

Sex Differences In Cognitive Decline: Sensory Abilities And Pathological Factors

In Different Profiles Of Mild Cognitive Impairment

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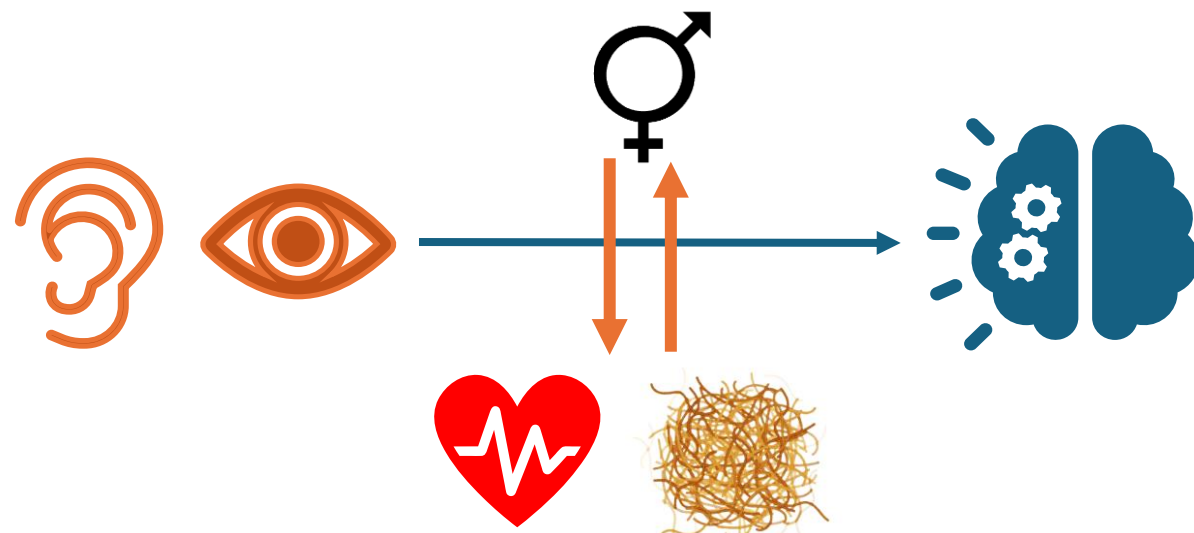
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BACKGROUND AND QUESTIONS

- 1) Sensory abilities $\approx$ 7% of preventable dementia risk factors, while vascular factors $\approx$ 2%
- 2) Intersectionality with sex and gender understudied, despite:
 - Men: more severe cardiovascular risk factors (CVRF), and vascular lesions in later life^[2]
 - Women: hypertension related to cognitive decline^[3], known impact of sensory impairment

QUESTION: How do sensory abilities predict cognition in people with different profiles of risk of dementia when considering:

- 1) Sex identity lived experience, and
- 2) CVRF, Alzheimer's pathology and brain vascular damage



