

Non-Alzheimer's Disease Dementias: Anatomic, Clinical, and Molecular Correlates

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Objective: To review the clinical and molecular features of non-Alzheimer's disease (non-AD) dementias, focusing on disorders associated with tau pathology (that is, frontotemporal lobar degeneration [FTLD], corticobasal ganglionic degeneration [CBD], and progressive supranuclear palsy [PSP]) or on disorders with synuclein pathology (that is, dementia with Lewy bodies [DLB] and multisystem atrophy [MSA]). We also discuss the pharmacologic treatment of these disorders.

Methods: We report a selective review of the literature on FTLD, CBD, PSP, DLB, and MSA.

Results: The non-AD dementias can present with a wide variety of cognitive and behavioural symptoms. Through common clinical features and shared molecular etiologies, neurodegenerative disorders previously thought to be distinct are now classified into tauopathies and synucleinopathies.

Conclusions: The unique cognitive and behavioural manifestations of the non-AD dementias can be mistaken for psychiatric disorders. Improved detection of tauopathies and synucleinopathies and their differentiation from AD is possible.

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Clinical Implications

- Better understanding and assessment of the cognitive and behavioural features of individuals suffering from dementia will improve diagnostic accuracy of the non-Alzheimer's disease (non-AD) dementias.
- Improved recognition and differentiation of dementing disorders will lead to more effective clinical management.
- Future treatment of non-AD dementias will be based increasingly upon the anatomic, molecular, and genetic pathology.

Limitations

- Only recently has attention been paid to the cognitive and behavioural symptoms of non-AD dementias.
- Given the overlapping clinical features, accurate differentiation of the tau-related disorders relies upon molecular and pathologic studies.
- Although growing, the literature on the pharmacologic treatment of neurodegeneration in tauopathies and synucleinopathies is small.

Key Words: dementia, frontotemporal dementia, tauopathy, synucleinopathy, review

The non-Alzheimer's disease (non-AD) dementias associated with tau and synuclein pathology present with profound changes in personality and behaviour, including disinhibition, delusions, hallucinations, apathy, obsessive–compulsive behaviour, hyperorality, and sleep disturbances.

These dementias have remarkable clinical overlap with schizophrenia, depression, obsessive–compulsive disorder, and personality disorder, and they are often initially misdiagnosed as psychiatric disorders. However, in contrast to primary psychiatric disorders, the anatomic and neurochemical basis of the

Table 1 Disorders associated with tau pathology

Alzheimer's disease
Amyotrophic lateral sclerosis-parkinsonism-dementia complex
Corticobasal degeneration
Creutzfeldt-Jakob disease
Down syndrome
Frontotemporal dementia with parkinsonism complex linked to chromosome 17
Pantothenate kinase-associated neurodegeneration (formerly Hallervorden-Spatz disease)
Pick disease
Progressive supranuclear palsy

tauopathies and synucleinopathies is known. Studies of frontotemporal lobar degeneration (FTLD) offer powerful insights into the anatomic underpinnings of personality, emotional blunting, empathy, and apathy, while research into dementia with Lewy bodies (DLB) has generated compelling new ideas about the anatomic and neurochemical basis for visual hallucinations and delusional misidentification.

The tauopathies and synucleinopathies have unique clinical, anatomical, neurochemical, and pathological profiles, and their differential diagnosis requires an understanding of these features. In this article, we describe the clinical syndromes, genetics, and molecular biology associated with 3 tauopathies—FTLD, corticobasal ganglionic degeneration (CBD), and progressive supranuclear palsy (PSP); and 2 synucleinopathies—DLB and multisystem atrophy (MSA). We also consider treatment approaches to these disorders.

