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ORIGINAL COMMUNICATION

Sustained attention failures on a 3-min reaction time task is a sensitive marker of dementia

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Abstract
The objective of the study is to determine the utility of a simple reaction time task as a marker of general cognitive decline across the frontotemporal lobar degeneration (FTLD) spectrum and in Alzheimer's disease (AD). One hundred and twelve patients presenting with AD or FTLD affecting behaviour (behavioural-variant frontotemporal dementia), language (progressive non fluent aphasia, logopenic progressive aphasia, semantic dementia) or motor function (corticobasal syndrome, progressive supranuclear palsy, frontotemporal dementia–motor neuron disease) and 25 age-matched healthy controls completed the Psychomotor Vigilance Task (PVT), a 3-min reaction time (RT) task. The proportion of lapses (RT > 500 ms) was significantly increased in dementia patients compared to healthy controls, except for semantic dementia, and correlated with all cognitive functions except language. Discrimination of individuals (dementia patients versus healthy controls) based on the proportion of lapses yielded the highest classification performance (Area Under the Curve, AUC, 0.90) compared to standard neuropsychological tests. Only the complete and lengthy neuropsychological battery had a higher predictive value (AUC 0.96). The basic ability to sustain attention is fundamental to perform any cognitive task. Lapses, interpreted as momentary shifts in goal-directed processing, can therefore, be used as a marker of general cognitive decline indicative of possible dementia.

Keywords Sustained attention · Vigilance · Neurodegenerative disorders · Dementia · Reaction time · Psychomotor vigilance task

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Introduction

Sustained attention, which reflects basic, bottom-up efficiency of information processing [1], is a cognitive process fundamental to many daily activities and behaviours [2] such as driving [3] or motor control [4]. Evidence suggests that attention processes are impaired in dementia. Reaction time (RT) measures, such as mean RT and RT variability have been found to differentiate individuals with dementia from controls [5–7], and to dissociate dementias (e.g., Alzheimer disease, Huntington disease, Lewy body dementia) from mild cognitive Impairment (MCI) [8]. Further, increased RT variability and slower mean RT are also associated with an increased risk of developing dementia over 4 years [9] or predict conversion from MCI to AD [10]. Currently, although AD and FTLD are the most common younger-onset dementia syndromes [11], evidence on RT performance across the frontotemporal lobar degeneration (FTLD) spectrum is lacking, apart from a small study ($n = 5$), which also reported increased RT variability [12].

These findings suggest that RT tasks to measure sustained attention may be useful for discriminating between individuals with and without dementia. Many of these tasks [13], however, are lengthy, lack reliability and have potential for practice effects. The Psychomotor Vigilance Task (PVT) is a brief (3-min) validated measure of sustained attention, with high test–retest reliability, and low learning effects [14]. The PVT measures sustained attention by capturing response times to randomly presented visual stimuli. This simple yet informative task has been used as a marker of attentional impairment following acute or chronic sleep loss, or in circadian misalignments after shift work [14, 15].

As such, the objectives of the current study were to (i) determine changes in sustained attention across the FTLD spectrum and in AD, (ii) compare its relation with other cognitive measures, and (iii) to test whether performance on the PVT can accurately discriminate between dementia patients and healthy controls. We hypothesised that if sustained attention deficits were present across all dementia syndromes tested here and were associated with performance on other cognitive tests, performance on the PVT could be used as a marker to discriminate between individuals with and without dementia.

Methods

Participants

One hundred fifty-one individuals (123 diagnosed with dementia; 28 healthy controls) were recruited from FRONTIER, the frontotemporal dementia research clinic based in Sydney, Australia, between February 2016 and December 2017. All participants underwent a comprehensive clinical assessment with an experienced neurologist, a neuropsychological assessment, and (in most cases) had a brain MRI. Diagnosis was established according to relevant clinical diagnostic criteria at the time of testing for probable behavioural-variant frontotemporal dementia (bvFTD) or possible bvFTD (bvFTD_Poss) [16], Alzheimer's disease (AD) [17], progressive non fluent aphasia (PNFA), semantic dementia (SD) or logopenic progressive aphasia (LPA) [18], corticobasal syndrome (CBS) [19], progressive supranuclear palsy (PSP) [20] or frontotemporal dementia-motor neuron disease (FTD-MND) [21]. Diagnosis was established by multidisciplinary agreement between the neurologist, neuropsychologist, and occupational therapist based on cognitive, clinical and (when available) imaging data.

