NRS	nonrestorative sleep
LEV	levetiracetam	NSAID	nonsteroidal anti-inflammatory drug
LF	low-frequency	NTS	nucleus tractus solitarius
LGMD	limb-girdle muscular dystrophy	NYHA	New York Heart Association
LH	lateral hypothalamus	OA	obstructive apnea
LH	luteinizing hormone	OAHI	obstructive apnea–hypopnea index
LKS	Landau–Kleffner syndrome	OCD	obsessive–compulsive disorder
LTG	lamotrigine	OCST	out-of-center sleep studies
LV	left-ventricular	OHS	obesity–hypoventilation syndrome
LVEF	left-ventricular ejection fraction	ONS	occipital nerve stimulation
LVIDd	left-ventricular internal diameter in diastole	OR	odds ratio
MA	monoamine	OSA	obstructive sleep apnea
MAD	mandibular advancement device	OSAS	obstructive sleep apnea syndrome
MAO	monoamine oxidase	OXC	oxcarbazepine
MAOI	monoamine oxidase inhibitor	PA	paroxysmal arousal
MCH	melanin-concentrating hormone	PaCO <sub>2</sub>	alveolar partial pressure of carbon dioxide
MCI	mild cognitive impairment	PaCO <sub>2</sub>	arterial partial pressure of carbon dioxide
MDD	major depressive disorder	PaO <sub>2</sub>	arterial partial pressure of oxygen
MDMA	3,4-methylenedioxymethamphetamine	PAP	positive airway pressure
MEMA	middle ear muscle activity	PARM	polyalanine repeat mutation
MEP	maximum expiratory pressure	PB	phenobarbital
MEP	motor evoked potential	PCO <sub>2</sub>	partial pressure of carbon dioxide
MG	myasthenia gravis	$P_{crit}$	critical closing pressure
MHA	morning headache	PD	Parkinson disease
MIBG	<i>meta</i> -iodobenzylguanidine	PDSS	Parkinson's Disease Sleep Scale
MIP	maximal inspiratory pressure	PE	pulmonary embolism
MMC	migrating motor complex	PeF	perifornical area
MMSE	Mini Mental State Examination	peri-LCa	peri-locus coeruleus alpha nucleus
MnPN	median preoptic nucleus	PET	positron emission tomography
MRI	magnetic resonance imaging	PFC	prefrontal cortex
MRS	magnetic resonance spectroscopy	PFT	pulmonary function tests
MS	multiple sclerosis	PGO	pontine–geniculate–occipital
MSA	multiple system atrophy	PH	posterior hypothalamus
MSLT	multiple sleep latency test	PHT	phenytoin
MT <sub>1</sub> , MT <sub>2</sub>	melatonin receptors	PIA	pontine inhibitory area
mTBI	minor traumatic brain injury	PIM/AIE	psychobiological inhibition/attention–intention–effort
MVC	maximum voluntary contraction	PIP	periorbital integrated potential
MWT	maintenance of wakefulness test	PLM	periodic leg/limb movements
MZ	monozygotic	PLMD	periodic limb movement disorder
NA	noradrenaline (norepinephrine)	PLMS	periodic leg/limb movements during sleep
nAChR	neuronal nicotinic acetylcholine receptor	PLMSI	PLMS index
NAVA	neurally adjusted ventilatory assist		
NC	narcolepsy with cataplexy		

PLMW	periodic leg/limb movements during wakefulness	SCN	suprachiasmatic nucleus
PM	polymyositis	SD	sleep deprivation
PMR	progressive muscle relaxation	SDB	sleep disordered breathing
PMS	proprio-spinal myoclonus	SE	sleep efficiency
