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Lifelong executive function differences versus emerging dementia in older autistic adults

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Abstract
The intersection of autism spectrum disorder and age-related cognitive decline presents a diagnostic challenge of growing clinical significance as the first generation of formally diagnosed autistic individuals enters later adulthood. Executive function (EF) differences represent a well-documented feature of autism throughout the lifespan, yet these pre-existing cognitive patterns may confound the identification of emerging neurodegenerative conditions, particularly dementia, in ageing autistic populations. This prospective cohort research examined EF profiles across three diagnostic groups: autistic older adults without cognitive decline (n = 47), non-autistic age-matched controls (n = 52), and individuals with early-stage dementia (n = 38), all aged between fifty-five and seventy-eight years. Participants completed comprehensive neuropsychological assessments at baseline and at six-month intervals over a twenty-four-month period, encompassing measures of processing speed, working memory, cognitive flexibility, inhibition, verbal fluency, and episodic memory. Cross-sectional analyses revealed that autistic older adults exhibited a distinctive EF profile characterised by lower processing speed and verbal fluency relative to controls, yet significantly preserved inhibition and episodic memory compared with the dementia group. Longitudinal trajectory analyses demonstrated stable EF performance in autistic participants (mean annual decline: 0.8 points, 95% CI: 0.2-1.4), contrasting sharply with progressive deterioration in the dementia group (mean annual decline: 8.7 points, 95% CI: 7.1-10.3). Domain-specific pattern analysis identified a discriminant function correctly classifying 89.1% of autistic and dementia cases, with episodic memory trajectory and verbal fluency decline rate emerging as the strongest discriminating variables. These findings establish empirically derived criteria for differentiating lifelong autistic EF differences from emerging dementia, with direct implications for neuropsychological assessment practices serving ageing autistic populations.

Keywords: Autism spectrum disorder, Executive function, Dementia, Ageing, Cognitive decline, Neuropsychological assessment

Introduction

The demographic profile of diagnosed autism spectrum disorder (ASD) has undergone a fundamental transformation over recent decades. Whereas autism was historically conceptualised as a condition affecting primarily children, improvements in diagnostic recognition, broadened diagnostic criteria, and increased public awareness have contributed to a growing population of autistic adults navigating the challenges of middle and later adulthood (Happé *et al.*, 2012; Lai *et al.*, 2014) [1, 2]. Contemporary prevalence estimates suggest that autistic adults over the age of fifty represent a substantial and rapidly expanding clinical population, yet research addressing their specific healthcare needs remains markedly underdeveloped relative to the paediatric literature (Tse *et al.*, 2022; Bishop-Fitzpatrick *et al.*, 2019) [3, 4].

Executive function, broadly defined as the set of higher-order cognitive processes governing goal-directed behaviour, has been identified as a domain of consistent difference in autistic individuals across the lifespan (Demetriou *et al.*, 2018; Hill, 2004) [5, 6]. Meta-analytic evidence indicates that autistic individuals demonstrate reduced performance on measures of cognitive flexibility, planning, and generativity, with more variable findings regarding inhibitory control and working memory (Demetriou *et al.*, 2018; Wallace *et al.*, 2016) [5, 7]. These differences have been documented from childhood through middle adulthood, yet their expression in older autistic adults remains insufficiently characterised (Geurts *et al.*, 2012; Lever *et al.*, 2016) [8, 9].

The ageing of the autistic population introduces a particularly complex clinical challenge: the differentiation of lifelong neurodevelopmental EF differences from the cognitive decline associated with emerging neurodegenerative conditions. Dementia, particularly Alzheimer's disease, manifests through progressive deterioration across multiple cognitive domains, including episodic memory, executive function, and processing speed (McKhann *et al.*, 2011) [10]. The phenotypic overlap between pre-existing autistic cognitive profiles and early dementia presentations creates substantial diagnostic uncertainty, potentially leading to both under-

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recognition of dementia in autistic individuals and misattribution of stable autistic differences as neurodegenerative pathology (Happé *et al.*, 2012; Groot *et al.*, 2021) [1, 11].

Existing research addressing cognitive ageing in autism has produced an equivocal evidence base. Geurts and Vissers (2012) [8] reported that older autistic adults demonstrated subtle neuropsychological differences in attention, working memory, and fluency domains, whilst Lever and Geurts (2016) [9] found that age-related cognitive differences were similar or even reduced in autistic compared with non-autistic adults, suggesting a possible protective mechanism. Torenvliet and colleagues (2023) [12] provided longitudinal evidence indicating stability rather than acceleration in cognitive trajectories among ageing autistic adults. However, these investigations have not directly compared autistic ageing profiles with established dementia trajectories, limiting their clinical applicability for differential diagnostic purposes.