Exclusion criteria for patients and controls included: concurrent psychiatric diagnosis, presence of other dementia or neurological syndrome, history of alcohol or substance abuse and/or use of medication with potential central nervous system (CNS) side effects. Only patients that scored > 40/100 on the Addenbrooke's Cognitive Examination-Third edition (ACE-III) [22] were included in the study to ensure proper understanding of the task. Healthy controls underwent the same comprehensive neuropsychological assessment and brain MRI protocol and were included only if they scored > 88/100 on the ACE-III.

All participants or their Person Responsible provided written informed consent in accordance with the Declaration of Helsinki. The South Eastern Sydney Local Health District and the University of New South Wales ethics committees approved the study.

Neuropsychological assessment

The ACE-III was used to assess general cognition [22]. All participants were tested on neuropsychological measures of attention (Digit Span Forward maximum span; Digits-F Max [23]), working memory (Digit Span Backward maximum span; Digits-B Max [23]), processing speed (Trail Making Test A [TMT-A] [24]), visuoconstruction (RCF Copy [25]), episodic memory (RCF Recall [25]), executive functioning (TMT Part B-A [24], Letter fluency [total of letters F, A and S] [26]) and language (confrontation naming subtest of the Sydney Language Battery [27]). Disease severity was assessed with the Frontotemporal Lobar Degeneration-Modified Clinical Dementia Rating Scale Sums of Boxes (CDR-FTLD SoB) [28].

Psychomotor vigilance task

Sustained attention was assessed with the Psychomotor Vigilance Task (PVT) (https://admin.joggleresearch.com/), administered on a portable tablet (Fig. 1). The PVT is a validated 3-min RT task measuring responses to visual stimuli

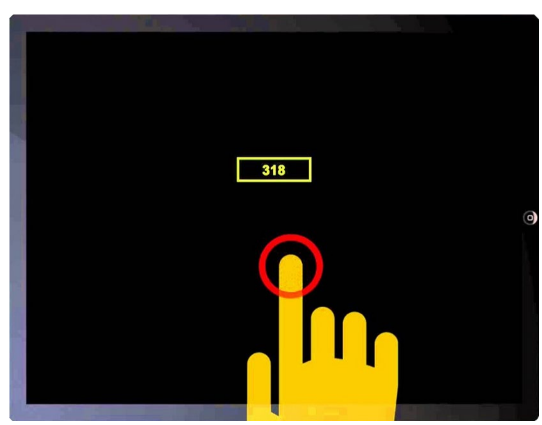

Fig. 1 Design of the Psychomotor Vigilance Task (PVT) on the tablet (reproduced with permission from Joggle Research)

occurring at random inter-stimulus intervals [14, 15]. For each trial, an empty box is presented on the screen, triggering a millisecond counter. Participants must press on the screen to stop the counter. The RT for that trial is then displayed for 1 s before the start of the next trial. Participants are instructed to respond as quickly as possible, while also avoiding pressing on the screen when the counter is not displayed (i.e., false starts). Four measures were included in the analyses: (1) PVT_Lapses (i.e., responses with RTs > 500 ms), (2) PVT_Median RT, (3) PVT_Stdev (RT standard deviation) and (4) PVT_FalseStarts (RTs < 100 ms) [14, 15]. Because of differences in RT across participants, the number of trials over 3 min ranged between 30 and 48. PVT_Lapses and PVT_FalseStarts were, therefore, expressed as a proportion (%) of total trials. Time of day of the PVT administration was also recorded so that potential differences in circadian timing across individuals could be considered.

To control for pure sensorimotor deficits, participants also completed the Motor Praxis Task (MPT) on the tablet. Participants were instructed to click on 20 squares that appear randomly on the screen, each smaller than the previous one, and therefore, more difficult to track. Performance was assessed by the speed (median RT) with which participants click on each square.

We also controlled for sleep quality using the Cambridge Behavioural Inventory-Revised (CBI-R) [29].

