

Relationship Between Menopausal Symptoms and Task-Induced Cortical Hemodynamic Response in Midlife: An fNIRS Study

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INTRODUCTION

- **Dementia disproportionately affects females**, and **perimenopause and early postmenopause** are increasingly recognized as **critical periods of neuro-aging**.
- Menopause research has largely focused on how **estradiol (E2) loss** affects brain structure and glucose metabolism. However, E2 also **acts on the cerebral vasculature**, promoting **vasodilation** that delivers blood to active brain tissue.
- **Functional near-infrared spectroscopy (fNIRS)** measures the **hemodynamic response function (HRF)**: the relative change in **oxygenated (HbO)**, **deoxygenated (Hb)** and **total hemoglobin (THb)** in cortical regions engaged during a task.
- A recent cross-sectional study (Zhou 2024) linked **greater menopausal symptom burden** to a **lower prefrontal HRF** in perimenopausal and postmenopausal females but relied on a single total symptom score and analyzed only HbO.
- Menopausal symptoms are **not one construct**, and the three hemoglobin signals **carry different information**.

OBJECTIVES & METHODS

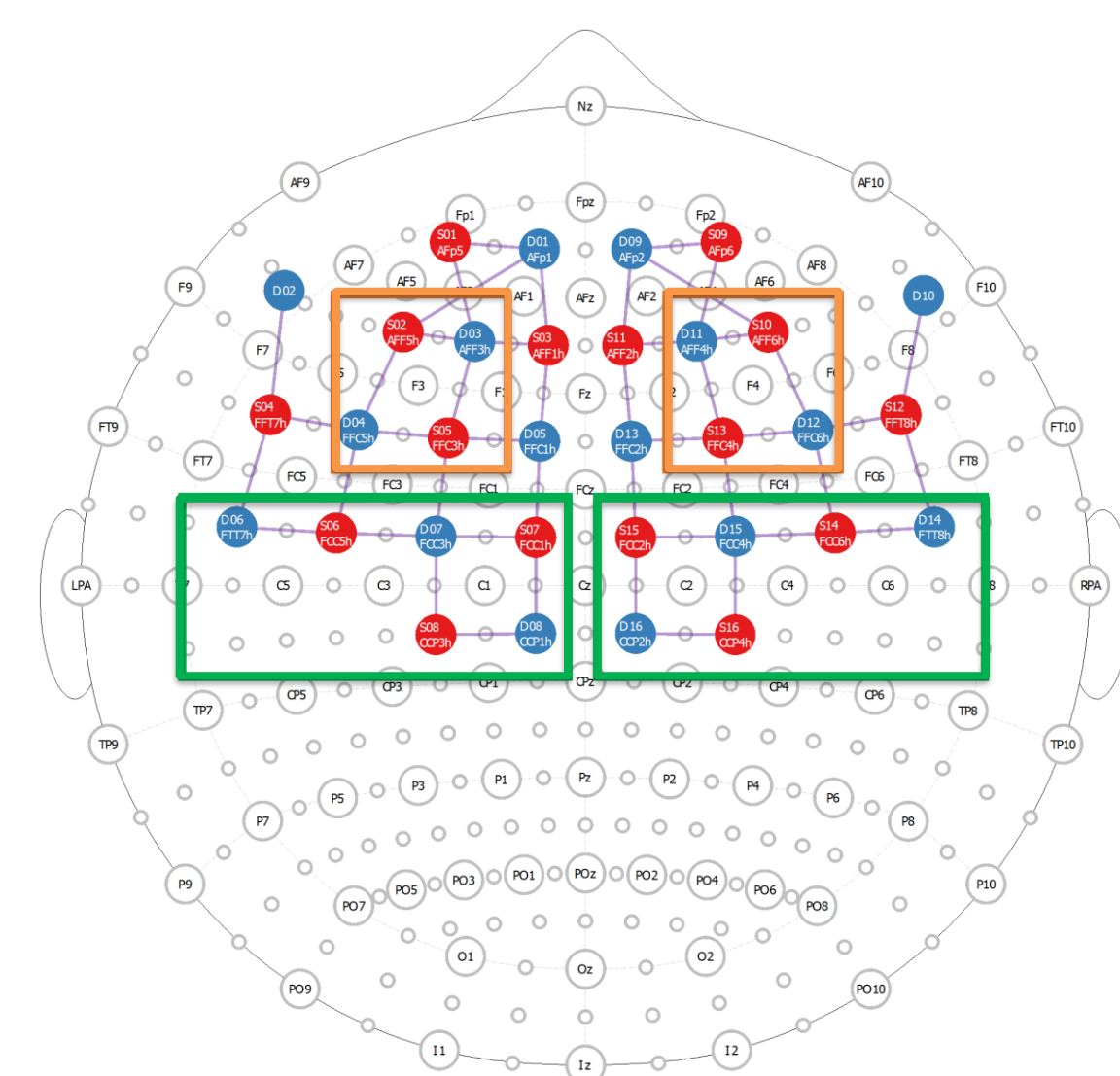
To determine how **reproductive stage** and **menopausal symptom subdomains** relate to the **task-induced HRF** across **all three hemoglobin signals** (HbO, Hb, THb) in midlife females.