PnC	pontis caudalis	SEP	somatosensory cortical evoked potential
PNE	primary nocturnal enuresis	Ser	serotonin
PnO	pontis oralis	SF-36	36-Item Short Form Health Survey
PNS	peripheral nervous system	SFMM	sleep-related faciomandibular myoclonus
PO <sub>2</sub>	partial pressure of oxygen	sIBM	sporadic inclusion-body myositis
POA	preoptic area	SIDS	sudden infant death syndrome
POAH	proptic nucleus of the anterior hypothalamus	SLD	sublaterodorsal nucleus
PPS	postpoliomyelitis syndrome	SLE	systemic lupus erythematosus
PPT	pedunculopontine	SMA	spinal muscular atrophy
PRM	primidone	SMR	sensorimotor rhythm
PROM	proximal myotonic myopathy	SN	substantia nigra
PrP	prion protein	SNA	sympathetic neural activity
PS	paradoxical sleep	SNIP	supine vital capacity nasal inspiratory pressure
PSG	polysomnography	SNP	single nucleotide polymorphism
PSM	proprio-spinal myoclonus	SNRI	serotonin and norepinephrine (noradrenaline)
PSP	progressive supranuclear palsy		reuptake inhibitor
PSQI	Pittsburgh Sleep Quality Index	SOL	sleep onset latency
PST	problem-solving therapy	SooS	sudden onset of sleepiness
PTSD	post-traumatic stress disorder	SOREMP	sleep onset REM period
PTT	pulse transit time	SOREMS	sleep onset REM sleep
PVDF	polyvinylidene fluoride	SPECT	single-photon emission computed tomography
PVR	peripheral vascular resistance	SRBD	sleep-related breathing disorder
PWS	Prader-Willi syndrome	SRED	sleep-related eating disorder
QoL	quality of life	SRMD	sleep-related movement disorder
R&K	Rechtschaffen & Kales	SSI	Standard Shiftwork Index
rACC	rostral anterior cingulate cortex	SSRI	selective serotonin reuptake inhibitor
RAM	reward activation model	SubC	subcoeruleus nucleus
RBD	REM sleep behavior disorder	SUDEP	sudden unexpected death in epilepsy
RBDSS	RBD Severity Scale	SUNCT	short-lasting unilateral neuralgiform headache with conjunctival injection and tearing
rCBF	regional cerebral blood flow		sleepwalking
RCT	randomized controlled trial	SW	slow-wave activity
RDI	respiratory disturbance index	SWA	slow-wave activity
REM	rapid eye movement	SWD	shift work sleep disorder
RERA	respiratory-effort-related arousal	SWD	sleep-wake disorder
RF	reticular formation	SWS	slow-wave sleep
RFM	rhythmic foot movement	SXB	sodium oxybate
RIA	radioimmunoassay	t-MHA	tele-methylhistamine
RIP	respiratory inductive plethysmography	T&A	tonsillectomy/adenoidectomy
RISP	recurrent isolated sleep paralysis	T2DM	type 2 diabetes mellitus
RLP	reduced light perception	TAC	trigeminal autonomic cephalgia
RLS	restless legs syndrome	TBI	traumatic brain injury
RMD	rhythmic movement disorder	Th	thalamocortical
RMg	nucleus raphe magnus	TH	tyrosine hydroxylase
RMMA	rhythmic masticatory muscle activity	THC	$\Delta^9$ -tetrahydrocannabinol
RSWA	REM sleep without atonia	TIA	transient ischemic attack
rtPCR	real-time polymerase chain reaction	TLC	total lung capacity
RV	residual volume	TMD	temporomandibular disorder