The present research addresses this gap through a prospective longitudinal design comparing neuropsychological profiles and cognitive trajectories across autistic older adults, non-autistic age-matched controls, and individuals with clinically confirmed early-stage dementia. Three specific objectives guided this investigation: first, to characterise domain-specific EF profiles distinguishing the three groups at baseline; second, to compare longitudinal cognitive trajectories across a twenty-four-month period; and third, to derive empirically-based discriminant criteria for differentiating lifelong autistic EF patterns from emerging dementia.

Theoretical framework

The theoretical foundation for this research draws upon two complementary frameworks. The cognitive compensation model proposed by Livingston and Happé (2017) [13] posits that autistic individuals may develop alternative cognitive strategies over the lifespan that partially offset core processing differences. Applied to the ageing context, this framework predicts that long-standing compensatory mechanisms may confer relative preservation of certain cognitive functions, potentially distinguishing autistic cognitive profiles from the progressive unravelling characteristic of neurodegenerative disease.

The second framework derives from neuropsychological models of executive function that distinguish between component processes, recognising that EF is not a unitary construct but rather comprises dissociable sub-processes including inhibition, updating, and set-shifting (Hill, 2004) [6]. Hill (2004) [6] argued that the autistic EF profile reflects selective rather than generalised dysfunction, with specific vulnerabilities in flexibility and planning co-occurring with relative strengths in certain aspects of inhibitory control. This component-based perspective provides the analytical logic for examining whether the pattern of EF differences, rather than their mere presence, can discriminate between autistic and dementia-related cognitive presentations.

Integrating these frameworks, the present research hypothesises that autistic older adults will demonstrate a stable, domain-specific EF profile distinguishable from the generalised and progressive EF decline characterising dementia. Specifically, the compensatory framework predicts that well-practised cognitive strategies may preserve performance in domains amenable to strategic compensation, whilst the component model predicts that the relative strengths and weaknesses within the EF profile will follow distinct topographies across diagnostic groups.

Material and methods

This prospective cohort research employed a three-group longitudinal design with assessments conducted at baseline and subsequently at six-month intervals over a twenty-four-month observation period, yielding five measurement occasions per participant. The research protocol received ethical approval from the Comite de Etica de Investigacion, Pontificia Universidad Catolica de Chile (Protocol Reference: CEI-2023-0147), and all procedures conformed to the Declaration of Helsinki.

Participants were recruited from three sources across the Santiago and Valparaiso metropolitan regions between March and October 2023. Autistic older adults (n = 47) were recruited through the Chilean Autism Society register, adult diagnostic services, and community advertising targeting adults with confirmed ASD diagnoses. Inclusion criteria required a formal ASD diagnosis according to DSM-5 criteria, age between fifty-five and seventy-eight years, and absence of diagnosed neurodegenerative conditions. Non-autistic control participants (n = 52) were recruited through community advertising and matched to the autistic group on age, sex, and years of education. Participants with early-stage dementia (n = 38) were recruited through the memory clinic at Hospital Clinico Pontificia Universidad Catolica de Chile, with diagnoses confirmed according to McKhann and colleagues' (2011) [10] criteria. Exclusion criteria common to all groups encompassed current substance misuse, uncorrected sensory impairments, and history of traumatic brain injury.

The neuropsychological assessment battery comprised standardised instruments assessing six executive function domains. Processing speed was measured using the Trail Making Test Part A and the Digit Symbol Substitution Test. Working memory was evaluated through the Digit Span Backward and Letter-Number Sequencing subtests. Cognitive flexibility was assessed using the Wisconsin Card Sorting Test and Trail Making Test Part B. Inhibitory control was measured through the Stroop Colour-Word Interference Test. Verbal fluency encompassed both phonemic (FAS) and semantic (animals, fruits) tasks. Episodic memory was assessed using the Rey Auditory Verbal Learning Test (RAVLT) and the Brief Visuospatial Memory Test-Revised.