Participants & Symptom Measures

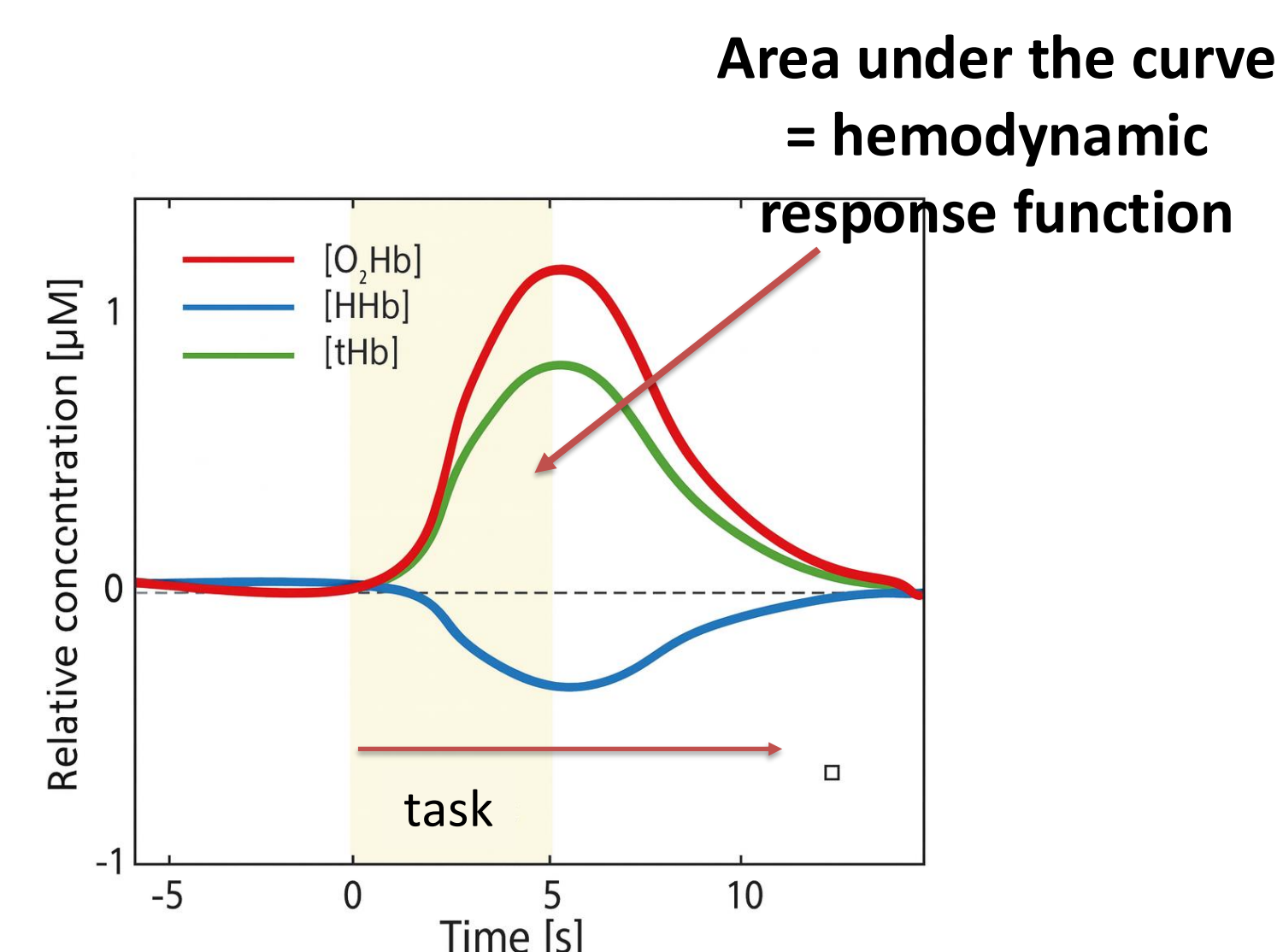
- **31 females aged 45–60** from the baseline assessment of the **SMART Brain pilot RCT**
- Reproductive stage by **STRAW+10 criteria**: **15 perimenopause** and **16 early postmenopause**
- **Menopause-Specific Quality of Life questionnaire (MENQOL)**: total score and **four subdomains** (**vasomotor, psychosocial, physical, sexual**); higher scores indicate greater symptom burden

