Although descriptions of the syndrome date back to the seventeenth century, akathisia has long seemed an orphan within neuropsychiatry, lacking until recently the serious attention it deserves. This book reviews the diverse published material on akathisia and related disorders, including restless legs syndrome, other forms of motor restlessness, and neuroleptic-induced dysphoria, and provides a comprehensive account of these important but insufficiently researched syndromes.

A historical overview of the underlying concepts sets the scene for a detailed exposition of current knowledge. The main focus is on drug-induced akathisia and its various subtypes, each of which is discussed in terms of the author's own criteria as well as those of other investigators. Dr Sachdev examines the relationship of drug-induced akathisia to the restlessness caused by other neurological disorders and presents a new synthesis of the underlying pathophysiological mechanisms. What constitutes akathisia is an important clinical and research question, and the author provides arguments for new operational criteria for the research diagnosis of drug-induced akathisia. Strategies for the measurement of akathisia are discussed, as are treatment approaches, and a fascinating appendix contains a translation of Haskovec's original account of the syndrome.

This is the first extended review of scientific and clinical aspects of akathisia and restlessness, and also suggests directions for their future investigation. It will be much valued by psychiatrists, neurologists and other physicians seeking a better understanding of these disabling syndromes.

AKATHISIA AND RESTLESS LEGS

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PERMINDER SACHDEV

University of New South Wales
The Prince Henry Hospital

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To Jagdeep, Sonal and Nupur

Contents

Foreword

In this era of rapidly proliferating scientific articles and texts, it is often difficult to identify and assimilate those publications which are truly useful additions to our knowledge base. Perminder Sachdev's scholarly and thorough review of akathisia and restless legs provides an extremely valuable synopsis of current information on this syndrome, and in fact represents a 'coming of age' of akathisia.

Akathisia has come to be associated with neuroleptic drug treatment; however, restless legs syndrome (also referred to as Ekbom's syndrome) as well as the akathisia seen in both postencephalitic and idiopathic parkinsonism may have some important common symptoms and pathophysiological features. Therefore, it is very helpful to have all of these syndromes discussed in one text. This volume thoroughly reviews the concept of restlessness, as well as its manifestations in a variety of clinical and nonclinical contexts. It also includes a compendium of instruments and techniques for assessing akathisia and restlessness.

A detailed discussion of the definition, assessment and diagnosis of drug-induced akathisia is provided and operational criteria for use in clinical research are proposed. Although neuroleptic-induced akathisia can produce a considerable degree of subjective dysphoria, the latter may apparently also occur independently of akathisia and is generally referred to as neuroleptic-induced dysphoria. Despite the paucity of data, the author reviews current knowledge and potential research implications of such dysphoria.

The epidemiology of akathisia has not been studied extensively, and the same conceptual and methodological problems that challenge differential diagnosis of the syndrome also preclude any firm conclusions regarding its incidence and prevalence. The existing database on this issue is thoroughly reviewed and critiqued, providing an important stepping-stone for further progress in this area. As new and potentially novel or superior antipsychotic

medications are introduced, it will become increasingly important to have well-developed methods for establishing the relative risk for syndromes such as akathisia associated with different drugs.

The treatment of akathisia, systematically discussed in this volume, takes on additional significance in light of the literature on the effects of akathisia on patient compliance with drug regimes, subjective well-being and suicidal and aggressive behaviour.

The relationship between acute akathisia and syndromes of chronic movement disorders such as tardive dyskinesia is crucial, both from a public health standpoint and heuristically. In addition, the potential existence of a syndrome labeled 'tardive akathisia' is an important issue in this context. Though there is still much controversy and need for further research, Sachdev suggests that the weight of the evidence supports the notion that tardive akathisia and tardive dyskinesia are separate syndromes, albeit with considerable overlap.

Perhaps the most challenging aspect of the text is the thorough review of hypotheses and data relating to pathophysiology. As with many clinical effects of antipsychotic medications, the implications for improving our understanding of neuropharmacological mechanisms of medication effects are extremely important, as are the implications for the prevention and treatment of adverse effects.

This volume contains important discussions of a number of other relevant areas, and the sum of all the parts amounts to a prodigious compilation and synthesis of data gathered from diverse fields. It will serve as an extremely valuable resource to clinicians and researchers alike.

JOHN M. KANE, MD

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Abbreviations

AA	acute akathisia
AC	adenyl cyclase
ACh	acetylcholine
ADHD	attention-deficit hyperactivity disorder
βA	β-adrenergic
BBB	blood–brain barrier
CA	chronic akathisia
CNS	central nervous system
CSF	cerebrospinal fluid
CT	computerized tomography
DA	dopamine
5,6DHT	5,6-dihydroxytryptamine
DIA	drug-induced akathisia
DIP	drug-induced parkinsonism
DWA	diskinesias while awake
ECG	electrocardiogram
ECT	electroconvulsive therapy
EEG	electroencephalogram
EL	encephalitis lethargica
EMG	electromyogram
EPSE	extrapyramidal side-effects
GABA	γ-aminobutyric acid
Glu	glutamate
GPe	globus pallidus externa
GPi	globus pallidus interna
HC	home cage
5HT	5-hydroxytryptamine (serotonin)
5HTP	5-hydroxytryptophan
ID	iron deficiency

LT	limb-truncal
MHPG	3-methoxy-4-hydroxyphenyl glycol
MI	movement index
MLMR	mesencephalic locomotor region
MSH	melanocyte-stimulating hormone
NCV	nerve conduction velocity
NDef	neuroleptic-induced defecation
NE	norepinephrine
NIA	neuroleptic-induced akathisia
NID	neuroleptic-induced dysphoria
NIP	neuroleptic-induced parkinsonism
NM	nocturnal myoclonus
NMDA	*N*-methyl D-aspartate
NREM	non–rapid eye movement sleep
OBLF	oral–buccal–lingual–facial
OCD	obsessive-compulsive disorder
OF	open field
pCPA	*p*-chlorophenylalanine
PD	Parkinson's disease
PET	positron emission tomography
PLMS	periodic leg movements in sleep
PLMT	painful legs and moving toes
POMS	profile of mood states
PPD	postpsychotic depression
REM	rapid eye movement
RLS	restless legs syndrome
ROC	receiver operating characteristic
SCN	suprachiasmic nucleus
SMA	supplementary motor area
SN	substantia nigra
SNr	substantia nigra pars reticulata
SP	supersensitivity psychosis
SRI	serotonin-reuptake inhibitor
STN	subthalamic nucleus
TA	tardive akathisia
TCA	tricyclic antidepressant
TD	tardive dyskinesia
TDt	tardive dystonia
TDys	tardive dysmentia
VTA	ventral tegmental area
WA	withdrawal akathisia