The AT(N) classification system for describing biological changes in Alzheimer's disease

ALZHEIMER'S DISEASE (AD) IS A PROGRESSIVE NEURODEGENERATIVE DISEASE AND THE MOST COMMON CAUSE OF DEMENTIA

CURRENT DIAGNOSTIC APPROACH

AD is diagnosed by assessing **cognitive & behavioral symptoms** (e.g. MMSE / MoCA) and rule out other causes of dementia

LIMITATIONS

Symptoms may not appear **early in AD**, because there is a **delay** between **biological changes and clinical onset**, resulting in late diagnosis

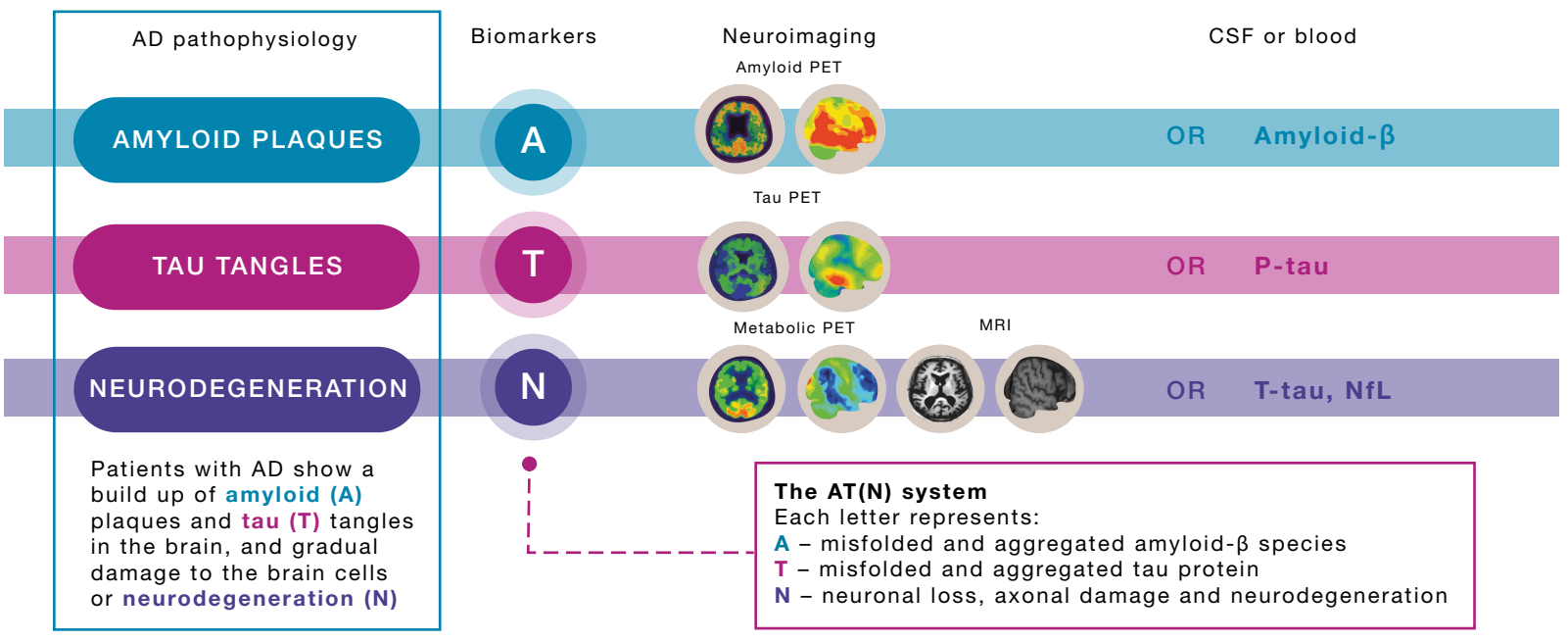
NEW DIAGNOSTIC APPROACH NEEDED

The AT(N) classification system was proposed to increase diagnostic accuracy and early diagnosis