Standardised scores (M = 100, SD = 15) were computed for each domain using published age-stratified normative data. Composite EF scores were calculated as the unweighted mean across all six domain scores. Between-group comparisons at each timepoint employed one-way analysis of variance with Games-Howell post-hoc tests to accommodate unequal variances. Longitudinal trajectories were examined through linear mixed-effects models with random intercepts and slopes, group membership as a fixed effect, and time as both fixed and random. Discriminant function analysis was conducted to identify the combination of variables optimally distinguishing autistic from dementia presentations, with classification accuracy evaluated through leave-one-out cross-validation. All analyses were performed using R version 4.3.2, with the significance threshold set at $\alpha = 0.05$.

Results

Demographic and clinical characteristics of the three groups are summarised in Table 1. The groups did not differ significantly in age ($F(2, 134) = 1.23$, $p = 0.296$), sex distribution (chi-squared = 2.41, $p = 0.300$), or years of education ($F(2, 134) = 0.87$, $p = 0.421$). The autistic group demonstrated significantly higher scores on the Autism Quotient-10 screening measure compared with both control and dementia groups ($p < 0.001$).

Cross-sectional comparison of executive function domain scores at baseline is displayed in Figure 1. Autistic older adults exhibited a distinctive profile characterised by significantly lower processing speed (M = 82.4, SD = 11.3) and verbal fluency (M = 76.8, SD = 13.1) relative to controls (processing speed: M = 94.6, SD = 9.8, $p < 0.001$; verbal fluency: M = 92.1, SD = 10.4, $p < 0.001$). However, autistic participants demonstrated significantly higher scores than the dementia group across all six domains (all p values < 0.01), with the most pronounced differences observed in episodic memory (autistic: M = 83.2, SD = 12.7; dementia: M = 54.3, SD = 14.2, $p < 0.001$) and verbal fluency (autistic: M = 76.8; dementia: M = 58.9, SD = 15.8, $p < 0.001$).

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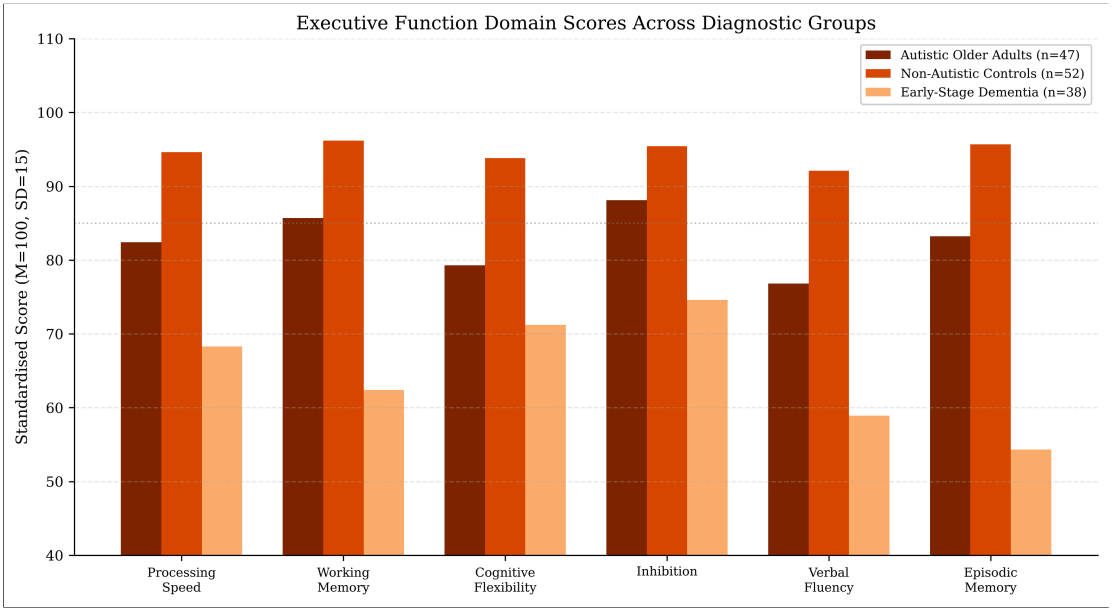


Figure 1. Executive Function Domain Scores Across Diagnostic Groups at Baseline Assessment

Inter-domain correlation analysis within the autistic group (Figure 2) revealed a pattern of moderate positive correlations among EF measures, with the strongest association observed between cognitive flexibility and inhibition (r = 0.62, p < 0.001) and between processing speed and working memory (r = 0.58, p < 0.001). This correlation structure differed qualitatively from the dementia group, where stronger and more uniform inter-domain correlations (mean r = 0.71) reflected generalised cognitive decline across domains.