Molecular–Clinical Correlations

The non-AD dementias are associated with abnormal protein aggregation within specific anatomic and chemical systems, and this neuronal specificity helps with differential diagnosis. Also, cognitive and behavioural decline frequently parallel the spread of pathological changes. The tauopathies often begin in the frontal or anterior temporal cortex, which dictates the distinctive psychiatric, linguistic, and cognitive syndromes associated with them. Synucleinopathies often begin in the brain stem dopaminergic neurons involved with sleep—in particular, the locus coeruleus—and the presence of rapid eye movement (REM) sleep disorder in the preclinical or prodromal stages of the disease suggests a diagnosis of DLB or MSA. With many of the dementing disorders, specific brain regions are spared from the underlying neurodegenerative pathology. Therefore, cognitive deficits and strengths in the early stages of a person's dementia mirror the

underlying anatomic localization and suggest the pathologic process. In the following section, we review the molecular biology of tau and alpha-synuclein and their association with neurodegenerative disease (Tables 1 and 2).

Tauopathies

Tau is a low molecular weight, microtubule-associated protein found in axons within the central and peripheral nervous system, but negligibly in oligodendrocytes and astrocytes or nonneuronal tissue. The tau protein is encoded by a single gene on chromosome 17q21. Alternative splicing of the messenger ribonucleic acid (mRNA) creates 3R and 4R, the major isoforms of the tau protein, both of which are equally distributed within normal neurons. A series of polymorphisms in the tau gene further define tau into H1 and H0 haplotypes (1). The association of the tau mutations, isoforms, and haplotypes with specific diseases has transformed the classification of the neurodegenerative disorders.

The assembly and stabilization of microtubules is a major function of tau; thus, it facilitates axonal transport and helps to build the neuronal cytoskeleton. Because tau is fundamental to these vital functions within neurons, it is not surprising that mutations in this protein lead to neurodegeneration. Abnormally increased phosphorylation of the tau protein is hypothesized to release tau from microtubules, thereby reducing its solubility. Insoluble tau then creates pathologic aggregates, contributing to neuronal degeneration.

Lynch and others (2) and Wilhelmson and others (3) noted a link to chromosome 17 (the location for tau) in a family with cognitive decline and parkinsonism associated with profound personality and behavioural changes. Subsequently, mutations in the tau gene were found in multiple frontotemporal dementia (FTD) families (4). Further genetic and pathological studies have implicated tau in CBD and PSP (5,6). The increased frequency of a specific haplotype of a tau isoform has been found in CBD and PSP, identifying the fact that these disorders with heterogeneous and shared clinical features share a genetic etiology (7).

Frontotemporal Lobar Degeneration

FTLD encompasses 3 syndromes: frontotemporal dementia (FTD), semantic dementia (SD), and primary progressive aphasia (PPA), all associated with focal degeneration in the frontal or anterior temporal lobes. Consensus diagnostic criteria define the core and supportive features of each disorder (8). In FTD, the onset and course of symptoms are gradual and progressive. AD and FTD have similar prevalence in the population aged 45 to 65 years. Thus, FTD is considered an early-onset dementia, with onset typically before age 65 years (9).

Unlike other neurodegenerative disorders, FTD is characterized by early and prominent behavioural disturbances affecting personal conduct and interpersonal interactions. Both disinhibited and socially inappropriate behaviour develop as insight and social skills decline. Antisocial behaviours, including crimes such as shoplifting, embezzlement, or indecent exposure can be the presenting features of the illness and are seen in many patients as the disease progresses. More subtle changes in social pragmatics are extremely common, and patients' interaction with others may become overfriendly and exhibit loss of personal boundaries. They may initiate detailed and personal conversations with complete strangers. Repetitive and stereotyped behaviour may appear as odd mannerisms or compulsions such as hoarding, collecting, or counting rituals. Similarly, mental rigidity can lead to obsessive adherence to fixed routines. Some individuals present with apathy or emotional blunting, often misdiagnosed as depression. Alterations in well-established political or religious ideologies occur in a minority of patients. Other supportive features of FTD are hyperorality and dietary changes, often manifested as gorging and gluttony. Individuals may also severely restrict their food choices or obsessively crave certain food types, especially carbohydrates or sweets.