METHODS

Variable	Cognitively Unimpaired			Amnesic MCI			Vascular MCI		
	Male (n=35)	Female (n=65)	Statistic	Male (n=121)	Female (n=67)	Statistic	Male (n=58)	Female (n=41)	Statistic
Demographics									
Non-caucasian background	n=2	n=3		n=16	n=10		n=8	n=4	
Caucasian background	n=33	n=62		n=105	n=57		n=50	n=37	
Age	70.16±5.66	69.76±6.1	-0.33	72.43±6.76	71.93±6.79	-0.47	77.61±6.27	74.37±5.64	-2.67**
Education	16.14±2.33	15.11±2.44	-2.09*	15.47±2.96	15.21±2.84	-0.58	15.6±2.81	14.05±2.57	-2.83**
MoCA	27.31±1.69	27.52±1.67	0.59	23.64±2.76	24.28±2.73	1.51	23.03±3.26	24.1±3.06	1.65
Sensory abilities									
CDTT	-10.08±2.52	-10.41±1.47	-0.72	-9.35±2.21	-9.68±2.08	-1	-7.39±3.5	-9.49±2.94	-3.22***
CS	1.7±0.21	1.74±0.15	0.89	1.66±0.16	1.7±0.14	1.69	1.59±0.2	1.62±0.17	0.83
Pathological / Risk variables									
rFSRP	5.09±2.9	5.54±3.65	0.68	5.84±3.28	5.34±3.13	-0.99	7.16±3.73	5.97±3.44	-1.61
Global WMH	15046.17±16382.55	10495.37±7872.7	-1.55	13479.44±10543.45	13238.66±8400.06	-0.17	42778.26±24310.01	29893.22±18415.11	-2.98**
Frontal WMH	6547.69±5864.68	4857±3721.63	-1.55	5723.86±3867.23	6332.43±4673.25	0.89	19733.67±13798.68	15227.3±9863.38	-1.89
Temp. WMH	2528.23±2097.9	1990.52±1220.68	-1.39	2483.83±1884.19	2238.57±1228.95	-1.03	5026.95±2704.1	3473.28±1799.8	-3.41***
Parietal WMH	4001±7391.68	2056.63±2522.63	-1.51	2999.14±4281.55	2955.57±2618.51	-0.08	13786.03±9816.68	8574.45±7107.66	-3.05***
Occip. WMH	1738.66±1900.61	1336.6±1062.6	-1.16	1994.02±1506.43	1444.72±1028.25	-2.84**	3913.62±2250.51	2293.57±2439.11	-3.33***
Aβ42/40 ratio	0.06±0.01	0.07±0.01	2.71*	0.06±0.01	0.06±0.01	-0.27	7.16±3.73	5.97±3.44	-1.61
Cognitive abilities									
CRT	0.64±0.15	0.64±0.13	0.01	0.7±0.15	0.78±0.14	3.45***	0.81±0.19	0.76±0.15	-1.47
nBRT	0.61±0.33	0.66±0.25	0.67	0.87±0.65	1.14±0.67	2.61**	1.26±1.07	1.27±0.95	0.05
DSST	63.06±14.69	66.45±12.56	1.16	54.75±11.7	55.34±15.93	0.24	44.9±13.29	51.55±11.65	2.62**

Table 1. Demographic and clinical data. MoCA= Montreal Cognitive Assessment; CDTT= Canadian Digit Triplet Test; CS= Contrast Sensitivity; rFSRP= revised Framingham Stroke Risk Profile; WMH = White Matter Hyperintensities; Aβ42/40 = plasma β-amyloid (TP 42 / 40); CRT= Choice Reaction Time; nBRT = n-1 Back Reaction Time. DSST= Digit Symbol Substitution Test; * = p<0.05; ** = p<0.01; *** = p < 0.001