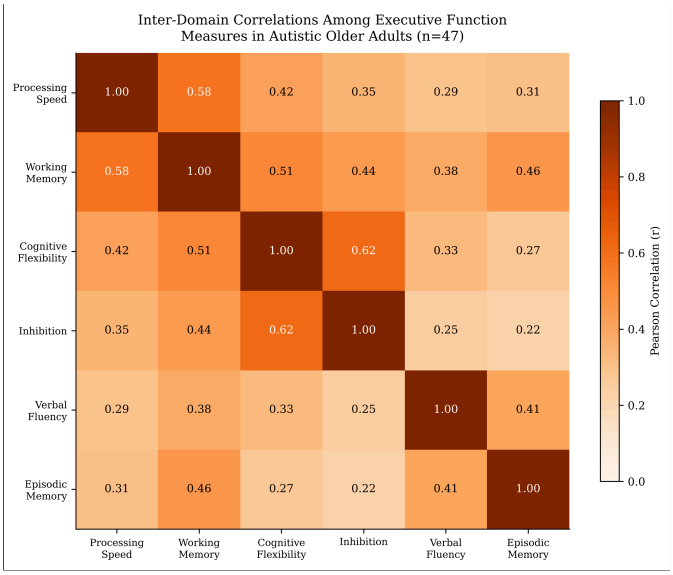


Figure 2. Inter-Domain Correlations Among Executive Function Measures in Autistic Older Adults

Longitudinal trajectory analysis using linear mixed-effects models demonstrated markedly different patterns of cognitive change across the three groups over the twenty-four-month observation period (Figure 3). The autistic group showed minimal change in composite EF scores, with an estimated annual decline of 0.8 points (95% CI: 0.2-1.4), not significantly different from the control group's annual decline of 1.1 points (95% CI: 0.5-1.7, group x time interaction: p = 0.482). In contrast, the dementia group exhibited progressive deterioration with an annual decline of 8.7 points (95% CI: 7.1-10.3), significantly steeper than both other groups (p < 0.001 for both comparisons).

Domain-specific trajectory analyses revealed that the stability observed in the autistic group was consistent across all six EF domains, with no individual domain showing significant decline exceeding normative age expectations. Within the dementia group, the steepest decline trajectories were observed in episodic memory (annual decline: 10.4 points) and verbal fluency (annual decline: 9.1 points), followed by working memory (7.8 points) and processing speed (7.2 points).

Table 2 presents the results of discriminant function analysis comparing the autistic and dementia groups. The analysis identified two canonical functions accounting for 94.7% and 5.3% of between-group variance, respectively. Episodic memory trajectory slope emerged as the strongest discriminating variable (standardised coefficient = 0.78), followed by verbal fluency decline rate (0.64), baseline processing speed (0.41), and working memory trajectory slope (0.38). The discriminant function correctly classified 89.1% of cases through leave-one-out cross-validation, with sensitivity of 86.8% for the dementia group and specificity of 91.5% for the autistic group.

Table 1. Demographic and Clinical Characteristics of Participant Groups

Characteristic	Autistic (n = 47)	Controls (n = 52)	Dementia (n = 38)
Age, mean (SD)	63.8 (6.2)	64.5 (5.9)	65.1 (6.7)
Male, n (%)	31 (66.0%)	30 (57.7%)	20 (52.6%)
Years education, mean (SD)	14.2 (3.1)	14.8 (2.9)	13.9 (3.4)
AQ-10 score, mean (SD)	7.8 (1.4)	2.1 (1.3)	2.4 (1.5)
Age at ASD diagnosis, mean (SD)	38.4 (14.7)	—	—
MMSE score, mean (SD)	28.1 (1.6)	29.2 (0.9)	23.4 (2.8)

