

Does Low Level of HIV Viral Replication in the CSF Relate to Neuropsychological Outcomes for People on Suppressive ART?

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1 Research Question

Does low level of HIV viral replication in the CSF (1) relate to neuropsychological outcomes (2) for people on suppressive ART (3)?

- 1) A viral load in CSF that is undetectable by the standard assay but detectable by the sensitive assay (roughly 8 cop/ml to 40 cop/ml).
- 2) Outcomes in terms of inflammatory biomarkers, neural injury, and neuropsychological functions.
- 3) On antiretroviral therapy (ART) with plasma viral load ≤ 100 cop/ml for more than 1 year.

2 Methods

Data Collection Plan

- 3 inclusion criteria: Adults (≥ 18 yrs) with confirmed HIV infection who has been on suppressive ART for more than 1 year.
- 3 sites: UNC, Yale, and UCSF
- 2 types of data:
 - Cross-sectional (individuals who, at the time of enrollment, satisfy the inclusion criteria.)
 - Longitudinal (individuals who, at the time of enrollment, are naive to ART. They will be followed for 1 year to decide whether to be included or not.)

For those enrolled, viral load in plasma and in CSF will be measured using a standard assay. At the same time, biomarkers are measured, and neuropsychological tests are performed. If the CSF viral load is undetectable by the standard assay, a sensitive assay will be performed.

Analysis Plan

- Independent variable: Categories by CSF viral load
- Dependent variable: Biomarkers and neuropsychological tests
- Correlation Measure: Kendall's Tau (Non-parametric, rank-based)
- Hypothesis Test: Kruskal-Wallis (Non-parametric equivalence of ANOVA)

