

Stress-sensitive Neuroendocrine Pathways Link Environmental Toxicants to Subjective Cognitive Decline in Aging

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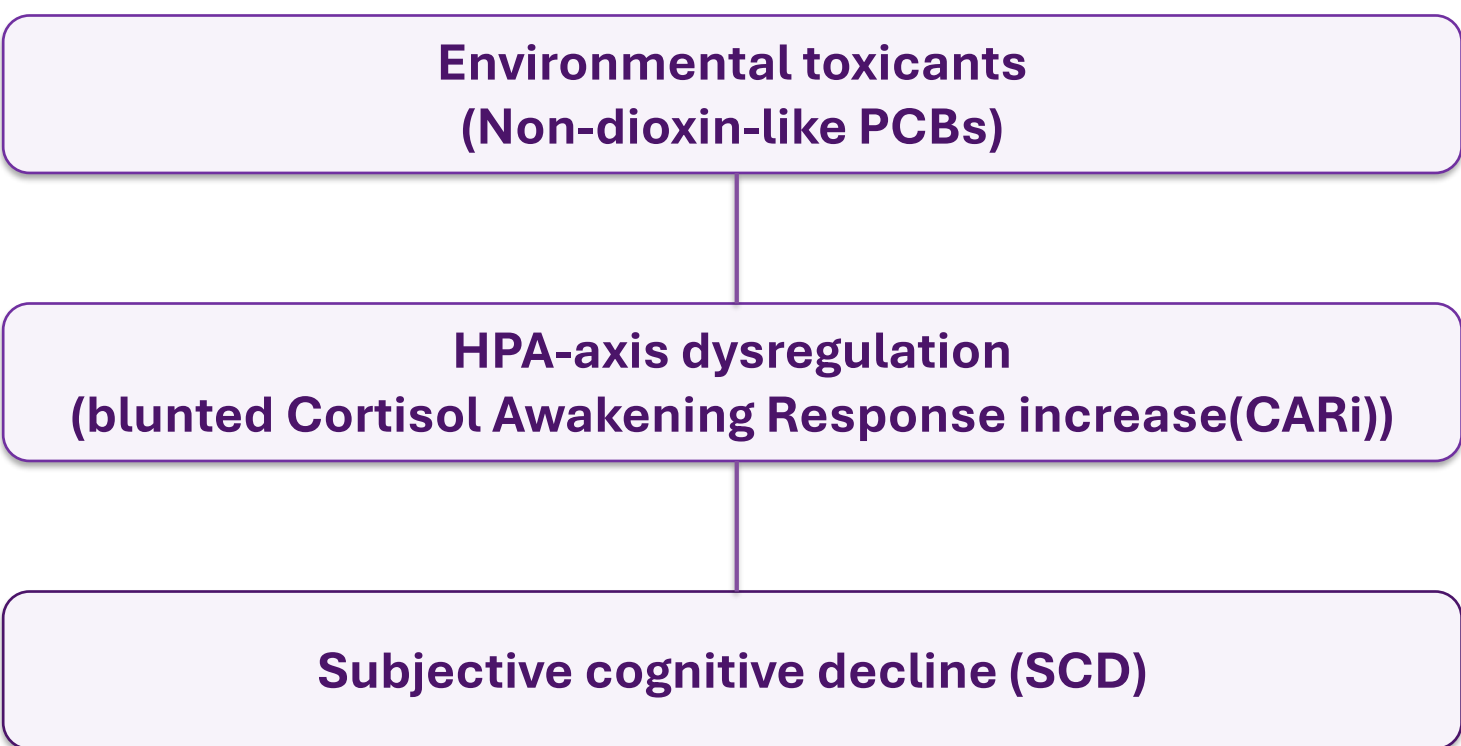
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INTRODUCTION

- Environmental toxicants are increasingly recognized as modifiable risk factors for cognitive aging, yet the early biological mechanisms remain unclear.
- Non-dioxin-like polychlorinated biphenyls(PCBs) may disrupt steroid hormone signaling and alter hypothalamic-pituitary-adrenal(HPA) axis function, a key stress-sensitive neuroendocrine pathway.
- Subjective cognitive decline can emerge before objective cognitive deficits; it may serve as an early indicator of toxicant-related cognitive vulnerability.
- To identify early neuroendocrine mechanisms linking environmental toxicant exposure to cognitive vulnerability, this study examined PCB-related HPA-axis dysregulation and subjective cognitive decline in cognitively unimpaired older adults.