Despite the profound behavioural changes, memory is relatively spared. As the disease progresses, individuals may perform poorly on formal tests of memory because of impulsive answers or intrusions from impaired monitoring of their own performance. The recall of stimuli is affected by deficits in frontally mediated retrieval, but cues and choices improve recall. In contrast, AD impairs encoding and formation of memory, thus resulting in poor recall, even with assistance. Paralleling their perseverative behaviour, individuals may exhibit press of speech, stereotyped language with repetition of certain words or phrases, or echolalia. In the apathetic forms of FTD, the person's verbal output becomes sparse and lacks spontaneity, leading to complete mutism. Spatial perception and construction are preserved throughout the disease course. The cognitive deficits in FTD are found on neuropsychological tests of frontal lobe function (that is, tests of abstraction, set-shifting, sequencing, and phonemic fluency. Imaging tends to show bilateral frontotemporal atrophy).

FTD associated with both familial and sporadic amyotrophic lateral sclerosis (ALS) has been reported (10–13). In many cases, the personality and behavioural changes of FTD preceded the onset of motor weakness in ALS by years, but in others, ALS preceded FTD (14).

The initial symptoms with PPA and SD usually involve speech or language, and the frontal lobe deficits prominent in FTD are less extensive. The 2 language subtypes of FTD are also characterized by relatively preserved memory and visuoconstructive ability.

Individuals with PPA develop a nonfluent aphasia with prominent word-finding difficulty and altered speech output (15). Consensus criteria for PPA define the syndrome as nonfluent speech with agrammatism, phonemic paraphasias, or anomia (8). While speech is initially fluent, word-finding and articulatory deficits lead to decreased verbal output. Behaviour is usually relatively preserved in PPA. Imaging shows atrophy in the left frontal and insular regions.

SD is characterized by loss of semantic knowledge and naming. Individuals with SD may report impaired naming and recognition of previously familiar objects or faces. They may be able to describe the function or physical characteristics of an object. Semantic paraphasias appear in association with the loss of word meanings. As more semantic information is lost, speech output becomes vague and devoid of content, with increased usage of words like "it" or "thing." Fluency remains intact, but the loss of word meaning results in impaired verbal and reading comprehension. In SD, the ability to spell orthographically irregular words declines. For example, the word "yacht" may be spelled or written as "yat." A similar supportive feature is surface dyslexia, where, for example, "gnat" is read to sound like "gunat."

Impaired personal and social conduct is also seen in SD but differs slightly from its manifestation in FTD. Repetitive behaviours with intense compulsions are common. Food fads and selective food preferences distinguish SD from the hyperorality in FTD (16). A focus on eating a single food or a series of food items is common. Individuals with SD also have impaired emotion processing, including impaired expression and comprehension of emotions (16,17). Diminished empathy for others and emotional coldness characterize the right temporal subtype of SD. Some affected individuals can exhibit irritability, mental rigidity, and eccentric clothing choice (18). Imaging shows often-asymmetric bilateral temporal and amygdala atrophy.

The clinical symptoms and cognitive deficits in the FTD subtypes reflect the distribution of focal frontal or temporal lobe degeneration and the laterality of disease. Impaired social judgement and interaction were found to be common in FTD with predominant right frontal damage (19). The nonfluent speech in PPA results from left hemisphere involvement, particularly the posterior frontal and insular region. Selective temporal lobe atrophy, often more left-sided, leads to the language deficits of SD. Behavioural changes in SD likely reflect damage to the amygdala, anterior temporal, and posterior orbitofrontal, especially if right-sided. In contrast, patients with left temporal damage tend to have more socially appropriate behaviour (18).