3 Analysis Population

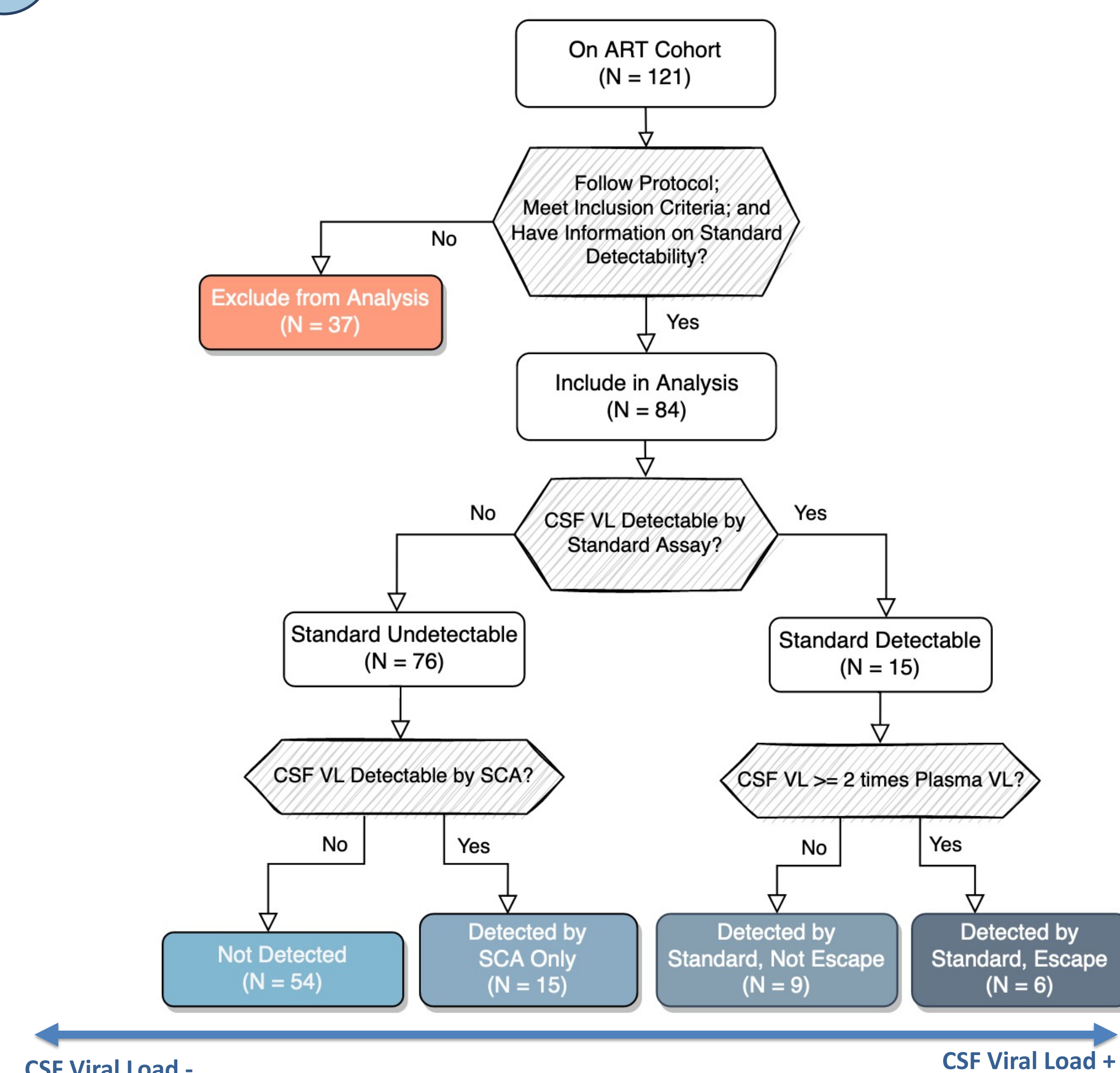
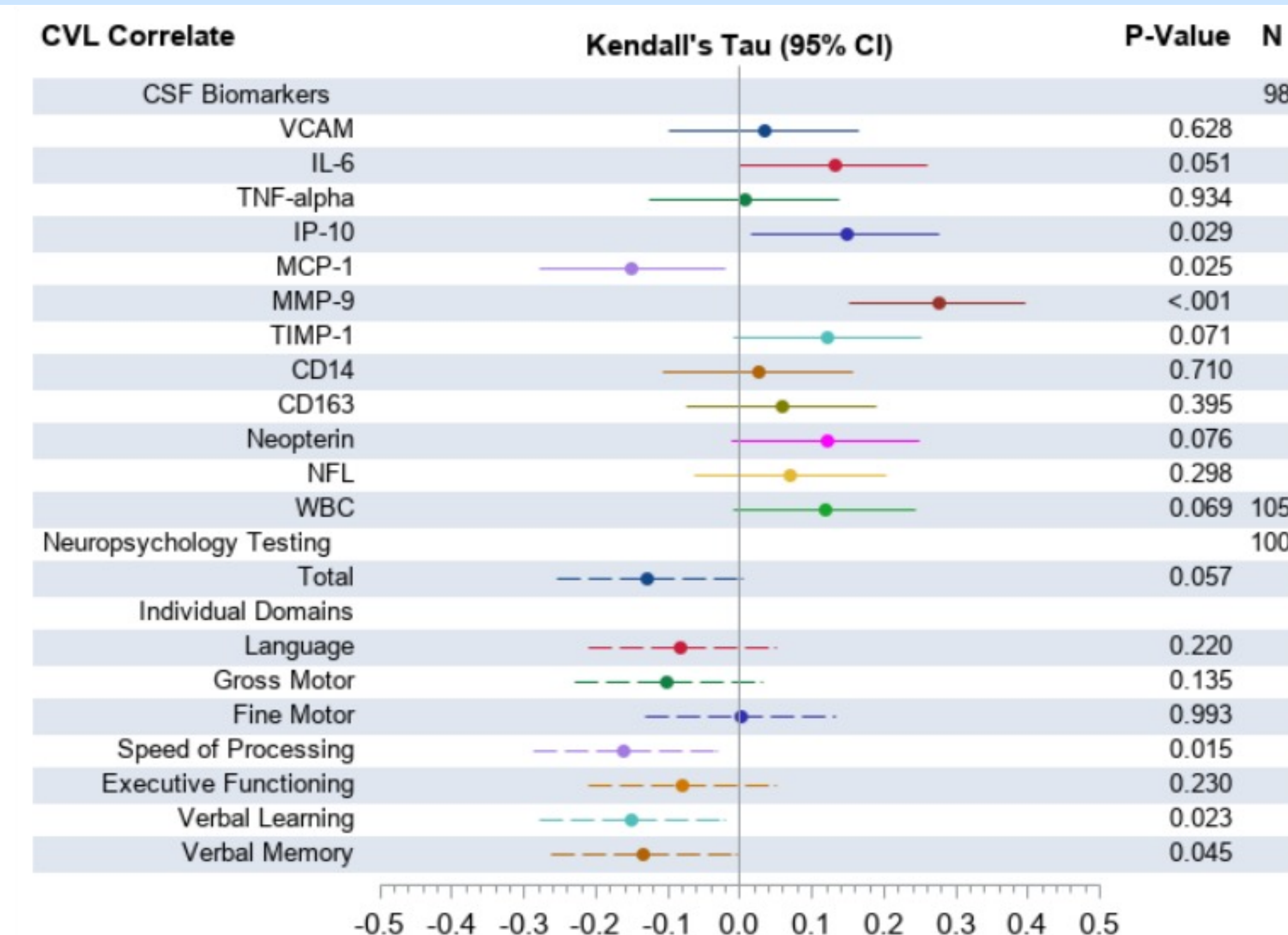