METHODS

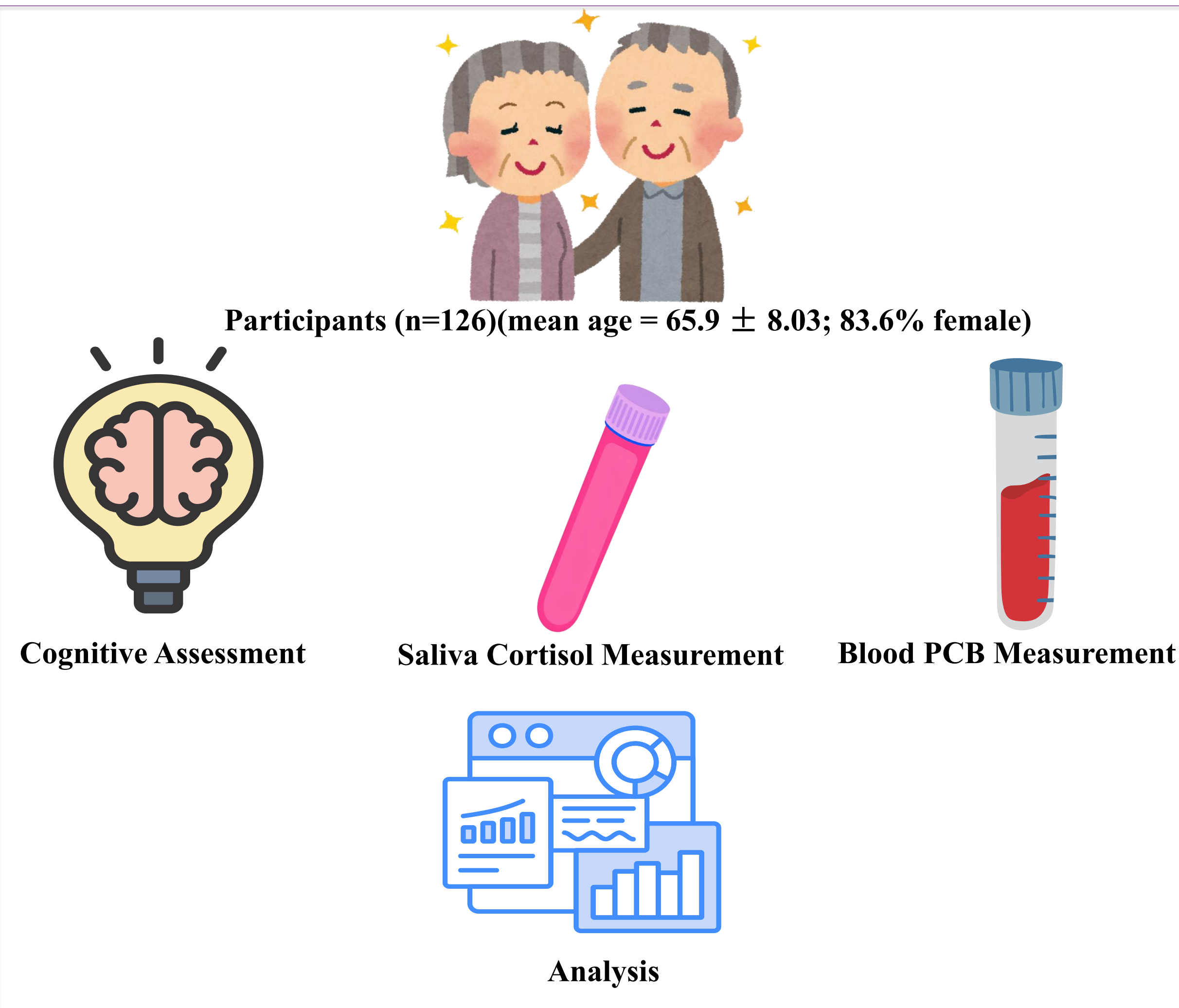
Measures

- Cross-sectional study of 126 cognitively unimpaired, community-dwelling adults aged ≥ 50 years
- Serum non-dioxin-like PCB concentrations were quantified using mass spectrometry
- Neurotoxic equivalency represents the resulting cumulative neurotoxicity-weighted PCB burden
- Salivary cortisol at awakening and +30 min over two consecutive days to derive CARi
- SCD assessed with Memory Assessment Complaint Questionnaire(MAC-Q)
- Objective cognition: global cognition, attention, memory, and executive function

