Utility of Event Related Potentials in a Memory Disorders Clinic

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Background

Event related potentials (ERPs) are a type of quantitative electroencephalogram (EEG) that may be a potential biomarker of Alzheimer's disease. ERP measures differ between mild AD patients and healthy older adults, and between patients with mild cognitive impairment due to AD versus those with MCI due to other etiologies. We investigate the sensitivity and specificity of ERPs as a potential biomarker of amyloid PET status.

Objectives

Explore sensitivity and specificity of neuropsychological measures and ERP to predict amyloid PET status
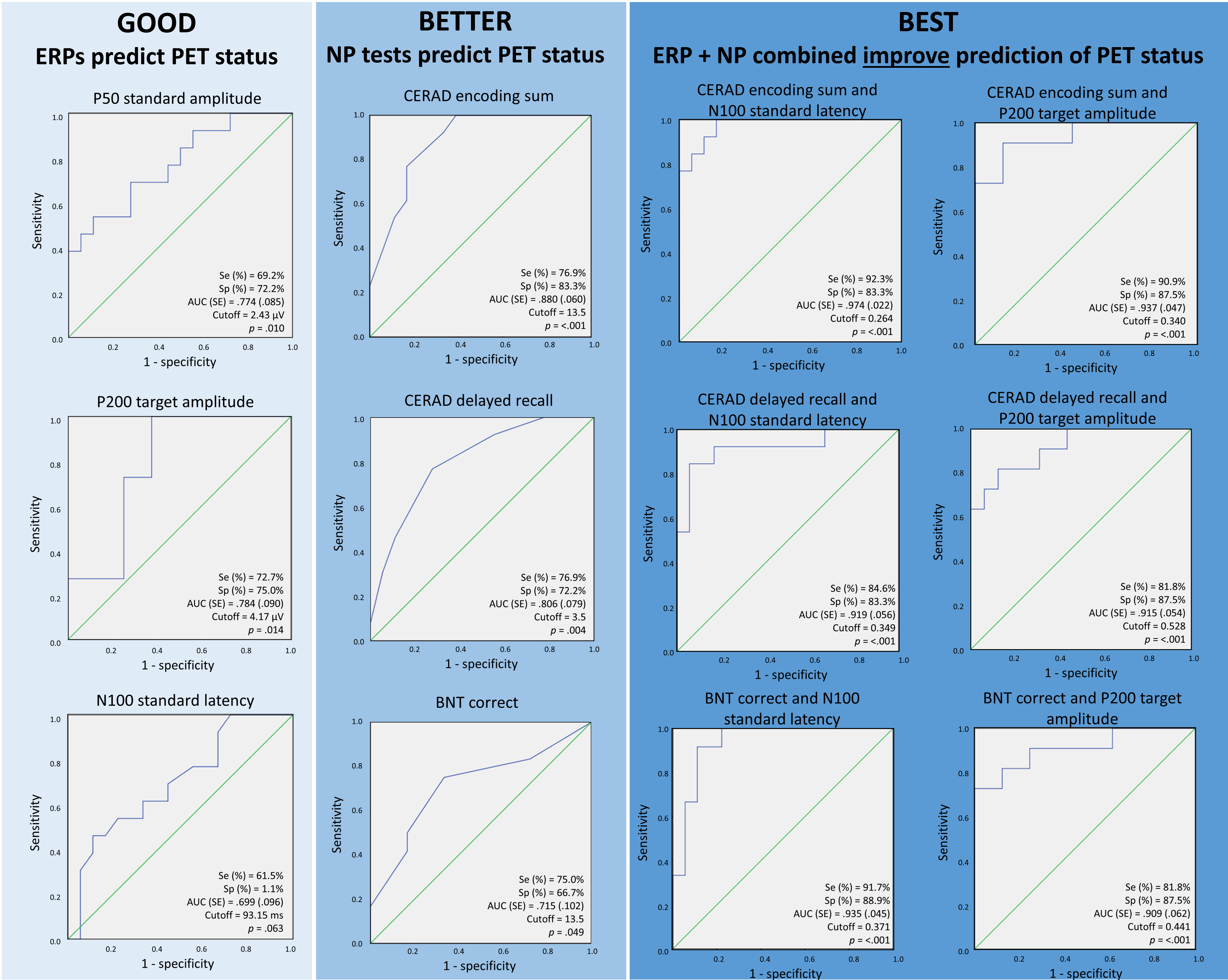
Methods

Thirty-one subjects who presented with memory loss underwent standard clinical workup including a neuropsychological (NP) battery, florbetapir positron emission tomography (PET), and an EEG with a three-tone auditory oddball task using a 10-electrode COGNISION™ rig. Predictive abilities of PET status was measured in individual ERP measures using bivariate logistic regression controlling for age, education, and medication status on SPSS (ver. 20). Significant ERP predictors were analyzed using receiver operating characteristic (ROC)-curves and logistic regression. Predictive abilities of ERP and NP combinations were analyzed individually using bivariate logistic regression (see chart 1).

Table 1. Descriptive statistics between groups.