Table 1: Demographics of Analysis Population

| | Not Detected (N=54) | Detected by SCA Only (N=15) | Detected by Standard, Not Escape (N=9) | Detected by Standard, Escape (N=6) | P-Value |
|----------------------------------|------------------------|-----------------------------------|---|---|---------|
| Characteristic | | | | | |
| Age, median (IQR) | 51 (44, 54) | 48 (36, 63) | 48 (45, 52) | 50 (42, 54) | 0.6581 |
| Sex at Birth, n (%) | | | | | |
| Male | 46 (85.2%) | 12 (80.0%) | 7 (77.8%) | 5 (83.3%) | 0.8781 |
| Female | 8 (14.8%) | 3 (20.0%) | 2 (22.2%) | 1 (16.7%) | |
| Race, n (%) | | | | | |
| Black | 27 (50.0%) | 6 (40.0%) | 5 (62.5%) | 3 (50.0%) | 0.5961 |
| White | 25 (46.3%) | 9 (60.0%) | 3 (37.5%) | 2 (33.3%) | |
| Other | 2 (3.7%) | 0 (0.0%) | 0 (0.0%) | 1 (16.7%) | |
| Ethnicity, n (%) | | | | | |
| Not Hispanic | 51 (94.4%) | 15 (100.0%) | 8 (88.9%) | 5 (83.3%) | 0.2813 |
| Hispanic | 3 (5.6%) | 0 (0.0%) | 1 (11.1%) | 1 (16.7%) | |
| Years of Education, median (IQR) | 14 (12,16) | 12 (12,17) | 12 (10,14) | 12 (12,13) | 0.2612 |

4 Results

Figure 1: Correlation between Neuropsychological Outcomes and CSF Viral Load



* For Neuropsychological Testing, the population is restricted to those having a total Z score; Those incapable of completing certain domain batteries are excluded. Thus, the results might be biased towards the null.

