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Predicting the Emergence of Primary Progressive Aphasia Variants from Unclassifiable Language Test Performance

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Introduction

For the majority of patients, primary progressive aphasia (PPA) is distinguished into one of three variants: semantic variant, non-fluent/agrammatic variant, or logopenic variant (Gorno-Tempini et al., 2011). However, 10-41% of individuals who meet consensus criteria for a diagnosis of PPA do not meet criteria for any one variant for a variety of reasons (Gil-Navarro et al., 2013; Harris et al., 2013; Matias-Guiu et al., 2014; Mesulam et al., 2012; Sajjadi et al., 2014; Wicklund et al., 2014). The ability to predict the eventual course of disease can provide valuable early information for care teams and families to assist in planning and managing expectations about the future. The aim of the present work was to determine whether performance during comprehensive cognitive-linguistic evaluation in which a patient receives an early unclassifiable PPA designation predicted the later emergence of a given variant.

Methods

Nineteen English-speaking individuals with an initially unclassifiable variant of PPA were identified from a pool of 256 patients who were followed in the outpatient clinic every 6 to 12 months until features sufficient to identify a variant emerged, often by the next visit. Patients were evaluated using a modified version of the National Alzheimer's Coordinating Center Uniform Dataset standardized evaluation battery frontotemporal lobar degeneration (FTLD) module version 2.0 (<https://nacccdata.org/data-collection/forms-documentation/ftld-2>), as well as the Hopkins Action Naming Assessment (HANA; Breining et al., in press), 30-item short form of the Boston Naming Test (BNT; Williams et al., 1989), 14-item Pyramids and Palm Trees Test (Breining et al., 2015; Howard & Patterson, 1992), 15-item Kissing and Dancing Test (Bak & Hodges, 2003), and the Berndt picture-word verification of nouns and verbs (Berndt et al., 1997; Breese & Hillis, 2004; Breining, 2011). Receiver operating characteristic curves were used to evaluate the binary ability of a given task to predict eventual classification as a given variant. Tasks with a high average area under the curve (AUROC ≥ 0.75 ; Hosmer et al., 2013) then were examined using regression analyses to determine their ability to predict variant among the three. Finally, in an exploratory examination, optimal cut-point scores were identified for any task that proved to be a significant independent factor in predicting variant using the regression analysis.

Results

High mean AUROC was observed for the written noun naming subtest of the FTLD module, BNT, HANA, and Berndt picture-word verification of verbs (Table 1). The BNT was the only test that, in isolation, resulted in a significant model, $\chi^2(32) = 49.91$, $p = 0.02$, and

high accuracy in classification. Optimal cut-point scores to identify each variant using the BNT were identified (Figure 1). A normal score of 28/30 or higher best predicted nfavPPA. Below 18/30 best predicted svPPA. LvPPA was best identified by a score of 20/30 or greater but did not perform as well at that cut-point.

Conclusions

Word-finding tasks performed best in parsing between eventual variants, despite this being a common deficit in PPA. The 30-item BNT emerged as a uniquely accurate basis for predicting which variant would emerge.

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Table 1: Predicting future classifications from task performance

