

A simple EEG visual score is highly associated with the diagnosis of dementia with Lewy bodies in the Amsterdam dementia cohort.

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- Frontal intermittent rhythmic delta activity (FIRDA) combined with slowing of the posterior dominant rhythm (s-FIRDA) was strongly associated with the diagnosis of dementia with Lewy bodies in routine EEGs from the Amsterdam Dementia Cohort (ADC).
- s-FIRDA demonstrated high specificity for DLB, being positive in 18% of cases, compared to only 1.7% of individuals with Alzheimer’s disease (AD) dementia and 0.8% of all the non DLB diagnoses aggregated.
- These performances would come with a positive predictive value (PPV) of around 90% for a diagnosis of DLB vs AD in settings with 50% pre-test probability, with meaningful diagnostic implications.

Background: the diagnosis of dementia with Lewy bodies (DLB) is mainly clinical¹, with disease-specific pathophysiological biomarkers currently lacking. In this context, differential diagnosis from Alzheimer’s disease (AD) is often complicated by overlapping presentation and high rates of AD co-pathology². Previous studies highlighted the potential utility visual EEG analysis in the diagnosis of DLB, by showing more severe dysregulation compared to other dementias, including higher likelihood of slowed dominant rhythm (PDR) and frontal intermittent delta activity (FIRDA)^{3,4,5}. Based on this background, we aimed to test the performance these two visual features combined for the differential diagnosis of DLB, using routine EEGs recorded in the Amsterdam dementia cohort (ADC).

Methods: 4211 individuals from the ADC with available EEG report and CSF status were enrolled (57.3% males). 160 (3.8%) had a diagnosis of DLB. All the EEG reports were searched for the presence of the combination of FIRDA and a slowed PDR below 8 Hz (s-FIRDA). To avoid confounding, FIRDA were only adjudicated if they were described outside clear phases of drowsiness (pure sleep-onset FIRDA were considered negative). Chi-squared tests were used to compare the proportions of positive s-FIRDA in individuals with DLB versus the whole remaining cohort and versus the subgroup with a diagnosis of AD-dementia (n 1211); the relative odds-ratios (OR)s were estimated. Positive predictive value (PPV) of s-FIRDA for the diagnosis of DLB in the full cohort was estimated. Analyses were performed in Rstudio.

Results: Clinical and demographic characteristics of the DLB and AD subcohorts are shown in Table 1. S-FIRDA was found in 18.1% of DLB patients against 0.8% of the remaining cohort, and only 1.7% of the individuals with AD (OR vs non-DLB: 26.1, 95% CI 13.5 – 34.5, p<0.001; OR vs AD: 13.2, 95% CI 7.2-24.0, p<0.001. Figure 1, Table 2). The finding of s-FIRDA had a 46% positive predictive value (PPV) for a diagnosis of DLB in the full cohort (Figure 2).

	DLB (n = 160)	AD (n = 1211)	p
Sex (M/F)	134/26	583/628	< 0.001
Age, mean(SD)	68.5 (6.5)	65 (7.7)	< 0.001
APOE4 carrier (%)	51.3	68.7	< 0.001
MMSE, mean (SD)	22.8 (4.4)	20.2 (5.2)	< 0.001
CDR, median (IQR)	1 (0.5 – 1)	1 (0.5 – 1)	0.9
Fazekas class, median (IQR)	1 (0 – 1)	1 (0 – 1)	0.25
CSF A+ (%)	56.2	100	/

Table 1: Clinical and demographic characteristics of the DLB and AD subgroups. CSF amyloid status is based on Aβ42 peptide level, as assessed by Innotech® or Elecsys®. Difference in continuous and categorical variables were tested with the Wilcoxon and the Chi-squared test, respectively. Abbreviations: Dementia with Lewy bodies (DLB), Alzheimer’s disease (AD), Male (M), Female (F), standard deviation (SD), Mini mental state examination (MMSE), Inter-quartile range (IQR) Clinical dementia rating scale (CDR), Cerebrospinal fluid (CSF)

	DLB	Non DLB
s-FIRDA positive	29	34
s-FIRDA negative	131	4017

Table 2: Confusion matrix for s-FIRDA in the differential diagnosis of dementia with Lewy bodies (DLB) versus non DLB diagnoses.