Figure 2: TNF-a, IL-6, and MMP-9 by CVL Categories

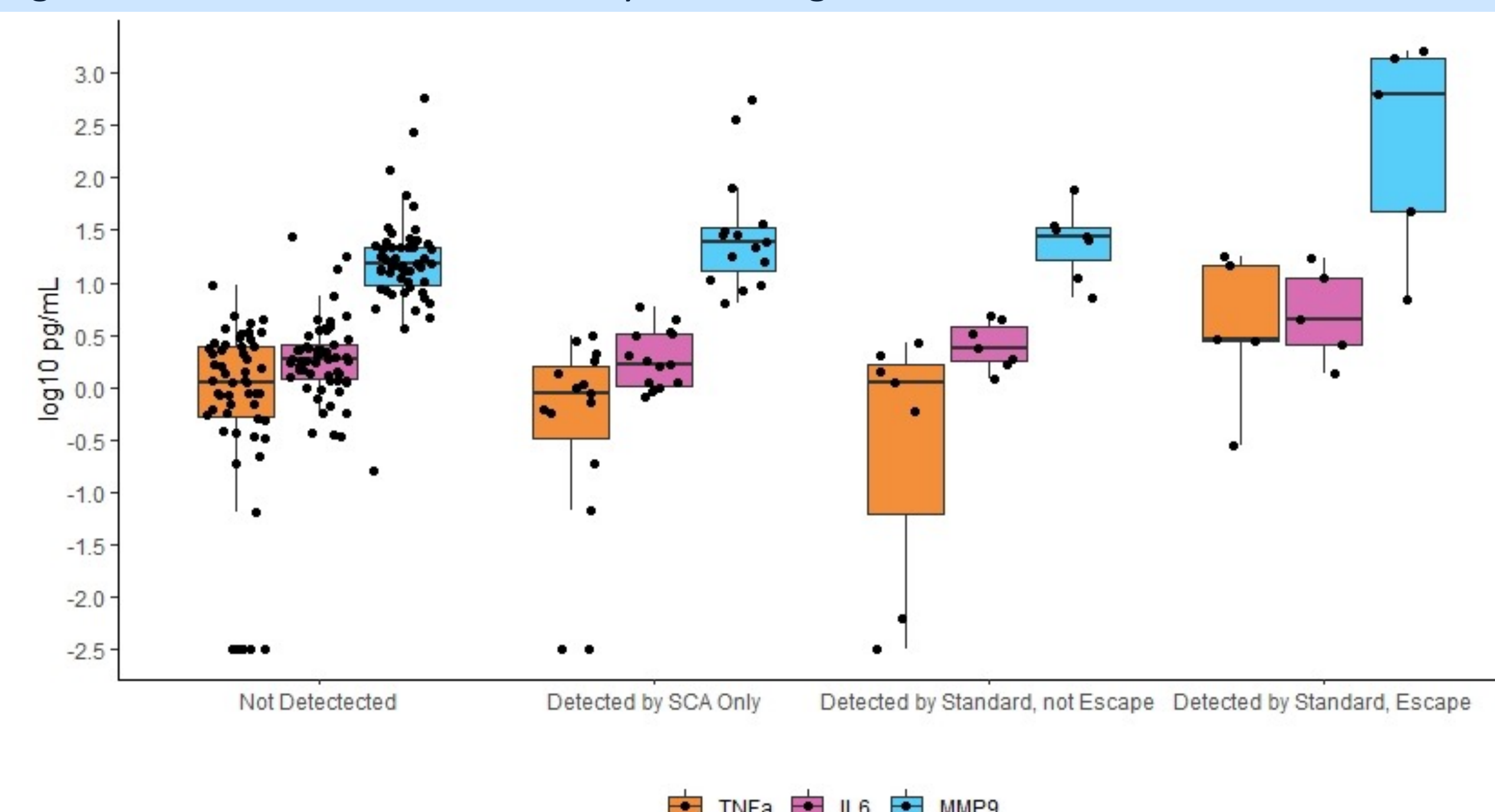


Figure 3: IP-10, MCP-1, and NFL (Age Corrected) by CVL Categories

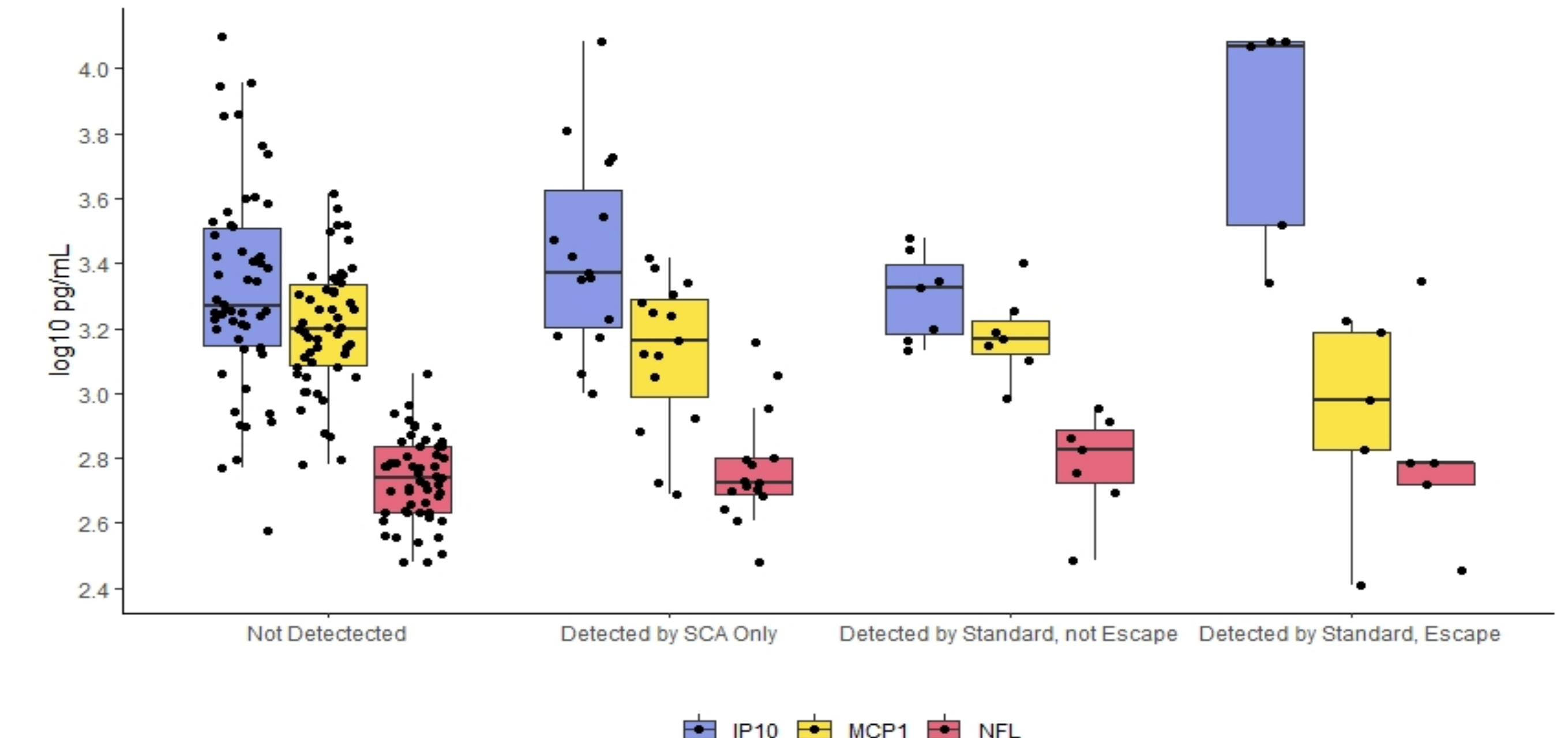


Figure 4: Neopterin by CVL Categories

