

The Symptomatic Non-alzheimer Cognitive Composite (SNACC): An objective, etiology-agnostic tool for monitoring cognitive change

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Introduction

Establishing an etiologic diagnosis in patients without dementia who lack Alzheimer’s disease (AD) biology is challenging and often requires years of longitudinal follow-up. An etiology-agnostic cognitive composite combined with a neurodegeneration biomarker such as plasma neurofilament light (NfL) may improve detection of individuals at higher risk of cognitive and functional deterioration. We evaluated the diagnostic and prognostic value of the Symptomatic Non-Alzheimer Cognitive Composite (SNACC), alone and combined with plasma NfL, in patients without dementia and negative AD biomarkers.

Results

Final diagnoses included Frontotemporal Lobar Degeneration (FTLD; n=89), Lewy Body disease (LBD; n=109), non-neurodegenerative conditions (No-ND; n=262), other neurodegenerative diagnoses (n=12), and uncertain etiology (n=93). At baseline, FTLD showed the highest plasma NfL levels and the lowest SNACC scores, followed by LBD, whereas No-ND showed the lowest NfL levels and the highest SNACC scores.

Characteristic	Overall (N=565)	FTLD-MND (N=89)	LBD (N=109)	No ND (N=262)	Other (ND) (N=12)	Uncertain (N=93)	p-value
Age (years)	69 (9)	71 (8)	73 (6)	67 (9)	73 (10)	70 (9)	<0.001
Sex							0.034
Man	286 (51%)	48 (54%)	64 (59%)	115 (44%)	5 (42%)	54 (58%)	
Woman	279 (49%)	41 (46%)	45 (41%)	147 (56%)	7 (58%)	39 (42%)	
Education (years)	11.7 (5.0)	12.7 (4.7)	11.1 (5.2)	12.2 (4.9)	11.6 (3.6)	10.3 (4.9)	0.002
Baseline MMSE	26.96 (2.33)	26.72 (2.35)	26.48 (2.40)	27.34 (2.14)	26.75 (3.47)	26.72 (2.47)	0.009
Plasma NfL (Z-score)	-0.45 (1.51)	0.66 (1.57)	-0.23 (1.48)	-0.89 (1.36)	-0.64 (0.94)	-0.50 (1.37)	<0.001
Stage							<0.001
GDS FAST 2	72 (13%)	2 (2.2%)	10 (9.2%)	51 (19%)	0 (0%)	9 (9.7%)	
GDS FAST 3	493 (87%)	87 (98%)	99 (91%)	211 (81%)	12 (100%)	84 (90%)	
SNACC Composite	-2.31 (2.89)	-3.11 (2.58)	-2.56 (2.80)	-1.70 (2.88)	-3.27 (3.61)	-2.84 (2.91)	<0.001
Memory Composite	-1.23 (1.11)	-1.42 (1.14)	-1.27 (1.03)	-1.06 (1.07)	-1.82 (1.12)	-1.40 (1.22)	0.002
Executive Composite	-0.98 (0.79)	-1.29 (0.88)	-0.98 (0.69)	-0.86 (0.77)	-1.06 (0.74)	-1.01 (0.80)	<0.001
Language Composite	-0.54 (0.78)	-0.76 (0.70)	-0.54 (0.74)	-0.42 (0.76)	-0.98 (0.98)	-0.62 (0.85)	<0.001
Visuospatial Composite	0.45 (1.44)	0.37 (1.38)	0.23 (1.47)	0.65 (1.42)	0.59 (1.82)	0.20 (1.43)	0.058