Statistical analyses

Data were analysed using IBM SPSS Statistics, 24.0 (SPSS Inc., Chicago, Ill., USA) and figures created with Canvas (ACDSee, Inc., Bellevue, WA, USA). The distribution normality of demographic, neuropsychological and behavioural data was first determined with Shapiro–Wilks tests. Normally distributed variables were compared across groups using one-way ANOVAs followed by Bonferroni post hoc tests. Variables not normally distributed were analysed by Kruskal–Wallis ANOVA followed by Mann–Whitney *U* tests, Bonferroni corrected. Chi square tests were used to analyse categorical measures (e.g., sex). Effect sizes are reported using the partial eta-square (η^2). As performance on RT tasks are known to be affected by demographic variables such as age, education and sex as well as sleep quality, time of testing and motor praxis, analyses were additionally performed using these covariates.

Logistic stepwise regression analyses were performed using the Enter method to identify significant predictors of binary group membership (dementia patients versus healthy controls). We then calculated the receiver operating characteristic curve (ROC) and area under the curve (AUC) of the PVT and neuropsychological tests to obtain optimal cut-off scores and determine the best sensitivity and specificity indices. Statistical significance for all analyses was set at $p < 0.05$.

Correlations between the significant PVT behavioural measures and neuropsychological measures were analysed using Spearman rank coefficient across all patients.

Results

Demographic and neuropsychological profiles

Out of the 151 individuals originally screened, 137 individuals were finally included in this study (112 diagnosed with dementia; 25 healthy controls). Five patients were excluded because their ACE-III was below 40, four patients did not understand the task and one patient did not complete the PVT and the MPT. One control was excluded as he scored < 88/100 on the ACE-III. Two controls and one patient were excluded due to technical problems with the PVT.

Participant groups were matched for sex ($p = 0.27$), age ($p = 0.26$) and education level ($p = 0.28$) (Table 1). Across the patient groups, disease duration was longer in the bvFTD_Poss than in the FTD–MND group. Overall, patient groups showed worse general cognition on the ACE-III compared to controls except for the bvFTD_Poss and PSP groups. Across patient groups, AD and LPA scored worst. Both bvFTD groups and the FTD–MND group demonstrated greater functional impairment (CDR-FTLD SoB) compared to controls. Across patients, AD had significantly greater functional impairment than PNFA.

On neuropsychological tests, all patients were similarly impaired on executive functions (Letter fluency) compared to controls. The AD group showed impaired performance across all neuropsychological tasks compared with controls and significantly worse performance than other patient groups on memory (RCF) and processing speed/executive functions (TMT) tests. The bvFTD group also demonstrated impaired performance across all neuropsychological tests compared to controls, except on testing of processing speed/executive functions (TMT), which were preserved. Two of the motor syndromes (PSP and CBS) showed specific deficits on processing speed and executive functions (TMT) compared to controls. The language syndromes (PNFA, LPA, SD) showed preserved performance on processing speed and executive functions tests, but impaired performance on Naming.

Sleep was variably impaired across groups ($F_{(9,136)} = 5.40$, $p < 0.001$, $\eta^2 = 0.28$). Both bvFTDs groups showed worse sleep quality compared to controls (all p values < 0.001).