fNIRS Outcomes

fNIRS tracked relative changes in **HbO, Hb and THb** over the **dorsolateral prefrontal cortex (DLPFC)** and **premotor cortex (PMC)** during a **2-back working memory task** (6 blocks: 35 s task, 20 s rest).



DLPFC (orange) and PMC (green)



HRF = area under the concentration curve during the task, relative to a pre-task baseline, for each hemoglobin signal and region.

Statistical Analysis: Separate linear regressions examined reproductive stage and each MENQOL score for every hemoglobin signal and region, adjusted for age, body mass index, education and hormone therapy use.

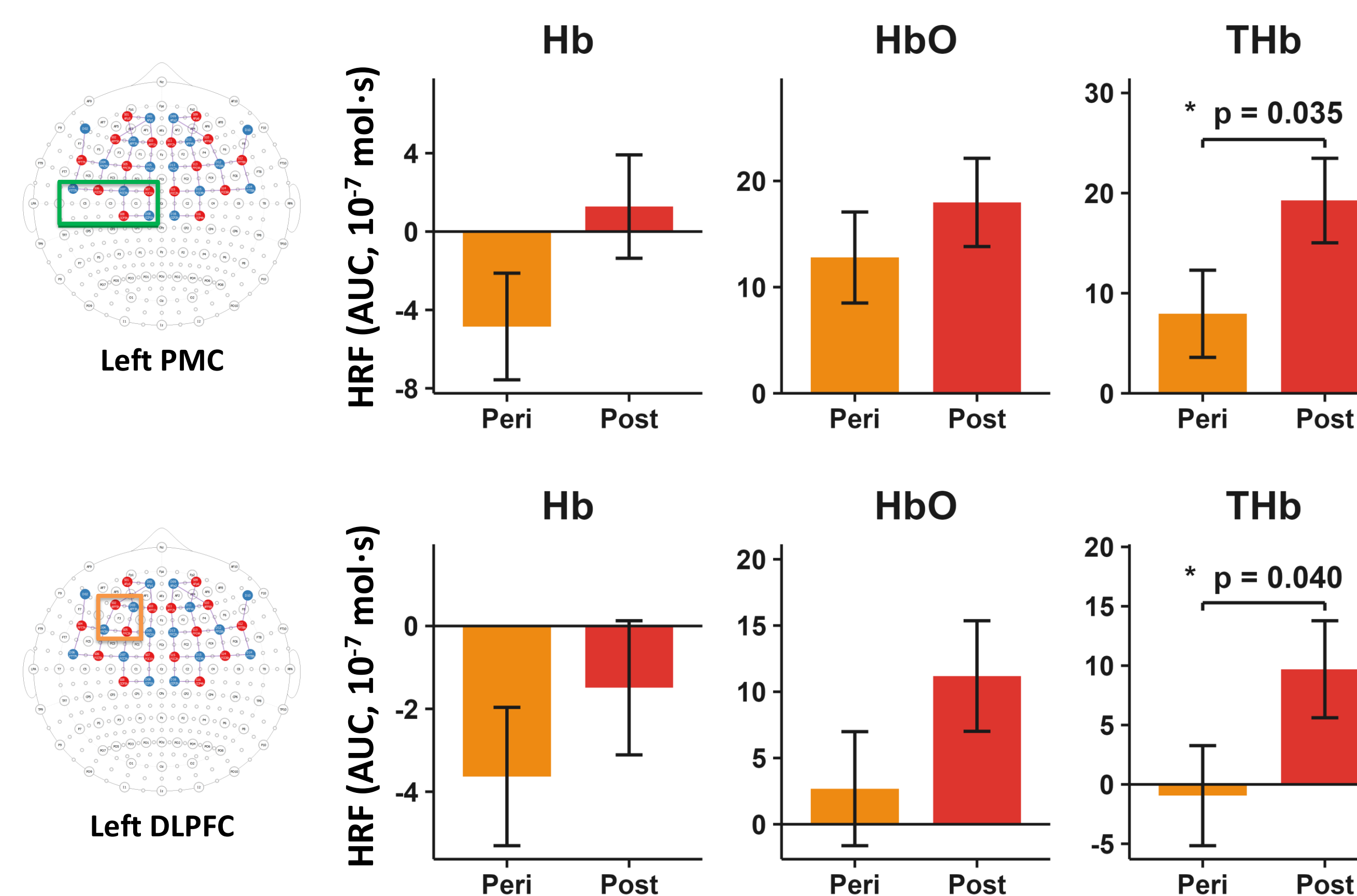
RESULTS

Table 1. Baseline Characteristics by Reproductive Stage

	Perimenopause (n = 15)	Early Postmenopause (n = 16)	p value
Age (years)	51.1 (4.1)	54.2 (3.4)	0.028
Body mass index (kg/m ²)	29.1 (9.3)	26.5 (4.5)	0.343
Master's degree or higher, n (%)	4 (27%)	7 (44%)	0.458
Hormone therapy use, n (%)	2 (13%)	2 (12%)	1.000
Estradiol (pg/ml)	379.3 (284.6)	66.8 (90.8)	0.001
Follicle stimulating hormone (pg/ml)	34.7 (31.3)	74.8 (26.0)	0.001
MENQOL total	2.5 (1.3)	2.9 (1.1)	0.319
Vasomotor	2.2 (2.0)	2.9 (2.4)	0.385
Psychosocial	2.9 (1.7)	2.7 (1.1)	0.790
Physical	2.6 (1.4)	2.9 (0.9)	0.435
Sexual	2.3 (1.6)	3.1 (2.5)	0.272

Mean (SD) unless noted. Bold: p < 0.05 between stages.

HRF by Reproductive Stage



HRF by reproductive stage: Early postmenopausal females had a greater THb response than perimenopausal females in the left PMC (p = 0.035) and left DLPFC (p = 0.040). No stage differences reached significance for HbO or Hb. Bars are estimated marginal means ± SE.

