

Treball de Fi de Màster

## Neuroenginyeria I Rehabilitació

# Electrocardiographic markers for cognitive decline detection.

### ANNEXES

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**Convocatòria:** 01.2023



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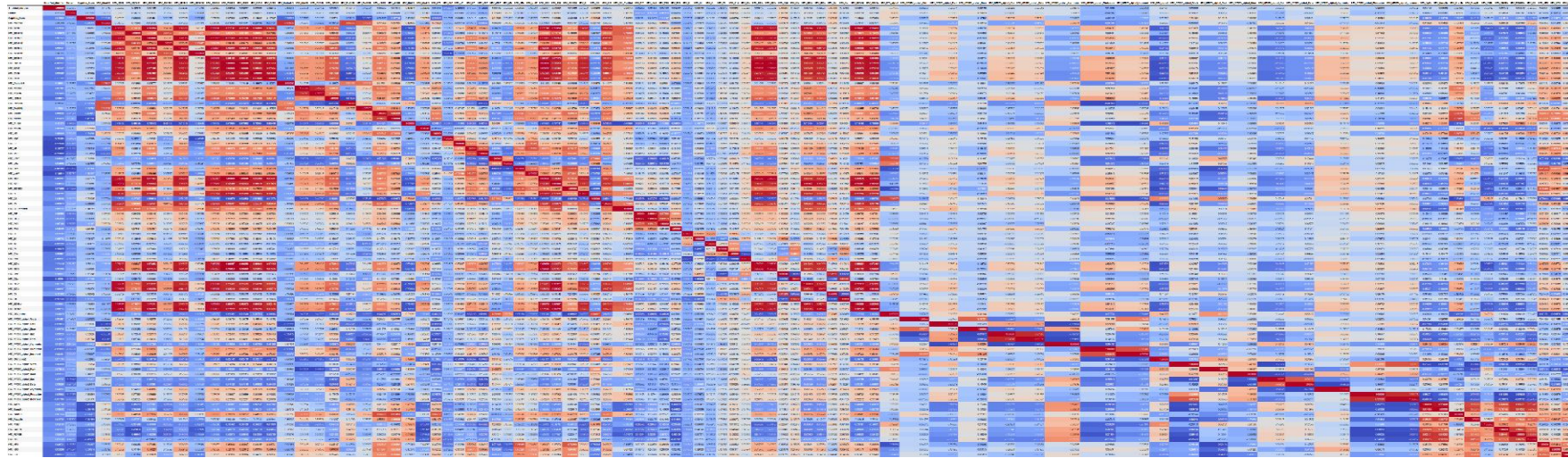
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# 1. Python packages used.

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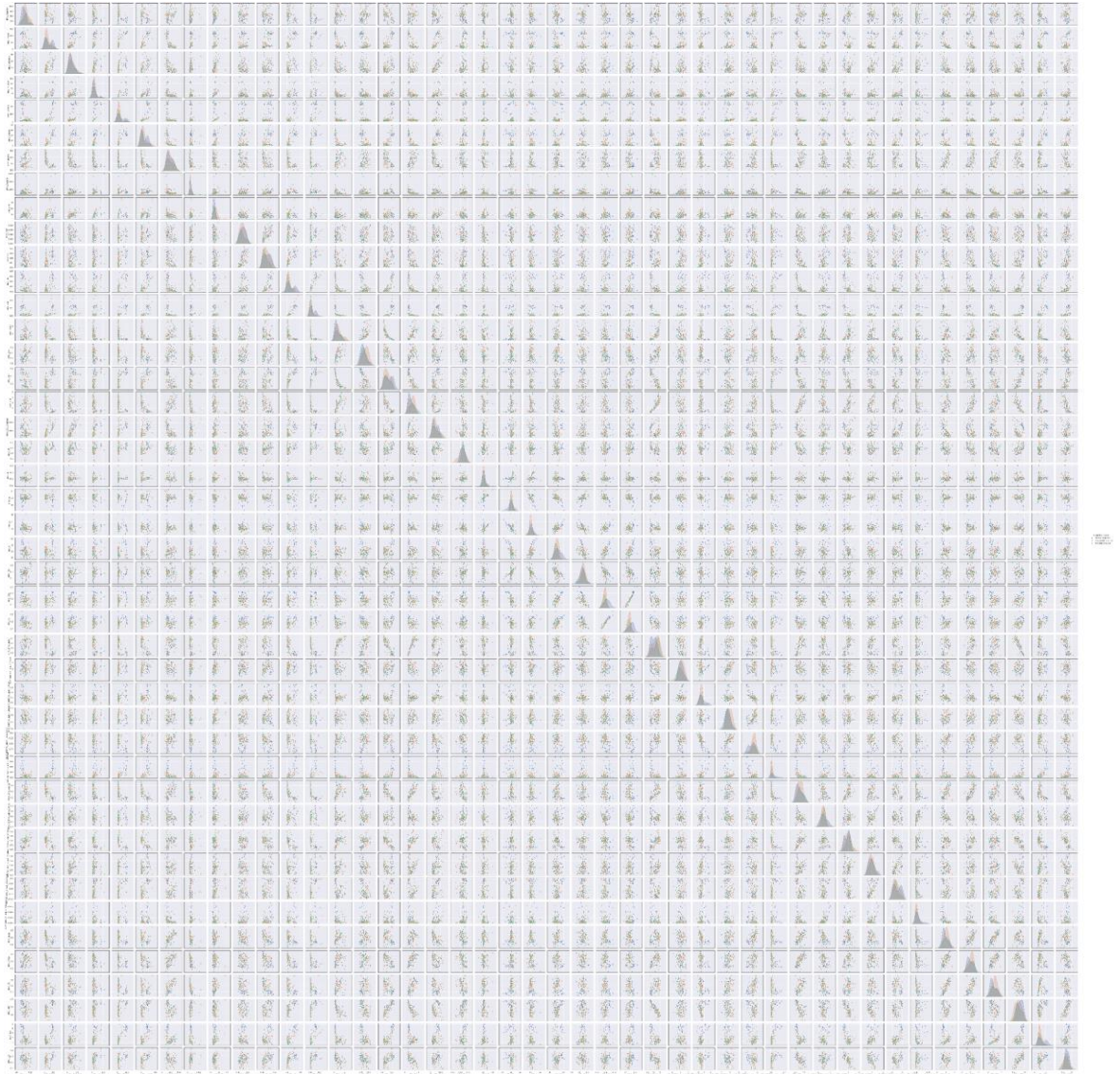
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## 2. Correlation matrix



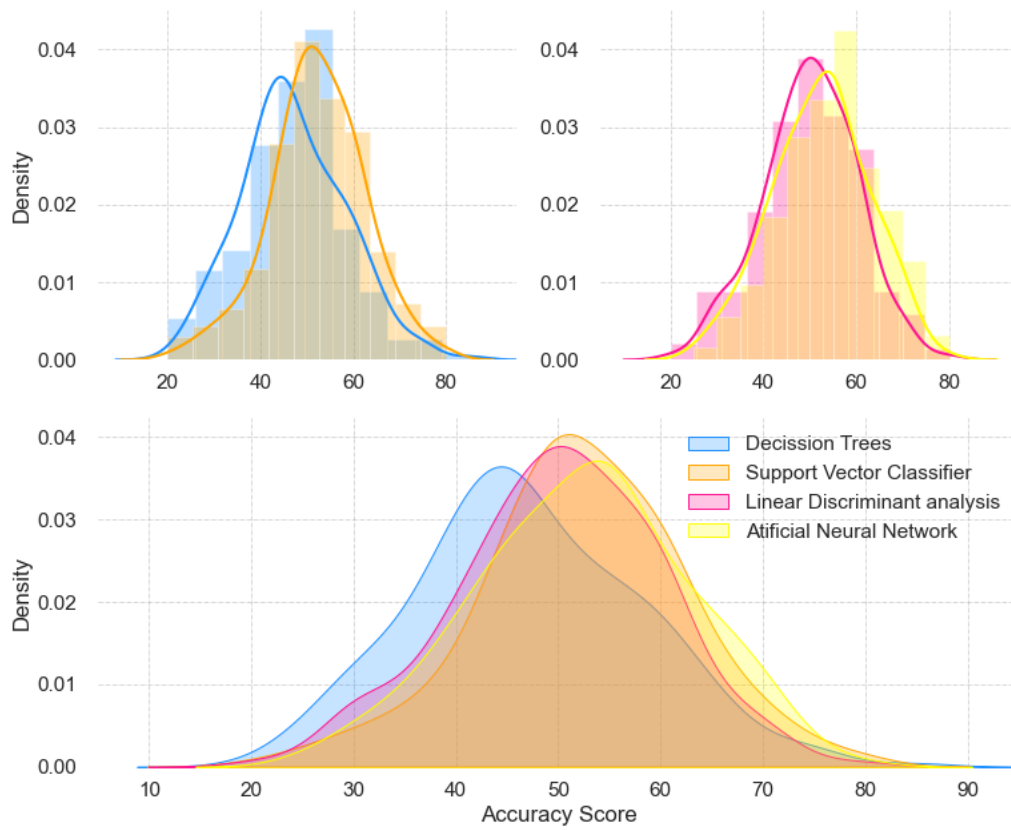
**Figure 1:** Correlation matrix of the total number of HRV extracted markers.  
 (Unfortunately, the maximum resolution allowed in PDF does not enable a clear view of this image).

### 3. Scatter Plot of Uncorrelated Markers



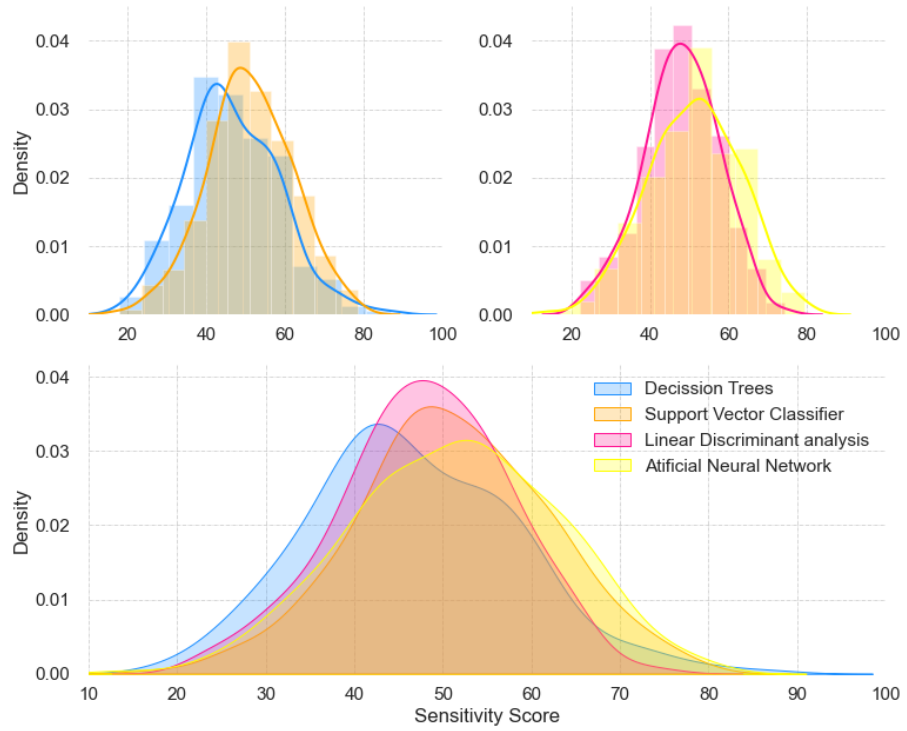
**Figure 2:** Scatter plot of the uncorrelated markers for the Elderly population of the Lemon database. (Unfortunately, the maximum resolution allowed in PDF does not enable a clear view of this image)

## 4. Cross Fold Validation

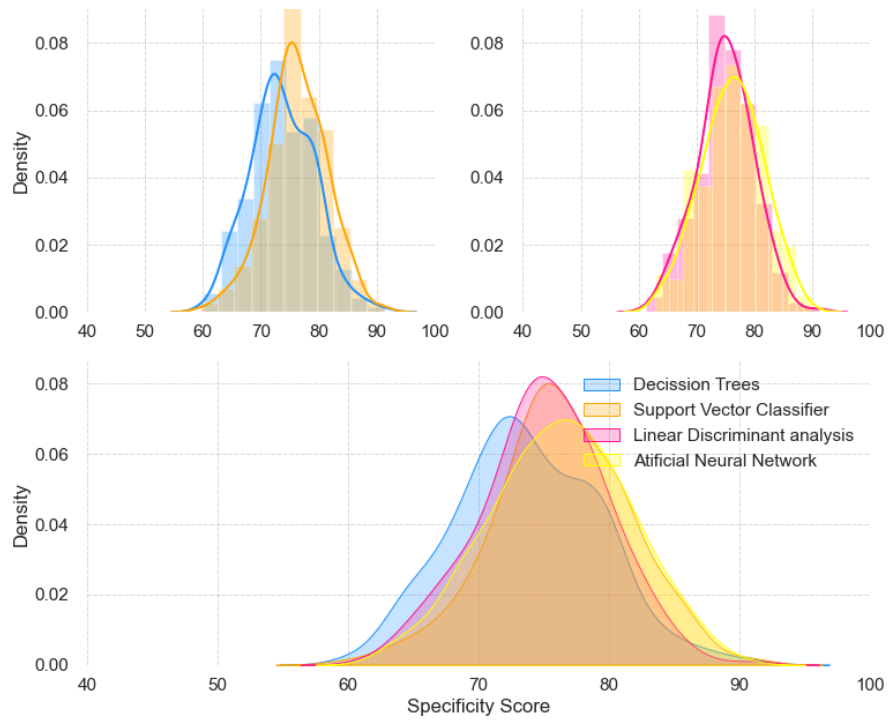


**Figure 3:** Averaged Cross Fold Accuracy Score (with PCA)

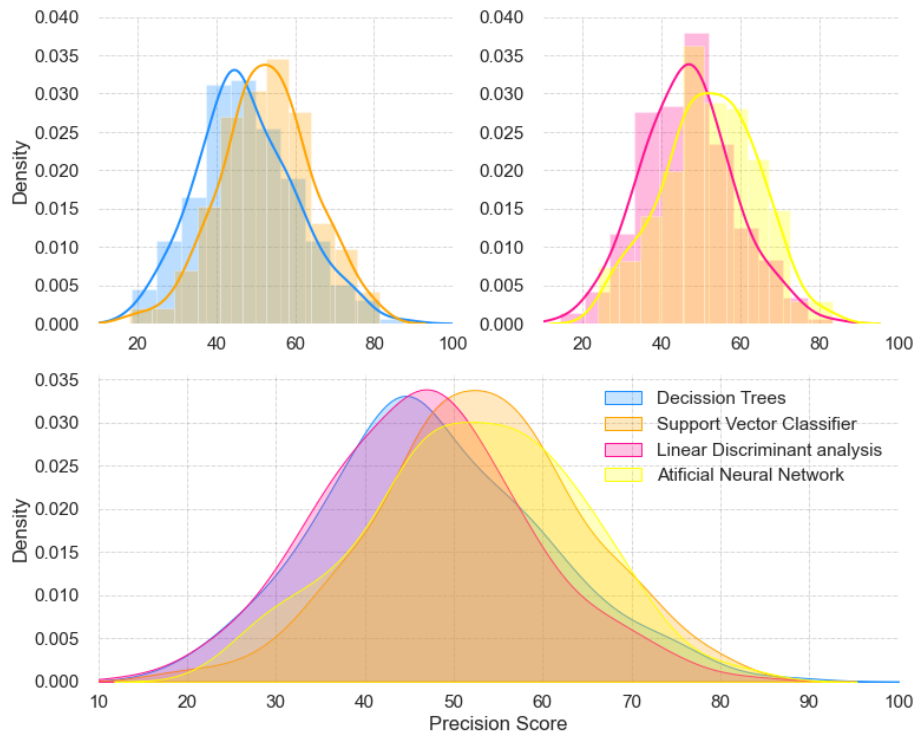




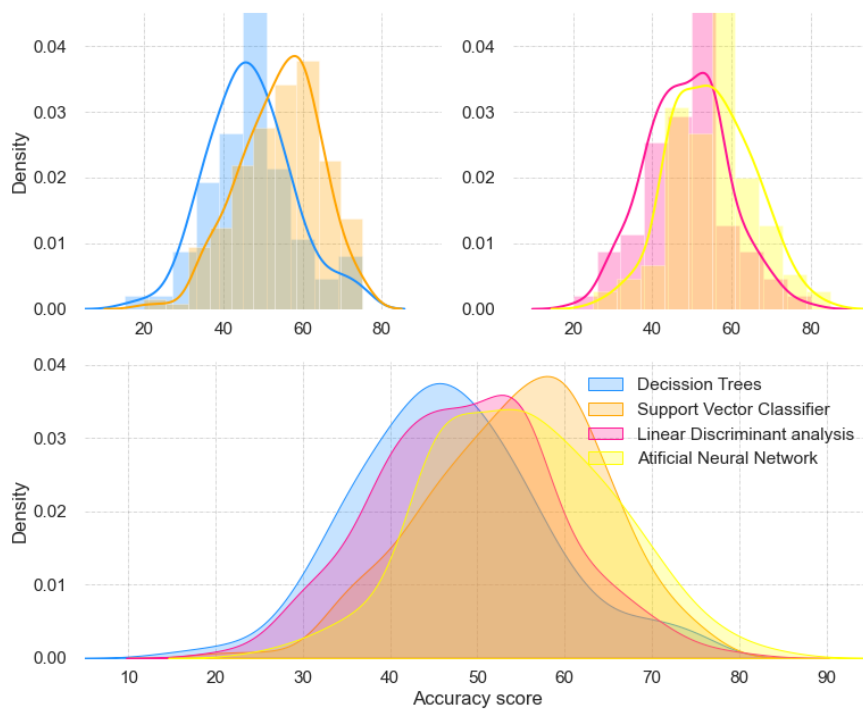
**Figure 4:** Averaged Cross Fold Sensitivity Score (with PCA)



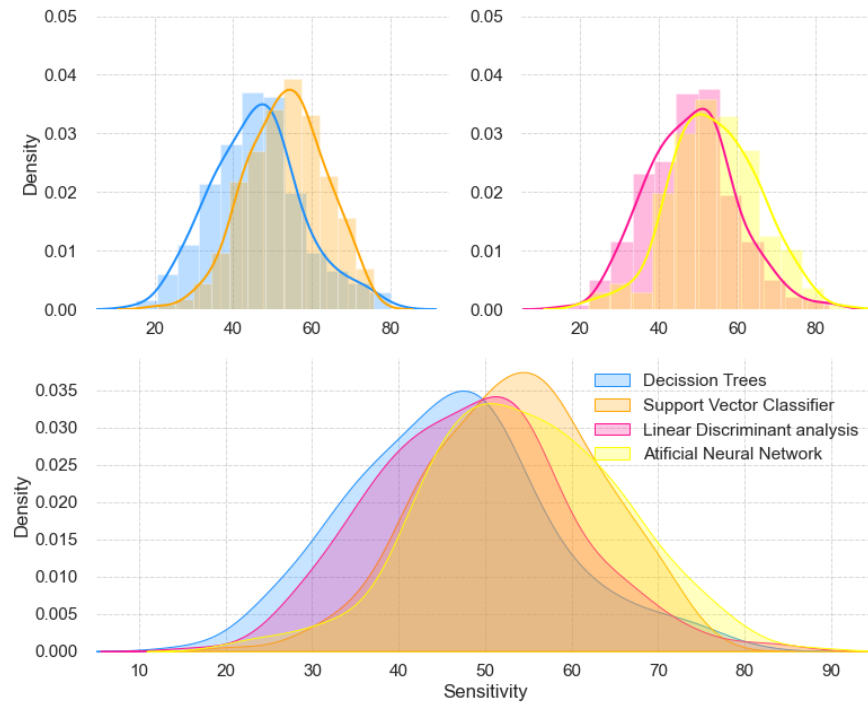
**Figure 5:** Averaged Cross Fold Specificity Score (with PCA)