Table 1 Demographic variables and cognitive profile according to group

	CTRL ($n=25$)	AD ($n=20$)	bvFTD ($n=35$)	bvFTD_Poss ($n=11$)	CBS ($n=6$)	FTD-MND ($n=8$)	PSP ($n=5$)	LPA ($n=11$)	PNFA ($n=7$)	SD ($n=9$)	p	Post hoc (Bonferroni)
Sex (M:F)	14:11	12:8	24:11	9:2	2:4	8:0	2:3	7:4	4:3	6:3	0.27*	
Age (years)	64.7 (6.5)	64.4 (9.0)	61.4 (8.7)	64.8 (10.1)	67.0 (2.7)	67.1 (8.4)	71.4 (5.2)	66.6 (7.4)	63.0 (8.5)	64.3 (5.9)	0.26†	
Education (years)	14.7 (3.2)	12.4 (2.6)	12.3 (2.8)	12.4 (3.4)	11.9 (5.8)	13.2 (3.0)	12.8 (2.7)	12.7 (2.9)	13.9 (4.0)	12.4 (2.7)	0.28†	
Disease duration (years)	NA	4.8 (4.3)	5.6 (3.9)	9.2 (5.2)	3.5 (1.3)	2.1 (1.6)	3.97 (2.3)	3.1 (1.5)	6.4 (3.0)	4.7 (2.5)	0.003$^{\#}$	bvFTD_Poss <FTD-MND
ACE-III (/100)	95 (2.7)	64.7 (13.1)	77.5 (12.0)	87.6 (6.1)	69.8 (13.1)	76.3 (6.1)	77.8 (9.4)	66.8 (14.5)	78.9 (17.5)	74.6 (16.2)	<0.001†	Patients (excl. bvFD_Poss, PSP) < CTRL; AD < bvFTD, bvFTD_Poss; LPA < bvFTD_Poss
CDR-FTDL Sob	0.21 (0.2)	4.9 (2.2)	4.3 (2.4)	4.4 (2.4)	2.9 (2.3)	3.4 (1.8)	3.3 (3.3)	2.4 (1.7)	1.6 (1.4)	2.8 (2.3)	<0.001†	AD, bvFTDs, FTD–MND < CTRL; AD < PNFA
RCF Copy (/36)	31.9 (2.4)	24.2 (7.3)	25.7 (7.1)	29.7 (6.1)	22.7 (5.9)	26 (9.0)	23.3 (3.1)	27.3 (9.7)	29.1 (4.3)	31.4 (2.3)	0.001†	AD, bvFTD < CTRL
RCF Recall (/36)	16.48 (3.4)	3.39 (3.6)	9.9 (6.3)	13.1 (8.3)	8.7 (5.7)	13.3 (9.3)	15.5 (8.5)	14.4 (10.3)	15.1 (4.3)	13.4 (6.0)	<0.001†	AD, bvFTD < CTRL; AD < all patients (excl. CBS)
SYDBAT Naming (/30)	27.4 (2.0)	20.6 (5.6)	22.1 (4.6)	26.0 (3.7)	21.2 (1.9)	21.0 (4.8)	24.8 (2.2)	17.4 (6.2)	17.0 (8.1)	15.7 (7.2)	<0.001†	AD, bvFTD, LPA, PNFA, SD < CTRL; LPA, PNFA, SD < bvFTD_Poss
Digits-F max	7.2 (1.4)	5.4 (1.3)	5.8 (1.3)	6.1 (1.5)	6.7 (1.9)	6.4 (1.4)	5.4 (0.5)	5.3 (1.3)	5.7 (1.4)	6.3 (1.2)	0.001†	AD, bvFTD, LPA < CTRL
Digits-B max	5.0 (1.1)	3.45 (0.8)	3.8 (1.1)	4.5 (1.6)	4.5 (1.3)	3.4 (1.6)	3.8 (1.3)	3.7 (1.1)	3.6 (0.7)	4.7 (0.5)	0.001$^{\#}$	AD, bvFTD, FTD–MND < CTRL
Letter fluency	48.0 (13.4)	26.3 (15.3)	24.5 (13.2)	25.9 (12.7)	16.2 (5.8)	21.6 (11.2)	15.4 (17.9)	21.0 (12.6)	14.9 (11.8)	31.1 (10.5)	<0.001$^{\#}$	Patients < CTRL
TMT A (s)	28.6 (7.3)	98.5 (81.1)	47.1 (17.4)	47.8 (22.7)	63.4 (29.9)	54.9 (19.6)	150.2 (98.7)	51.9 (30.3)	75.1 (67.9)	38.7 (19.8)	<0.001$^{\#}$	AD, PSP < CTRL; PSP < bvFTD

Table 1 (continued)

	CTRL ($n=25$)	AD ($n=20$)	bvFTD ($n=35$)	bvFTD_Poss ($n=11$)	CBS ($n=6$)	FTD-MND ($n=8$)	PSP ($n=5$)	LPA ($n=11$)	PNFA ($n=7$)	SD ($n=9$)	*p*	Post hoc (Bonferroni)
TMT B-A (s)	42.2 (17.3)	198.4 (124.2)	100.1 (75.6)	98.3 (75.6)	445.2 (426.5)	342.0 (385.5)	476.4 (379.7)	356.3 (391.4)	166.6 (272.8)	55.1 (25.3)	<0.001#	AD, CBS < CTRL; AD < SD