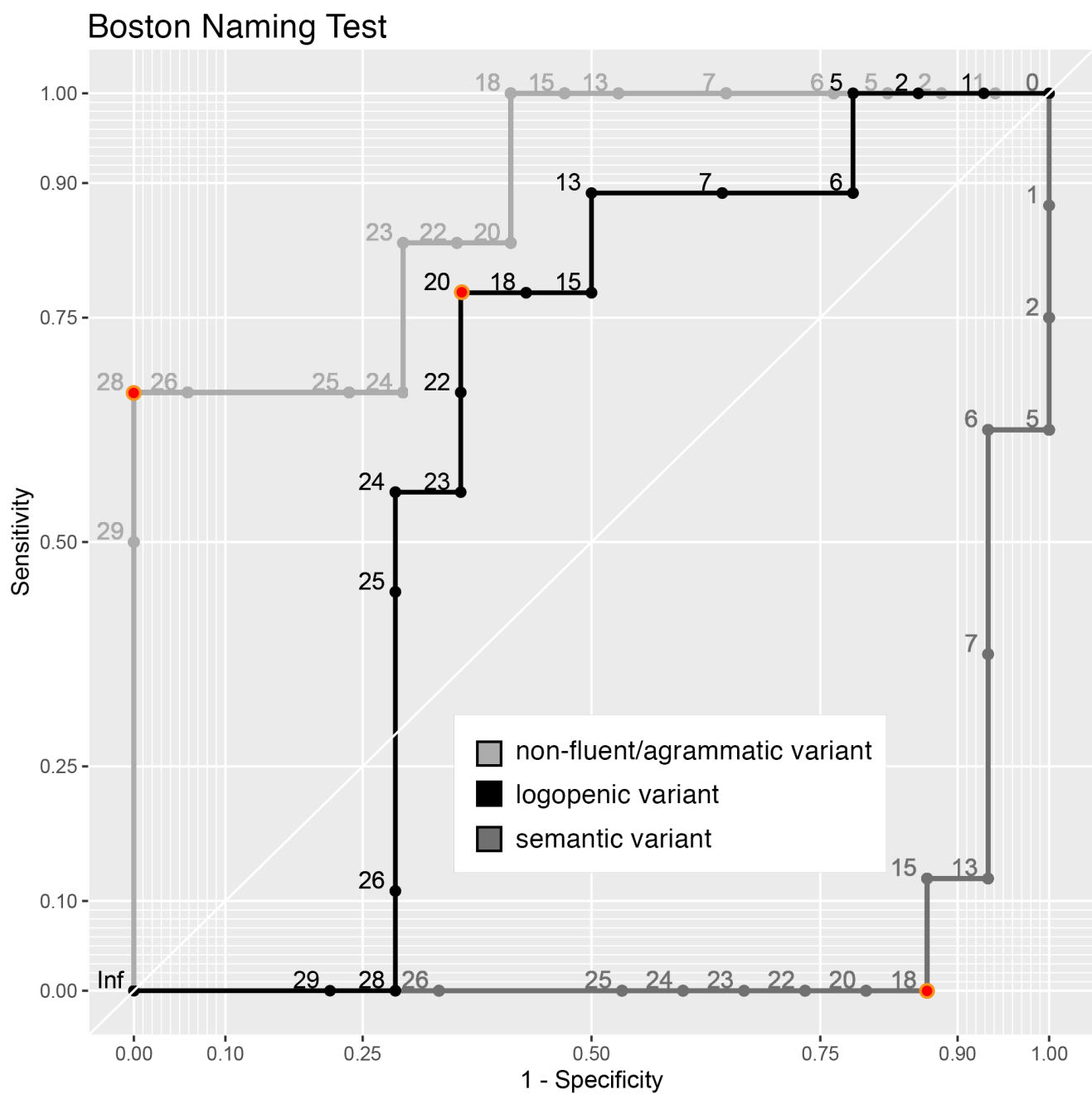
Assessment	lvPPA	nfavPPA	svPPA	Mean AUROC
Written noun naming*	0.74	0.74	0.98†	0.82
BNT*	0.62	0.88	0.95†	0.82
HANA*	0.65	0.76	0.92†	0.78
Berndt picture-word verification - verbs*	0.93	0.54†	0.85†	0.77
Oral noun naming	0.61	0.75	0.84†	0.73
Benson delayed figure copy	0.73	0.73	0.73†	0.73
Written verb naming	0.80	0.54	0.84†	0.73
Berndt picture-word verification - nouns	0.73	0.62	0.83†	0.72
Verbal fluency	0.85	0.59†	0.70†	0.72
Oral reading	0.67	0.67	0.81†	0.71
Semantic association	0.58	0.73	0.78†	0.70
Pyramids & Palm Trees	0.65	0.64	0.79†	0.70
Oral verb naming	0.68	0.58	0.76†	0.67
Semantic word picture matching	0.68	0.58	0.72†	0.66
Sentence repetition	0.60	0.62	0.69†	0.64
Sentence reading	0.67	0.58†	0.57†	0.61
Benson direct figure copy	0.67	0.58†	0.58†	0.61
Kissing & Dancing	0.59	0.56	0.63†	0.59

AUROC: Area under the receiver operating characteristics curve.

*Tests with a mean AUROC of ≥ 0.75 . All tests with at least one AUROC value ≥ 0.75 are bolded.

†ROC curves were inverted to calculate maximum AUROC. Lower performance was associated with greater predictive accuracy.

Figure 1: Boston Naming Test receiver operating characteristics curves by variant



Optimal cut-point scores are marked in red.