Table 2 Disorders associated with synuclein pathology

Alzheimer's disease (familial)
Amyotrophic lateral sclerosis
Dementia with Lewy bodies
Down syndrome
Multiple system atrophy
Pantothenate kinase-associated neurodegeneration (formerly Hallervorden-Spatz disease)
Parkinson's disease (sporadic and familial)
Pick disease

Table 3 Categories of tau pathology and clinical diagnoses

Inclusion type	Insoluble tau form	Most likely diagnoses
Tau-positive	3R	<ul style="list-style-type: none"> • Pick disease • FTDP-17
Tau-positive	4R	<ul style="list-style-type: none"> • CBD • PSP • FTDP-17
Tau-positive	3R and 4R	<ul style="list-style-type: none"> • Neurofibrillary tangle dementia • FTDP-17
Tau-negative Ubiquitin-negative	Undetectable	<ul style="list-style-type: none"> • DLDH
Tau-negative Ubiquitin-positive	Undetectable	<ul style="list-style-type: none"> • FTD with MND • FTD with MND-type inclusion but without MND

CBD = corticobasal ganglionic degeneration; DLDH = Dementia lacking distinctive histopathology; FTDP = frontotemporal dementia and parkinsonism ; MND = motor neuron disease PSP = progressive supranuclear palsy

The neuropathology seen with FTD clinical presentations is varied, but many exhibit tau or ubiquitin inclusions, while others show bland histology (Table 3; 20). However, AD, Pick disease, CBD, and dementia lacking distinctive histopathology have been found in some instances (21,22).

Corticobasal Degeneration

The clinical features of CBD are attributable to asymmetric focal cortical and basal ganglionic degeneration. Initial case reports described motor abnormalities, with relative sparing of cognitive function (23). Subsequent cases demonstrated "generalized intellectual impairment" (24). Owing to these early reports, CBD has traditionally been viewed as a

movement disorder with asymmetric rigidity, dystonia, and apraxia. Other motor symptoms include alien limb phenomenon and myoclonus. Individuals with an alien limb may describe a hand, and less frequently a foot, that moves involuntarily. The alien hand will grab and grope nearby objects or, in rare instances, resist the action of the normal other hand. Cortical sensory loss involving the primary sensory modalities or higher functions (astereognosis) appears.

Subsequent reports have emphasized the cognitive and emotional deficits in CBD (25–27). Dementia was the most common presenting symptom in one study of pathologically confirmed CBD. However, two-thirds of the patients were diagnosed with dementing disorders other than CBD (26). On neuropsychological measures, impairment in attention and executive function was more severe than in AD (25). Likely reflecting the frontal dysfunction of CBD, memory retrieval was improved with cues. Nearly one-half of individuals with CBD had language deficits, with anomia and nonfluent aphasia being most prominent (27). The cognitive symptoms of CBD overlap those found in FTD and PPA (28). Depression is extremely common with CBD. Growing awareness of the similarities between CBD and PPA has led to recent reassessment of the clinical and pathological definitions of CBD.

The neuropathological findings in CBD parallel the heterogeneous clinical features. Early pathological descriptions of CBD reported frontoparietal atrophy, with inclusions in the substantia nigra similar to those in Pick disease and globose neurofibrillary tangles also seen in PSP (24). Several reports have found a wide range of neuropathology for clinically diagnosed CBD. AD, Pick disease, PSP, Jakob-Creutzfeldt disease, and DLB pathology have been reported (29,30). Recent criteria for CBD included achromatic cortical neurons, as well as tau-positive neuronal inclusions, coiled bodies, astrocytic plaques, and thread-like lesions (31). However, the tau-positive pathology alone was insufficient to distinguish CBD from FTDP-17. Clinical information and molecular tau typing was recommended (31). The terms corticobasal degeneration syndrome and corticobasal syndrome have been used to emphasize the clinical and pathological heterogeneity of CBD (28,32).