Demographic and clinical information for Controls (Ctrl), Alzheimer's disease (AD), probable behavioural variant frontotemporal dementia (bvFTD), possible bvFTD (bvFTD_Poss), corticobasal syndrome (CBS), FTD–motor neuron disease (FTD–MND), progressive supranuclear palsy (PSP), logopenic progressive aphasia (LPA), progressive non fluent aphasia (PNFA), semantic dementia (SD). Values are mean ± standard deviation. *χ^2 test, †analysis of variance (ANOVA). #Kruskal–Wallis test. *ACE-III* Addenbrooke's Cognitive Examination—Third edition, *FRS* Frontotemporal Dementia Rating Scale. Higher scores denote higher functioning; *CDR-FTLD SoB* Frontotemporal Lobar Degeneration-Modified Clinical Dementia Rating Scale Sums of Boxes (CDR-FTLD SoB), *RCF* Rey Complex Figure, *SYDBAT* Sydney Language Battery, *Digits* Digit Span Forward and Backwards, *TMT* Trail Making Test. Missing Scores: education (CTRL 1, bvFTD_Poss 1); Disease duration (AD 1, CBS 1, FTD–MND 1); CDR-FTLD SoB (CTRL 1, bvFTD 2, bvFTD_Poss 3, CBS 1, FTD–MND 1, LPA 2, SD 1); RCF Copy (AD 1, bvFTD 2, bvFTD_Poss 1, CBS 1, PSP 1); RCF Recall (AD 1, bvFTD 2, bvFTD_Poss 1, CBS 1, PSP 1, LPA 1); SYDBAT (bvFTD 13, FTD–MND 1, SD 2); Letter fluency (CBS 1, LPA 1); TMT A (CTRL 1, CBS 1); TMT B-A (AD 9, bvFTD 3, CTRL 1, CBS 3, FTD–MND 2, PSP 2, LPA 3, PNFA 2)

Psychomotor vigilance task results

Group differences were observed on all measures of interest (Fig. 2): PVT_Lapses ($\chi^2(9)=51.25$, $p<0.001$, $\eta^2=0.32$), PVT_Median RT ($\chi^2(9)=51.43$, $p<0.001$, $\eta^2=0.17$), PVT_Stdev ($\chi^2(9)=39.40$, $p<0.001$, $\eta^2=0.17$) and PVT_FalseStarts ($\chi^2(9)=21.13$, $p=0.012$, $\eta^2=0.19$). All patient groups, except the SD group ($p=0.09$), had significantly more lapses than controls (all $p<0.001$, Bonferroni corrected). Across patient groups, the PSP group performed worse than the SD group ($p=0.01$). Regarding PVT_Median RT, only patients with PSP were significantly slower than controls ($p<0.001$), with no differences between patient groups. The AD, CBS, and PSP groups showed greater RT variability (PVT_Stdev) compared to controls (all $p<0.001$), but no differences between patient groups following Bonferroni correction. Importantly, these results remained unchanged after correcting for demographic variables (sex, age, education), time of testing, sleep and motor praxis (MPT).

Although time of testing during the day varied across groups ($\chi^2(9)=17.74$, $p=0.038$, $\eta^2=0.13$), no group differences survived Bonferroni correction.

Classification of healthy controls and dementia patients

Nearly 84% of participants were correctly classified as dementia patients or healthy controls based on PVT variables, but only PVT_Lapses was significant in the logistic regression model ($p=0.026$). A separate model that included the 8 neuropsychological measures correctly classified 93.5% of participants. The addition of PVT_Lapses significantly improved the model ($\Delta R^2=5.3\%$, $p=0.005$) with 94.6% of participants correctly classified, this measure being the only remaining significant variable in the model ($p=0.047$; Online Resource 1).

The AUC for PVT_Lapses was the highest compared to other neuropsychological measures (AUC 0.90, $p<0.001$; Online resource 1), which denotes high diagnostic accuracy according to standard models [30]. A proportion of lapses ≥ 9.5 classified group membership (dementia patients versus healthy controls) with a sensitivity of 83.5% and a specificity of 87.5% (Fig. 3). Among all the measures, only the ACE-III classified healthy controls versus dementia patients with greater accuracy (AUC 0.96; $p<0.001$).