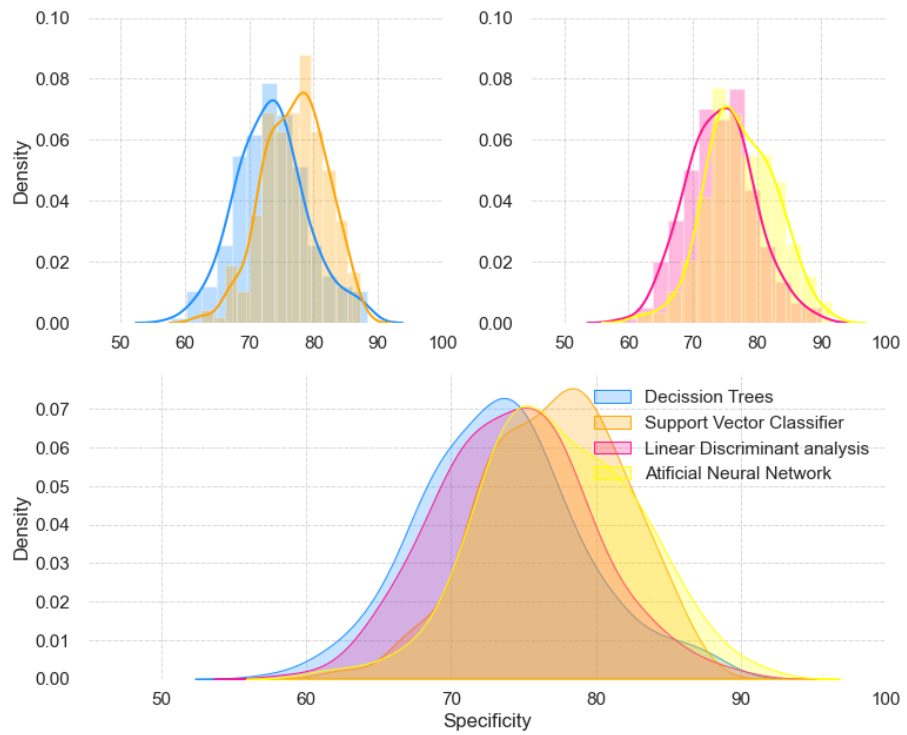
**Figure 6:** Averaged Cross Fold Precision Score (with PCA)



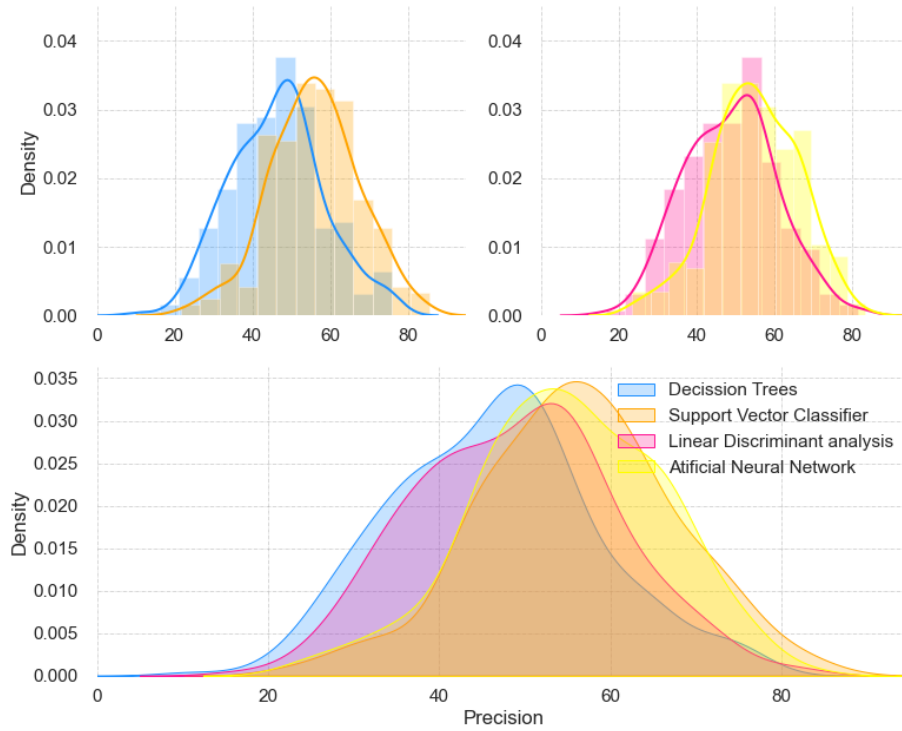
**Figure 7:** Averaged Cross Fold Accuracy Score (without PCA)



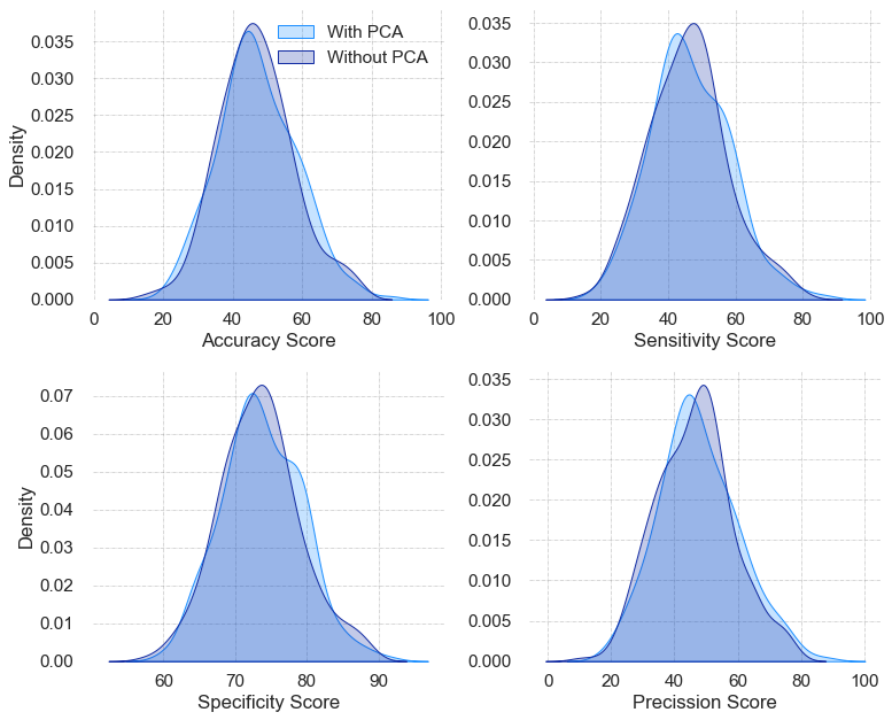
**Figure 8:** Averaged Cross Fold Sensitivity Score (without PCA)



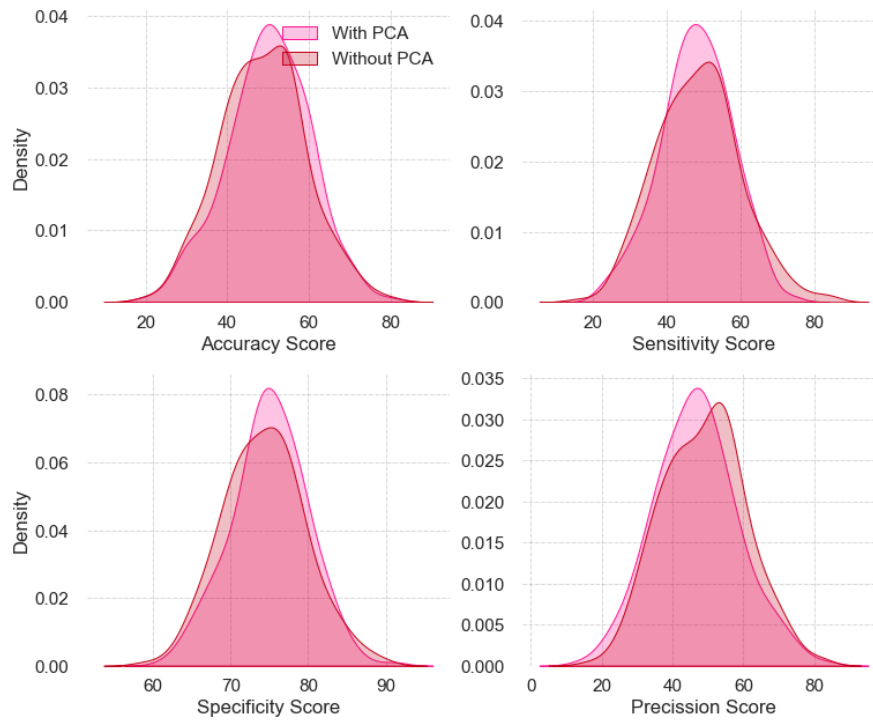
**Figure 9:** Averaged Cross Fold Specificity Score (without PCA)



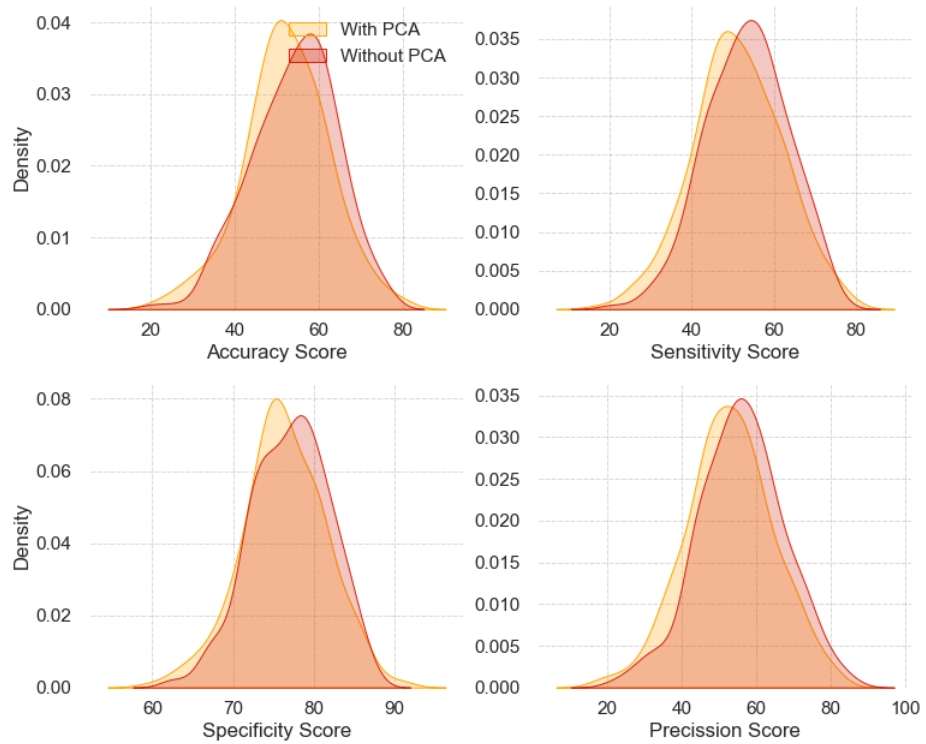
**Figure 10:** Averaged Cross Fold Precision Score (without PCA)



**Figure 11:** Decision Trees averaged Scores



**Figure 12:** Linear Discriminant Analysis averaged scores



**Figure 13:** Support Vector Machine averaged scores



Figure 14: Artificial Neural Network averaged scores

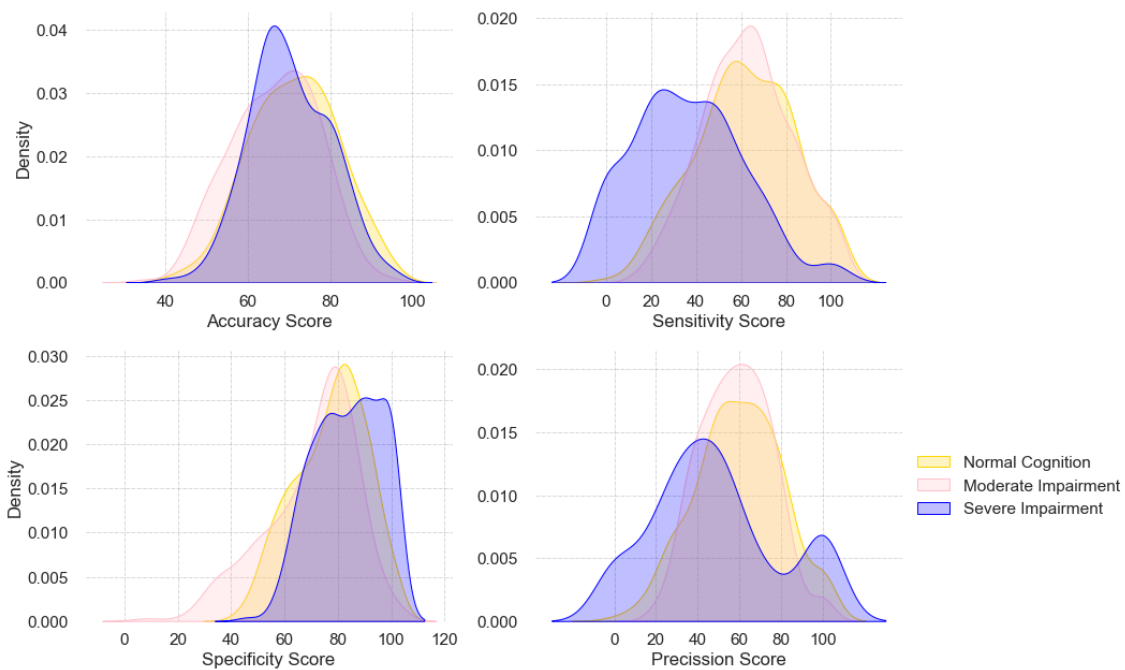
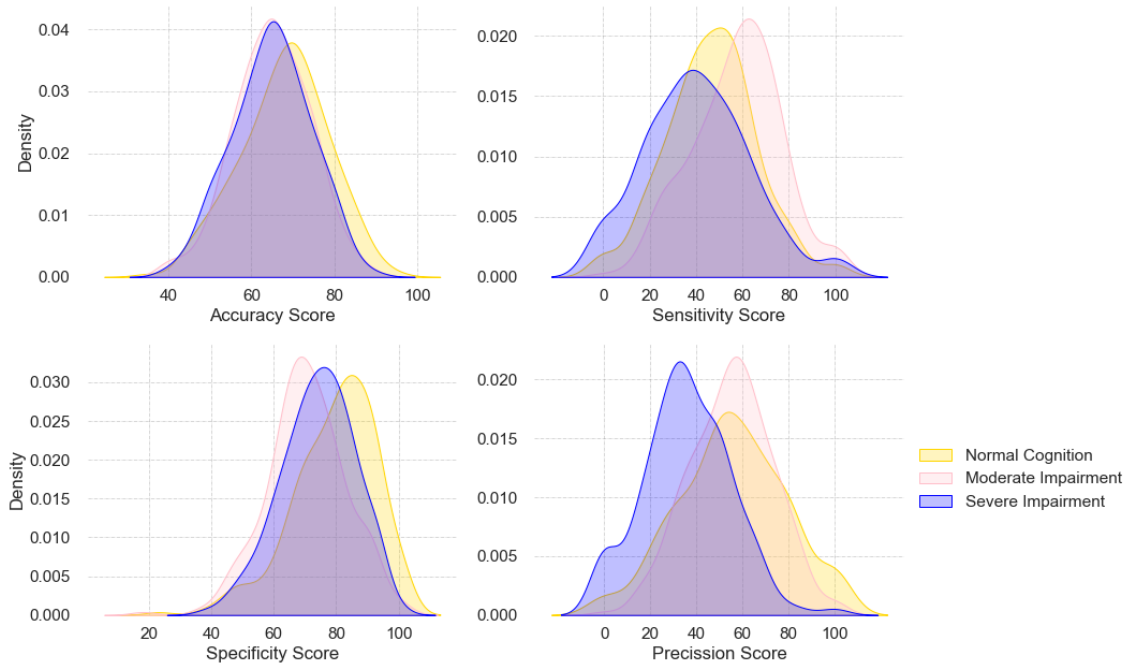
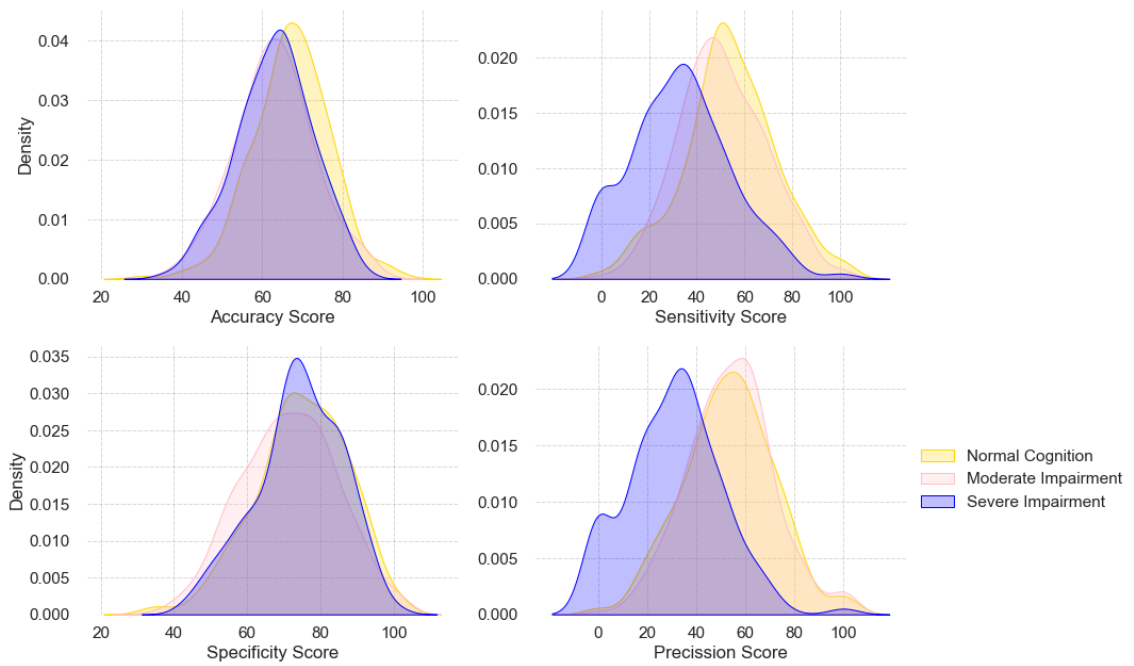


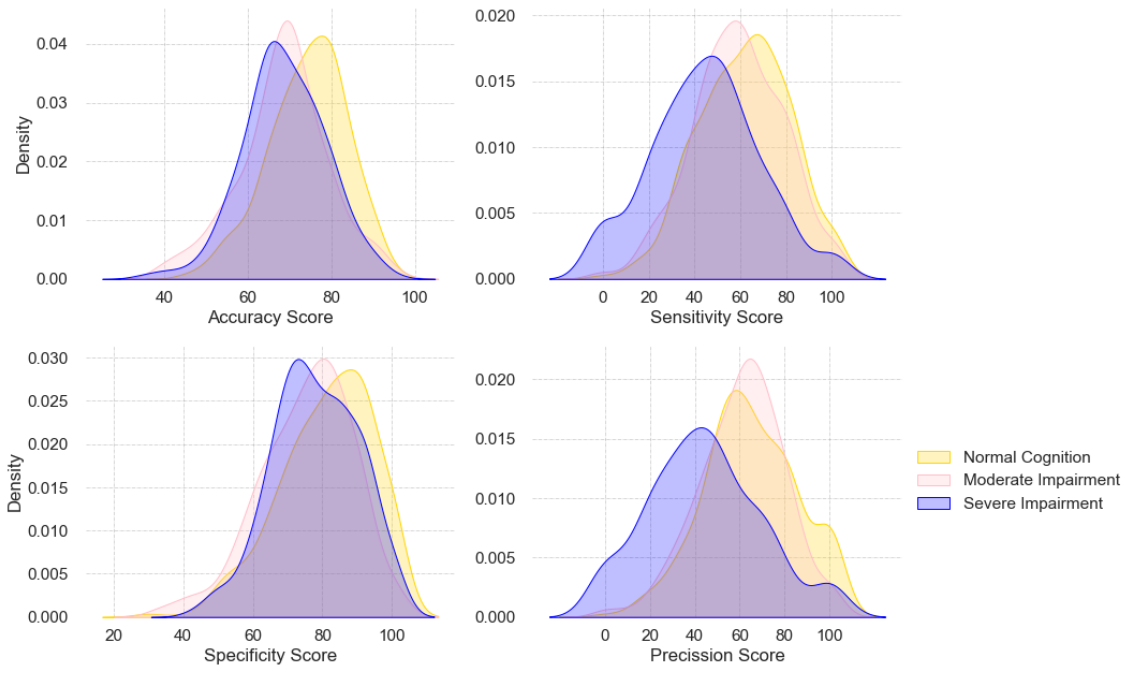
Figure 15: Decision Trees Score per cognitive category.