	DLB	AD
s-FIRDA positive	29	20
s-FIRDA negative	131	1191

Table 3: Confusion matrix for s-FIRDA in the differential diagnosis of dementia with Lewy bodies (DLB) versus Alzheimer’s disease (AD).

Conclusions: The simple EEG score s-FIRDA was associated with a diagnosis of DLB in nearly 50% of cases in the ADC, despite a pre-test probability of only 3.8%, prompting careful DLB consideration when found. Specifically, s-FIRDA was notably more prevalent in DLB compared to AD. If confirmed, these performances would imply more than 90% PPV for the diagnosis of DLB versus AD with a pre-test probability of 50%, underscoring its potential utility in the presence of dementia with suggestive clinical features. In consideration of the EEG affordability and high availability in most clinical and geographical settings, s-FIRDA might assist the diagnosis of DLB when more expensive tests are unavailable.

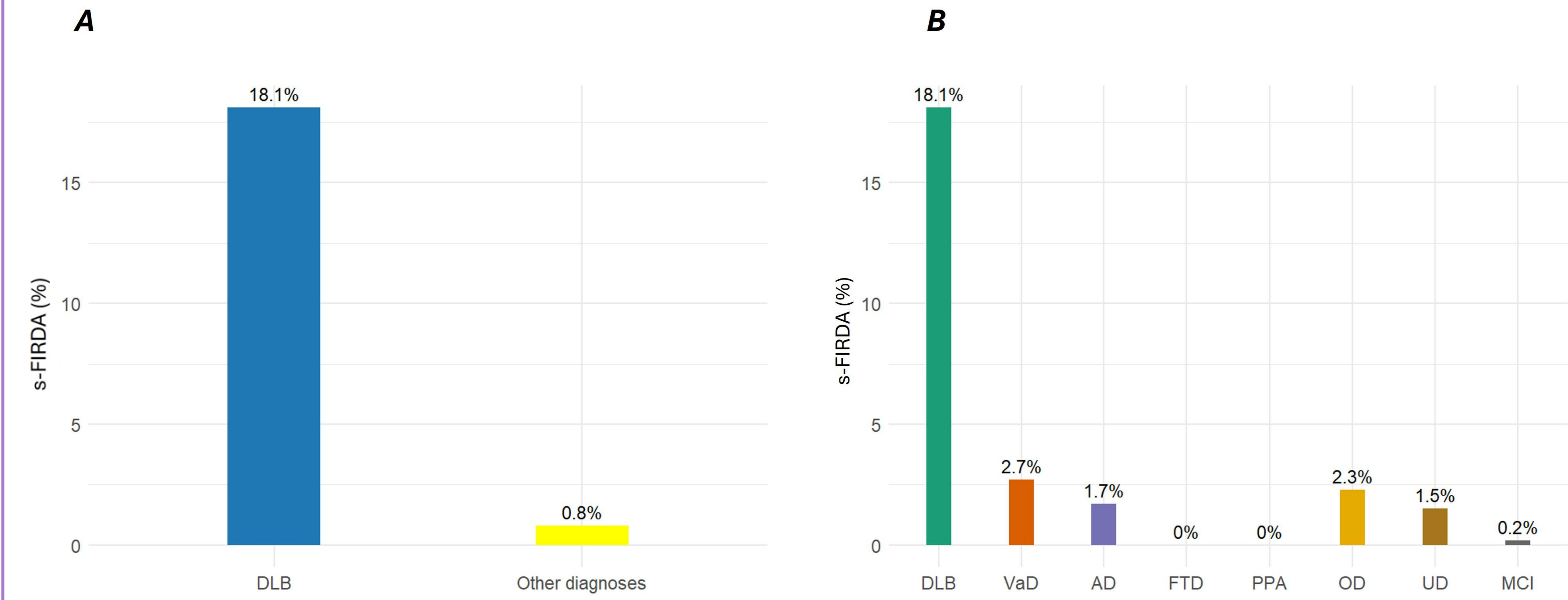


Figure 1: Prevalence of s-FIRDA in the ADC. A) s-FIRDA in the DLB population vs the whole non-DLB cohort; B) Detail of s-FIRDA prevalence in the individual diagnostic subpopulations. Abbreviations: Amsterdam dementia cohort (ADC), Dementia with Lewy bodies (DLB), frontotemporal dementia (FTD), primary progressive aphasia (PPA), other dementia (OD), unclear diagnosis (UD), mild cognitive impairment (MCI)