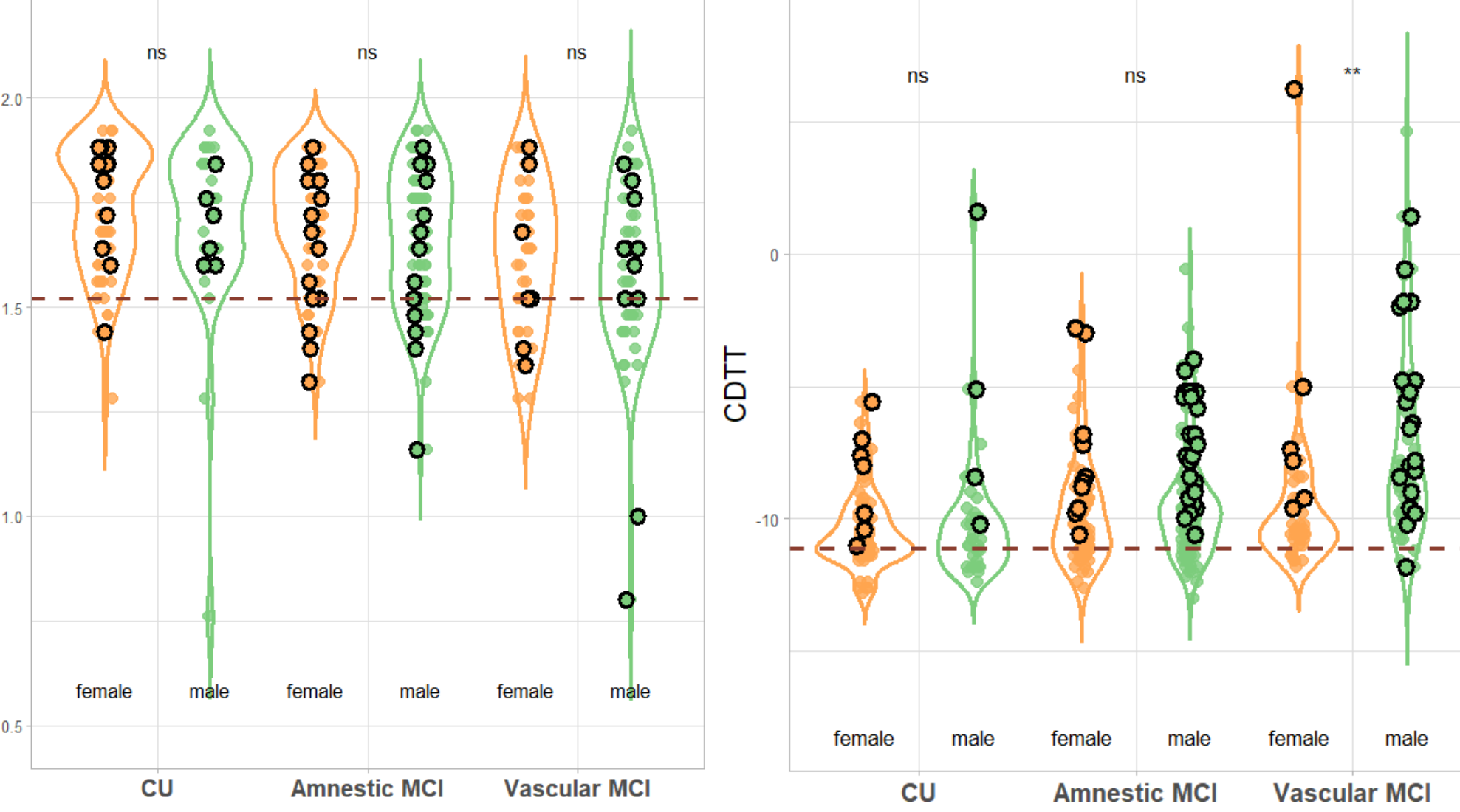


Figure 1. Violin plots from sensory abilities per group. Highlighted individuals have reported wearing sensory aids in daily life. Dashed line indicates the threshold for normative data of such sensory measure for populations of > 60 y.o. (Note: for CDTT values, the more negative, the better the hearing capacities; for CS values, the more positive, the better the visual capacities). NS = non-significant; ** = p<0.01

Sample recruited from COMPASS-ND study⁽⁴⁾ with no stroke history and assessed in :

- Sensory testing: Hearing (Canadian Digit-Triple Test, **CDTT**) and Vision (Contrast Sensitivity, **CS**)
- Neuropsychological battery, including: Perception (Choice Reaction Times, **CRT**), Working memory (n-1 Back Reaction Times, **BRT**) and Incidental learning (Digit Symbol Substitution Test, **DSST**)
- White Matter Hyperintensities (**WMH**) extracted from all lobes (T1-FLAIR sequence)
- Revised Framingham Stroke Risk Profile⁽⁵⁾ (**rFSRP**), with CVRF such as diabetes, smoking, CV events, etc.

ANALYSIS

1. Correlational analysis between predictors (sensory abilities / pathological factors) and outcomes (cognitive abilities).
2. Hierarchical regression models of processing speed / reaction times controlling for age, sex, education (**Model 1**), adding pathological factors (CVRF, Aβ-42/40, Global WMH) (**Model 2**), and finally hearing and vision (**Model 3**). A last step includes the interaction of each sensory ability and sex (added in separated models).
3. Finally, sex-stratified regressions are performed.