**Figure 16:** Linear Discriminant Analysis Score per cognitive category



**Figure 17:** Support Vector Machine Scores per cognitive category



**Figure 18:** Artificial Neural Network Scores per cognitive category



### 4.1. PCA eigenvalues for Subject Out Validation

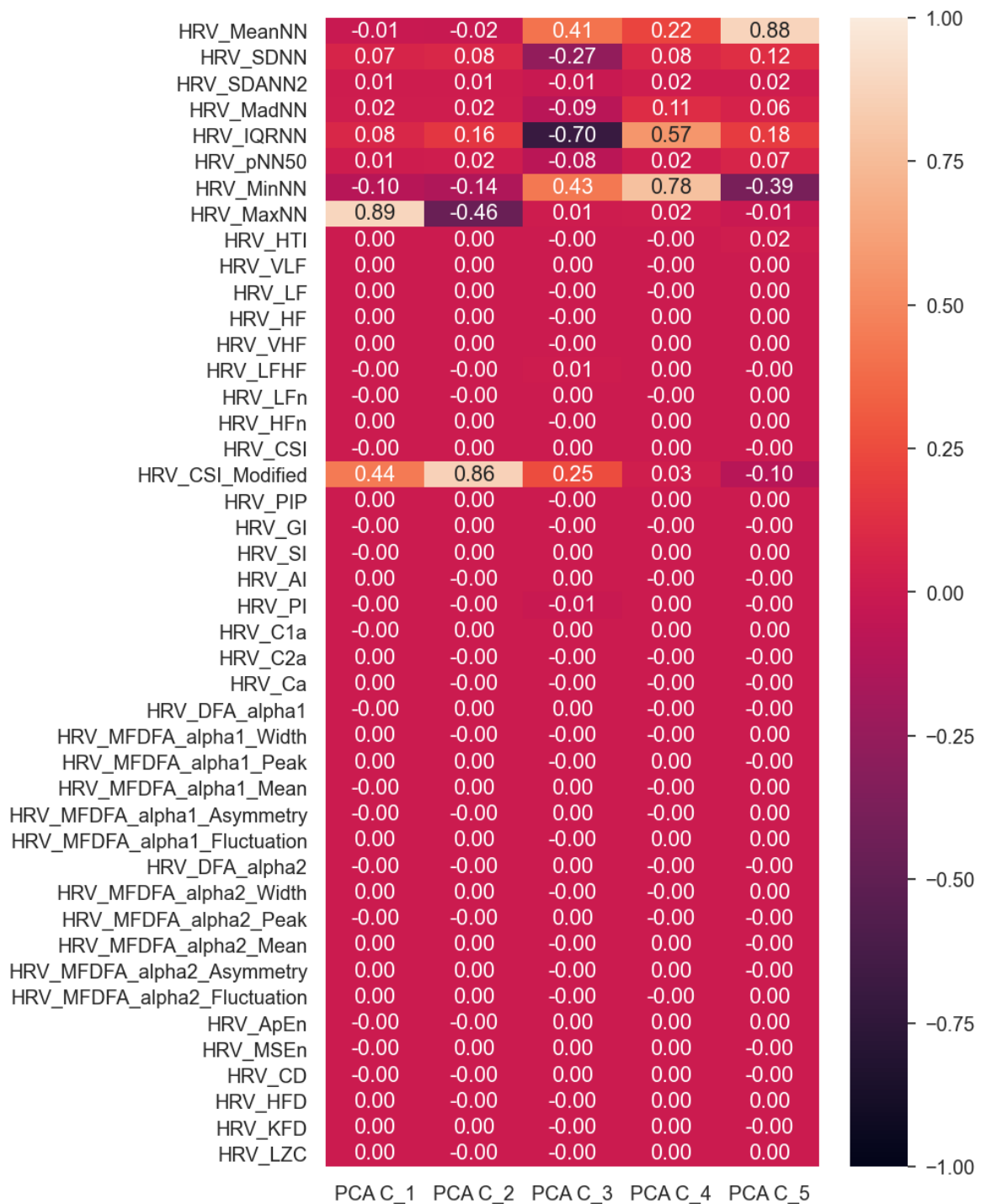


Figure 19: PCA Eigenvalues with Subject Out validation (second subject considered)

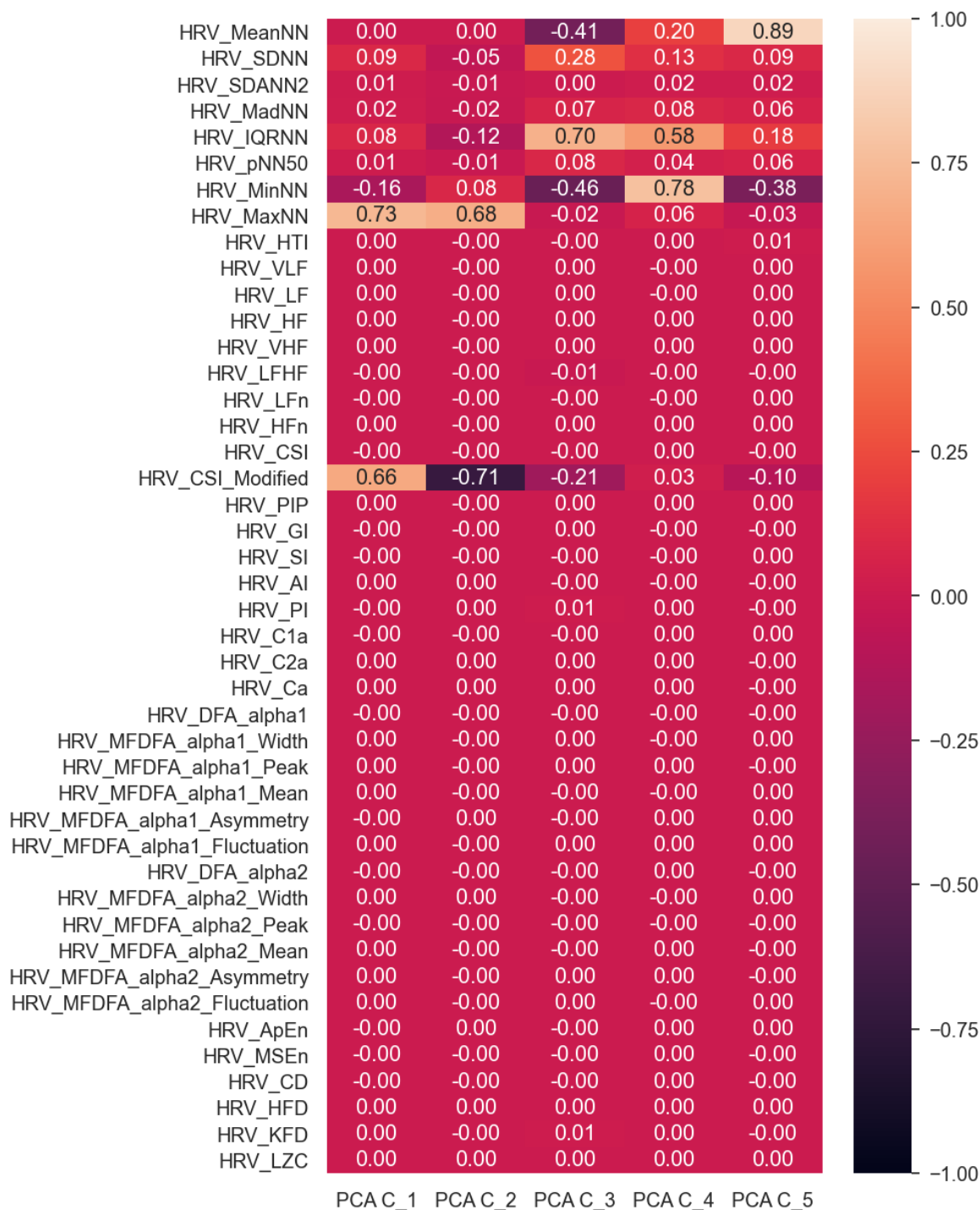


Figure 20: PCA Eigenvalues with Subject Out validation (third subject considered)

## 5. Subject Out Validation

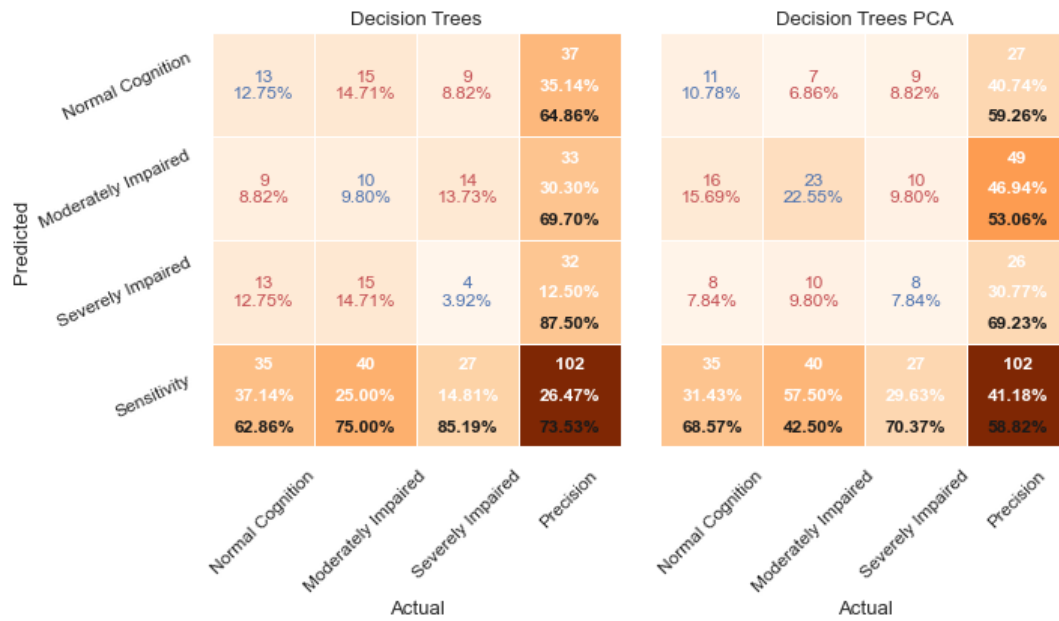


Figure 21: Confusion Matrix of Subject Out classification for Decision Trees.

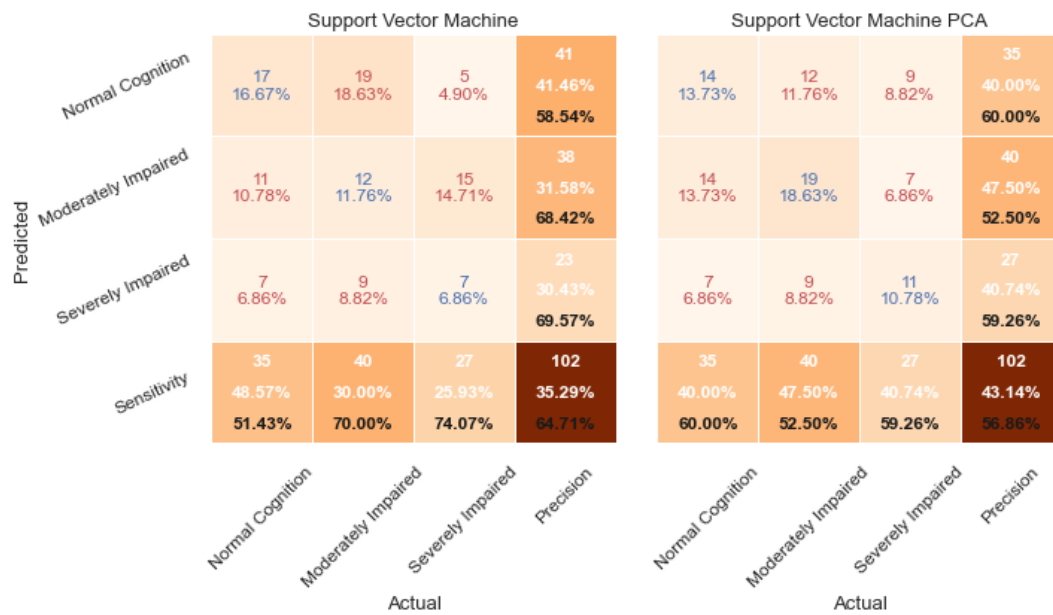


Figure 22: Confusion Matrix of Subject Out classification for Support Vector Machine.

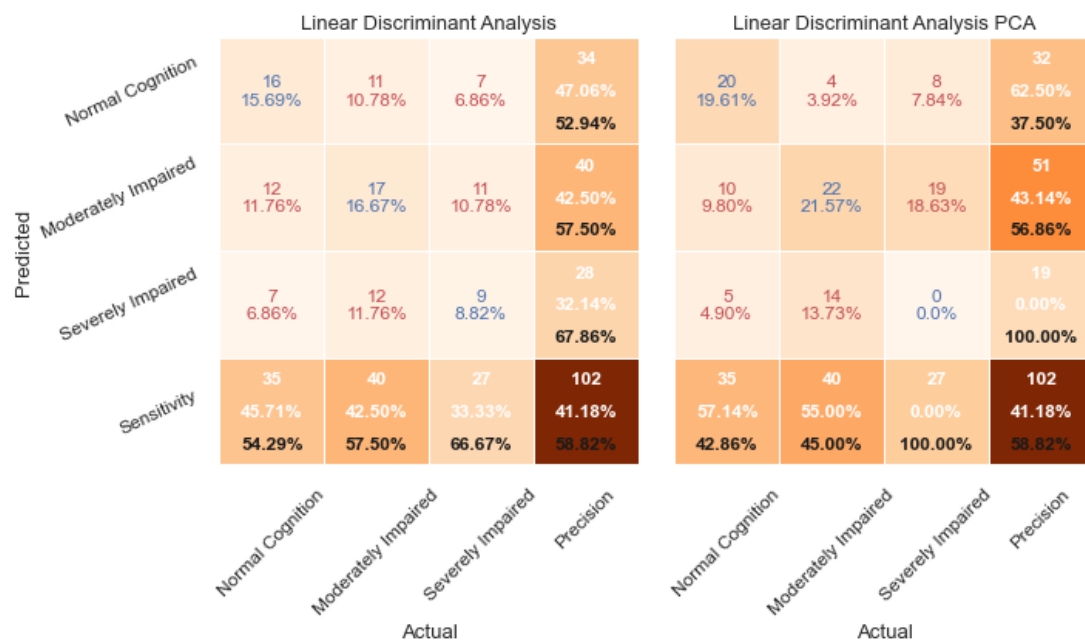


Figure 23: Confusion Matrix of Subject Out classification for Linear Discriminant Analysis.

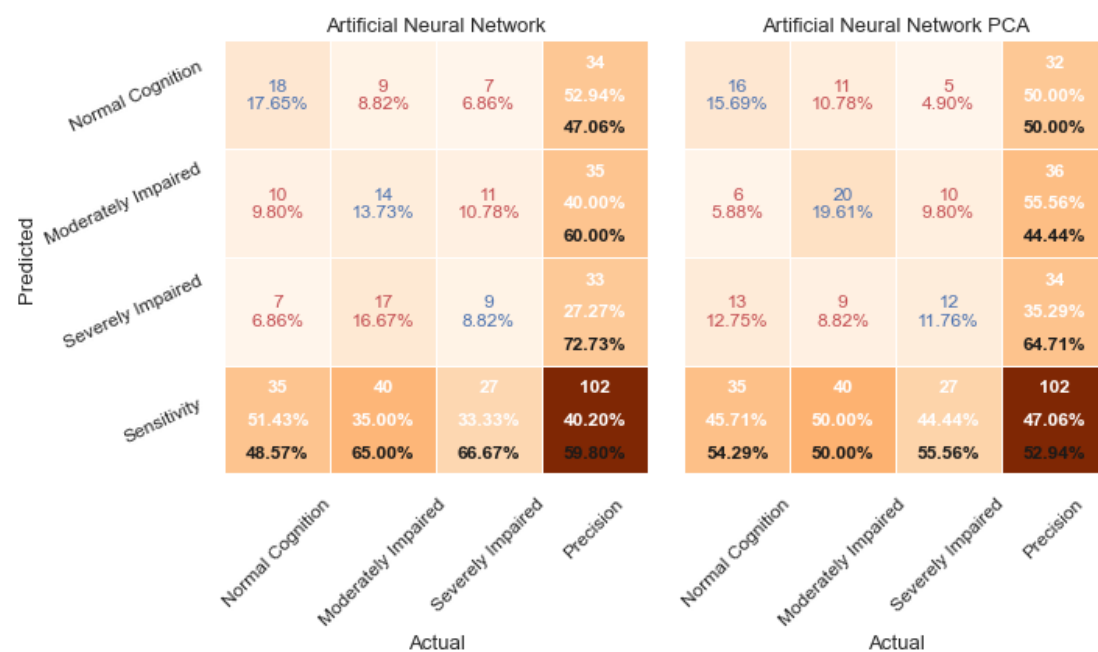


Figure 24: Confusion Matrix of Subject Out classification for Artificial Neural Network.