THE AT(N) CLASSIFICATION SYSTEM

was designed to overcome the conceptual limitations of conventional diagnostic classifications that are based on clinical symptoms

AT(N) BIOMARKERS (OBJECTIVE MEASURES OF BODY PROCESSES, CONDITION OR DISEASES)



THE EIGHT AT(N) PROFILES

(Based on NIA-AA Research Classification 2018)

Profile	A	T	N	Biomarker category
A- T- (N)-				Normal biomarkers
A+ T- (N)-	✓			AD pathologic change
A+ T+ (N)-	✓	✓		AD
A+ T+ (N)+	✓	✓	✓	AD
A+ T- (N)+	✓		✓	AD and concomitant suspected non-AD pathological change
A- T+ (N)-		✓		Non-AD pathologic change
A- T- (N)+			✓	Non-AD pathologic change
A- T+ (N)+		✓	✓	Non-AD pathologic change

AD CONTINUUM

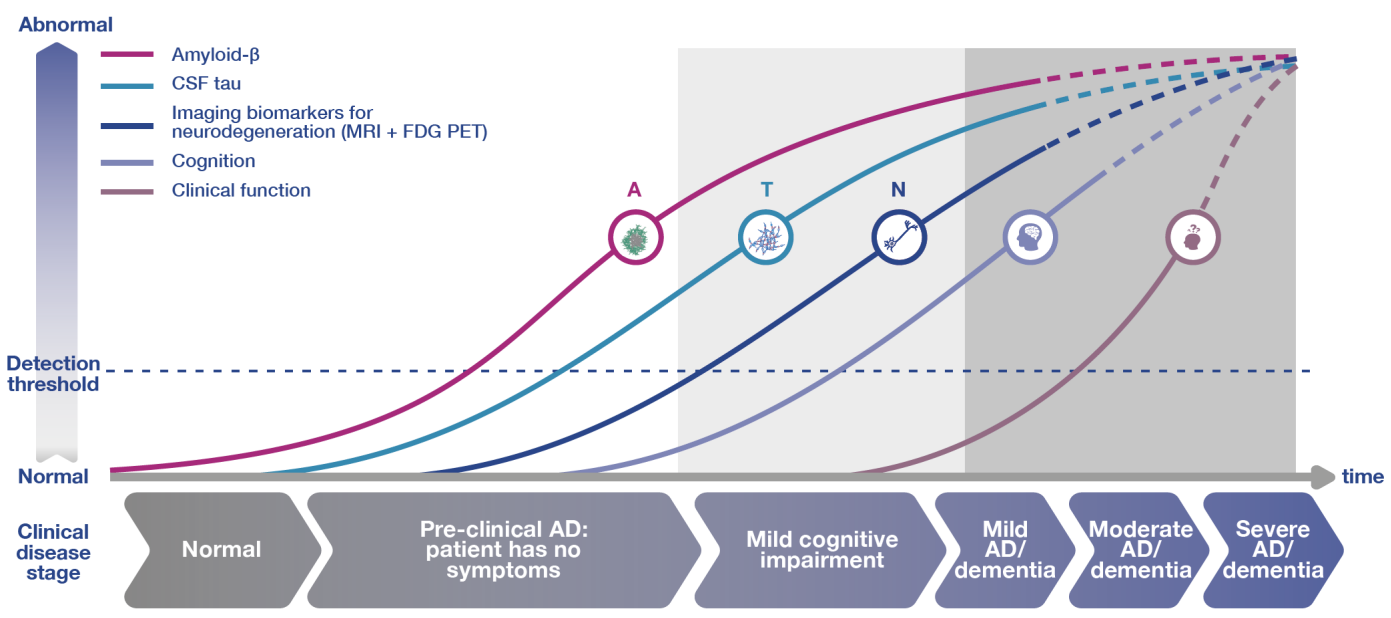
As AD progresses with time, AT(N) status can change from negative (-) to positive (+)