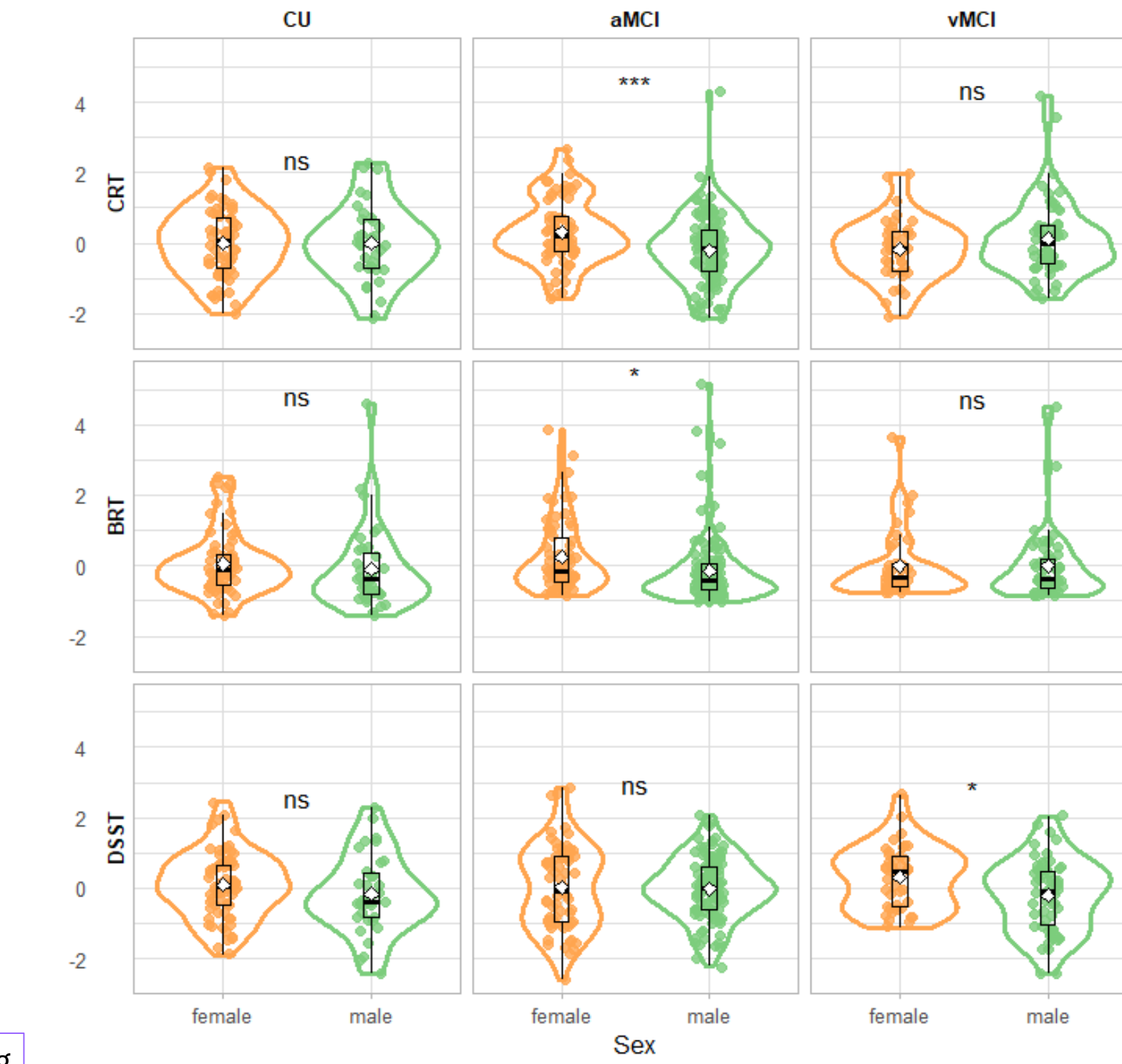


Figure 2. Violin plots from cognitive abilities per group (centered values per group). NS= non-significant; * = p<0.05; *** = p < 0.001