### 5.1. PCA eigenvalues with Subject Out Validation

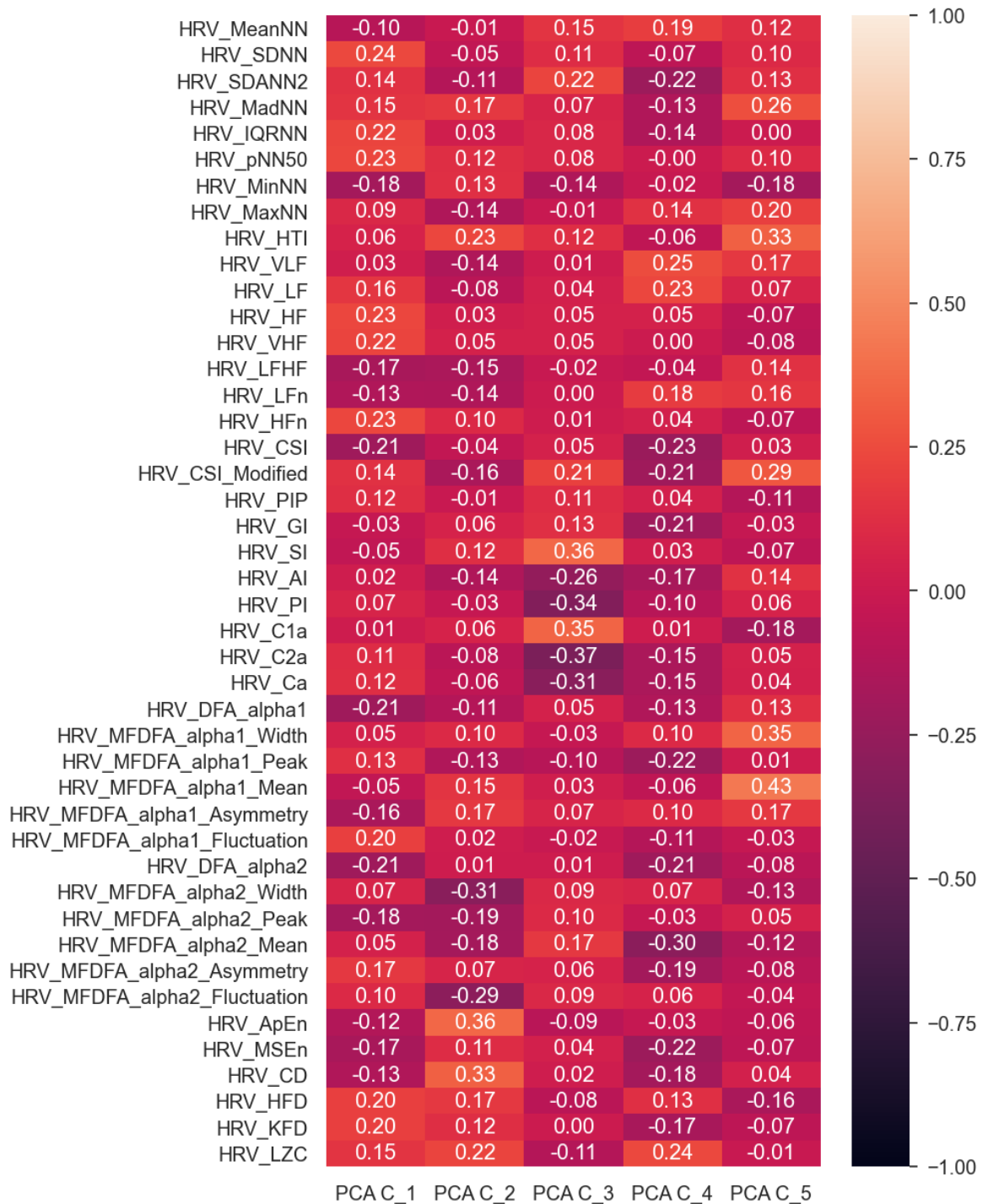


Figure 25: PCA Eigenvalues with Subject Out validation (second subject considered)

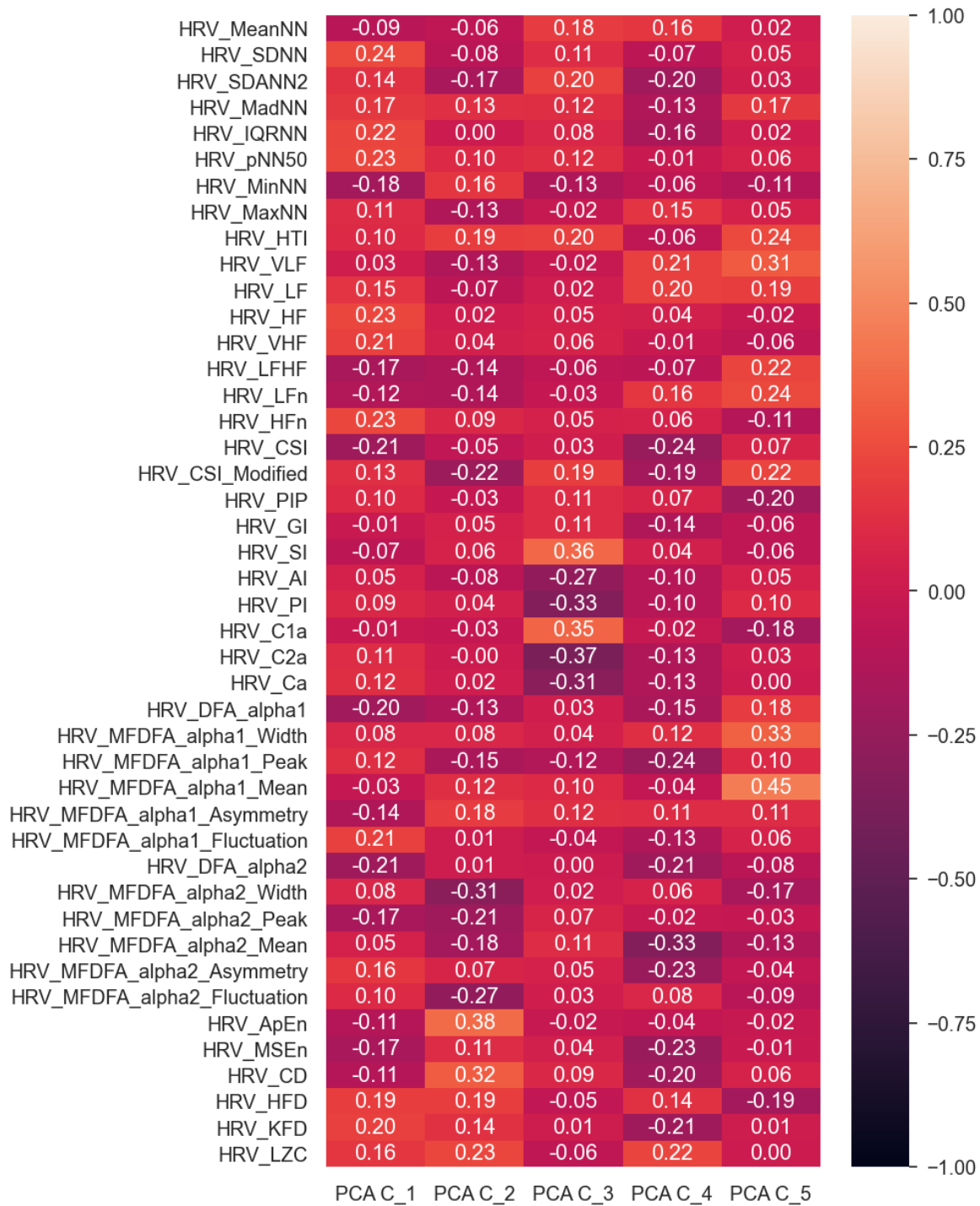


Figure 26: PCA Eigenvalues with Subject Out validation (third subject considered)

## 6. Cognitive tests correlation – CVLT, RWT and LPS

### California Verbal Learning Test

Six words must be memorized by participants. This test provides information about different learning strategies.

*CVLT\_6*: sum of all correct recalls from first until fifth trial

*CVLT\_10*: number of correct recalls when category cues are presented (short delay)

*CVLT\_12*: number of correct recalls when category cues are presented (long recall)

Only one marker reported statistical significance, indicating a low correlation between this test and the ECG uncorrelated markers, Table 1.

**Table 1:** Regression results with CVLT for the Elder Group and the Complete Database (*r* - regression coefficient, *CI* - confidence interval)

CVLT	Elderly Group			Complete Database		
	<i>r</i>	<i>CI (95%)</i>	<i>p-value</i>	<i>r</i>	<i>CI (95%)</i>	<i>p-value</i>
<b>CVLT_6</b>						
<i>KFD</i>	0.369	[0.07 0.61]	0.018	0.078	[-0.08 0.23]	0.332
<i>Alpha1 Fluct.</i>	0.285	[-0.03 0.54]	0.071	0.111	[-0.05 0.26]	0.166
<b>CVLT_10*</b>						
<i>PIP</i>	-0.219	[-0.49 0.09]	0.169	-0.124	[-0.27 0.03]	0.120
<i>HFD</i>	-0.216	[-0.49 0.10]	0.174	-0.073	[-0.23 0.08]	0.361
<b>CVLT_12</b>						
<i>C2a</i>	0.276	[-0.03 0.54]	0.080	0.158	[0.01 0.31]	0.048
<i>Ca</i>	0.276	[-0.03 0.54]	0.080	0.162	[0.01 0.31]	0.042
<i>C1a</i>	-0.274	[-0.54 0.04]	0.083	-0.157	[-0.31 -0.00]	0.049

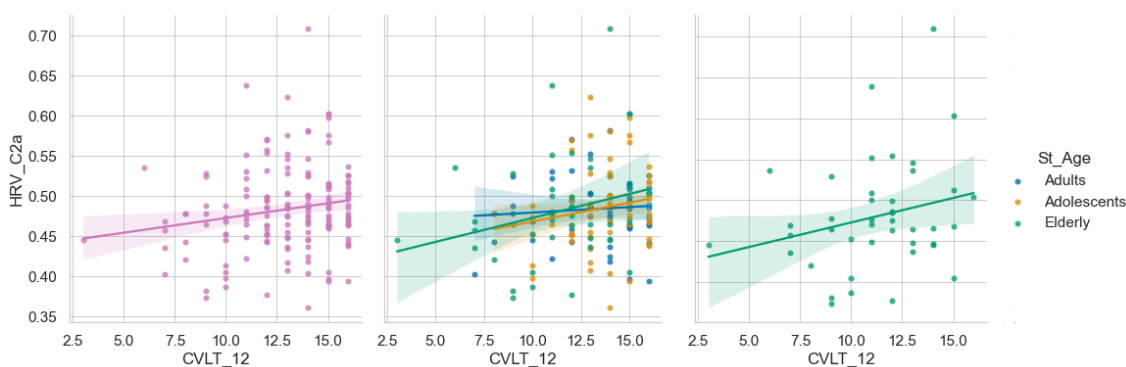
Several studies found a connection between HRV and memory performance [1], [2], even after adjusting for clinical and demographic covariates. Higher HRV levels are associated with improved memory regulation [3]. Both short-term and long-term verbal memory skills are negatively correlated with lower HRV [1], [2]. However, some studies reported no relationship between verbal memory and HRV [4]–[6].

Direct relation between HRV measures and CVLT is found in [7]. Results indicate that lower heart rate variability, independent of age or gender, is linked to decreased cognitive performance and may be a precursor to sympathovagal imbalance. Low performance users score on CVLT total recall was  $48.18 \pm 6.69$  while high performance individuals were  $63.34 \pm 4.31$ . Respectively, they had  $0.61 \pm 0.97$  and  $0.36 \pm 1.18$  for LF/HF ratio and  $43.30 \pm 21.18$ ms and  $49.93 \pm 19.95$ ms for SDNN in both cases with a p-value lower than 0.05 and  $n = 114$  [7].

Higher SDNN was cross-sectionally related with better performance of working memory [7], [8]. In contrast to SDNN, RMSSD, HF, and LF/HF indices, LF was strongly influenced by age and sex [7].

Another study stated that HRV indices, especially SDNN, pNN50, and RMSSD were significantly higher in normal cognition individuals while performing working memory tasks relative to their cognitively impaired counterparts [9]. Lower levels of HF-HRV response and poorer working memory performance were correlated to subjective memory deterioration (measured by lower scores on memory stability) [10].

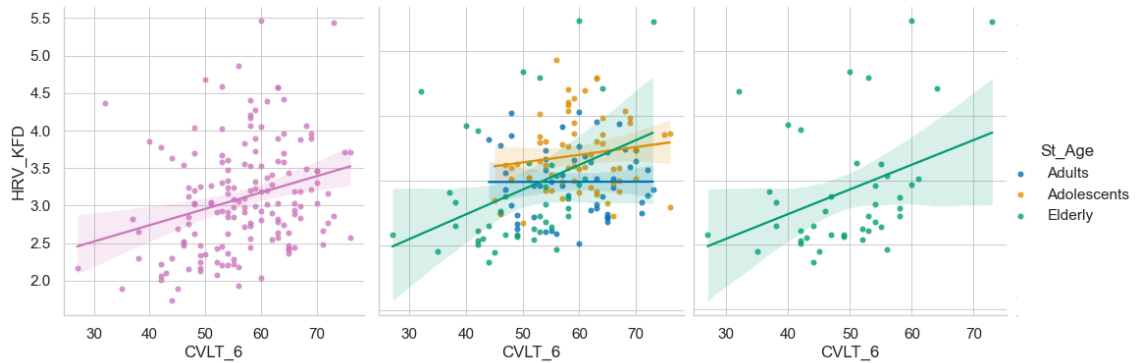
None of the markers with literary significance shows a low positive correlation in the present study with the exception of the fragmentation ratios C2a, C1a and Ca (E. CLVT\_12 –  $r: 0.274$  and  $-0.276$ , p-value: 0.080 and  $-0.083$ ), Figure 27. In the heart rate fragmentation study a negative correlation of this markers with cognitive decline scores was demonstrated [11]. Only one of our fragmentation markers has a negative regression, C1a, being the regression coefficient for the remaining ratios positive.



**Figure 27:** Regression plots between CVLT\_12 and C2a (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



Also noteworthy is the result obtained for KFD (E. CLVT\_12 –  $r$ : 0.369,  $p$ -value: 0.018) Figure 28, which shows a positive correlation for the elderly group. For both the database as a whole and the individual adolescent and adult group study a practically null correlation is reported. This pattern is repeated in most of the cognitive tests studied.



**Figure 28:** Regression plots between CVLT\_6 and KFD (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)

### Logical Deductive Thinking

Measures Global logical or inferential thinking and quantifies fluid intelligence. 40 rows with 8 symbols each were presented, and participants had to identify in each of the rows the one symbol that did not fit. The time limit for the task is 3 min.

LPS\_1: how many symbol-rows did the participant process correctly.

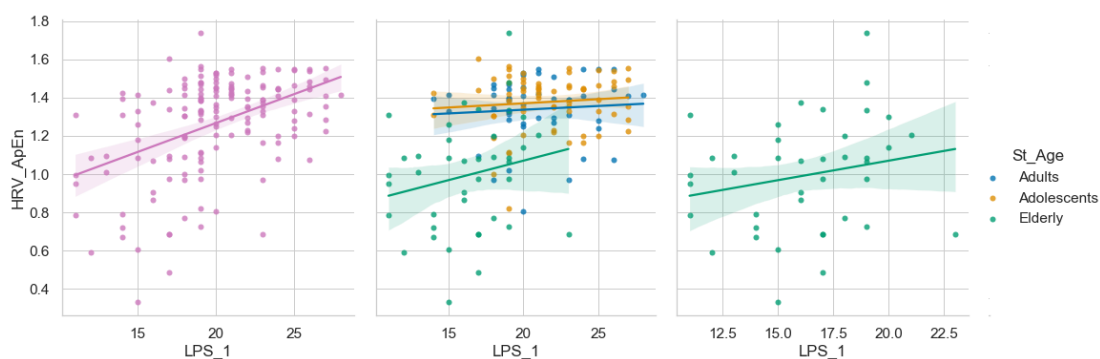
Within the Logical Deductive Thinking results, no marker is statistically significant, Table 2. This is indicative of practically non-existent correlation between the different extracted markers and LPS.

**Table 2:** Regression results with LPS for the Elder Group and the Complete Database ( $r$  - regression coefficient, CI - confidence interval)

LPS	Elderly Group			Complete Database		
	$r$	CI (95%)	$p$ -value	$r$	CI (95%)	$p$ -value
LPS_1						
ApEn	0.257	[-0.06 0.52]	0.105	0.091	[-0.07 0.25]	0.263
CSI_Modified.	-0.235	[-0.51 0.08]	0.139	-0.107	[-0.26 0.05]	0.185

Just one study identified an association of HRV with visual intelligence [1]. Even after adjusting the data for demographic, clinical, and behavioural confounding factors, lower HRV was associated with worse visuospatial ability.

Since the results of the regressions are additionally very unfavourable, the interest in studying this test is reduced. The only worth to mention marker is ApEn (E. LPS\_1 – r: 0.257, p-value: 0.105). Despite not providing a statistically significant p-value, a positive correlation is visually observed in both the Elderly group and the entire database, thus following the same patters as literary described. No markers validated in the literature (HF, LF, RMMS or SDNN) [1] provides a considerable statistical value.



**Figure 29:** Regression plots between LPS\_1 and ApEn (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)

### Regensburg Word fluency test

This test quantifies verbal fluency. Participants had 2 minutes of time to verbally list as many words as possible starting with the letter S.

RWT\_1: how many s-words did the participant's name during the first minute.

RWT\_12: how many s-words did the pp. name in total - repetitions -rule breaks.

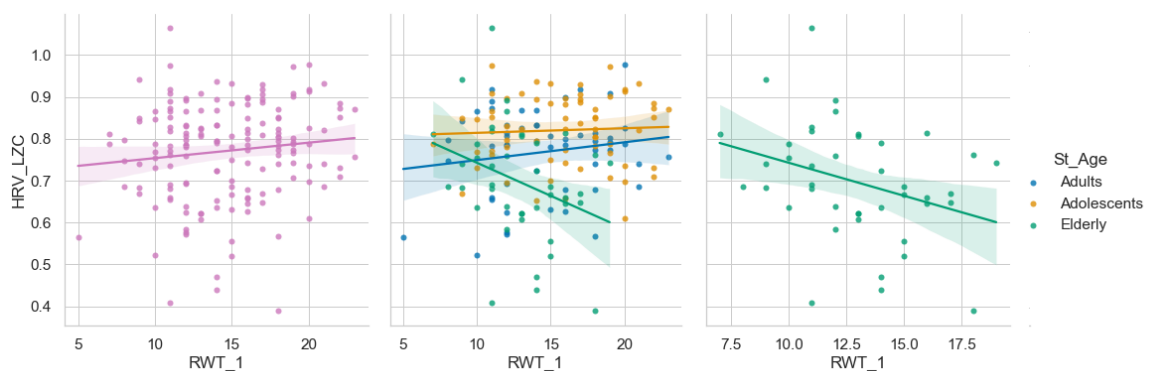
RWT\_24: how many animals did the pp. name in total - repetitions -rule breaks.

With Regensburg Word Fluency Test several markers reported statistical significance, Table 3. The best markers for each subtest will be briefly emphasized. An interesting observation is the lack of any previously described and literature-evidenced traditional markers (SDNN, HF, RMSSD) within this subset of tests.

**Table 3:** Regression results with RWT for the Elder Group and the Complete Database (*r* - regression coefficient, *CI* - confidence interval)

RWT	Elderly Group			Complete Database		
	<i>r</i>	<i>CI</i> (95%)	<i>p</i> -value	<i>r</i>	<i>CI</i> (95%)	<i>p</i> -value
<b>RWT_1</b>						
LZC	-0.332	[-0.58 -0.03]	0.034	-0.014	[-0.17 0.14]	0.859
HFD	-0.308	[-0.56 -0.01]	0.050	-0.095	[-0.25 0.06]	0.235
<b>RWT_12</b>						
Alpha2 Mean	0.332	[0.02 0.58]	0.036	0.042	[-0.11 0.2]	0.600
Alpha2 Width	0.299	[0.03 0.55]	0.036	0.055	[-0.10 0.21]	0.489
<b>RWT_24</b>						
SI	0.356	[-0.07 0.53]	0.046	0.137	[-0.02 0.29]	0.088

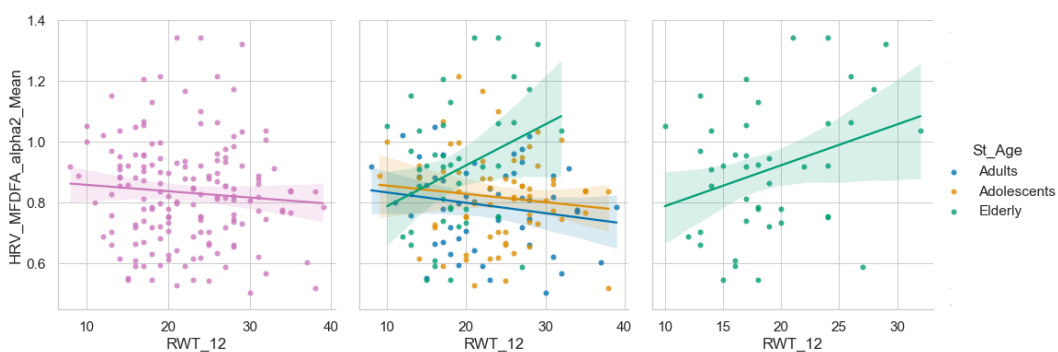
One study reported that [1], even after data adjustments for demographic, clinical, and behavioural confounding factors, lower HRV is related with worse language skills. In contrast, another study found no association between HRV and verbal performance [6]. No more articles were found relating linguistic performance and HRV parameters.