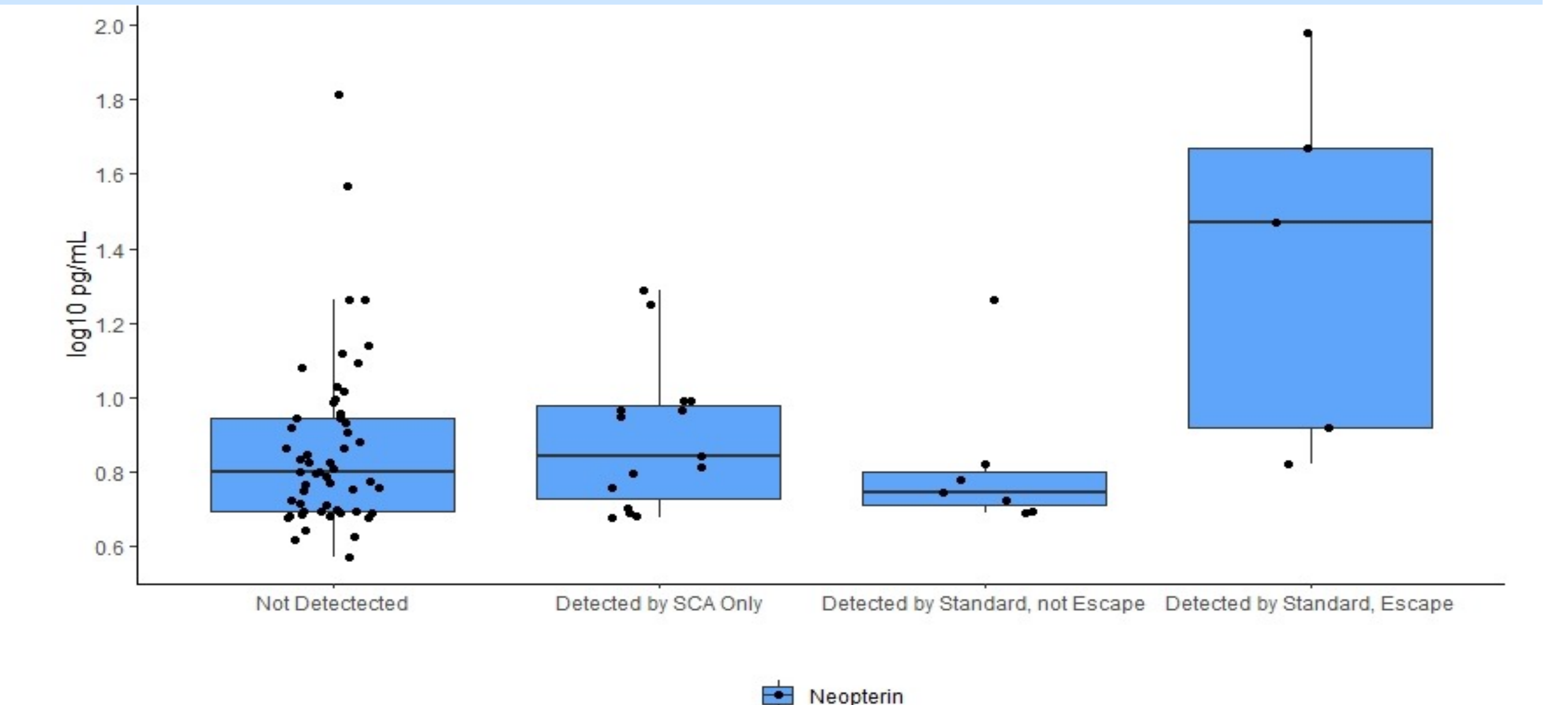
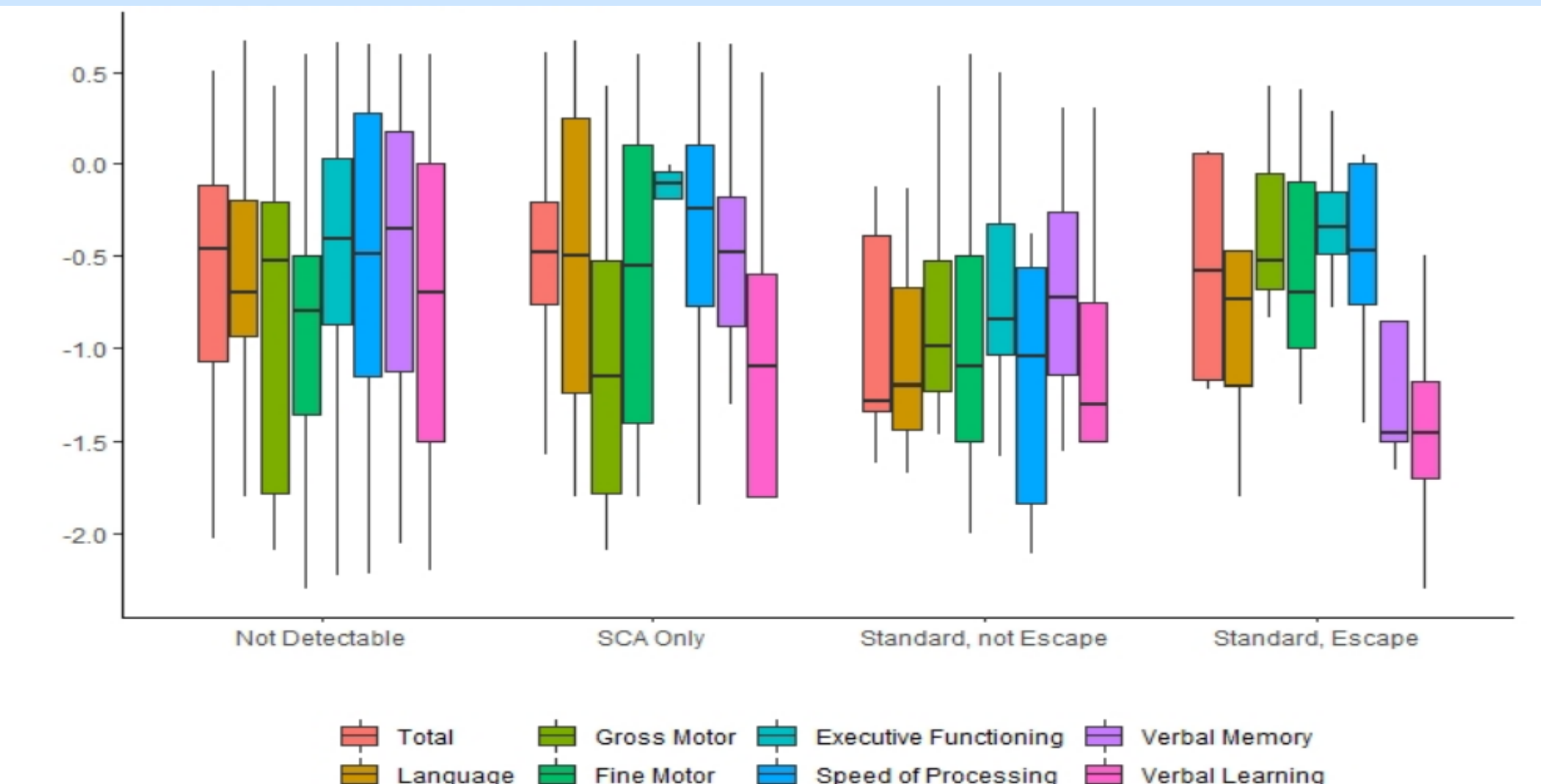


Figure 5: Neuro-physiological Testing Scores by CVL Categories



5 Conclusions & Next Steps

- Does any relation exist?
 - Probably not. There is not enough evidence to support significant correlations.
 - The significant biomarkers (TNF α and IP-10) shown in Figure 1 might be due to values at the limit of quantification. MMP-9 showed Escape as a different category, but given the limited sample size, it is questionable whether a conclusion can be reached.
- Major concerns & Further investigation?
 - Unbalanced categories and small sample sizes; Measurements at the limit of quantification; Definition of Escape and whether we should consider them as a separate category; Ambiguous unit of measure for some data entries.