

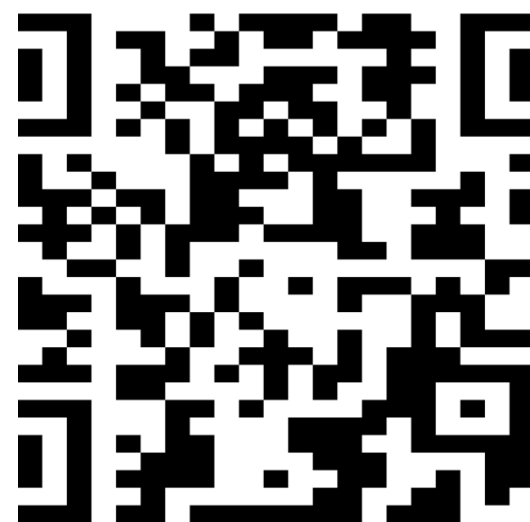
The Timing Of Psychotic Symptoms Onset In Mild Behavioural Impairment And Their Impact On Cognitive Function In Older Adults

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Psychotic symptoms in MBI are preceded by subtle executive-attentional deficits and become associated with broader cognitive impairment once clinically manifest. Individuals who later develop psychotic symptoms already show subtle cognitive deficits before symptom onset. Self-rated MBI appears more sensitive than proxy-rated assessments in identifying early cognitive changes associated with psychotic symptoms.

