was seen to occur in patients with both idiopathic and postencephalitic parkinsonism.[2] Nowadays, however, the most important presentation of akathisia is in patients taking neuroleptic drugs.[3]

Akathisia has two components: subjective (psychological) and objective (motor). The subjective symptoms include a feeling of tension, an inability to tolerate being still, and an urge to move; the motor component (which is believed to be secondary to the psychological symptoms) consists of restlessness and hyperactivity—shuffling and tapping of feet, rocking of the body, or, in more severe forms, inability to remain seated, standing, or lying (impatience musculaire); and continuous changing of the position of the body, pacing, or even running (tasikinesia).[4-7] The psychological symptoms and motor signs usually coexist, but in the mildest form of akathisia only the psychological component may be present.[7] The term pseudoakathisia has been used to describe a syndrome of motor restlessness without the psychological symptoms of true akathisia.[8 9]

Akathisia induced by neuroleptics may be due to reserpine, phenothiazines, thioxanthenes, and butyrophenones; more potent neuroleptics such as trifluoperazine and haloperidol are more likely to cause the syndrome than less potent ones such as chlorpromazine or thioridazine.[10] Other neuroleptic-like drugs which block central dopamine receptors such as metoclopramide[11] and amoxapine[12] may produce the syndrome. Akathisia is the most common motor side effect of treatment with neuroleptics; the overall incidence has been reported to be around 20%.[7 10] The neuronal basis of akathisia is not clear: possibly it may reflect the blockade of dopamine receptors in the frontal cortex innervated by the mesocortical dopamine pathway.[13 14]

Although akathisia may occur in isolation it is often combined with other extrapyramidal syndromes induced by neuroleptics, such as parkinsonism[7] or dyskinesia.[9 15] Akathisia may appear early or late in the course of treatment with neuroleptics. Acute akathisia usually develops within a few days of the start of treatment, is dose dependent, and disappears if the dose is reduced or the drug is stopped. It often responds to anticholinergic drugs, and if treatment is continued it commonly subsides after two to three months.[9 10] Tardive akathisia, by contrast, like tardive dyskinesia, appears after several months of continuous treatment, is not dose dependent, does not respond to anticholinergic drugs, and is made worse by stopping treatment.[8 15] Tardive akathisia is often of the "pseudoakathisia" type.[5 8 9] Another clinical variant is prolonged or persistent akathisia.[9 15] This is the continuation of the acute akathisia syndrome over several months; this syndrome usually merges with tardive dyskinesia.[9]

The differential diagnosis includes conditions simulating either the psychological or the motor components of the syndrome. The tension and inner restlessness of akathisia may be mistaken for the agitation of some psychotic and depressive states, leading the clinician to increase the dosage of the neuroleptic.[5 9] The motor restlessness may be confused with dyskinesia[5 8] and some neurological disorders affecting the legs, such as restless leg syndrome and meralgia paraesthetica.[5]

The most effective treatment of acute akathisia is reduction of dosage or withdrawal of the offending drug, or substitution of a less potent neuroleptic. Anticholinergics,[7 15] benzodiazepines,[16] β adrenoceptor antagonists,[17] clonidine,[18] and amantadine[19] have been reported to alleviate akathisia induced by neuroleptics.

The early recognition of akathisia induced by neuroleptics is of considerable clinical importance: a subjectively distressing condition,[6 20] it may lead to acts of violence,[21] suicide,[22] and to discontinuation of neuroleptic treatment by the patient.[23]

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Subcortical dementia

A characteristic slowness of response and mental processing has been recognised for many years in patients suffering from disease of cerebral subcortical structures. The response to a proposition is considerably delayed, but ultimately the response is accurate and appropriate—a simple slowing down of the thought process. Some of these patients may be found to have frontal gliomas, and their slow responses are accompanied by specific neurological signs produced by the presence of the tumour. In 1974 Albert and his colleagues used the term subcortical dementia to describe the intellectual deterioration seen in progressive supranuclear palsy,[1] and in 1975 McHugh and Folstein described a similar pattern of deterioration in patients suffering from Huntington's chorea.[2] These workers suggested that the forgetfulness and slowness of thought processes, the altered personality with specific apathy and depression, and the impaired ability to manipulate acquired knowledge constituted a specific syndrome; and they contrasted it with the dementia of Alzheimer's disease.

Further study of the subcortical dementias might possibly lead towards treatment and they give neurologists an opportunity to study the progressive memory loss associated with

dementing processes.[3] Aphasia, alexia, agnosia, and amnesia are absent in Huntington's chorea—in contrast with the dementias of Alzheimer's disease and of Jakob-Creutzfeldt disease, in which these changes are common.