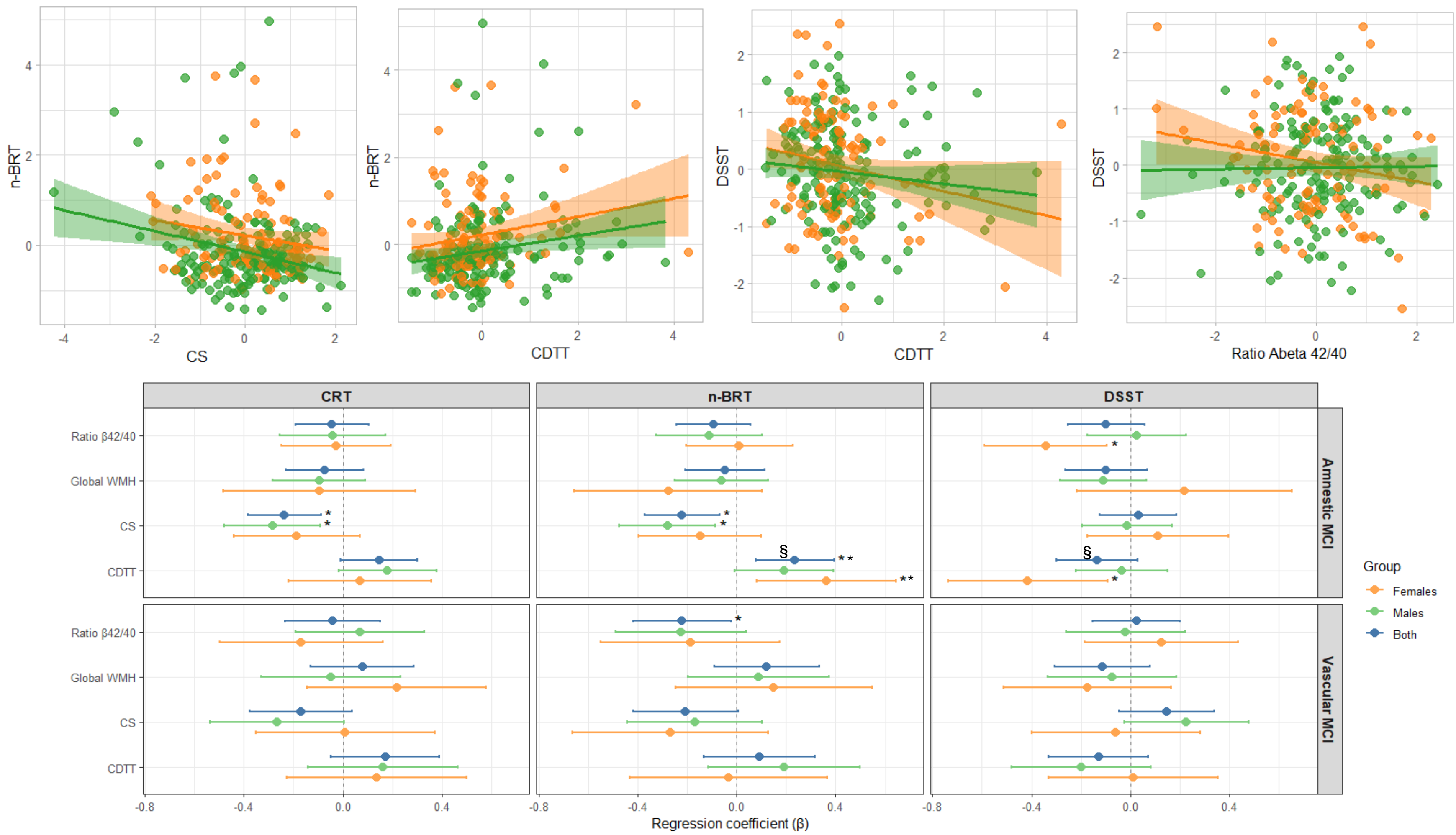
CONCLUSION

- 1) Sensory health may be a resilient factor against dementia factors, depending on the underlying pathology
- 2) Analyses per sex of risk factors of dementia may reveal important dissociations with potential for better prevention of cognitive decline

DISCUSSION

- **Speech-to-noise discrimination** associated to worse performance in visual tasks only in **MCI females**, whereas **contrast sensitivity** associated to worse performance only in **MCI males** → Possible intermodal influence?
- Differences of pathological factors found more in MCI subgroups, but only plasma-measured Aβ-42/40 seems to be associated to worse performance → sensory resilience over CVRF?