Progressive Supranuclear Palsy

PSP represents a neurodegenerative disorder with tau pathology similar to CBD and FTD. A core feature of PSP is vertical supranuclear gaze palsy manifested as impaired voluntary ocular pursuits and saccades but intact reflexive eye movements. Another major symptom is postural instability leading to falls. Axial rigidity is more prominent than appendicular rigidity. Increased axial tone results in an upright, occasionally overly erect, neck and body posture. Diagnostic criteria use signs and symptoms of CBD and FTD as exclusionary

features (33). However, the neuropsychological profile in PSP shows executive dysfunction, memory impairments, and motor-planning deficits similar to those found in CBD (25).

In addition to the similar cognitive deficits, commonalities between PSP, CBD, and FTD are found at the molecular and genetic levels. The pathological hallmark of PSP is intraneuronal globose neurofibrillary tangles that are immunoreactive for tau (34). The predominant tau isoform in PSP is 4R tau, also found in CBD and FTD (4,35,36). Further evidence of the overlap between PSP and CBD has come from association of the H1 tau haplotype with both disorders, which reinforces their shared genetic feature (7,37).

Synucleinopathies

The synucleins are a family of intracellular proteins that arise from 3 distinct genes. Synuclein proteins range in size from 113 to 143 amino acids and are abundant in neural tissue. Most relevant to neurodegenerative disorders is alpha-synuclein, a 14 kDa protein expressed in both neuronal and nonneuronal cell types, including dopaminergic and noradrenergic neurons, endothelial cells, and platelets (38). Although not a synaptic vesicle protein, alpha-synuclein plays a role in membrane trafficking and cytoskeletal organization in the presynaptic terminal; it also plays a role in the physiological regulation of synaptic enzymes, transporters, and neurotransmitter vesicles (39–41). Mouse models lacking alpha-synuclein show a reduced dopamine level in the striatum and a reduced reserve pool of synaptic vesicles in the hippocampus. Phenotypically, the mice show normal lifespan and behaviour but axonal damage of motor neurons and denervation of neuromuscular junctions (42,43).

An association between alpha-synuclein and neurodegenerative syndromes was first noted in families with autosomal dominant Parkinson's disease (PD) who also had point mutations in the alpha-synuclein gene (44). Ensuing studies revealed that abnormal alpha-synuclein filaments are the main component of Lewy bodies seen in PD and DLB, as well as in the glial cytoplasmic inclusions of multiple system atrophy (MSA) (45,46). The filaments bind to beta-amyloid peptide and facilitate its aggregation *in vitro*, suggesting that these alpha-synuclein fragments may facilitate plaque formation and contribute to neurodegeneration in AD.

Studies of alpha-synuclein and the associated disorders have so far revealed that it has an important correlative, though not causative, role in the development of neurodegenerative diseases. PD, DLB, and MSA are linked by this common protein aggregate and show abnormal alpha-synuclein and Lewy body inclusions in the similar brain regions, yet each has its unique clinical manifestations.

Dementia With Lewy bodies

DLB is characterized by progressive loss of cognitive function. Its features include fluctuating levels of cognition, visual hallucinations, and parkinsonism (47). Disease progression usually occurs over years, and it can be more rapid than in AD. Fluctuating cognition often confuses the diagnosis of DLB, as the person can oscillate between near-normal levels and severe confusion over a period of seconds to weeks (48). Individuals with DLB are also very sensitive to metabolic fluctuations and thus often present with delirium. The cognitive decline associated with DLB can precede the onset of parkinsonian symptoms and is associated with prominent impairment in visuospatial and executive function. Visuospatial deficits can manifest clinically as a loss of the ability to negotiate familiar surroundings. Formal neuropsychological testing shows impaired executive function and working memory (49). Individuals are slow to perform tasks of set-shifting and spatial working memory. In contrast to AD, short-term memory is relatively intact in DLB.