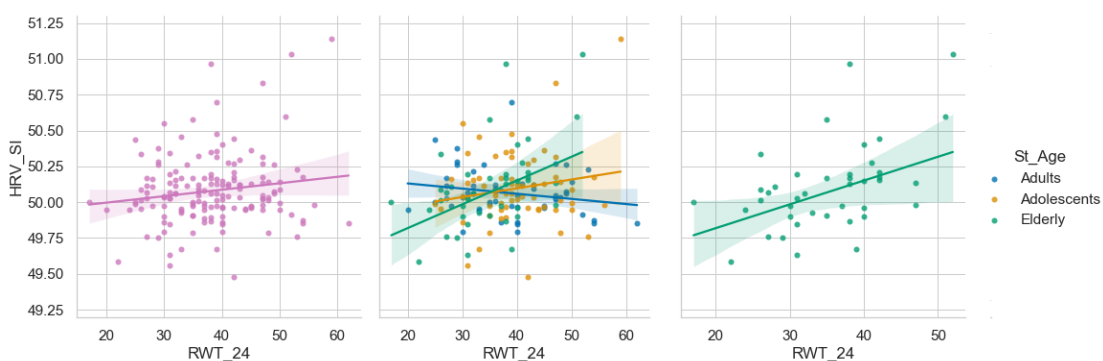
**Figure 30:** Regression plots between RWT\_1 and LZC (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)

LZC only exhibits correlation with RWT (E. RWT\_1 – *r*: 0.332, *p*-value: 0.034), no other subset of tests shows significant regression for this marker. The regressions performed both for the complete database as well as for the adult and adolescent group exhibit a positive trend, Figure 30. Pattern reversed when dealing with the Elderly group. At the same time, HFD (E. RWT\_1 – *r*: 0.308, *p*-value: 0.050) shows similar regression values within this first subtest, and when observing its visual representation in the annexes, a nearly equal tendency to LZC is observed. Considering that HFD appears only correlated within this test, this might indicate a direct relationship between both markers.

The previously aforementioned tendency is reversed when dealing with Alpha 2 Mean (E.  $RWT_{12} - r: -0.332$ ,  $p\text{-value}: 0.036$ ) and SI (E.  $RWT_{24} - r: 0.356$ ,  $p\text{-value}: 0.193$ ), Figure 31 and Figure 32. For Alpha 2 Mean, while a positive regression is shown in the Elderly group, the overall trend as well as for the younger groups is slightly negative. In SI, depending on the age group studied a different trend is observed, having the complete database and the Elderly group a positive correlation.



**Figure 31:** Regression plots between  $RWT_{12}$  and Alpha 2 Mean (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



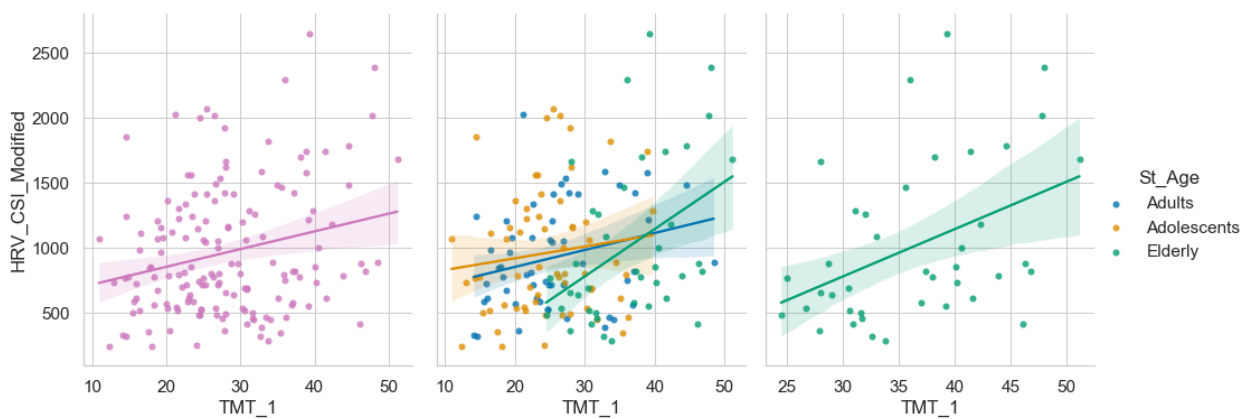
**Figure 32:** Regression plots between  $RWT_{24}$  and SI (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)

## 7. Cognitive Tests – Extra figures and tables

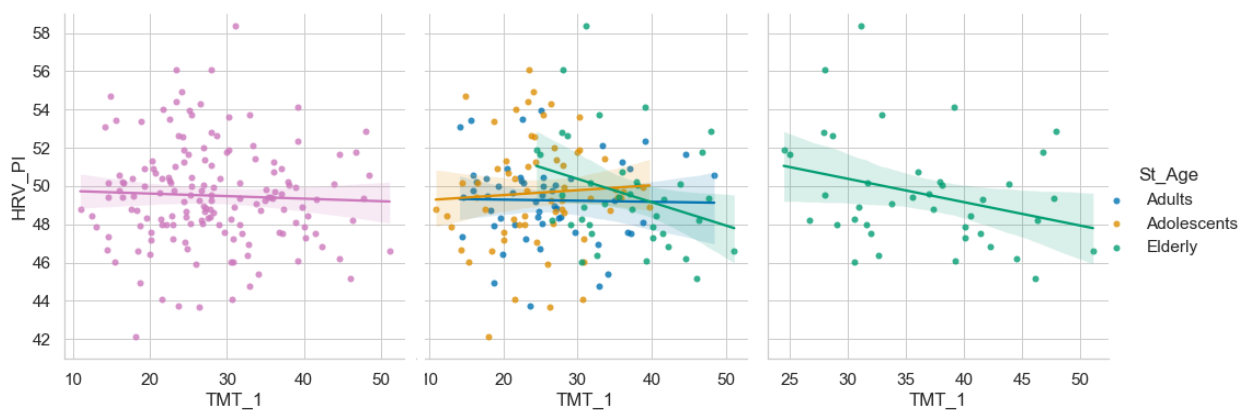
**Table 4:** Regression results with TMT for the Elder Group and the Complete Database (*r* - regression coefficient, *CI* - confidence interval)

TMT	Elderly Group			Complete Database		
	<i>r</i>	<i>CI</i> (95%)	<i>p</i> -value	<i>r</i>	<i>CI</i> (95%)	<i>p</i> -value
<b>TMT_1</b>						
CSI_Modified	0.515	[0.24 0.71]	0.001	0.226	[0.07 0.37]	0.005
PI	-0.429	[-0.65 -0.14]	0.006	-0.078	[-0.23 0.08]	0.333
SDANN2	0.452	[0.16 0.67]	0.003	0.139	[-0.02 0.29]	0.084
pNN50	0.449	[0.16 0.67]	0.004	0.029	[-0.13 0.19]	0.716
MadNN	0.346	[0.04 0.59]	0.029	0.127	[-0.03 0.28]	0.117
PIP	0.341	[0.15 0.66]	0.004	-0.008	[-0.17 0.15]	0.917
C1a	0.301	[-0.05 0.54]	0.094	0.093	[-0.07 0.25]	0.250
HTI	0.264	[-0.05 0.53]	0.100	0.076	[-0.08 0.23]	0.348
MeanNN	0.257	[-0.06 0.53]	0.109	-0.044	[-0.2 0.11]	0.586
Alpha2 Mean	0.250	[-0.07 0.52]	0.119	0.183	[0.03 0.33]	0.022
<b>TMT_5</b>						
C2a	-0.386	[-0.62 -0.08]	0.014	-0.139	[-0.29 0.02]	0.081
Alpha1 Assy.	0.385	[0.08 0.62]	0.014	0.090	[-0.07 0.24]	0.259
Alpha2 Peak	0.367	[0.06 0.61]	0.020	0.232	[0.08 0.37]	0.003
Alpha1 Peak	-0.352	[-0.60 -0.05]	0.026	-0.001	[-0.16 0.16]	0.995
PI	-0.351	[-0.60 -0.04]	0.026	-0.127	[-0.28 0.03]	0.111
KFD	-0.329	[-0.58 -0.02]	0.038	-0.215	[-0.36 -0.06]	0.007
LFHF	0.315	[0.01 0.57]	0.047	0.204	[0.05 0.35]	0.010
CSI	0.299	[-0.01 0.56]	0.060	0.248	[0.10 0.39]	0.002
MeanNN	0.286	[-0.03 0.55]	0.073	0.018	[-0.14 0.17]	0.819
HFD	-0.278	[-0.54 0.04]	0.082	-0.215	[-0.36 -0.06]	0.006
Alpha1	0.270	[-0.05 0.54]	0.092	0.194	[0.04 0.34]	0.014
HTI	0.268	[-0.05 0.54]	0.094	0.077	[-0.08 0.23]	0.332
SI	0.265	[-0.05 0.53]	0.098	0.137	[-0.02 0.29]	0.084

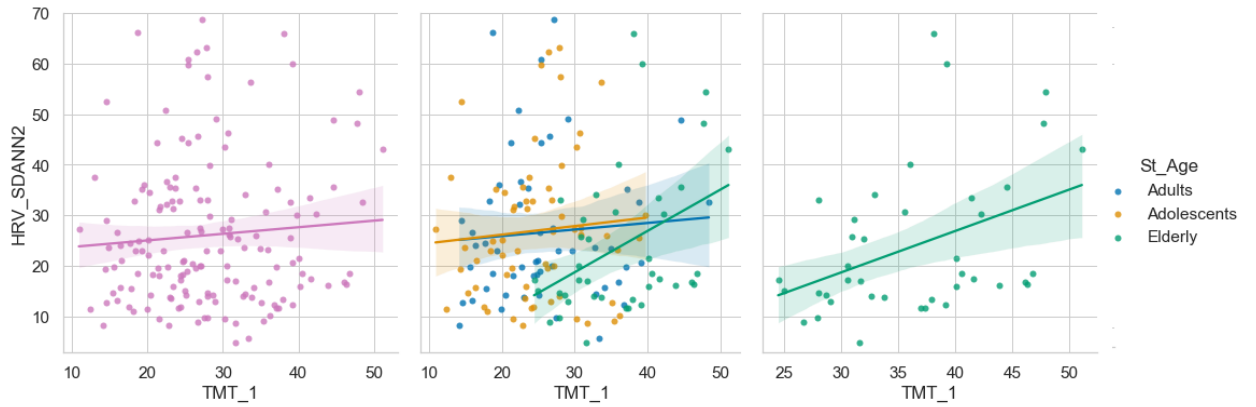
<i>TMT_mean</i>	<i>r</i>	<i>CI (95%)</i>	<i>p-value</i>	<i>r</i>	<i>CI (95%)</i>	<i>p-value</i>
<i>CSI_Modified</i>	0.373	[0.07 0.61]	0.016	0.250	[0.1 0.39]	0.002
<i>MadNN</i>	0.347	[0.04 0.59]	0.026	0.169	[0.01 0.32]	0.033
<i>MaxNN</i>	0.296	[0.04 0.59]	0.026	0.221	[0.07 0.36]	0.005
<i>PI</i>	-0.294	[-0.55 0.01]	0.062	-0.117	[-0.27 0.04]	0.140
<i>MinNN</i>	-0.277	[-0.54 0.03]	0.080	-0.152	[-0.3 0.00]	0.055
<i>SDANN2</i>	0.260	[-0.05 0.53]	0.100	0.134	[-0.02 0.28]	0.090
<i>C2a</i>	-0.255	[-0.52 0.06]	0.107	-0.119	[-0.27 0.04]	0.135



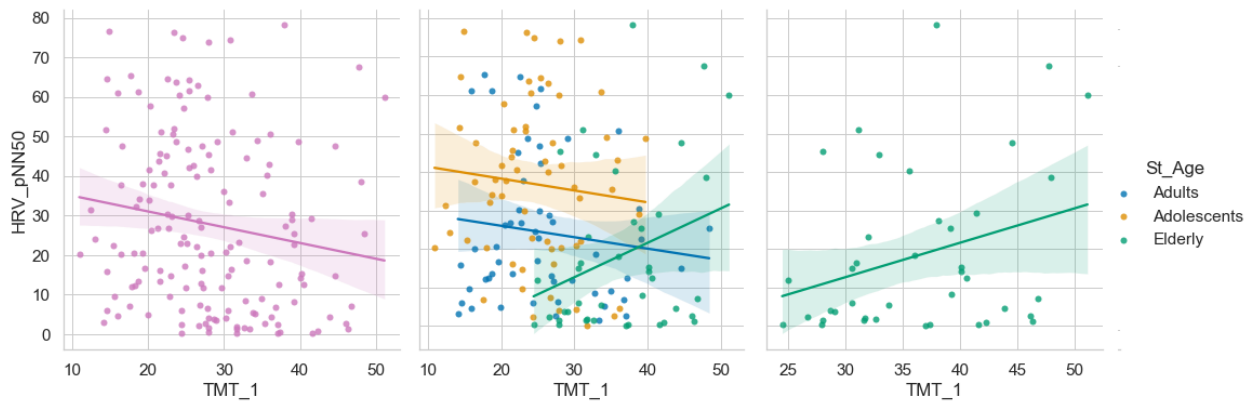
**Figure 33:** Regression plots between *TMT\_1* and *CSI\_Modified* (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



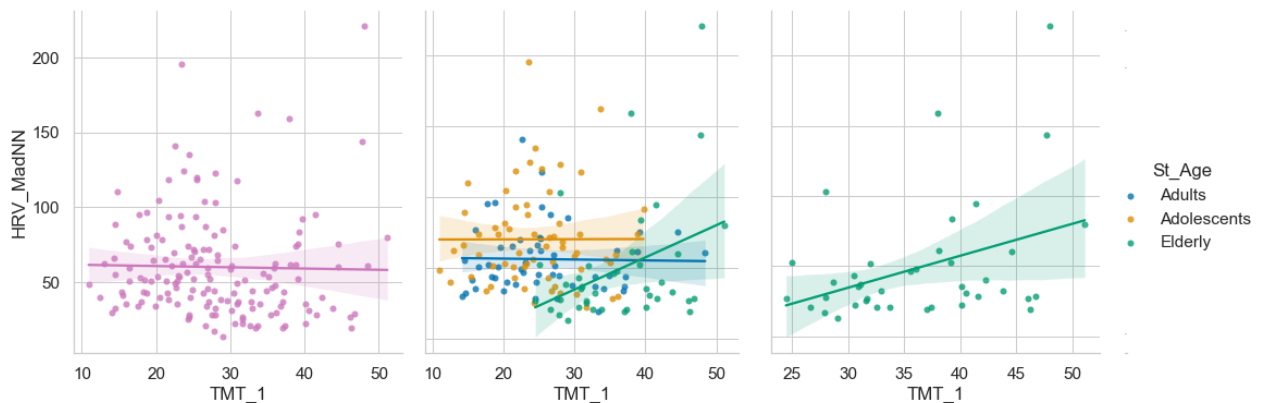
**Figure 34:** Regression plots between *TMT\_1* and *PI* (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



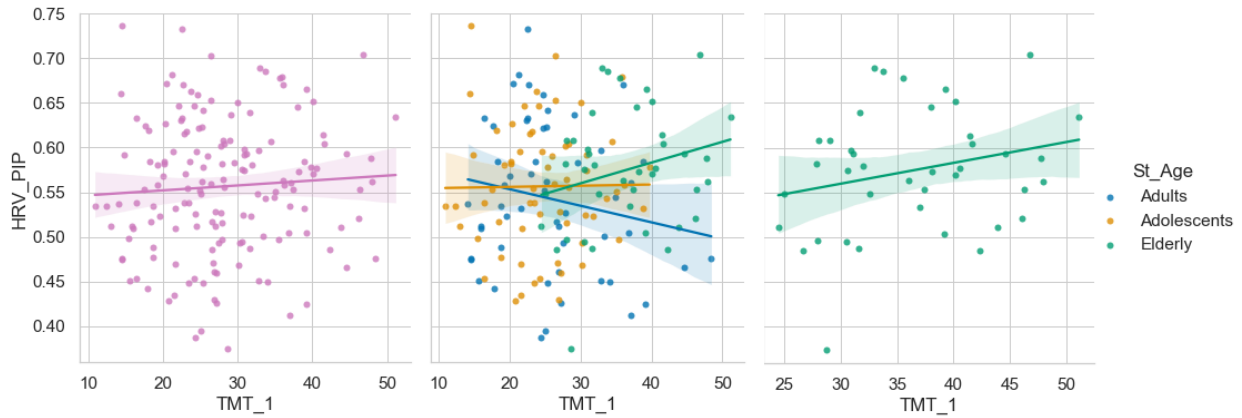
**Figure 35:** Regression plots between TMT\_1 and SDANN2 (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



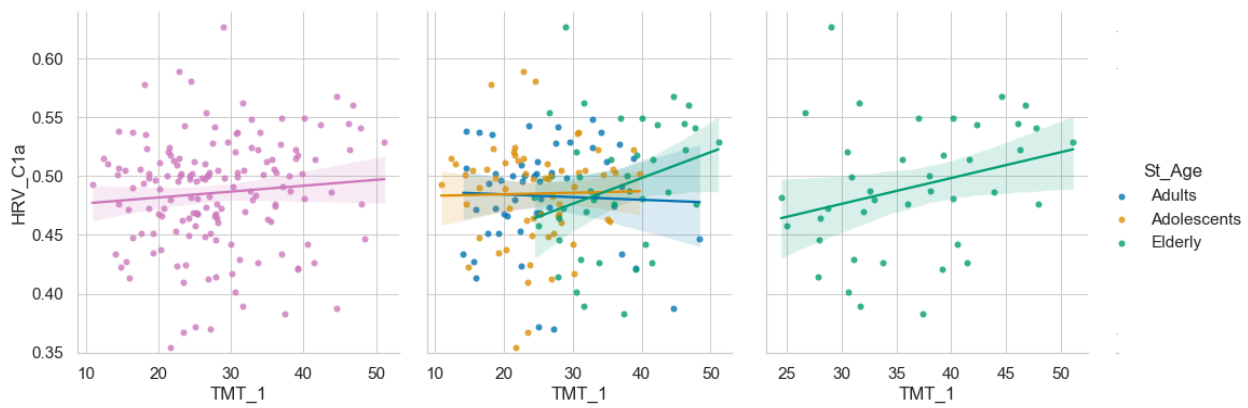
**Figure 36:** Regression plots between TMT\_1 and pNN50 (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



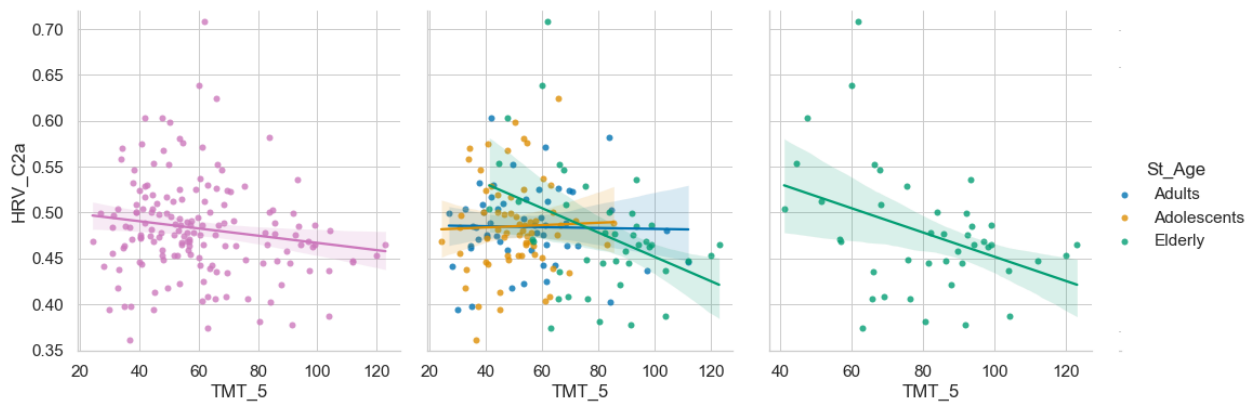
**Figure 37:** Regression plots between TMT\_1 and MadNN (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