Characteristics	PET− (n=18)	PET+ (n=13)
Age	66.1 (1.8)	67.1 (1.9)
Years of Education	14.1 (0.7)	13.5 (0.7)
MOCA*	22.1 (1.1)	16.0 (1.6) [p = .003]
MMSE*	26.0 (0.6)	22.2 (1.1) [p = .004]
Button press accuracy (%)	88.7 (3.5)	84.9 (5.2)
False alarms (%)	1.1 (0.3)	1.1 (0.3)
Median reaction time (ms)	448.7 (25.8)	524.6 (39.6)

* denotes significance <.05

GOOD
ERPs predict PET status

P50 standard amplitude
Se (%) = 69.2%
Sp (%) = 72.2%
AUC (SE) = .774 (.085)
Cutoff = 2.43 µV
p = .010

P200 target amplitude
Se (%) = 72.7%
Sp (%) = 75.0%
AUC (SE) = .784 (.090)
Cutoff = 4.17 µV
p = .014

N100 standard latency
Se (%) = 61.5%
Sp (%) = 1.1%
AUC (SE) = .699 (.096)
Cutoff = 93.15 ms
p = .063

BETTER
NP tests predict PET status

CERAD encoding sum
Se (%) = 76.9%
Sp (%) = 83.3%
AUC (SE) = .880 (.060)
Cutoff = 13.5
p = <.001

CERAD delayed recall
Se (%) = 76.9%
Sp (%) = 72.2%
AUC (SE) = .806 (.079)
Cutoff = 3.5
p = .004

BNT correct
Se (%) = 75.0%
Sp (%) = 66.7%
AUC (SE) = .715 (.102)
Cutoff = 13.5
p = .049

BEST
ERP + NP combined <u>improve</u> prediction of PET status

CERAD encoding sum and N100 standard latency
Se (%) = 92.3%
Sp (%) = 83.3%
AUC (SE) = .974 (.022)
Cutoff = 0.264
p = <.001

CERAD encoding sum and P200 target amplitude
Se (%) = 90.9%
Sp (%) = 87.5%
AUC (SE) = .937 (.047)
Cutoff = 0.340
p = <.001

CERAD delayed recall and N100 standard latency
Se (%) = 84.6%
Sp (%) = 83.3%
AUC (SE) = .919 (.056)
Cutoff = 0.349
p = <.001

CERAD delayed recall and P200 target amplitude
Se (%) = 81.8%
Sp (%) = 87.5%
AUC (SE) = .915 (.054)
Cutoff = 0.528
p = <.001

BNT correct and N100 standard latency
Se (%) = 91.7%
Sp (%) = 88.9%
AUC (SE) = .935 (.045)
Cutoff = 0.371
p = <.001

BNT correct and P200 target amplitude
Se (%) = 81.8%
Sp (%) = 87.5%
AUC (SE) = .909 (.062)
Cutoff = 0.441
p = <.001

Results

◀ ROC analyses were carried out with ERP and NP variables that were individually found to be significant predictors of PET status. Combined ROC analyses were conducted using predictive probabilities obtained from logistic regression containing both ERP and NP variables and controlling for age, education, and medication status (donepezil).

Chart 1. Predicting PET status combining NP and ERP.

		β (SE)	Wald	p	Odds ratio	95% CI Lower	95% CI Upper
A ^*	CERAD encsum	-1.628 (0.985)	2.730	.098	0.196	0.028	1.354
	N100 std lat	0.216 (0.120)	3.208	.073	1.241	0.980	1.570
B ^*	CERAD encsum	-0.695 (0.373)	3.474	.062	0.499	0.240	1.036
	P200 tgt amp	0.614 (0.384)	2.548	.110	1.847	0.869	3.924
C ^*	CERAD delayed	-0.992 (0.591)	2.815	.093	0.371	0.116	1.181
	N100 std lat	0.092 (0.048)	3.705	.054	1.097	0.998	1.204
D ^	CERAD delayed	-0.953 (0.509)	3.514	.061	0.385	0.142	1.044
	P200 tgt amp	0.505 (0.299)	2.856	.091	1.658	0.922	2.979
E ^*	BNT correct	-0.649 (0.374)	3.005	.083	0.523	0.251	1.089
	N100 std lat	0.118 (0.054)	4.705	.030	1.125	1.011	1.251
F ^*	BNT correct	-0.747 (0.392)	3.641	.056	0.474	0.220	1.020
	P200 tgt amp	0.630 (0.336)	3.524	.060	1.878	0.973	3.628

^ model p <.005 ; * block p < .05 when ERP is added onto the NP regression model (block significance); D trends toward significance (p = .055). Each model run independently controlling for age, education, Donepezil (block 1), NP only (block 2), ERP (block 3).

Conclusions

- When assessed independently, ERP measures did not predict PET status more sensitively or specifically than NP tests alone
- The utility of N100 and P200 may be in combination with other aspects of the neurological workup
- Results suggest that early ERP waveforms which are typically thought of as stereotyped responses may provide valuable information regarding underlying amyloid pathology
- Future efforts will evaluate how ERP features align with other biomarkers of neurodegeneration including quantitative MRI cortical volume measurements