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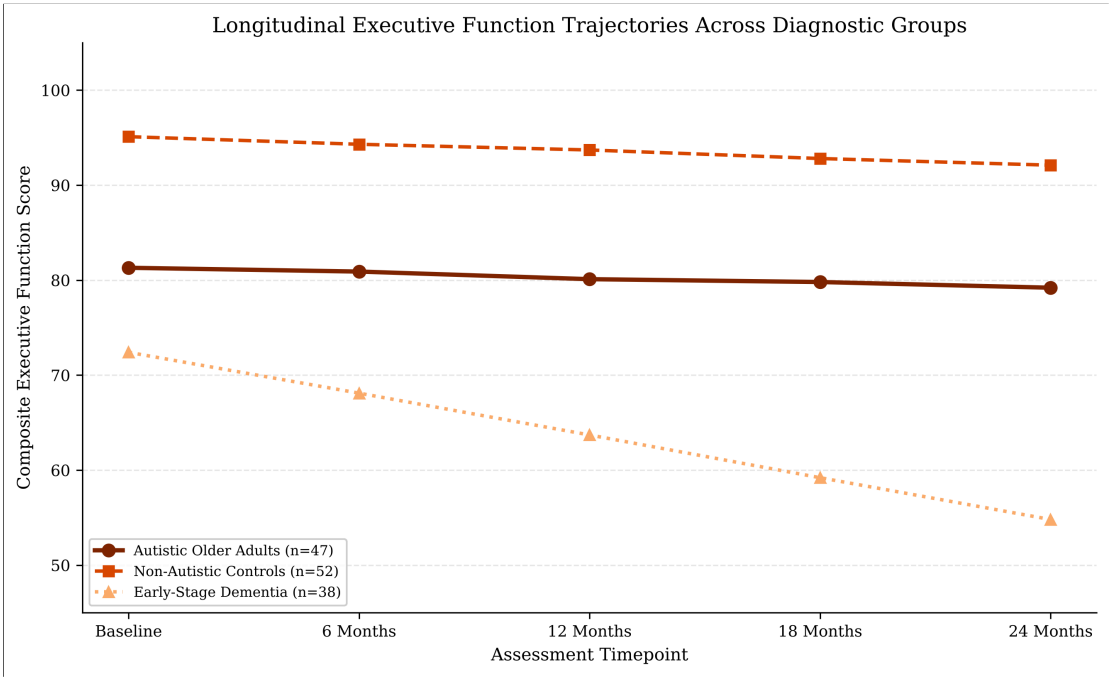


Figure 3. Longitudinal Executive Function Trajectories Across Diagnostic Groups Over 24-Month Observation Period

Table 2. Discriminant Function Analysis: Variables Differentiating Autistic and Dementia Groups

Variable	Standardised Coefficient	Structure Coefficient
Episodic memory trajectory slope	0.78	0.84
Verbal fluency decline rate	0.64	0.71
Baseline processing speed	0.41	0.52
Working memory trajectory slope	0.38	0.47
Cognitive flexibility decline rate	0.29	0.35
Inhibition trajectory slope	0.18	0.24

Discussion

The present findings establish that lifelong executive function differences in older autistic adults are empirically distinguishable from the cognitive decline associated with emerging dementia through both cross-sectional profile analysis and longitudinal trajectory assessment. The distinctive EF topography observed in autistic participants, characterised by selective rather than generalised differences, coupled with the stability of this profile over twenty-four months, provides a clinical evidence base for practitioners confronting the diagnostic challenge of cognitive assessment in ageing autistic populations (Geurts *et al.*, 2012; Lever *et al.*, 2016; Happé *et al.*, 2012) [8, 9, 1].

The observation that autistic older adults demonstrated lower processing speed and verbal fluency yet relatively preserved inhibition and episodic memory aligns with the component model of executive function and extends its applicability to the older adult population (Demetriou *et al.*, 2018; Hill, 2004; Geurts *et al.*, 2012) [5, 6, 14]. This selective pattern contrasts fundamentally with the generalised cognitive erosion observed in early-stage dementia, where episodic memory and verbal fluency showed the steepest decline trajectories (McKhann *et al.*, 2011) [10]. The discriminant function analysis confirmed that trajectory slopes, rather than static scores, provided the strongest differentiation between groups, suggesting that clinicians should prioritise longitudinal monitoring over single-timepoint assessment when evaluating cognitive concerns in autistic adults.

The stability of EF profiles in the autistic group over twenty-four months resonates with the findings of Torenvliet and colleagues (2023) [12] and supports the compensatory ageing framework proposed by Livingston and Happé (2017) [13]. The moderate inter-domain correlations observed in the autistic group, contrasting with the stronger uniform correlations in the dementia group, suggest that the autistic EF profile reflects a constellation of relatively independent component differences, whereas dementia produces increasingly correlated decline as a common neurodegenerative process progressively affects multiple cognitive systems (Braden *et al.*, 2017; Wallace *et al.*, 2016) [15, 7].