INTRODUCTION		RESULTS		CONCLUSIONS																																																																																				
Mild Behavioural Impairment (MBI) is a late-life syndrome characterized by emergent changes in behaviour and is associated with increased dementia risk¹. Psychotic symptoms are the least common MBI domain but are associated with faster progression to dementia^{2,3}. However, it remains unclear whether cognitive alterations associated with psychotic symptoms are already present before symptom onset in later life. We aim to investigate the relationship between psychotic symptoms and cognition in cognitively unimpaired older adults and whether cognitive differences are detectable before the emergence of psychotic symptoms in both self-rated and proxy-rated MBI assessments.		 N (self-rated) NS: 9708 IP: 610 PB: 305 N (proxy-rated) NS: 5335 IP: 405 PB: 309 PROTECT Choort Study SELF-RATED MBI – COGNITIVE PERFORMANCE <i>Multivariable linear regression (adjusted for age, sex, education)</i> <table><tr><th rowspan="2">Cognitive domain</th><th rowspan="2">Measure</th><th colspan="2">Incident psychosis (n = 610)</th><th colspan="2">Baseline psychosis (n = 305)</th></tr><tr><th>Estimate (β)</th><th>p-value</th><th>Estimate (β)</th><th>p-value</th></tr><tr><td rowspan="2"> Attention</td><td>Vigilance accuracy</td><td>↓ − 0.082</td><td>< .001</td><td>↓ − 0.096</td><td>< .001</td></tr><tr><td>Vigilance reaction time</td><td>↓ 0.111</td><td>.003</td><td>↓ 0.163</td><td>.002</td></tr><tr><td> Verbal memory</td><td>Verbal memory (immediate recall)</td><td>↓ 0.038</td><td>.242</td><td>↓ 0.153</td><td>.001</td></tr><tr><td rowspan="2"> Executive functioning</td><td>Executive functioning (verbal fluency)</td><td>↓ − 0.066</td><td>.040</td><td>↓ − 0.106</td><td>.017</td></tr><tr><td>Span total</td><td>↓ − 0.039</td><td>.233</td><td>↓ − 0.179</td><td>< .001</td></tr><tr><td> Inhibitory control</td><td>Inhibitory control (DPICO accuracy)</td><td>↓ − 0.100</td><td>.004</td><td>↓ − 0.054</td><td>.262</td></tr></table> PROXY-RATED MBI – COGNITIVE PERFORMANCE <i>Multivariable linear regression (adjusted for age, sex, education)</i> <table><tr><th rowspan="2">Cognitive domain</th><th rowspan="2">Measure</th><th colspan="2">Incident psychosis (n = 405)</th><th colspan="2">Baseline psychosis (n = 309)</th></tr><tr><th>Estimate (β)</th><th>p-value</th><th>Estimate (β)</th><th>p-value</th></tr><tr><td rowspan="2"> Attention</td><td>Vigilance accuracy</td><td>↓ − 0.027</td><td>.203</td><td>↓ − 0.091</td><td>< .001</td></tr><tr><td>Simple reaction time</td><td>↓ − 0.047</td><td>.299</td><td>↓ 0.084</td><td>.012</td></tr><tr><td> Verbal memory</td><td>Verbal memory (immediate recall)</td><td>↓ − 0.040</td><td>.314</td><td>↓ − 0.071</td><td>.114</td></tr><tr><td> Executive functioning</td><td>Executive functioning (verbal fluency)</td><td>↓ − 0.078</td><td>.044</td><td>↓ − 0.060</td><td>.168</td></tr><tr><td> Inhibitory control</td><td>Inhibitory control (DPICN accuracy)</td><td>↓ 0.013</td><td>.716</td><td>↓ − 0.126</td><td>.002</td></tr></table> ↓ = worse performance Higher reaction time values (RT) indicate slower responses = worse performance		Cognitive domain	Measure	Incident psychosis (n = 610)		Baseline psychosis (n = 305)		Estimate (β)	p-value	Estimate (β)	p-value	 Attention	Vigilance accuracy	↓ − 0.082	< .001	↓ − 0.096	< .001	Vigilance reaction time	↓ 0.111	.003	↓ 0.163	.002	 Verbal memory	Verbal memory (immediate recall)	↓ 0.038	.242	↓ 0.153	.001	 Executive functioning	Executive functioning (verbal fluency)	↓ − 0.066	.040	↓ − 0.106	.017	Span total	↓ − 0.039	.233	↓ − 0.179	< .001	 Inhibitory control	Inhibitory control (DPICO accuracy)	↓ − 0.100	.004	↓ − 0.054	.262	Cognitive domain	Measure	Incident psychosis (n = 405)		Baseline psychosis (n = 309)		Estimate (β)	p-value	Estimate (β)	p-value	 Attention	Vigilance accuracy	↓ − 0.027	.203	↓ − 0.091	< .001	Simple reaction time	↓ − 0.047	.299	↓ 0.084	.012	 Verbal memory	Verbal memory (immediate recall)	↓ − 0.040	.314	↓ − 0.071	.114	 Executive functioning	Executive functioning (verbal fluency)	↓ − 0.078	.044	↓ − 0.060	.168	 Inhibitory control	Inhibitory control (DPICN accuracy)	↓ 0.013	.716	↓ − 0.126	.002	Cognitive alterations are detectable in individuals with psychotic symptoms. Subtle cognitive deficits, particularly in inhibitory control, may already be present before the clinical emergence of psychotic symptoms. Self- and proxy- reported MBI may be particularly useful for identifying these early changes.	
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METHODS		CONTACT																																																																																						
MBI assessed using self- and proxy-rated questionnaires Participants classified into: - No psychotic symptoms (NS) - Incident psychotic symptoms (onset during follow-up, IP) - Psychotic symptoms present at baseline (PB) Cognition was evaluated across multiple domains		 Barbara Blasutto: Barbara.Blasutto@uniroma1.it Dr. Byron Creese, PhD: Byron.Creese@brunel.ac.uk ALZHEIMER'S ASSOCIATION AAIC 26																																																																																						
REFERENCES		¹ Creese, B., Brooker, H., Ismail, Z., Wesnes, K. A., Hampshire, A., Khan, Z., ... & Ballard, C. (2019). Mild behavioral impairment as a marker of cognitive decline in cognitively normal older adults. <i>The American Journal of Geriatric Psychiatry</i>, 27(8), 823-834. ² Liew, T. M. (2020). Neuropsychiatric symptoms in cognitively normal older persons, and the association with Alzheimer's and non-Alzheimer's dementia. <i>Alzheimer's Research & Therapy</i>, 12(1), 35. ³ Creese, B., Arathimos, R., Aarsland, D., Ballard, C., Brooker, H., Hampshire, A., ... & Ismail, Z. (2023). Late-life onset psychotic symptoms and incident cognitive impairment in people without dementia: Modification by genetic risk for Alzheimer's disease. <i>Alzheimer's & Dementia: Translational Research & Clinical Interventions</i>, 9(2), e12386																																																																																						