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PURPOSE

Investigate sex-specific risk factors (RF) differences in Alzheimer’s disease (AD) and healthy controls with network analyses

HYPOTHESIS

Networks would significantly differ between males and females within AD group and across the cognitive spectrum

KEY FINDINGS

Sex hormones were linked to cerebrovascular health in patterns that varied by sex, age and hormonal stage.

Background

- Incidence of dementia is projected to double in the next 10 years<sup>1</sup>:
  - Over 60% of dementia cases are females<sup>2-3</sup>
- Common RF for Alzheimer’s dementia (AD) include:
  - Hypertension, APOE ε4, depression and smoking<sup>4-5</sup>.
- Sex differences are prominent in RF of AD:
  - Females at higher risk of AD when hypertension and APOE ε4 are present<sup>6-7</sup>
  - Males risk is greater with depression, and obesity<sup>8-9</sup>
- Here, we employed a high-level statistical analysis for identifying sex-based RF for AD, called a network analysis<sup>10-11</sup>

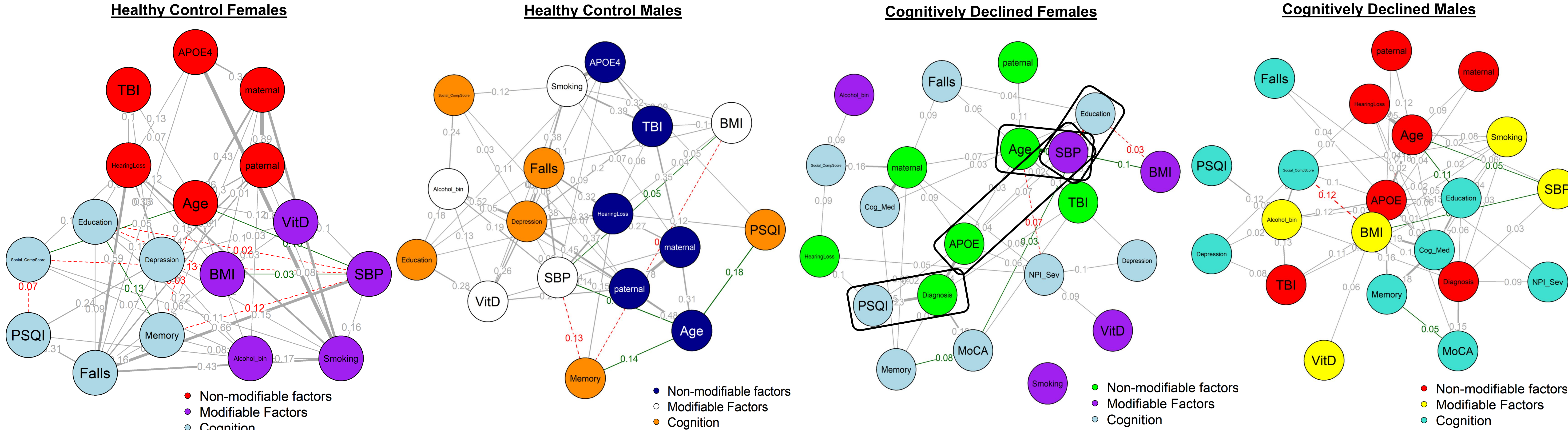
Methods

- 570 participants from the Canadian Consortium for Neurodegeneration in Aging<sup>12</sup> and the Ontario Neurodegenerative Research Initiative<sup>13</sup> total comprised of:
  - Healthy controls (HC); Individuals with mild cognitive impairment and those with AD combined to form cognitively declined (CD) group
- Measured non-modifiable RF (e.g., age); modifiable RF (e.g., hypertension [SBP]); and cognitive functions
- Mathematical approach, network analysis, employed to create sex-specific networks

	Age	APOE ε4	Education	MoCA	PSQI	Smoker	SBP	Depression
HCF	64.9	56.6%	15.6	27.9	5.7	20.9%	127.5	36.8%
HCM	64.5	57.3%	16.0	27.5	4.3	17.6%	131.6	19.8%
CDF	70.7	55.8%	15.7	22.5	5.1	26.3%	129.9	26.5%
CDM	72.3	43.7%	15.3	22.5	5.0	23.7%	130.5	16.6%
Significance	*, #, §	*, #, §		*, #, †	#, †	*	†	*, †

HCF = Healthy control females  
HCM = Healthy control males  
CDF = Cognitively declined females  
CDM = Cognitive declined males  
\*significantly different between CD females and HC Females;  
#significantly different between CD males and HC males;  
§ CD females and CD males are significantly different;  
† significantly different between HC females and HC males

Results



The black line surrounding risk factors indicates these were significantly different relationships in the network of CDF compared to CDM

Discussion

- Sex-specific profiles revealed: APOE ε4 was most central in CDF, while cognitive scores were most influential in CDM.
- HCF showed more interconnected network than CDF suggesting disruption of protective factors (e.g., education, vascular health).
- CDM demonstrated a reorganization of networks rather than loss of connectivity strength.
- Support the need for sex-specific dementia prevention strategies:
  - Addressing APOE and vascular in females; enhancing cognitive monitoring in males.
- Future longitudinal work is needed to track the evolving network patterns across disease progression.

References

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