Behavioural symptoms are more frequent and occur earlier in DLB, compared with AD (50). Recurrent, well-formed, detailed visual hallucinations are a core feature of DLB (47); one study found delusions in 27.8% of cases (51). Delusional misidentification is surprisingly common, and patients often complain that their spouse or child has been replaced by an impostor (Capgras syndrome). The selective degeneration of the amygdala, a brain region involved with identifying familiar faces, appears to be the anatomic substrate of this syndrome. The delusions and visual hallucinations seen in DLB have been associated with upregulation of cholinergic muscarinic receptors caused by decreased cholinergic levels (52).

Also, when associated with dementia or parkinsonism, REM sleep behaviour disorder (RBD) reliably predicts an underlying synucleinopathy (53). RBD presents clinically as acting out of dreams during REM sleep, with the individual punching, flailing arms, or kicking legs. Paralleling the comorbidities of other dementias, apathy, anxiety, and depression are common in DLB (54).

The pathological characteristics of DLB explain its psychiatric and cognitive features. The characteristic fluctuations in cognition have been linked to changes in high-affinity nicotinic receptor binding in the temporal cortex of DLB patients (55). These cholinergic changes occur early in the course of DLB pathology and may account for the early progression of DLB dementia, as well as for the wide fluctuations in cognitive performance. Decreased frontal and temporal volumes on imaging may also account for the impairments seen on executive functioning tasks (56).

In addition to decreased cholinergic levels and function, dopamine transporters and the amount of striatal dopamine are diminished in DLB. The locus coeruleus demonstrates

decreased neuronal counts, reduced norepinephrine levels, and increased numbers of norepinephrine receptor sites (57,58).

Multiple System Atrophy

The term "multiple system atrophy" (MSA) was first proposed by Graham and Oppenheimer when they suggested that the presentations of olivopontocerebellar atrophy (OPCA), idiopathic orthostatic hypotension, Shy-Drager syndrome, and striatonigral degeneration were "the expression of a single neuronal atrophy syndrome that occurred in a variety of overlapping combinations" (59). MSA is characterized by sporadic onset of parkinsonism, cerebellar signs, pyramidal tract dysfunction, and autonomic insufficiency in varying combinations. Current terminology of the MSA subtypes is based upon the major features present, either cerebellar signs (MSA-C) or parkinsonism (MSA-P). Parkinsonian features can include akinesia with rigidity, postural instability, hypokinetic speech and tremor. Cerebellar signs include nystagmus and dysarthria, as well as gait and limb ataxia. Pyramidal features include extensor plantar responses and hyperreflexia. Autonomic dysfunction includes orthostatic hypotension, bladder and rectal atony, loss of sweating, urinary and rectal incontinence, and impotence in men.

MSA is commonly associated with sleep disorders, including RBD, which occurs in approximately one-half of patients with MSA-related sleep disorders (53,60). In contrast to DLB, psychiatric symptoms are not considered a major feature of MSA, with the possible exception of depression (61). One study demonstrated emotional blunting in patients with striatonigral type MSA (62).

The neuropsychological features of MSA include deficits in learning, recognition memory, and verbal fluency (63). Frontal lobe dysfunction has been demonstrated on tests of verbal fluency, spatial working memory, attentional set-shifting, and planning (64,65). Other neuropsychological impairments associated with MSA include weakness on measures of immediate memory and learning, as well as in retrieval and recognition on a verbal list-learning task (63). Impaired psychomotor speed is also demonstrated in MSA (63).

Neuropathological changes related to MSA include neuronal loss, gliosis, and intracellular cytoplasmic inclusions throughout the basal ganglia, brain stem, cerebellum, and spinal cord (66). The diffuse nature of the inclusions and neuronal loss explains the variety of symptoms seen in MSA and the degree of variability of systems affected.