Correlational analyses

Across all patients, the number of lapses correlated significantly with all neuropsychological tests, with the exception of Naming and Digit Span Forward Max span (Table 2). PVT_Lapses did not correlate with sleep ($r_{(110)}=-0.11$, $p=0.24$) or circadian time ($r_{(110)}=0.13$, $p=0.18$).

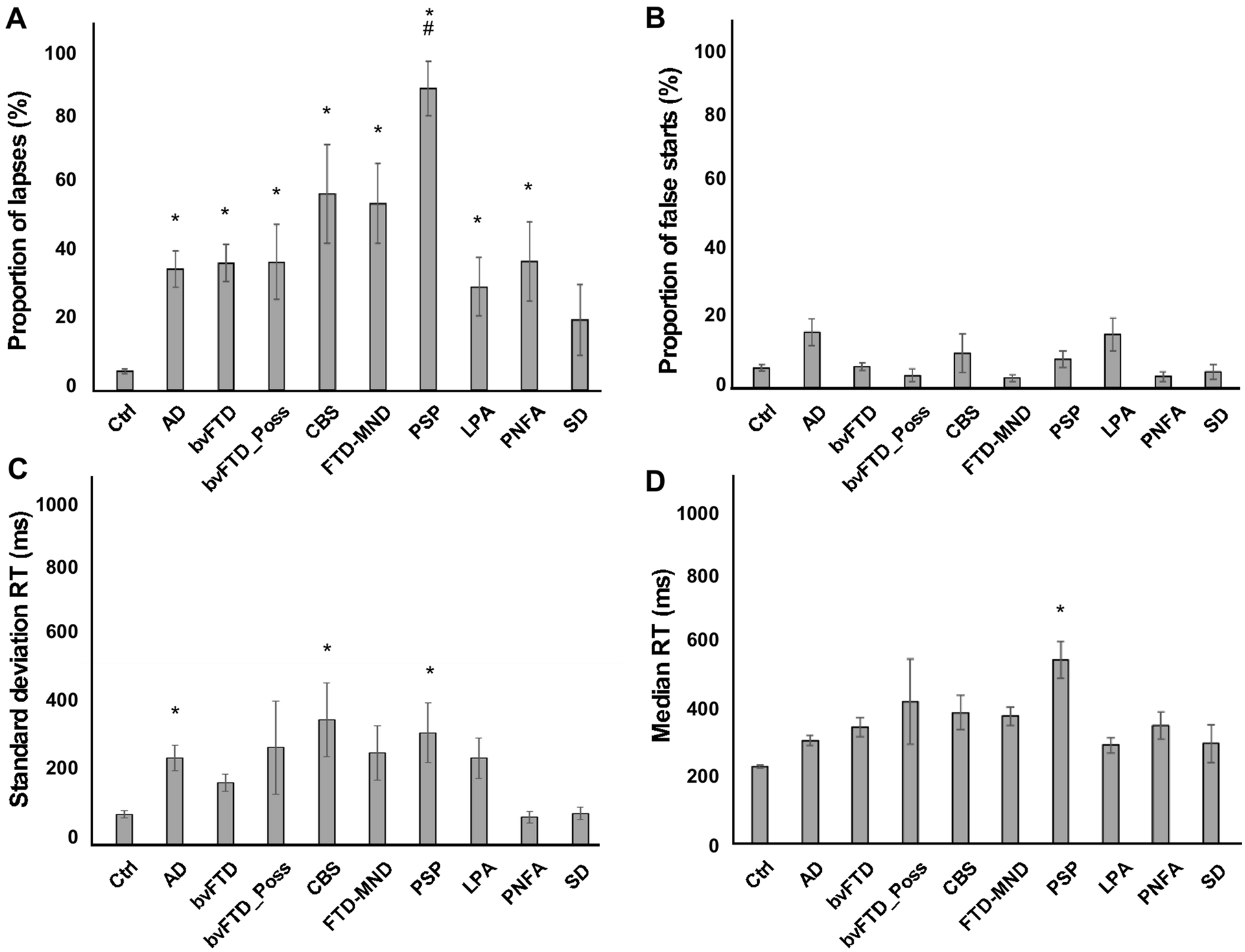

Fig. 2 Behavioural results on the Psychomotor Vigilance Task (PVT) for PVT_Lapses (**a**) PVT_FalseStarts (**b**), PVT_Stdev (**c**) and PVT_Median_RT (**d**) across all patient groups and controls. Controls (Ctrl), Alzheimer's disease (AD), probable behavioural-variant frontotemporal dementia (bvFTD), possible bvFTD (bvFTD_Poss), corticobasal syndrome (CBS), FTD–motor neuron disease (FTD-MND), progressive supranuclear palsy (PSP), logopenic progressive aphasia (LPA), progressive non fluent aphasia (PNFA), semantic dementia (SD). Main effects of Group significant for all variables (all $p<0.012$). The results remain unchanged when correcting for age, sex, education, sleep quality, circadian time and motor praxis. Bonferroni corrected significant difference compared to: *Ctrl, #SD. Bars represent mean and SEM

Discussion

This study demonstrates that the presence of delayed responses during a simple psychomotor vigilance task is a sensitive measure that successfully differentiates dementia patients from healthy controls. Specifically, dementia patients showed a higher proportion of lapses compared with healthy controls, a difference which remained unchanged after controlling for age, sex, education, sleep quality, circadian timing and motor praxis. Increased proportion of lapses was further associated with deficits on the majority of cognitive tests, including processing speed, working and episodic memory, visuospatial processing and executive functions. In contrast, none of the other measures of attention, such as mean RT, response variability and presence of impulsive responses (i.e. false alarms) differentiated between patients and controls. These results confirm that sustained attention is a fundamental component to many cognitive processes, a finding previously reported in aging, MCI, AD and sleep deprivation populations [5, 10]. This finding supports the conceptual framework presenting skills as a pyramid, with basic skills situated at the base of the pyramid and subsequently more complex skills at the apex.

Critically, our study shows that above a particular threshold, the presence of attentional lapses reliably discriminates between healthy controls and dementia patients and more so than standard neuropsychological tests. Indeed, while attentional disturbance has been previously found to predict

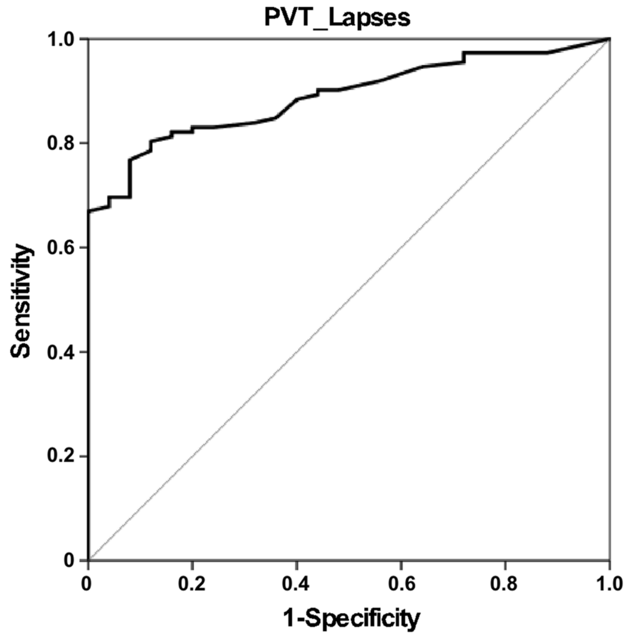

Fig. 3 Receiver operator curve (ROC) demonstrating an area under the curve (AUC) of 0.90 for PVT_Lapses in the diagnosis of dementia patients compared with healthy controls

Table 2 Correlations between PVT_Lapses and neuropsychological tests across all patients

	PVT_Lapses
ACE-III	−0.228*
CDR-FTLD SoB	0.221*
RCF copy	−0.325**
RCF recall	−0.233*
SYDBAT naming	−0.05
Digits-F max	−0.104
Digits-B max	−0.269**
Letter fluency	−0.361**
TMT A (s)	0.599**
TMT B-A (s)	0.480**

Correlations across all patients ($n = 112$)

ACE-III Addenbrooke's Cognitive Examination—Third Edition, *RCF* Rey Complex Figure, *SYDBAT* Sydney language battery, *Digits* Digit Span Forward and Backwards, *TMT* trail making test

*$p < 0.05$; **$p < 0.01$

conversion from MCI to AD [9, 10], here, we demonstrate that the presence of lapses is a sensitive measure of dementia in the FTLD spectrum, as well as in AD. The only test which predicted group membership with greater accuracy than the PVT was the ACE-III, a general cognition screening test, which combines most higher-order cognitive functions but takes 15–20 min to administer and 5–10 min to score [22], compared to 3 min for the PVT.