T+
A+ combined with a T+ status is a hallmark of AD

N+
N+ is not specific to AD, therefore, it is represented in parentheses

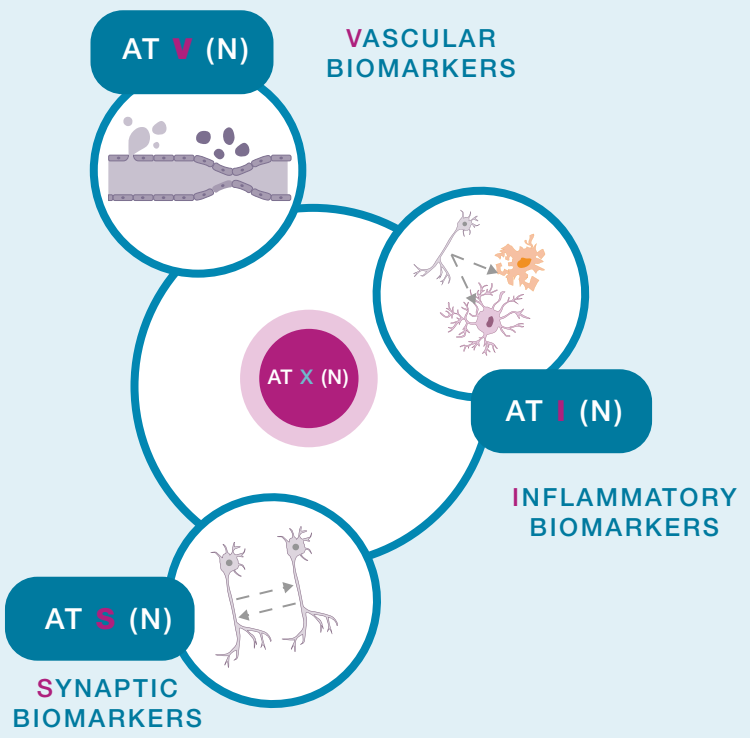
TEMPORAL EVOLUTION OF AT(N)

Abnormal changes in biomarkers are detected years before the onset of clinical symptoms. These changes may occur at different times and follow distinct time trajectories across the AD continuum



Adapted from Jack CR Jr et al. Lancet Neurol. 2013;12(2):207-16

THE AT(N) SYSTEM COULD EVOLVE INTO THE ATX(N) SYSTEM, WHERE "X" REPRESENTS AN ARRAY OF BIOMARKERS THAT REFLECT OTHER BIOLOGICAL CHANGES IN AD



KEY TAKEAWAYS

The AT(N) system:

- Remains a **research framework**, and more work is required to integrate it into clinical practice
- Is designed to increase diagnostic confidence.
- Could evolve into the **ATX(N)** system where "X" represents other biomarkers that contribute to AD pathophysiology.
- Is an ever-changing classification system
- In the **future**, the ATX(N) system may help provide more accurate diagnosis and timely treatment of AD

REFERENCES:
1. Hampel H, Cummings J, Blennow K, et al. Developing the ATX(N) classification for use across the Alzheimer disease continuum. Nat Rev Neurol. 2021;17(9):580-589.
2. Hampel H, Elhage A, Cummings J, et al. The AT(N) system for describing biological changes in Alzheimer's disease: a plain language summary. Neurodegener Dis Manag. 2022;12(5):231-239.
3. Jack CR Jr, Bennett DA, Blennow K, et al. NIA-AA Research Framework: toward a biological definition of Alzheimer's disease. Alzheimer's Dement. 2018;14(4):535-562.

ABBREVIATIONS:
AD, Alzheimer's disease; A, amyloid; Amyloid-β, amyloid-beta; CSF, Cerebrospinal fluid; MMSE, Mini-Mental State Exam; MoCA, Montreal Cognitive Assessment; MRI, magnetic resonance imaging; N, neurodegeneration; NfL, neurofilament light chain; NIA-AA, National Institute on Aging and Alzheimer's Association; P-Tau, phosphorylated tau; PET, positron emission tomography; T, tau; T-tau, total tau.

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More info? Scan here for references