**Figure 38:** Regression plots between TMT\_1 and PIP (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)

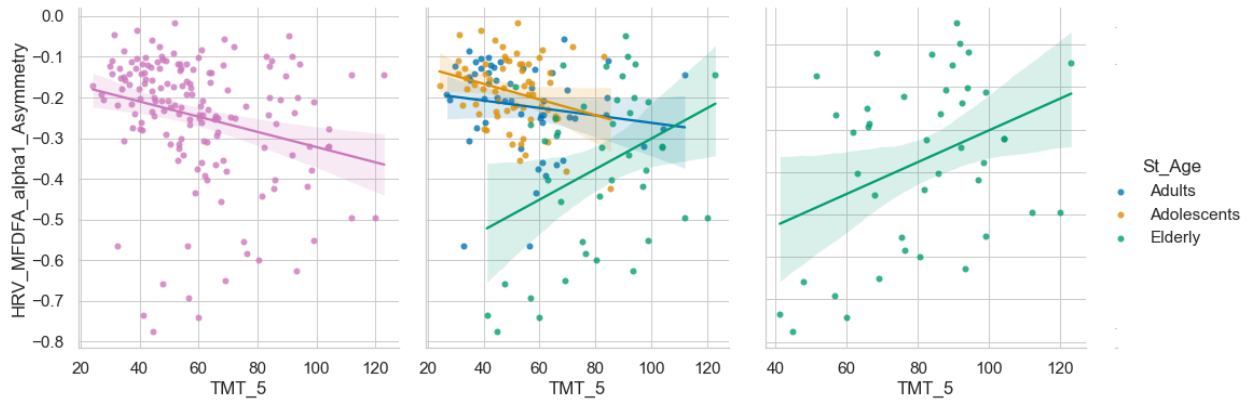


**Figure 39:** Regression plots between TMT\_1 and C1a (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)

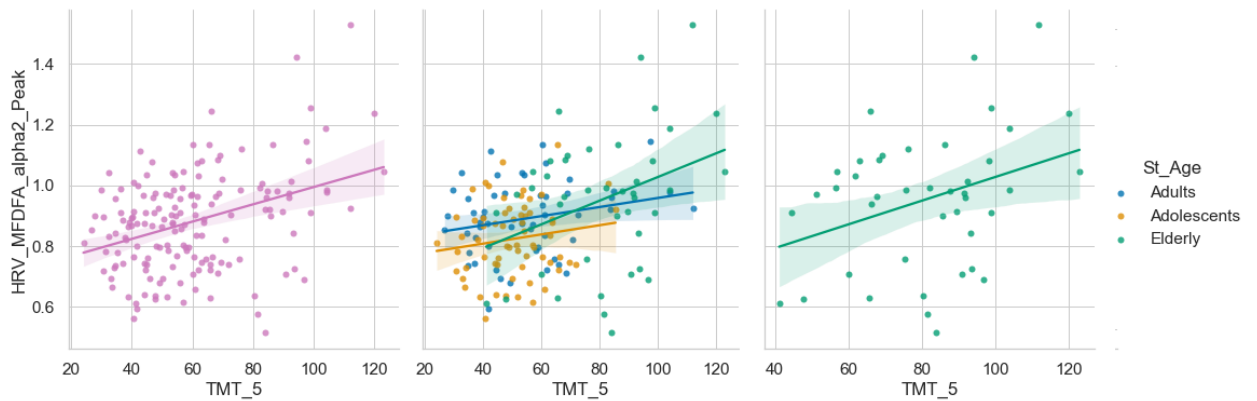


**Figure 40:** Regression plots between TMT\_5 and C2a (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)

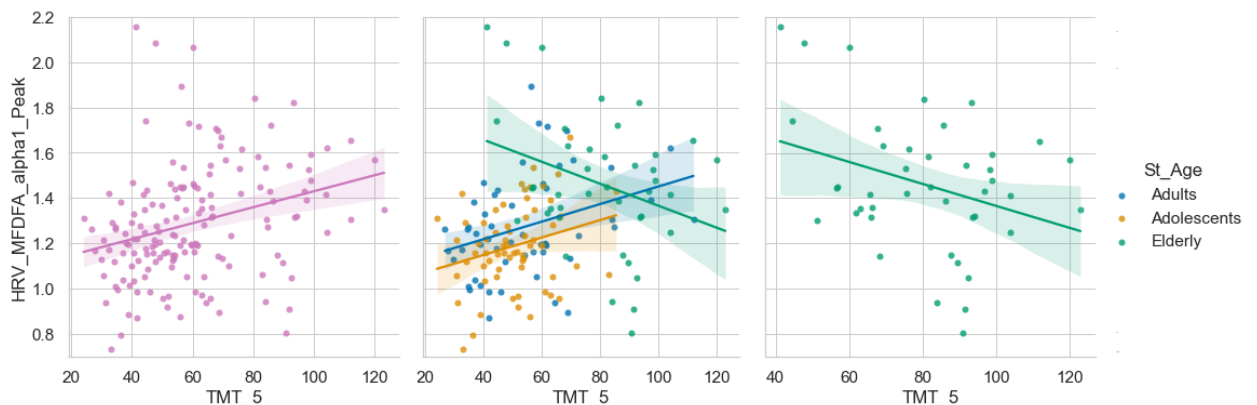




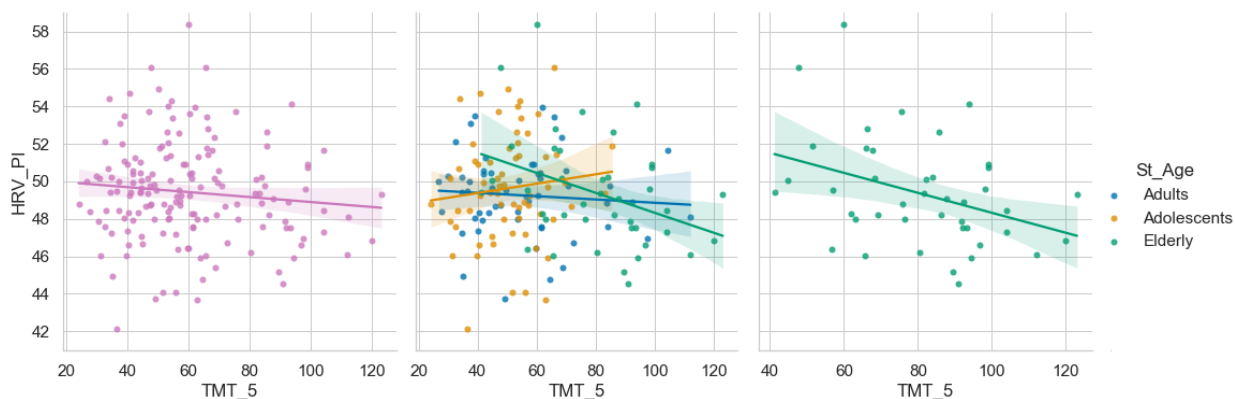
**Figure 41:** Regression plots between TMT\_5 and Alpha 1 Asymmetry (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



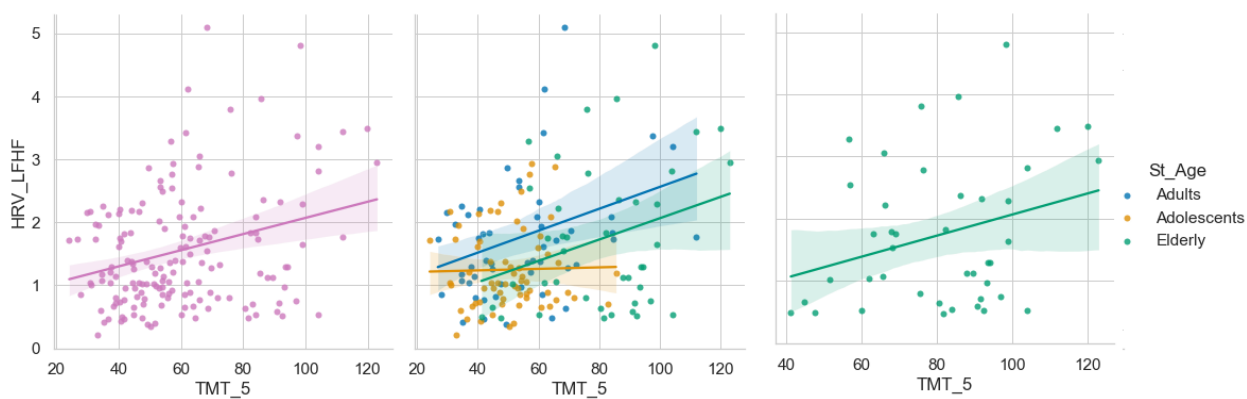
**Figure 42:** Regression plots between TMT\_5 and Alpha 2 Peak (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



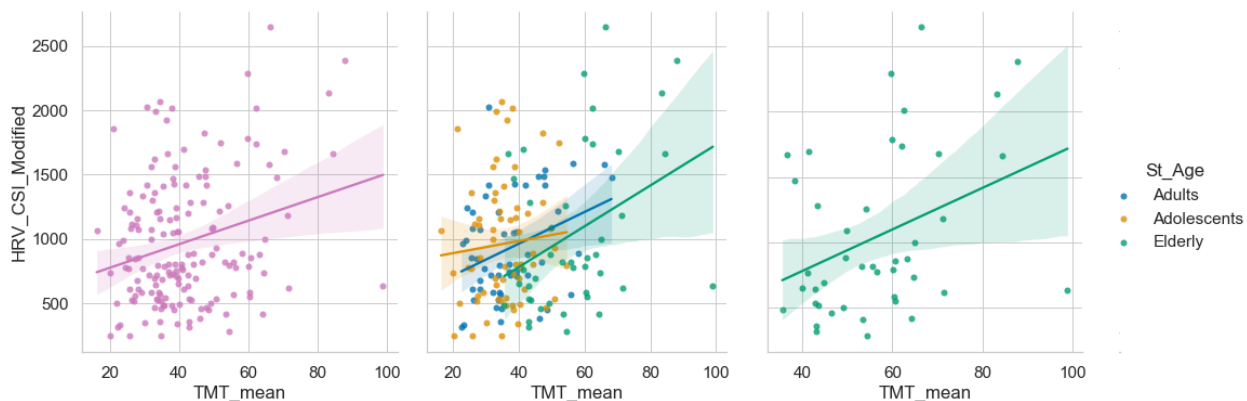
**Figure 43:** Regression plots between TMT\_5 and Alpha 1 Peak (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



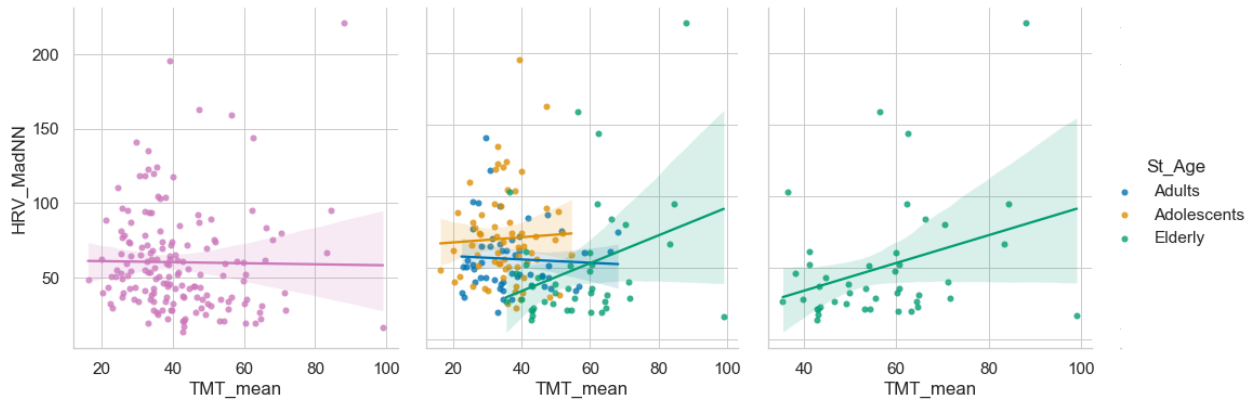
**Figure 44:** Regression plots between TMT\_5 and PI (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



**Figure 45:** Regression plots between TMT\_5 and LFHF (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



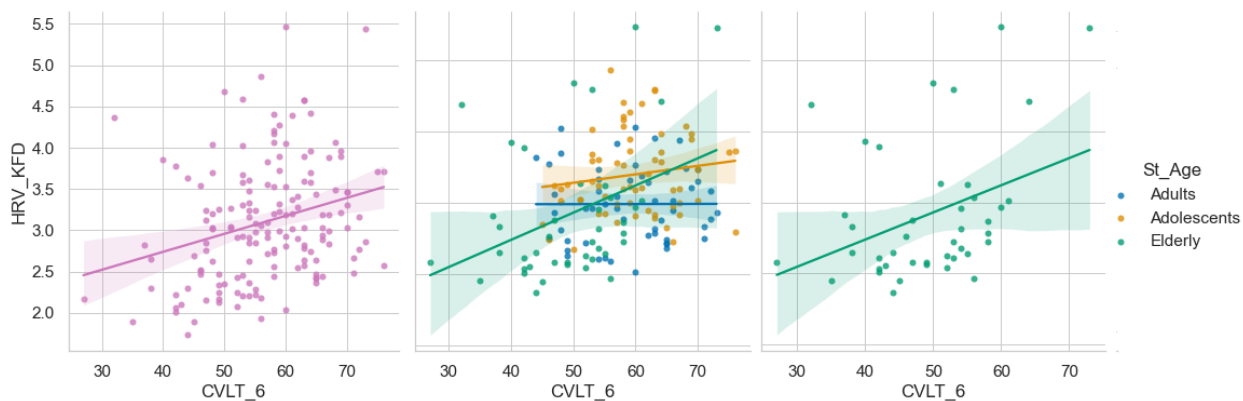
**Figure 46:** Regression plots between TMT\_mean and CSI\_Modified (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



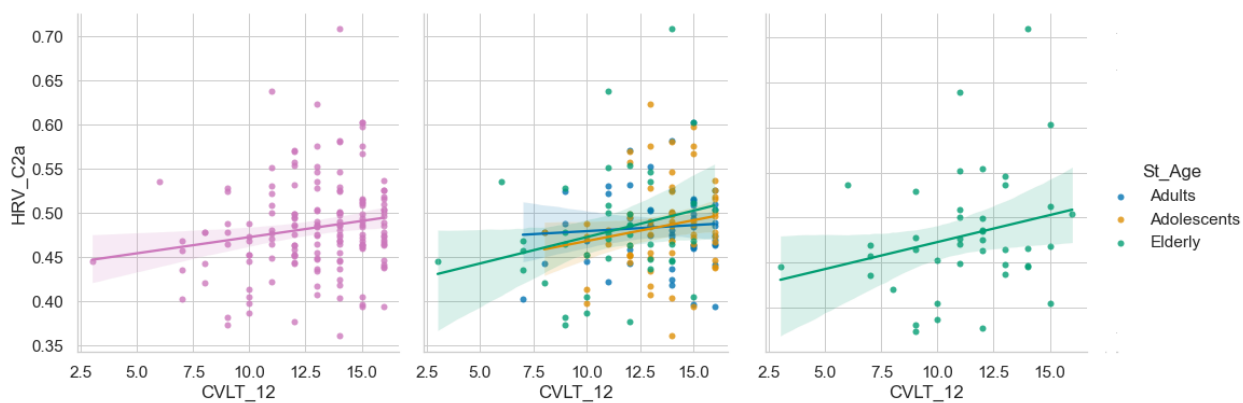
**Figure 47:** Regression plots between *TMT\_mean* and *MadNN* (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)

**Table 5:** Regression results with CVLT for the Elder Group and the Complete Database (*r* - regression coefficient, *CI* - confidence interval)

CVLT	Elderly Group			Complete Database		
	<i>r</i>	<i>CI</i> (95%)	<i>p-value</i>	<i>r</i>	<i>CI</i> (95%)	<i>p-value</i>
<b>CVLT_6</b>						
<i>KFD</i>	0.369	[0.07 0.61]	0.018	0.078	[-0.08 0.23]	0.332
<i>Alpha1 Fluct.</i>	0.285	[-0.03 0.54]	0.071	0.111	[-0.05 0.26]	0.166
<i>Alpha1 Mean</i>	0.261	[-0.05 0.53]	0.100	0.092	[-0.07 0.25]	0.249
<b>CVLT_10*</b>						
<i>PIP</i>	-0.219	[-0.49 0.09]	0.169	-0.124	[-0.27 0.03]	0.120
<i>HFD</i>	-0.216	[-0.49 0.10]	0.174	-0.073	[-0.23 0.08]	0.361
<b>CVLT_12</b>						
<i>C2a</i>	0.276	[-0.03 0.54]	0.080	0.158	[0.01 0.31]	0.048
<i>Ca</i>	0.276	[-0.03 0.54]	0.080	0.162	[0.01 0.31]	0.042
<i>C1a</i>	-0.274	[-0.54 0.04]	0.083	-0.157	[-0.31 -0.00]	0.049



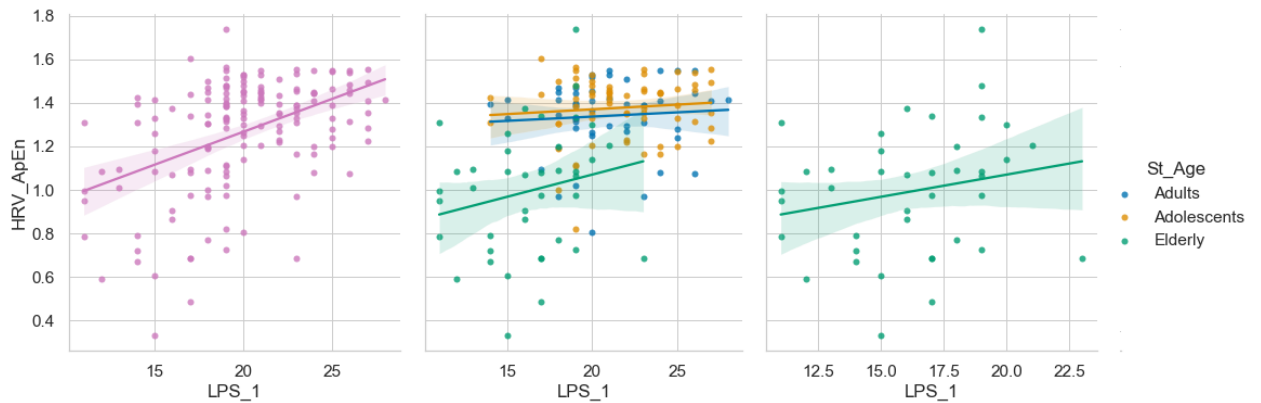
**Figure 48:** Regression plots between CVLT\_6 and KFD (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



**Figure 49:** Regression plots between CVLT\_12 and C2a (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)

CI - confidence interval)

LPS	Elderly Group			Complete Database		
	<i>r</i>	CI (95%)	<i>p</i> -value	<i>r</i>	CI (95%)	<i>p</i> -value
ApEn	0.257	[-0.06 0.52]	0.105	0.091	[-0.07 0.25]	0.263
CSI_Modified.	-0.235	[-0.51 0.08]	0.139	-0.107	[-0.26 0.05]	0.185