The dysfunction in subcortical dementia may result from pathological changes in subcortical structures including the striatum, the thalamus, and possibly brain stem nuclei. The concept has recently been enlarged to include the dementia associated with Parkinson's disease and also the intellectual deterioration occurring in other extrapyramidal syndromes including Wilson's disease, the spinocerebellar degenerations, and idiopathic calcification of the basal ganglia.[4] Possibly, too, the dementia associated with depression may be of subcortical type,[5] and similar clinical features may be recognised in patients suffering from multiple lacunar strokes.[6]

Nevertheless, a strict division into two forms of dementia or two distinct clinical types of dementia seems difficult to accept, for all dementing processes must affect widespread areas of the brain both cortical and subcortical. The dementia of Parkinson's disease may simply represent a coincidental development of the changes of Alzheimer's disease[7-9]—a suggestion based on the similar pathological findings in the two disorders—namely, senile plaques and neurofibrillary tangles. Indeed, even the dementia of Alzheimer's disease has been suggested to be subcortical in origin, resulting from a degeneration primarily in the basal nucleus of Meynert.[10 11] Though an anatomical classification is not necessarily acceptable, the clinical distinction seems fairly clear.

The clinical syndrome of subcortical dementia consists, then, of acquired intellectual impairment with features of forgetfulness and slowing of mental processes as the primary abnormality; the intellectual deterioration is characterised by difficulty in manipulating acquired knowledge, and there are also personality and effective changes, including apathy and depression. The functions of language, calculation, and learning remain intact, and the proponents of the division insist that these features contrast sharply with the manifestations of cortical dysfunction in Alzheimer's disease and its analogues where aphasia, amnesia, and agnosia are salient features and intellectual impairment is paramount.

There is some neurochemical evidence to support the concept. Cummings and Benson described the intellectual changes of Huntington's chorea and drew attention to their similarity to the intellectual changes of Parkinson's disease.[6] They suggested that the dementia of Huntington's chorea was related to the thalamic and striatal changes rather than to cortical changes, and indeed studies of cerebral metabolism in the disorder have shown no abnormality—in contrast with the profound metabolic reduction in the caudate nuclei.

In Parkinson's disease, too, the neurochemical evidence suggests that the dementia does not simply represent coincidental Alzheimer's disease. The main neurochemical change is loss of dopamine from the nigrostriatal pathways and the ventral tegmental area, whereas in Alzheimer's disease the cholinergic system is preferentially affected and the amounts of acetylcholine related enzymes are reduced in the cerebral cortex. The administration of levodopa partially reverses the intellectual impairment in Parkinson's disease[12] but has no effect on the cognitive deficits of Alzheimer's disease.

In a more recent review Huber and Paulson included among the conditions in which the dementia has been considered subcortical Wilson's disease, traumatic encephalopathy, and multiple sclerosis.[3] They contrasted the clinical features of Alzheimer's disease with those of the subcortical dementias, emphasising the slowing of mental operations together with the progressive impairment of memory. They selected Huntington's chorea as the ideal model for studying subcortical dementias; subtle changes of memory function might be the first indications of the disease, antedating the chorea by several years and offering the possibility of experimental neuropsychological investigation. The predictable course of the disease and the absence of language or perceptual problems should, they said, allow study of the specific memory changes.

In his original description Parkinson described "the senses and the intellects being uninjured,"[13] and yet today most observers recognise that intellectual deterioration is a common associated feature. Lieberman *et al* have suggested that the form of Parkinson's disease associated with dementia is distinct from paralysis agitans itself, arising at a later age and having a shorter duration and responding less well to levodopa.[14] Huber and Paulson considered the possibility of the coincidental development of Alzheimer's disease, but from their own studies they submitted that the subcortical structures were primarily affected—and they discussed the possibility that treatment with levodopa might have been the cause of the dementia, but they concluded that the issue was not yet settled. Their main aim in reviewing the concept, they said, was to encourage researchers to study the mental processes, particularly the memory disturbances, in patients with subcortical dementia. They regarded Korsakoff's syndrome as a pure amnesic condition with no associated dysfunction of intelligence, language, or attention, and suggested that the subcortical dementias were somewhat similar. They suggested some specific neuropsychological procedures to be adopted in these studies and hoped that once the concept of subcortical dementia was established it might be possible to find pharmacological means to improve subcortical timing and activation. Unfortunately, as yet the subdivision of the cortical and subcortical dementias has led to no remarkable therapeutic advance in the treatment of either.

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