Treatment

Improved understanding of the cellular and chemical changes occurring in the tauopathies and synucleinopathies has led to novel, yet rational, approaches to pharmacologic treatment. Unlike the cholinergic deficit in AD, atrophy of the pathways between frontal cortex and subcortical structures interrupts serotonergic circuits; this provides the rationale for using selective serotonin reuptake inhibitors to control the behavioural disturbances in FTD. An uncontrolled, unblinded study showed that fluoxetine, sertraline, or paroxetine improved disinhibition, depression, carbohydrate craving, and

compulsions (67). In another open-label, uncontrolled study of 16 individuals with FTD, paroxetine reduced behavioural symptoms and caregiver stress (68). There was also improvement in abstraction with proverb interpretations.

In 2 recent studies, the monoamine oxidase inhibitors selegiline and moclobemide were also used to target the serotonergic deficit in FTD (69,70). The Neuropsychiatric Inventory (71) scores and number of errors on the Stroop Test (72) decreased with selegiline (69). Depression, irritability, mental rigidity, and motor and speech perseverations improved with moclobemide (70).

The cholinergic deficits in DLB provided the rationale for using cholinesterase inhibitors. In early uncontrolled studies, donepezil improved general cognition (73,74). The frequency of, and agitation related to, visual hallucinations also improved with donepezil (73). Similarly, following treatment with rivastigmine, apathy, delusions, agitation, and hallucinations decreased (75). A randomized, double-blind, placebo-controlled study also found that behavioural symptoms responded to rivastigmine and that speed on attention tests improved (76).

The cholinesterase inhibitors have mixed effects on the parkinsonian features of DLB. In an early study, one-third of individuals had worsened parkinsonism with donepezil. The increased parkinsonian signs improved with levodopa-carbidopa therapy (73). Studies of rivastigmine showed both no change and significant improvement (75,76). In conjunction with the dopaminergic deficits, the variable response of motor symptoms justifies combining cholinesterase inhibitors and dopaminergic agents, such as levodopa-carbidopa, to treat the psychiatric and motor symptoms of DLB.

Summary

Focal degeneration in dementing disorders can lead to atypical clinical symptoms and cognitive deficits that may not be recognized as degenerative in origin. The late-life onset of such behaviour as altered eating habits, social disinhibition, and obsessions-compulsions may reflect atrophy of selective brain regions. Further, neurodegenerative dementias may present with cognitive deficits other than impaired memory. The anatomic underpinnings of cognition and behaviour are particularly evident in FTD and SD.

The growing body of literature on the neuropsychology and genetics of non-AD dementias has led to greater awareness of the clinical and molecular overlap among the tauopathies and synucleinopathies. Recent advances in the treatment of FTD and DLB have focused on anatomy and neurotransmitter alterations and serve as models for future development of therapy for the non-AD dementias.

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Résumé : Les démences de type non-Alzheimer : corrélations anatomiques, cliniques et moléculaires

Objectif : Étudier les caractéristiques cliniques et moléculaires des démences de type non-Alzheimer, en mettant l'accent sur les troubles associés à la pathologie tau (c'est-à-dire, la dégénérescence lobaire frontotemporale [DLFT], la dégénérescence ganglionnaire corticobasale [DGC], et la paralysie supranucléaire progressive [PSP]), ou sur les troubles ayant une synucleopathie (c'est-à-dire, la démence à corps de Lewy [DCL] et les atrophies multisystématisées [AMS]). Nous discutons également du traitement pharmacologique de ces troubles.

Méthodes : Nous faisons rapport sur une étude sélective de la documentation sur la DLFT, la DGC, la PSP, la DCL et les AMS.

Résultats : Les démences de type non-Alzheimer peuvent présenter une grande variété de symptômes cognitifs et comportementaux. À l'aide des caractéristiques cliniques communes et des étiologies moléculaires partagées, les maladies neurodégénératives que l'on croyait distinctes auparavant sont désormais classées comme tauopathies ou comme synucleopathies.

Conclusions : Les manifestations cognitives et comportementales uniques des démences de type non-Alzheimer peuvent être confondues avec d'autres troubles psychiatriques. Une meilleure détection des tauopathies et des synucleopathies ainsi que de leur différenciation de la maladie d'Alzheimer est possible.