Attentional lapses appear to reflect a component of attention that is independent from response variability or basic processing speed [1]. Lapses have been linked to perceptual, processing or executive failures, declines of intrinsic alertness, or momentary failures in goal-directed processing [31, 32], and have been associated with detrimental real-life behaviours such as increased traffic accidents [33] and work-related injuries [32]. In clinical populations, increased lapses have been reported in patients with traumatic brain injury (TBI) [34], attention-deficit hyperactivity disorder (ADHD) [35] and AD [6]. Our study provides the first evidence of increased lapses across the FTLD spectrum.

Among all dementia groups, SD was the only group showing similar proportion of lapses compared with controls ($p = 0.16$). Arguably, the number of SD patients was relatively small and standard deviation wide and will need replication with a larger sample. Nevertheless, whether sustained attention is required for naming remains under debate, with mixed evidence [36]. Here, when collapsed across all patients, however, naming did not correlate with the proportion of lapses.

From a biological viewpoint, lapses of attention have been associated with reduced frontoparietal activation [37] and reduced deactivation of the default-mode network [38] which have been hypothesized to reflect inefficient suppression of task-irrelevant processes or allocation of resources towards behaviourally relevant stimuli [37]. Reaction times are also sensitive to frontal lobe lesions [39] and reduced integrity of white matter tracts connecting frontal and parietal regions [40]. Degeneration of the frontal and temporal lobes, and/or basal ganglia is commonly found in AD and FTLD [41]. Presence of increased lapses in ADHD and TBI [34, 35], disorders characterised by frontal dysfunctions/lesions, further underlines the importance of frontal regions and connected networks towards sustained attention capacity.

These findings highlight the potential of the PVT as a screening tool for general cognitive and functional decline in a range of dementia syndromes. The PVT is an attractive time- and cost-effective biomarker as it has the advantages of being portable, easily administered and scored by professionals, applicable to linguistically and culturally diverse populations and minimally affected by aptitude or learning effects [15]. Moreover, the PVT has high ecological validity as it has been associated with risk in real-world and attention-demanding situations such as driving [15]. Altogether, the PVT appears to be an accurate test to rapidly screen and identify individuals in need of further cognitive examination.

The present findings should be considered with some limitations. Undoubtedly, patient groups varied in size. Our main aim, however, was to identify sensitive markers of dementia, broadly defined, based on PVT and neuropsychological tests. Larger sample sizes will be required to investigate group differences and determine within-group correlations with the PVT. Performance decline on the PVT has been previously associated with demographic variables such as older age, female sex or lower education [7] as well as circadian fluctuations or sleep quality [14, 15]. Importantly, however, our results remained unchanged after controlling for these variables, suggesting that the increased proportion of lapses in dementia patients is independent of these factors. In addition, studies using unselected controls, not just "super" controls, will be valuable to fully capture the range of performance of individuals presenting for investigations. Importantly, a recent study showed reliable discrimination between individuals with dementia and those with memory impairment but who do not fulfil the diagnostic criteria for MCI or dementia presenting at memory clinics [8].

Whilst we excluded patients taking medications with potential CNS side effects, we cannot rule out that some medication influenced performance on the PVT by altering motor performance [42, 43] or increasing sustained attention [44]. A recent study showed that prediction of incident dementia based on response time remained significant after adjusting for current medical status including antihypertensive medication [9] suggesting the impact of medication on sustained attention is minor.

Future studies will also need to determine whether an increased proportion of lapses on the PVT is a sensible indicator of future dementia. Promising findings demonstrated that slower RT at study entry increased the risk of developing dementia over 4 years by 60% in non-demented community-living older adults [9].

In conclusion, our study shows that the proportion of lapses on a 3-min simple RT task discriminates with greatest accuracy between patients with dementia and healthy individuals. Such tasks, which can easily be deployed in assessment settings, can therefore, be used as a marker of general cognitive decline indicative of possible dementia.

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Compliance with ethical standards

Conflicts of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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