RWA	REM sleep without atonia	TMN	tuberomammillary nucleus
SAHS	sleep apnea-hypopnea syndrome	TMS	transcranial magnetic stimulation
SaO <sub>2</sub>	arterial oxygen saturation	TNF	tumor necrosis factor
SB	sleep bruxism	TPM	topiramate
SBD	sleep-related breathing disorder	TSH	thyroid-stimulating hormone
SCA	spinocerebellar ataxia	TST	total sleep time
SCD	sickle cell disease	TST	total sleep time

TTH	tension-type headache	VNS	vagus nerve stimulation
UA	upper airway	VNTR	variable number tandem repeat
UARS	upper airway resistance syndrome	VPA	valproate
UES	upper esophageal sphincter	VPSG	video-polysomnography
UPPP	uvulopalatopharyngoplasty	VRG	ventral respiratory group
VBM	voxel-based morphometry	VTa	ventral tegmental area
VC	vital capacity	W	wake
vGlut2	vesicular glutamate transporter 2	WASM	World Association of Sleep Medicine
vlPAG	ventrolateral part of the periaqueductal gray matter	WASO	wake after sleep onset
VLPO	ventrolateral preoptic nucleus	WED	Willis–Ekbom disease
		ZI	zona incerta

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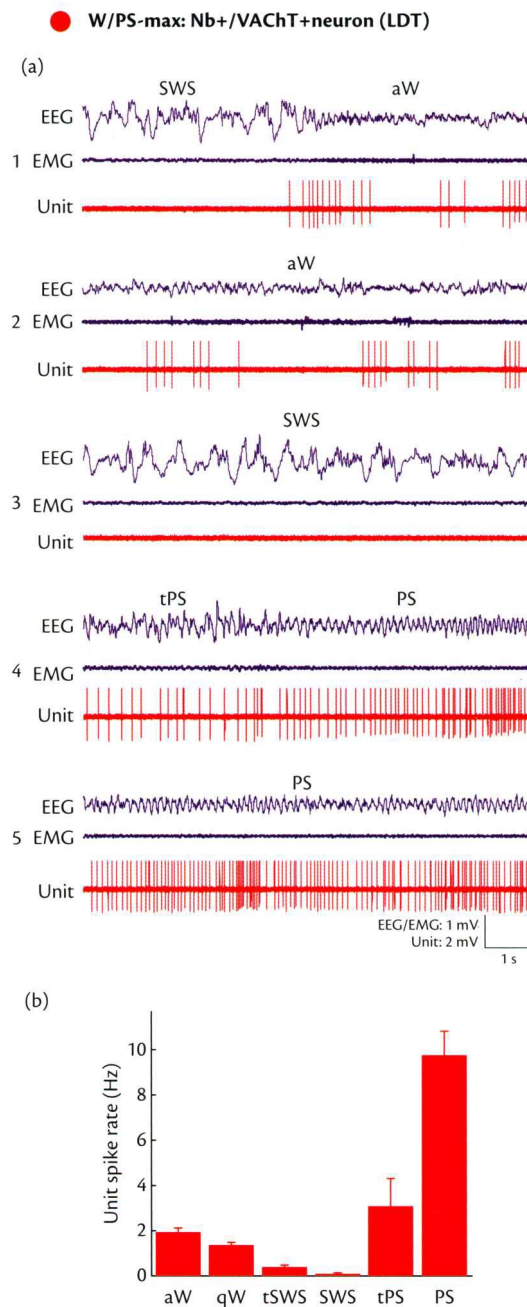
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**Fig. 4.2** Discharge of cholinergic W/PS-max active unit across sleep-wake states in rat. Data from a recorded, Neurobiotin (Nb)-labeled cell (#CBS28U03) that was identified as immunopositive for vesicular ACh transporter (VAcHT) and located in the LDT. (a) Polygraphic records from 10 s epochs or periods of the unit together with EEG (from retrosplenial cortex) and EMG activity during a transition from SWS to aW (1), aW (2), SWS (3), a transition from tPS to PS (4), and PS (5). (b) Bar graph showing mean spike rate of the unit across sleep-wake stages. Note that during W (2), the unit discharged tonically at a slow rate (1.91 Hz) with prominence of fast EEG activity, ceased firing during SWS (3) (0.06 Hz) in association with slow EEG activity (~1–4 Hz), and discharged maximally and tonically to reach its highest rates during PS (5) (9.70 Hz) in association with prominent rhythmic theta (~6–8 Hz) along with fast EEG activity. It changed its rate of discharge prior to cortical activation in the transition from SWS to aW (1) and prior to PS during tPS (4) as EEG activity progresses to theta. The unit discharge was significantly positively correlated with EEG gamma ( $r = 0.37$ ) along with theta activity ( $r = 0.93$ ). aW: active wake; qW: quiet wake; tSWS: transition to slow-wave sleep; SWS: slow-wave sleep; tPS: transition to paradoxical sleep; PS: paradoxical sleep. Reproduced from *J Neurosci*, 34(13), Boucetta S, Cisse Y, Mainville L, Morales M, Jones BE, Discharge Profiles across the Sleep-Waking Cycle of Identified Cholinergic, GABAergic, and Glutamatergic Neurons in the Pontomesencephalic Tegmentum of the Rat, pp. 4708–27, Copyright (2014), with permission from Society for Neuroscience.