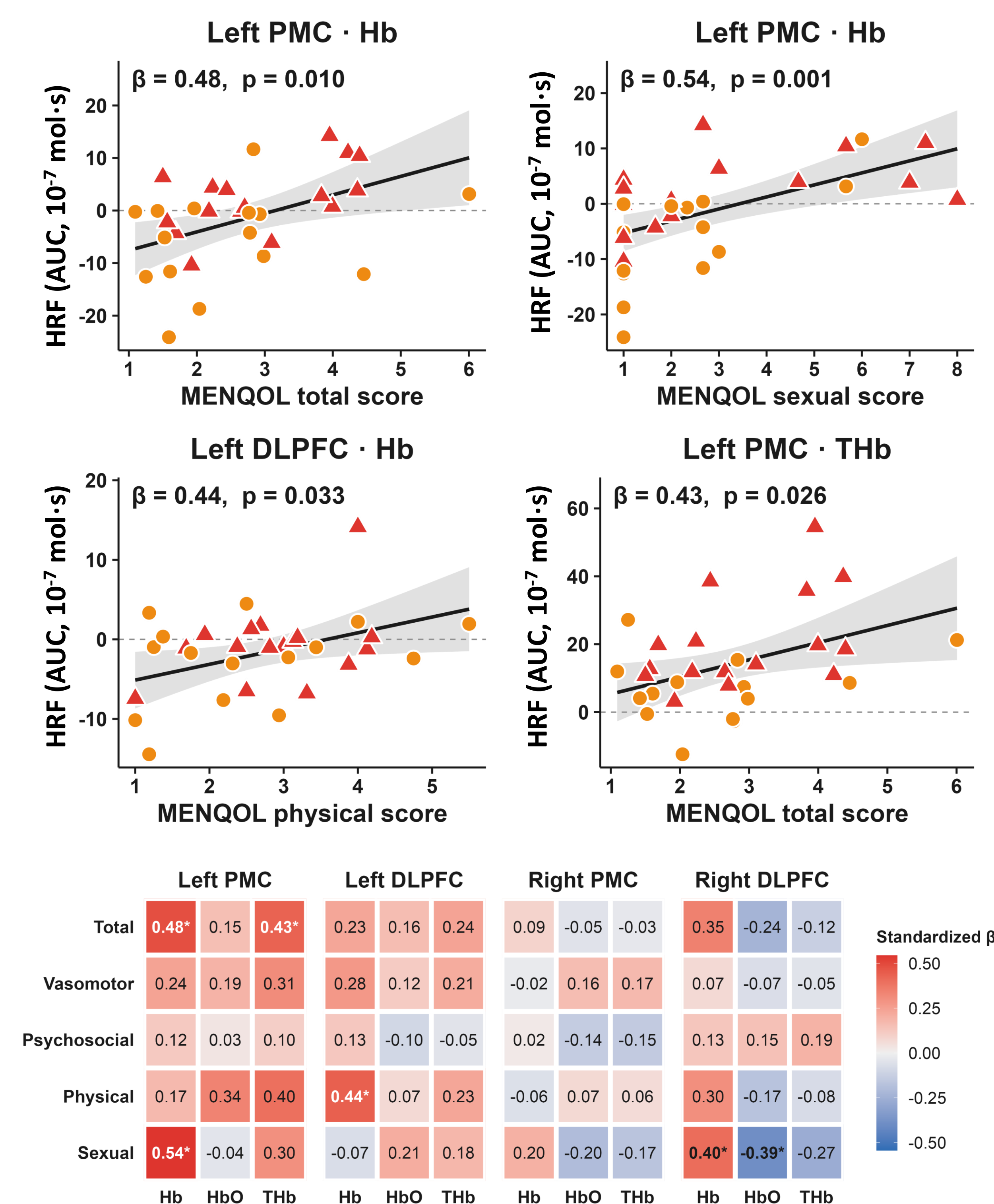
CONCLUSIONS & LIMITATIONS

- In contrast to a previous study, our results suggest that **task-induced cerebral blood flow increased, not decreased, in early postmenopause versus perimenopause**.
- **Sexual and physical symptoms** of menopause were related with a greater hemodynamic response; vasomotor and psychosocial symptoms were not.
- As **estradiol loss** underlies both menopausal symptoms and reduced vasodilation, greater **sexual and physical symptom burden** may indicate a **brain blood supply not as well matched to demand** during a cognitive task.
- These effects appeared in **total and deoxygenated hemoglobin** and would have been **missed if analyzing oxygenated hemoglobin alone**.

Limitations: 1. Small sample size; 2. Cross-sectional design; 3. Exploratory analyses, not corrected for multiple comparisons

Perimenopause Early Postmenopause

HRF and Menopausal Symptoms



Menopause Symptoms and HRF: Greater total symptom burden was associated with a larger Hb (p = 0.010) and THb (p = 0.026) response in the left PMC. By subdomain, sexual symptoms were related to left PMC Hb (p = 0.001) and physical symptoms to left DLPFC Hb (p = 0.033). HbO showed no association in the left hemisphere. In the right DLPFC, sexual symptoms were related to higher Hb (p = 0.023) and lower HbO (p = 0.039). Heatmap: standardized β ; * p < 0.05.

ACKNOWLEDGMENTS

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