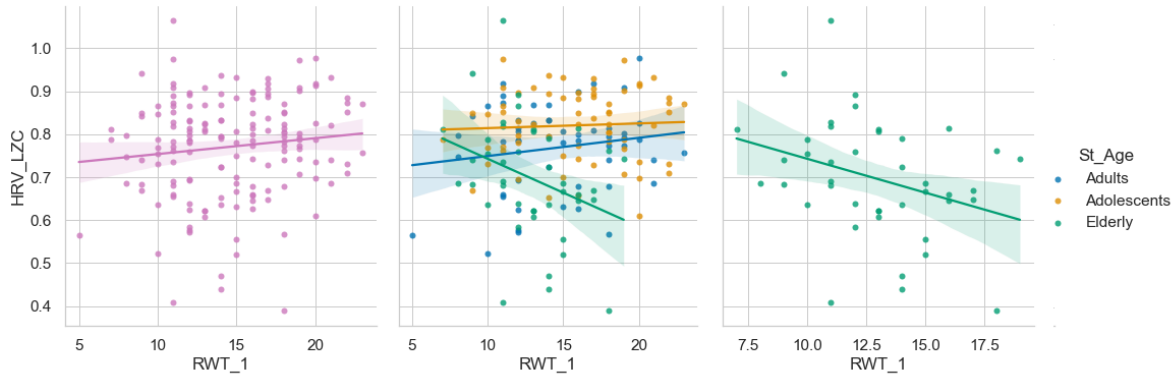


**Figure 50:** Regression plots between LPS\_1 and ApEn (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)

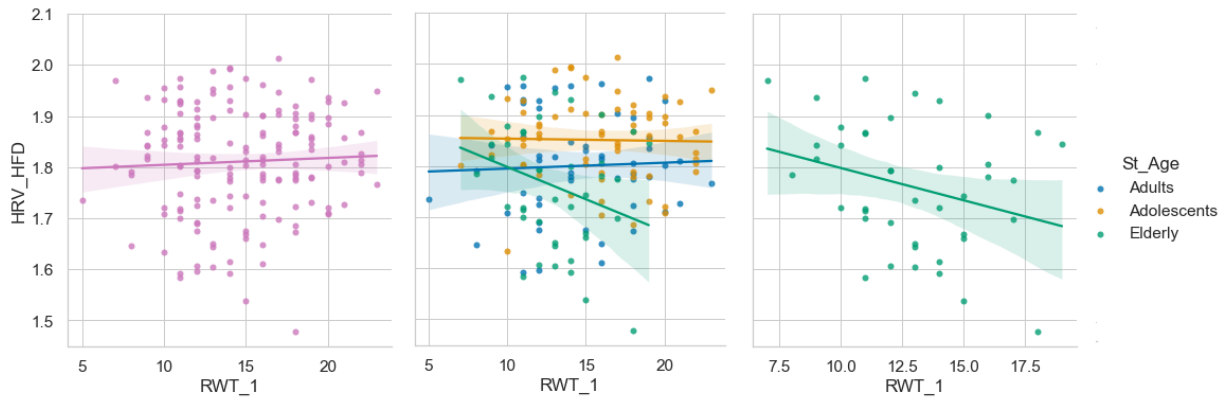
**Table 6:** Regression results with RWT for the Elder Group and the Complete Database (r - regression coefficient, CI - confidence interval)

RWT	Elderly Group			Complete Database		
<i>RWT_1</i>	<i>r</i>	<i>CI (95%)</i>	<i>p-value</i>	<i>r</i>	<i>CI (95%)</i>	<i>p-value</i>
<i>LZC</i>	-0.332	[-0.58 -0.03]	0.034	-0.014	[-0.17 0.14]	0.859
<i>HFD</i>	-0.308	[-0.56 -0.01]	0.050	-0.095	[-0.25 0.06]	0.235
<i>Alpha2 Width</i>	0.291	[-0.02 0.55]	0.065	0.088	[-0.07 0.24]	0.272
<i>ApEn</i>	-0.279	[-0.54 0.03]	0.077	-0.057	[-0.21 0.10]	0.474
<i>Alpha1 Mean</i>	-0.269	[-0.53 0.04]	0.089	0.022	[-0.13 0.18]	0.780
<i>Alpha1 Width</i>	-0.263	[-0.53 0.05]	0.096	0.050	[-0.11 0.20]	0.530
<i>SI</i>	0.257	[-0.06 0.52]	0.105	0.074	[-0.08 0.23]	0.353
<i>Alpha2 Fluct.</i>	0.251	[-0.06 0.52]	0.113	0.055	[-0.10 0.21]	0.488
<i>RWT_12</i>	<i>r</i>	<i>CI (95%)</i>	<i>p-value</i>	<i>r</i>	<i>CI (95%)</i>	<i>p-value</i>
<i>Alpha2 Mean</i>	0.332	[0.02 0.58]	0.036	0.042	[-0.11 0.2]	0.600
<i>Alpha2 Width</i>	0.299	[0.03 0.55]	0.036	0.055	[-0.10 0.21]	0.489
<i>ApEn</i>	-0.250	[-0.52 0.07]	0.120	-0.010	[-0.17 0.15]	0.900
<i>C2a</i>	0.255	[-0.07 0.52]	0.128	0.058	[-0.10 0.21]	0.464
<i>RWT_24</i>	<i>r</i>	<i>CI (95%)</i>	<i>p-value</i>	<i>r</i>	<i>CI (95%)</i>	<i>p-value</i>
<i>SI</i>	0.356	[-0.07 0.53]	0.046	0.137	[-0.02 0.29]	0.088

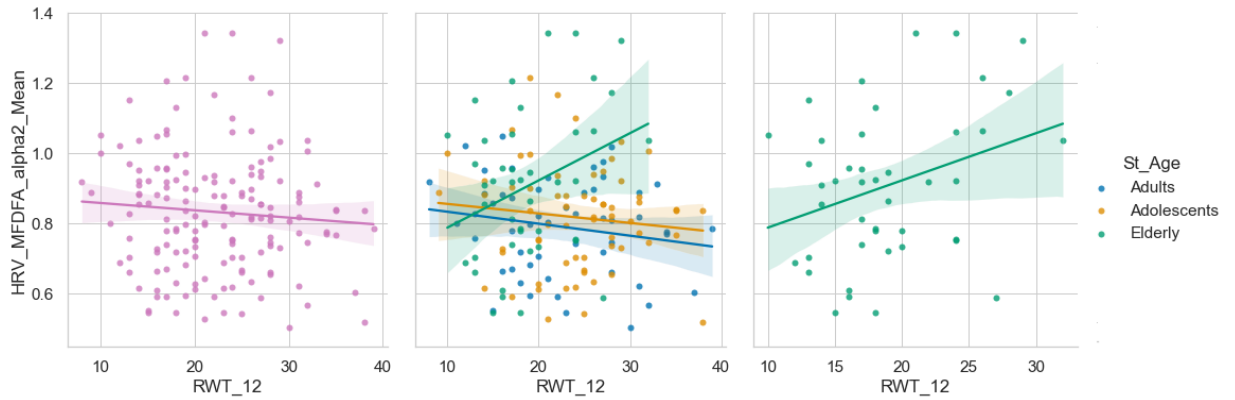
<i>Alpha1 Width</i>	0.193	[-0.13 0.48]	0.240	0.096	[-0.06 0.25]	0.232
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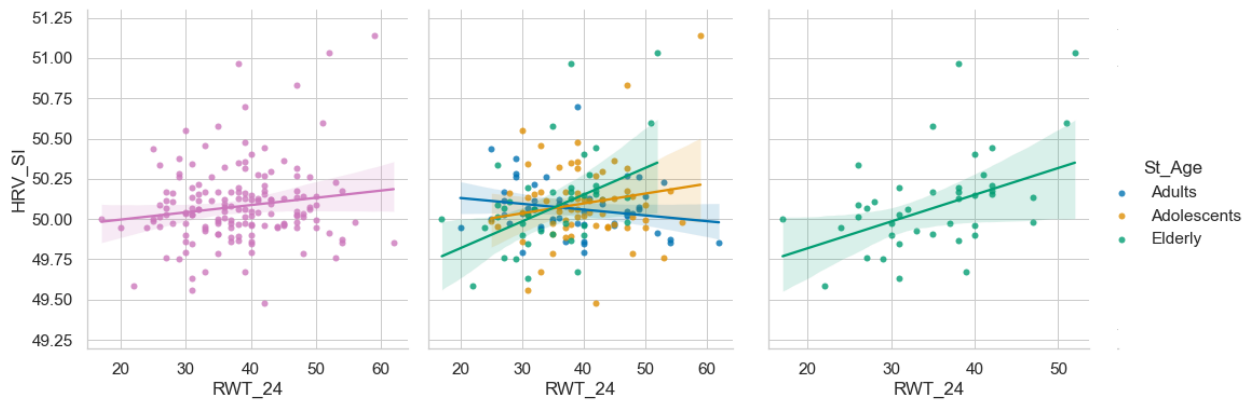
**Figure 51:** Regression plots between RWT\_1 and LZC (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



**Figure 52:** Regression plots between RWT\_1 and HFD (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



**Figure 53:** Regression plots between RWT\_12 and Alpha 2 Mean (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)

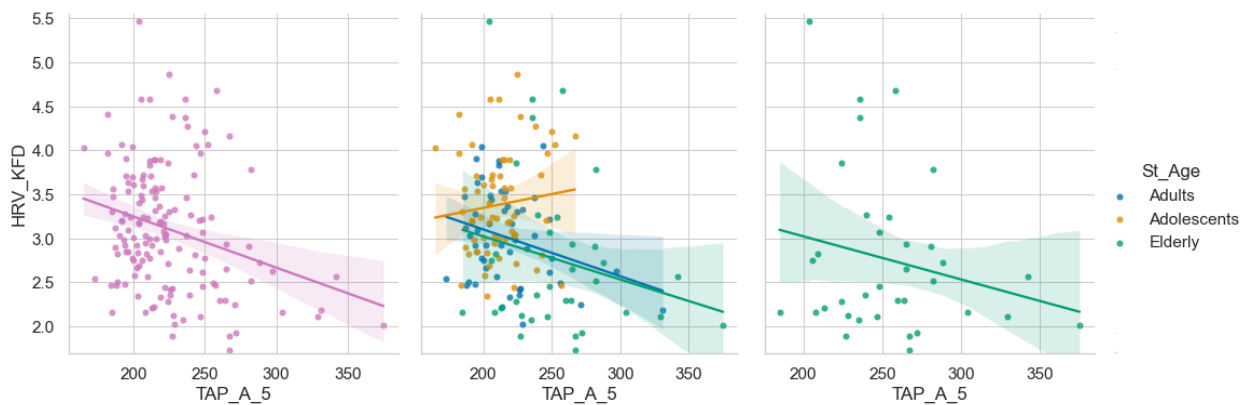


**Figure 54:** Regression plots between RWT\_24 and SI (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)

**Table 7:** Regression results with TAP-A for the Elder Group and the Complete Database (*r* - regression coefficient, *CI* - confidence interval)

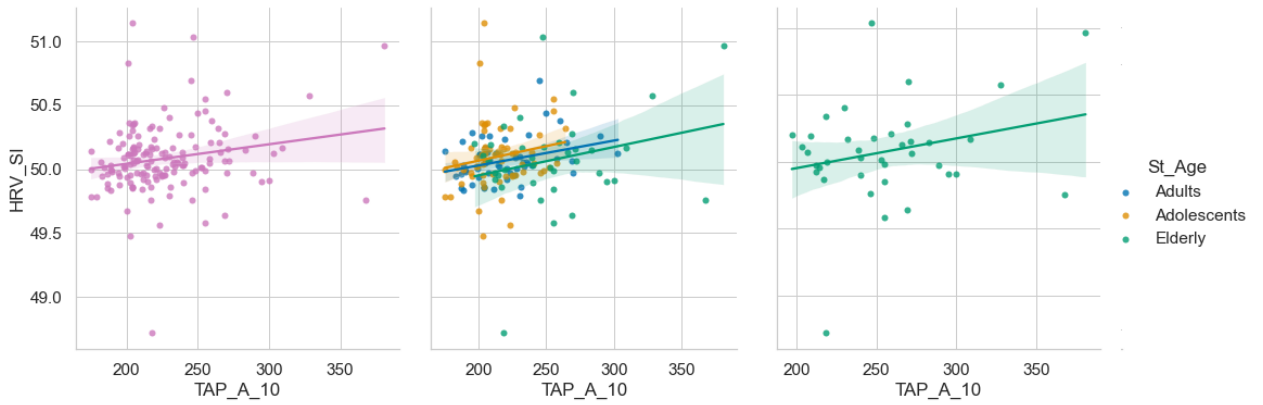
TAP-A	Elderly Group			Complete Database		
	<i>r</i>	<i>CI</i> (95%)	<i>p</i> -value	<i>r</i>	<i>CI</i> (95%)	<i>p</i> -value
<i>KFD</i>	-0.314	[-0.57 -0. ]	0.048	-0.174	[-0.33 -0.01]	0.034
<i>VLF</i>	-0.294	[-0.56 0.02]	0.065	-0.014	[-0.17 0.15]	0.866
<i>Pnn50</i>	-0.294	[-0.55 0.02]	0.066	-0.138	[-0.29 0.02]	0.094
<i>Alpha2 Fluct.</i>	-0.293	[-0.55 0.02]	0.066	-0.142	[-0.3 0.02]	0.085
<i>SDNN</i>	-0.284	[-0.55 0.03]	0.075	-0.131	[-0.29 0.03]	0.112
<i>HF</i>	-0.269	[-0.54 0.05]	0.093	-0.120	[-0.28 0.04]	0.145

<i>Alpha1 Fluct.</i>	-0.268	[-0.53 0.05]	0.095	-0.129	[-0.28 0.03]	0.116
<i>VHF</i>	-0.255	[-0.53 0.06]	0.112	-0.097	[-0.25 0.06]	0.237
<b>TAP_A_10</b>	<b>r</b>	<b>CI (95%)</b>	<b>p-value</b>	<b>r</b>	<b>CI (95%)</b>	<b>p-value</b>
<i>SI</i>	0.091	[-0.23 0.40]	0.582	0.265	[0.11 0.41]	0.001
<i>IQRNN</i>	0.227	[-0.09 0.51]	0.164	0.262	[0.11 0.40]	0.001
<b>TAP_A_16</b>	<b>r</b>	<b>CI (95%)</b>	<b>p-value</b>	<b>r</b>	<b>CI (95%)</b>	<b>p-value</b>
<i>C1a</i>	-0.362	[-0.60 -0.06]	0.020	-0.157	[-0.31 0.00]	0.053
<i>CSI_Modified</i>	-0.351	[-0.59 -0.05]	0.024	-0.216	[-0.36 -0.06]	0.007
<i>SDANN2</i>	-0.303	[-0.56 0.01]	0.054	-0.149	[-0.30 0.01]	0.067
<i>MinNN</i>	0.295	[-0.01 0.55]	0.061	0.155	[-0.00 0.31]	0.057
<i>MadNN</i>	-0.281	[-0.54 0.03]	0.075	-0.178	[-0.33 -0.02]	0.028
<i>SDNN</i>	-0.280	[-0.54 0.03]	0.076	-0.220	[-0.37 -0.06]	0.006
<i>IQRNN</i>	-0.255	[-0.52 0.06]	0.108	-0.195	[-0.34 -0.04]	0.016

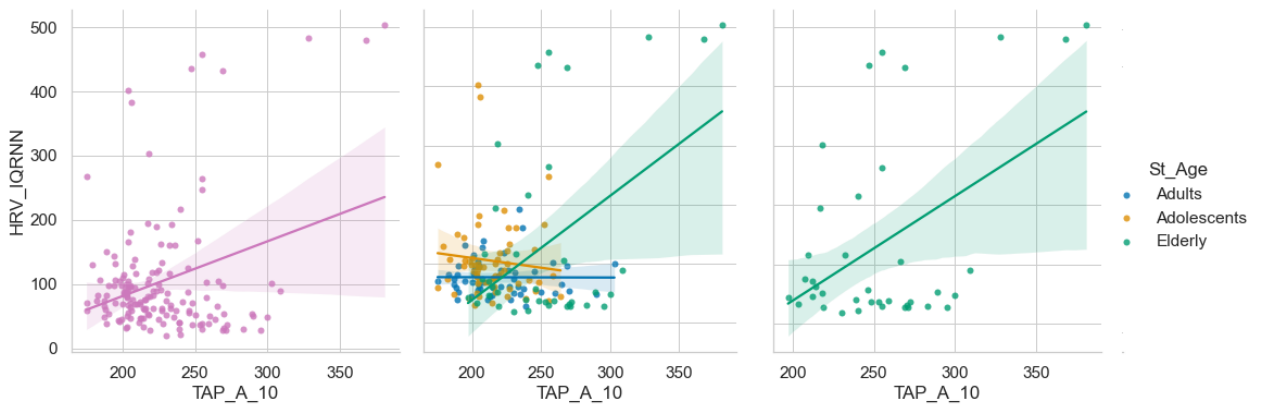


**Figure 55:** Regression plots between TAP\_A\_5 and KFD (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)

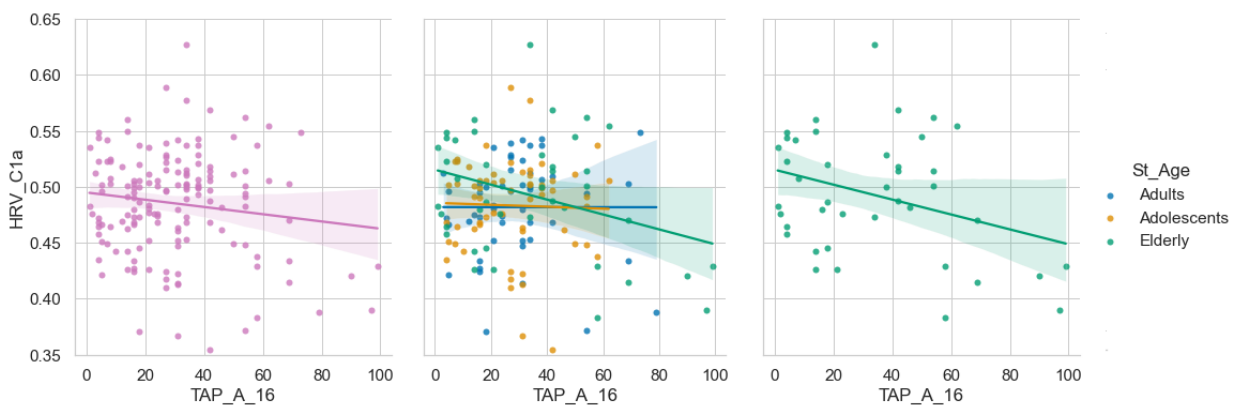




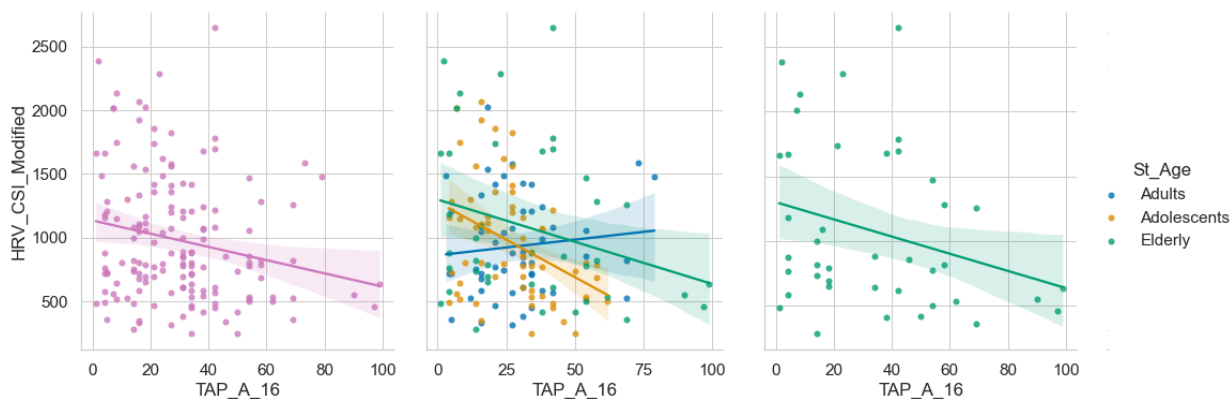
**Figure 56:** Regression plots between TAP\_A\_10 and SI (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