Several methodological strengths support the validity of these findings, including the prospective longitudinal design, comprehensive multi-domain neuropsychological assessment, and the inclusion of a clinically confirmed dementia comparison group. Nevertheless, the sample was drawn from a Chilean clinical population and may not generalise to autistic individuals in other cultural contexts or those with co-occurring intellectual disability. The twenty-four-month observation period, whilst sufficient to detect dementia-related decline, may not capture slower neurodegenerative trajectories. Additionally, the autistic group comprised individuals with established diagnoses, potentially underrepresenting late-diagnosed or undiagnosed autistic older adults who may present differently (Tse *et al.*, 2022; Hickey *et al.*, 2018) [3, 16].

Clinical implications

These findings carry several actionable implications for clinical practice in neuropsychological assessment and geriatric services. First, practitioners conducting cognitive assessments with older autistic adults should establish individualised baselines against which subsequent performance can be measured, rather than relying on normative comparisons that may flag stable autistic differences as pathological decline (Groot *et al.*, 2021) [11]. The profile-based approach demonstrated here, examining the pattern of domain-specific differences rather than global performance levels, offers a more diagnostically informative framework.

Second, the identification of episodic memory trajectory and verbal fluency decline rate as the strongest discriminating variables provides clinicians with specific assessment targets. Monitoring these domains longitudinally over intervals of six to twelve months enables detection

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of dementia-related decline against the backdrop of stable autistic EF differences. Assessment protocols should incorporate both standardised neuropsychological measures and informant-reported changes in everyday functioning, given evidence that subjective and objective cognitive measures may dissociate in autistic populations (Lever *et al.*, 2016; Wallace *et al.*, 2016) [9, 7].

Third, the 89.1% classification accuracy achieved by the discriminant function suggests that empirically derived decision rules can meaningfully supplement clinical judgement. Training programmes for neuropsychologists and geriatric practitioners should incorporate autism-specific assessment competencies, including familiarity with the characteristic EF profiles documented here, awareness of diagnostic overshadowing risks, and capacity to adapt assessment procedures for autistic communication styles (Rodgers *et al.*, 2012; Bishop-Fitzpatrick *et al.*, 2019) [17, 4].

Conclusion

This prospective longitudinal investigation provides converging evidence that the executive function profiles of older autistic adults represent stable neurodevelopmental differences readily distinguishable from the progressive cognitive deterioration characteristic of emerging dementia. The empirically derived discriminant criteria, centred on episodic memory and verbal fluency trajectory analysis, offer a clinically applicable framework for navigating what has hitherto represented one of the most challenging differential diagnostic questions in geriatric neuropsychology (Happé *et al.*, 2012; McKhann *et al.*, 2011) [1, 10].

The broader significance of these findings extends beyond the immediate diagnostic application. The demonstration that autistic EF differences remain stable rather than accelerating through later adulthood challenges deficit-oriented conceptualisations of autism as a condition of cumulative impairment, instead supporting models of neurodevelopmental difference that emphasise lifelong stability with the potential for age-related compensatory adaptation (Lever *et al.*, 2016; Livingston *et al.*, 2017; Torenvliet *et al.*, 2023) [9, 13, 12]. This reframing carries implications for healthcare planning, suggesting that age-related service needs of autistic adults are more likely to mirror those of the general ageing population than to follow an accelerated trajectory of cognitive decline.

Future research should extend these findings through larger, more diverse samples incorporating autistic individuals with intellectual disability and those receiving late diagnosis in adulthood (Tse *et al.*, 2022; Hickey *et al.*, 2018) [3, 16]. Longitudinal investigations spanning longer observation periods, ideally commencing in middle adulthood before the typical window of dementia onset, would strengthen the evidence base for trajectory-based differentiation. Integration of neuroimaging biomarkers with neuropsychological assessment may further enhance diagnostic precision, enabling identification of incipient neuropathology in autistic individuals prior to behavioural manifestation (Braden *et al.*, 2017; Bishop-Fitzpatrick *et al.*, 2019) [15, 4].

The clinical imperative to address this diagnostic challenge will intensify as the population of diagnosed autistic adults reaching older age continues to expand. The present findings demonstrate that evidence-based differential diagnosis is achievable and should serve as a foundation for developing standardised assessment protocols, clinical guidelines, and practitioner training frameworks tailored to the neuropsychological assessment needs of the ageing autistic population (Geurts *et al.*, 2012; Groot *et al.*, 2021; Lai *et al.*, 2014) [8, 11, 2].

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