Analysis

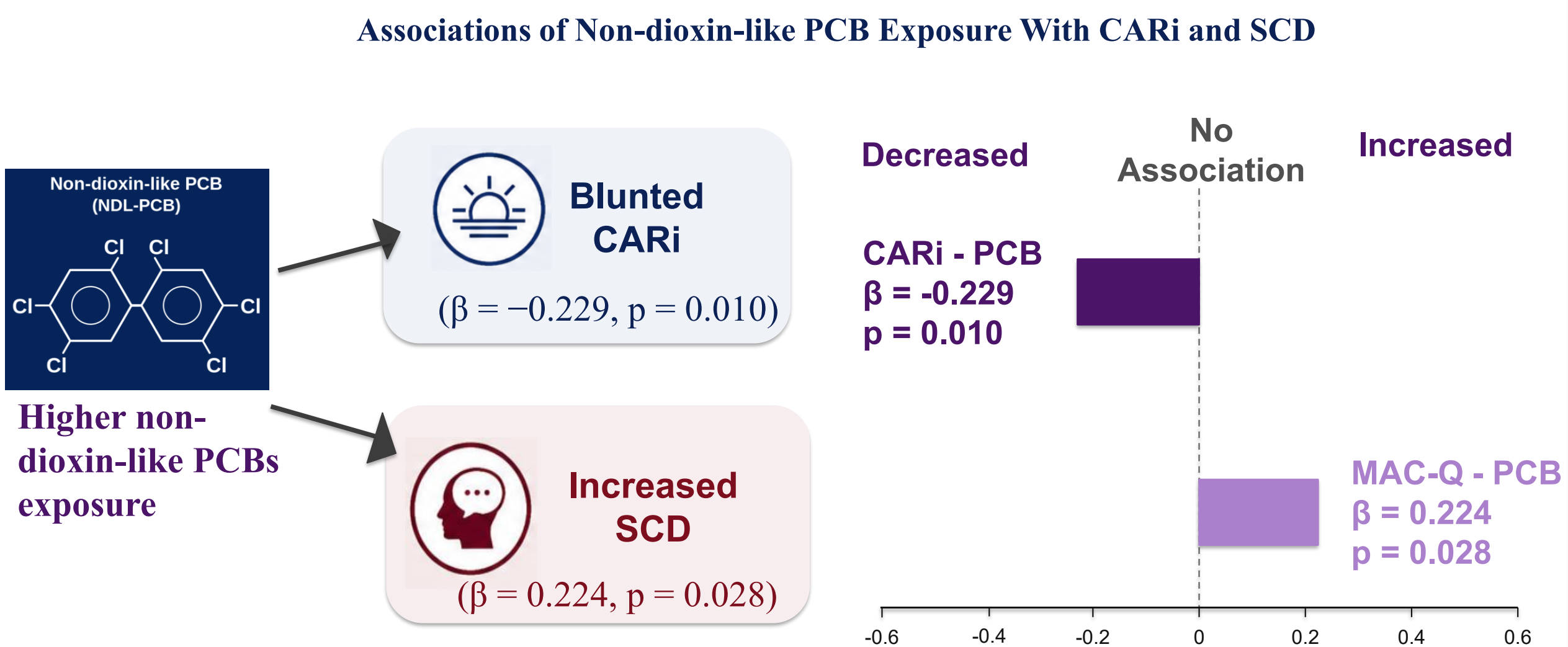
- Linear regression models tested PCB associations with CARi and cognitive outcomes, adjusted for age, sex, and education.

STUDY DESIGN



RESULTS

- Higher PCB concentrations were associated with blunted CARi ($\beta = -0.229$, $p = 0.010$).
- Higher NDL-PCBs levels were associated with increased MAC-Q scores adjusted for sex, age and education ($\beta = 0.224$, $p = 0.028$). ($= -0.218$, $p = .031$), indicating more frequent memory complaints.
- No significant associations were observed between PCB exposure and objective cognition across measured domains (all $p > 0.05$).



CONCLUSIONS

- Higher non-dioxin-like PCB exposure was linked to blunted CARi and greater subjective cognitive decline.
- Findings support HPA-axis dysregulation as a potential early pathway connecting environmental toxicants to cognitive vulnerability in aging.
- Subjective cognitive decline may signal PCB-related cognitive vulnerability before objective deficits are detectable.
- Subjective cognitive decline could serve as a sentinel marker of environmental neurotoxicity, warranting further investigation through longitudinal and mechanistic studies.

IMPLICATIONS

- This study highlights stress-sensitive neuroendocrine disruption as a potential early mechanism linking environmental toxicants to cognitive vulnerability in aging.
- Findings suggest that subjective cognitive decline and CARi may help identify early toxicant-related risk before objective cognitive impairment emerges.
- Reducing environmental toxicant exposure may represent a modifiable target for promoting cognitive health and dementia prevention.
- This work is significant in that it provides insight into how lifelong environmental toxicant exposure may contribute to cognitive vulnerability in aging, a key step toward improving understanding of environmental influences on brain health for early prevention.

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KEY TAKEAWAY

Toxicant exposure + Stress biology may reveal early cognitive vulnerability

Environmental toxicants may contribute to early cognitive vulnerability in aging by disrupting stress-sensitive HPA-axis function, with subjective cognitive decline emerging before objective cognitive deficits are detectable.