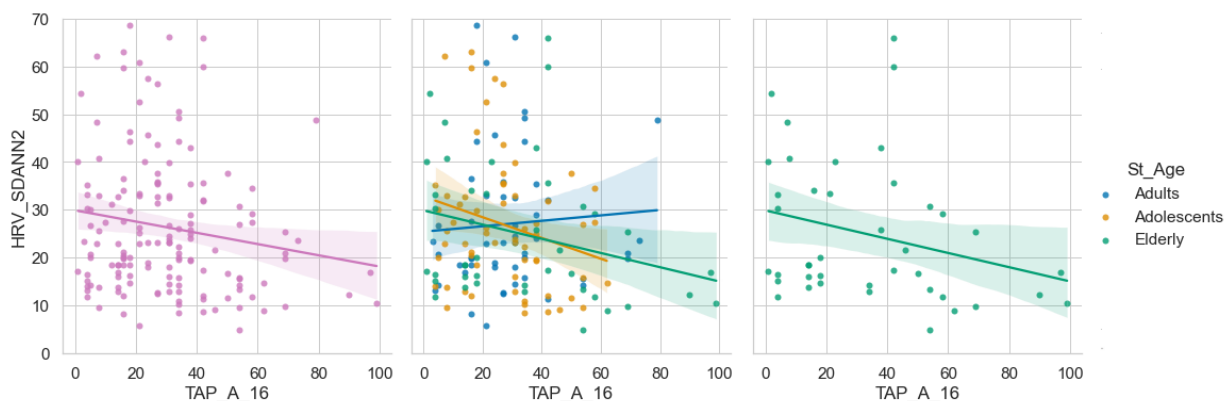
**Figure 57:** Regression plots between TAP\_A\_10 and IQRNN (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



**Figure 58:** Regression plots between TAP\_A\_16 and C1a (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



**Figure 59:** Regression plots between TAP\_A\_16 and CSI\_Modified (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)

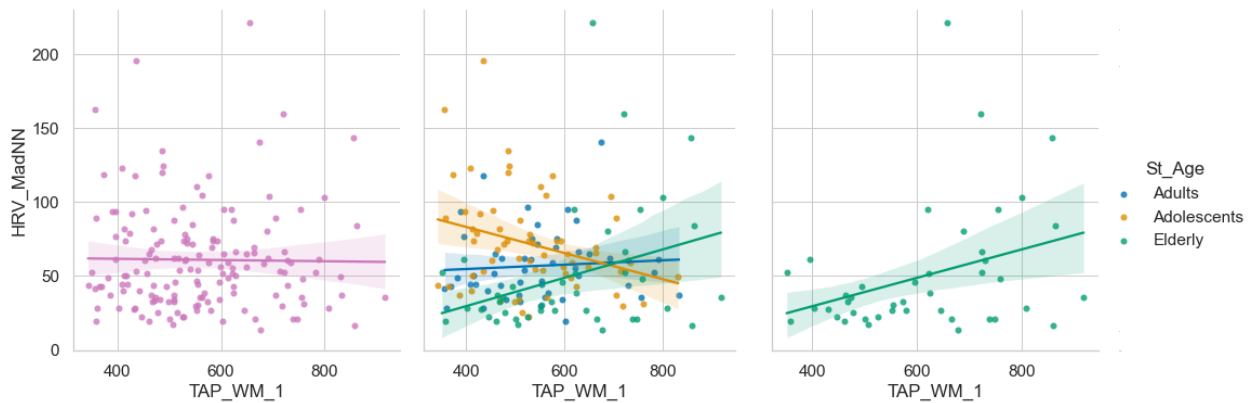


**Figure 60:** Regression plots between TAP\_A\_16 and SDANN2 (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)

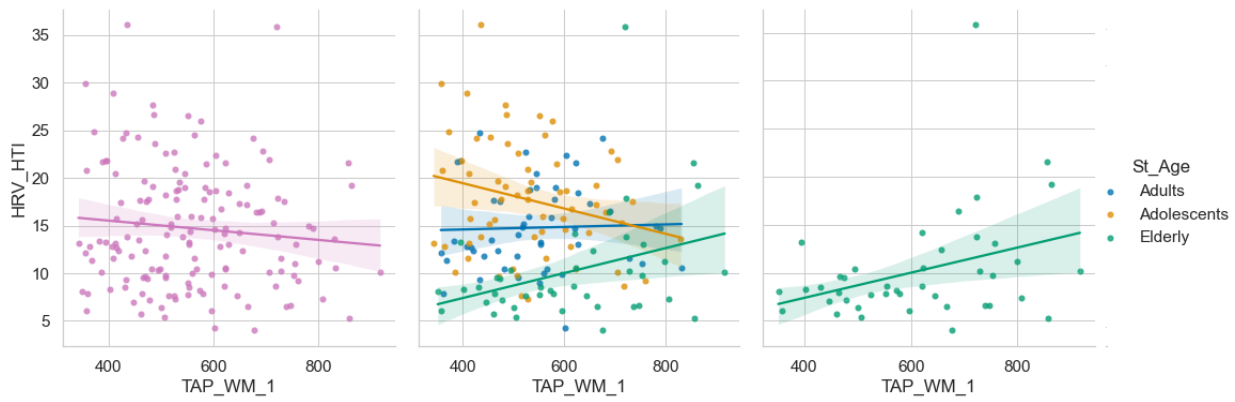
**Table 8:** Regression results with TAP-WM for the Elder Group and the Complete Database (*r* - regression coefficient, *CI* - confidence interval)

TAP-WM	Elderly Group			Complete Database		
	<i>r</i>	CI (95%)	<i>p</i> -value	<i>r</i>	CI (95%)	<i>p</i> -value
MadNN	0.381	[0.08 0.62]	0.014	0.060	[-0.1 0.22]	0.460
HTI	0.380	[0.08 0.62]	0.014	0.032	[-0.13 0.19]	0.698
SDANN2	0.333	[0.03 0.58]	0.033	0.009	[-0.15 0.17]	0.912
CSI_Modified	0.329	[0.02 0.58]	0.036	0.094	[-0.07 0.25]	0.248
SI	0.285	[0.08 0.62]	0.014	0.065	[-0.1 0.22]	0.428

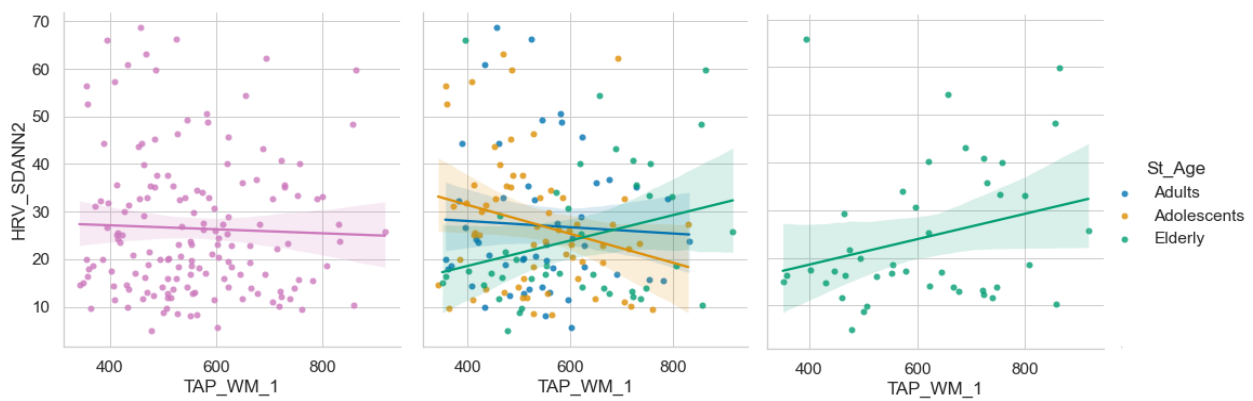
<i>GI</i>	0.283	[-0.03 0.54]	0.073	0.024	[-0.14 0.18]	0.769
<i>MinNN</i>	-0.267	[-0.53 0.04]	0.091	-0.028	[-0.19 0.13]	0.733
<i>pNN50</i>	0.259	[-0.05 0.53]	0.101	0.050	[-0.11 0.21]	0.539
<i>SDNN</i>	0.258	[-0.05 0.52]	0.103	0.055	[-0.11 0.21]	0.503
<b>TAP_WM_6</b>	<b><i>r</i></b>	<b><i>CI (95%)</i></b>	<b><i>p-value</i></b>	<b><i>r</i></b>	<b><i>CI (95%)</i></b>	<b><i>p-value</i></b>
<i>CD</i>	-0.392	[-0.63 -0.09]	0.012	-0.247	[-0.39 -0.09]	0.002
<i>ApEn</i>	-0.355	[-0.60 -0.05]	0.024	-0.163	[-0.31 -0.00]	0.045
<i>Alpha1 Fluct.</i>	0.264	[-0.05 0.53]	0.099	0.101	[-0.06 0.26]	0.217
<b>TAP_WM_7</b>	<b><i>r</i></b>	<b><i>CI (95%)</i></b>	<b><i>p-value</i></b>	<b><i>r</i></b>	<b><i>CI (95%)</i></b>	<b><i>p-value</i></b>
<i>CD</i>	0.363	[0.05 0.61]	0.023	0.294	[0.14 0.43]	0.000
<i>Ca</i>	-0.280	[-0.55 0.04]	0.084	-0.159	[-0.31 0.00]	0.052
<i>ApEn</i>	0.272	[-0.05 0.54]	0.094	0.196	[0.04 0.35]	0.016



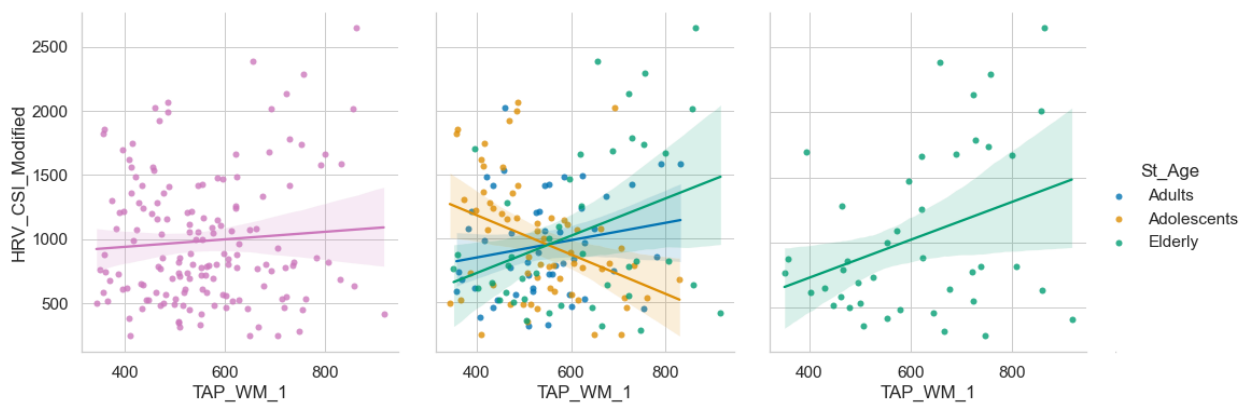
**Figure 61:** Regression plots between TAP\_WM\_1 and MadNN (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



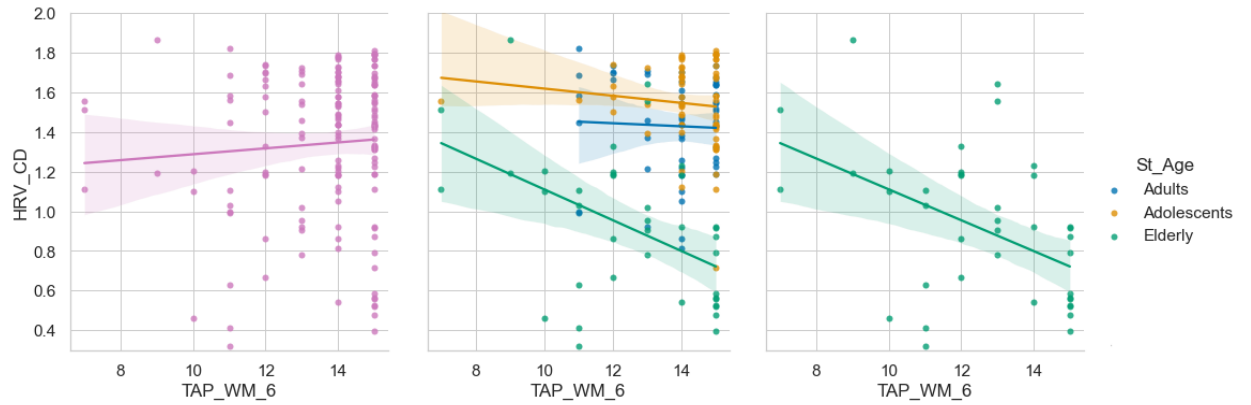
**Figure 62:** Regression plots between TAP\_WM\_1 and HTI (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



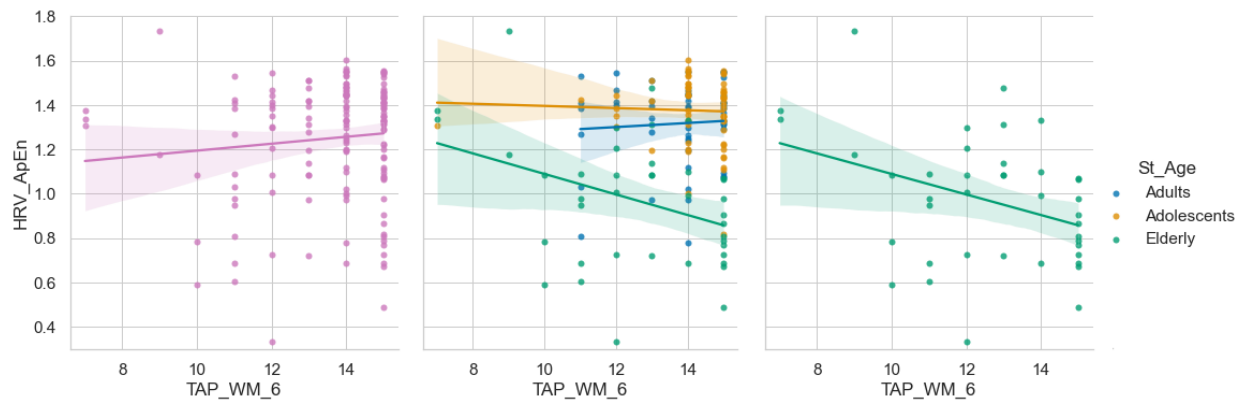
**Figure 63:** Regression plots between TAP\_WM\_1 and SDANN2 (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



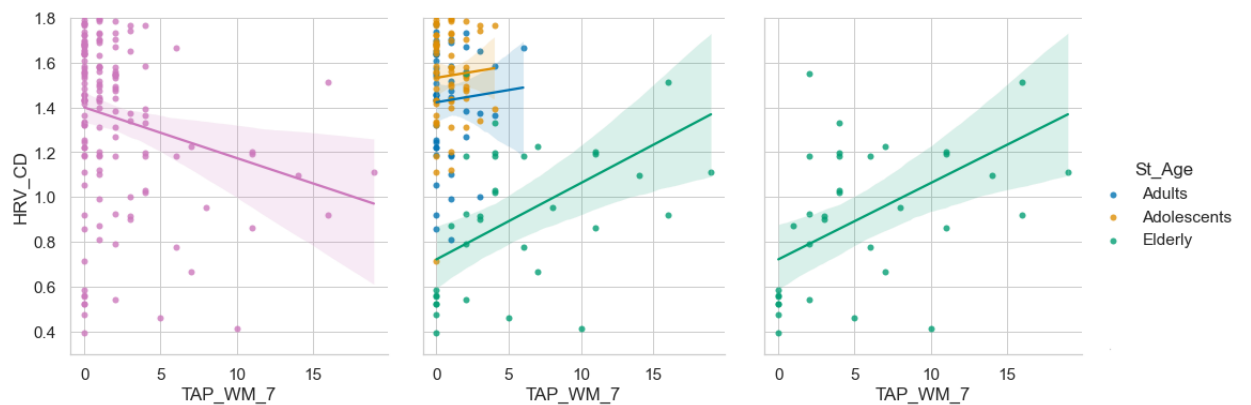
**Figure 64:** Regression plots between TAP\_WM\_1 and CSI\_Modified (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



**Figure 65:** Regression plots between TAP\_WM\_6 and CD (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



**Figure 66:** Regression plots between TAP\_WM\_6 and ApEn (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)



**Figure 67:** Regression plots between TAP\_WM\_1 and MadNN (left plot - complete database; central plot - complete database with age groups differentiation; right plot - Elder Group)

**Table 9:** Regression results with WST for the Elder Group and the Complete Database (*r* - regression coefficient, *CI* - confidence interval)

<b>WST</b>	<b>Elderly Group</b>			<b>Complete Database</b>		
	<i>r</i>	<i>CI (95%)</i>	<i>p-value</i>	<i>r</i>	<i>CI (95%)</i>	<i>p-value</i>
<b>WST_1</b>						
<i>MadNN</i>	0.377	[0.08 0.61]	0.015	0.126	[-0.03 0.28]	0.115
<i>SDANN2</i>	0.375	[0.08 0.61]	0.016	0.123	[-0.03 0.27]	0.125
<i>IQRNN</i>	0.370	[0.07 0.61]	0.017	0.171	[0.02 0.32]	0.032
<i>CSI_Modified</i>	0.346	[0.04 0.59]	0.027	0.116	[-0.04 0.27]	0.147
<i>SDNN</i>	0.297	[-0.01 0.55]	0.059	0.131	[-0.03 0.28]	0.101
<i>Alpha1 Fluct.</i>	0.277	[-0.03 0.54]	0.080	0.092	[-0.07 0.24]	0.253
<i>Ca</i>	0.265	[-0.05 0.53]	0.094	0.174	[0.02 0.32]	0.029
<i>Alpha1 Assy.</i>	-0.264	[-0.53 0.05]	0.096	-0.085	[-0.24 0.07]	0.291
<b>WST_3</b>	<i>r</i>	<i>CI (95%)</i>	<i>p-value</i>	<i>r</i>	<i>CI (95%)</i>	<i>p-value</i>
<i>SDANN2</i>	0.408	[0.11 0.64]	0.008	0.140	[-0.02 0.29]	0.078
<i>MadNN</i>	0.405	[0.11 0.63]	0.009	0.125	[-0.03 0.28]	0.115
<i>CSI_Modified</i>	0.362	[0.06 0.60]	0.020	0.119	[-0.04 0.27]	0.133
<i>SDNN</i>	0.311	[0.00 0.56]	0.048	0.131	[-0.03 0.28]	0.100
<i>Alpha1 Fluct.</i>	0.277	[-0.03 0.54]	0.079	0.083	[-0.07 0.23]	0.299
<i>Alpha1 Peak</i>	0.269	[-0.04 0.53]	0.089	0.086	[-0.07 0.24]	0.278
<i>Alpha1 Assy.</i>	-0.266	[-0.53 0.05]	0.092	-0.106	[-0.26 0.05]	0.181
<i>Ca</i>	0.266	[-0.05 0.53]	0.093	0.129	[-0.03 0.28]	0.103

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