RESULTS



Figures 4 and 5. Forest plots with standardized regression coefficients from prediction models (Model 3) of each outcome in both clinical groups, and scatterlots of selected residualized outcomes and residualized predictors in MCI participants. No significant predictors were found for control participants. Predictors marked with § also showed a significant interaction with sex in the overall prediction models (regardless of their main effect)

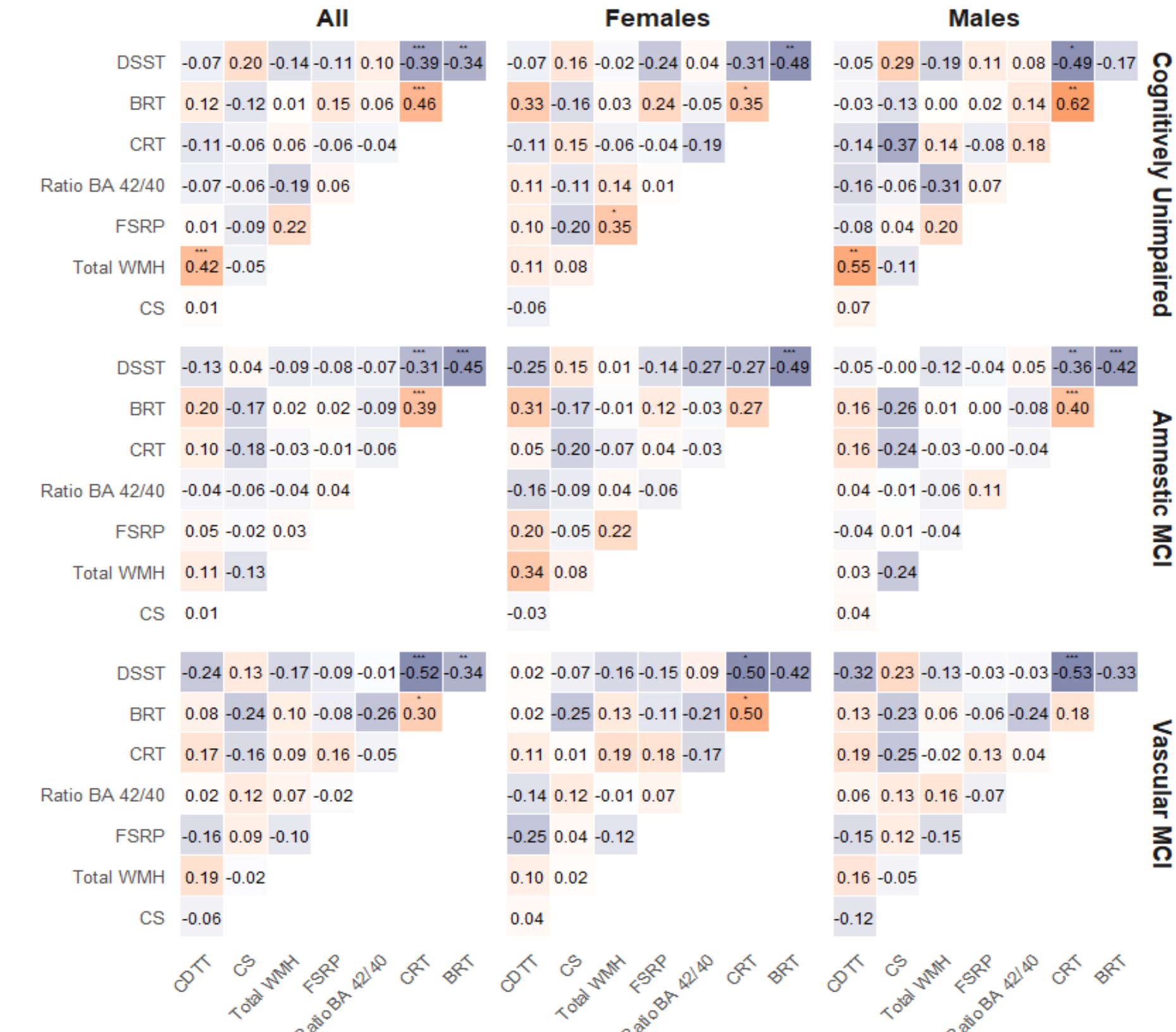


Figure 3. Correlation matrices among candidate predictors and outcomes across groups, controlling for age. All correlation are adjusted by BH method * = p<0.05; ** = p<0.01; *** = p < 0.001

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[1] Livingston et al., *The Lancet*.2024; [2] Gong et al. *BMC medicine*, 2021; [3] Czoeker & Goodwill, *Alzheimers & Dement*, 2018; [4] Phillips et al. *CJA*, 2025; [5] Wolf et al. *Stroke*, 1991

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