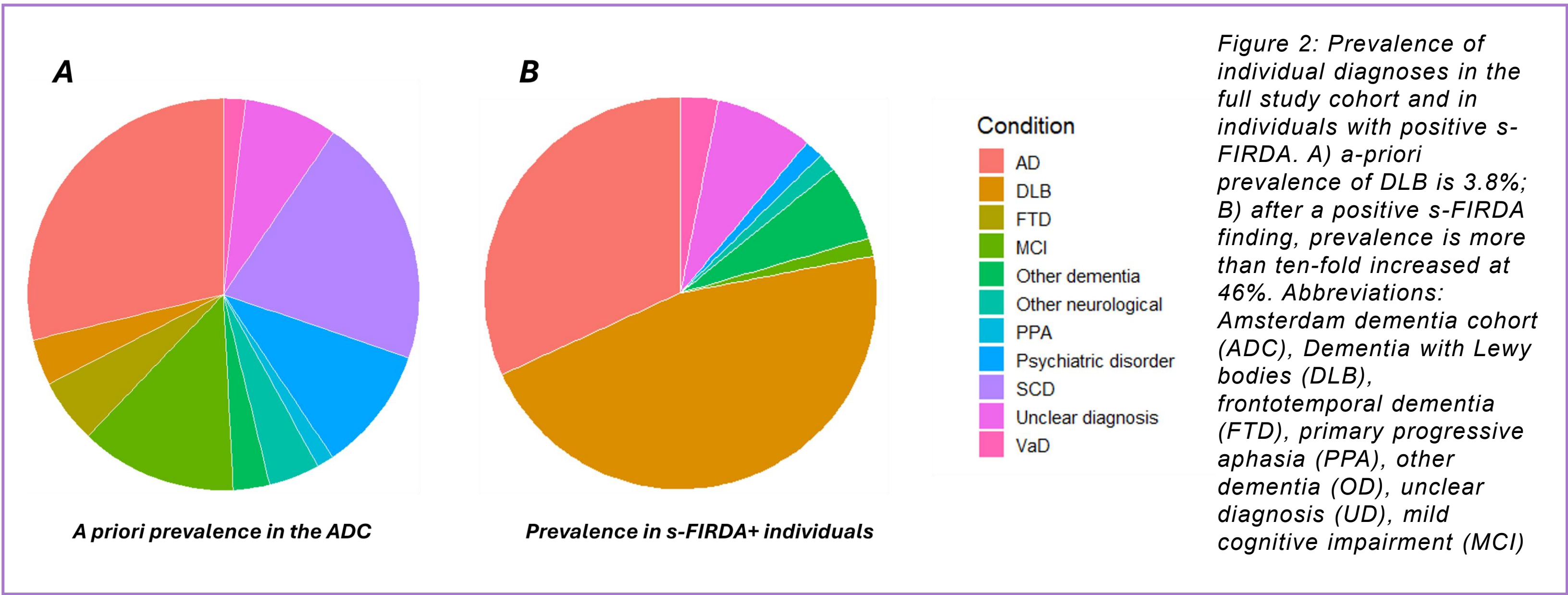


Figure 2: Prevalence of individual diagnoses in the full study cohort and in individuals with positive s-FIRDA. A) a-priori prevalence of DLB is 3.8%; B) after a positive s-FIRDA finding, prevalence is more than ten-fold increased at 46%. Abbreviations: Amsterdam dementia cohort (ADC), Dementia with Lewy bodies (DLB), frontotemporal dementia (FTD), primary progressive aphasia (PPA), other dementia (OD), unclear diagnosis (UD), mild cognitive impairment (MCI)

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