

Distilling Heterogeneity in Alcohol Effects on Neurocognitive Health

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Alcohol Consumption and Neurocognitive Development

The National Academies of Sciences, Engineering, and Medicine's
Review of Evidence on Alcohol and Health Committee Meeting
3/28/2024

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CHRONIC EXCESSIVE ALCOHOL
CONSUMPTION: AUD

Neurobiobehavioral Concomitants: AUD

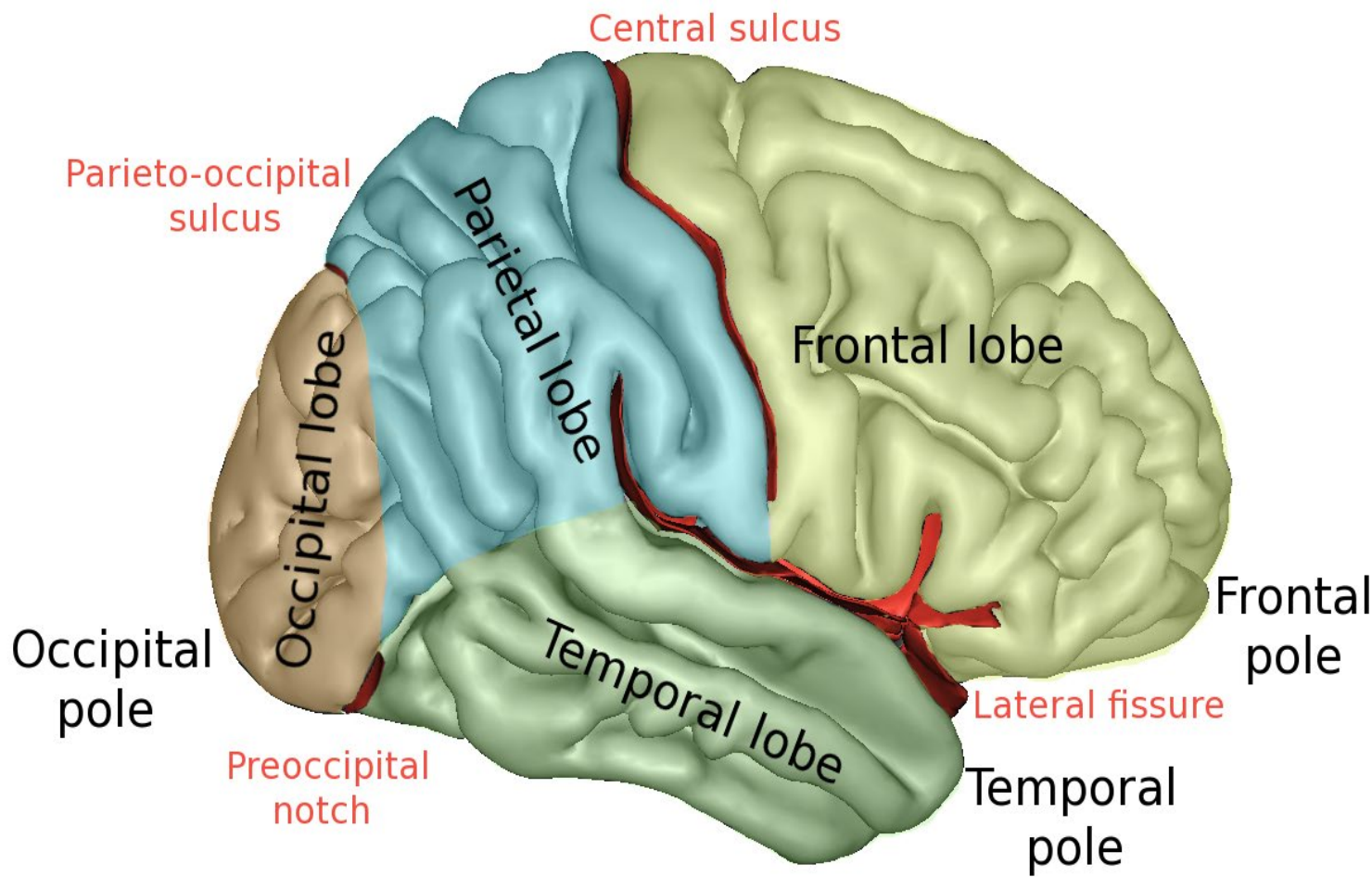
OVERVIEW

- Residual cognitive consequences
- DSM-5: ~ 30-40% of individuals meeting criteria for Alcohol Use Disorder (AUD) demonstrate clinically significant cognitive impairment
- Studies: 50%-80% (AUD) show significant deficits when compared to age/education equivalent cohorts
- Impairments: In absence of confounding comorbidities

TYPICAL STUDY POPULATION

- Men and women meeting criteria for AUD and engaged in treatment
- Detoxification completed
- No continuing use of significant psychoactive medications (e.g., treatment for psychotic disorders)
- No indication of significant medical condition that would confound interpretation
- Typically evaluated ≥ 21 days after last use

Neuropsychology & Functional Domains

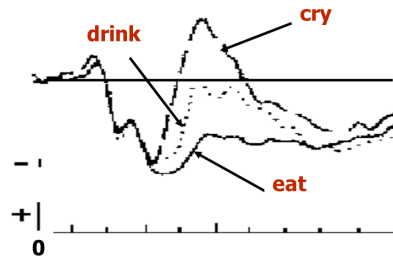


- Executive functions /Problem-solving/Abstracting
- Verbal Learning and Memory
- Visual-spatial Learning and Memory
- Perceptual –motor skills
- Language reception/production

Neurophysiology

- Non-invasive scalp electrodes
- Temporal dynamics of underlying neural activity
- Time-locked to specific stimuli or responses- Event-Related Potentials
- ERPs are presumed to reflect underlying cognitive processes

The pizza was too hot to ____.

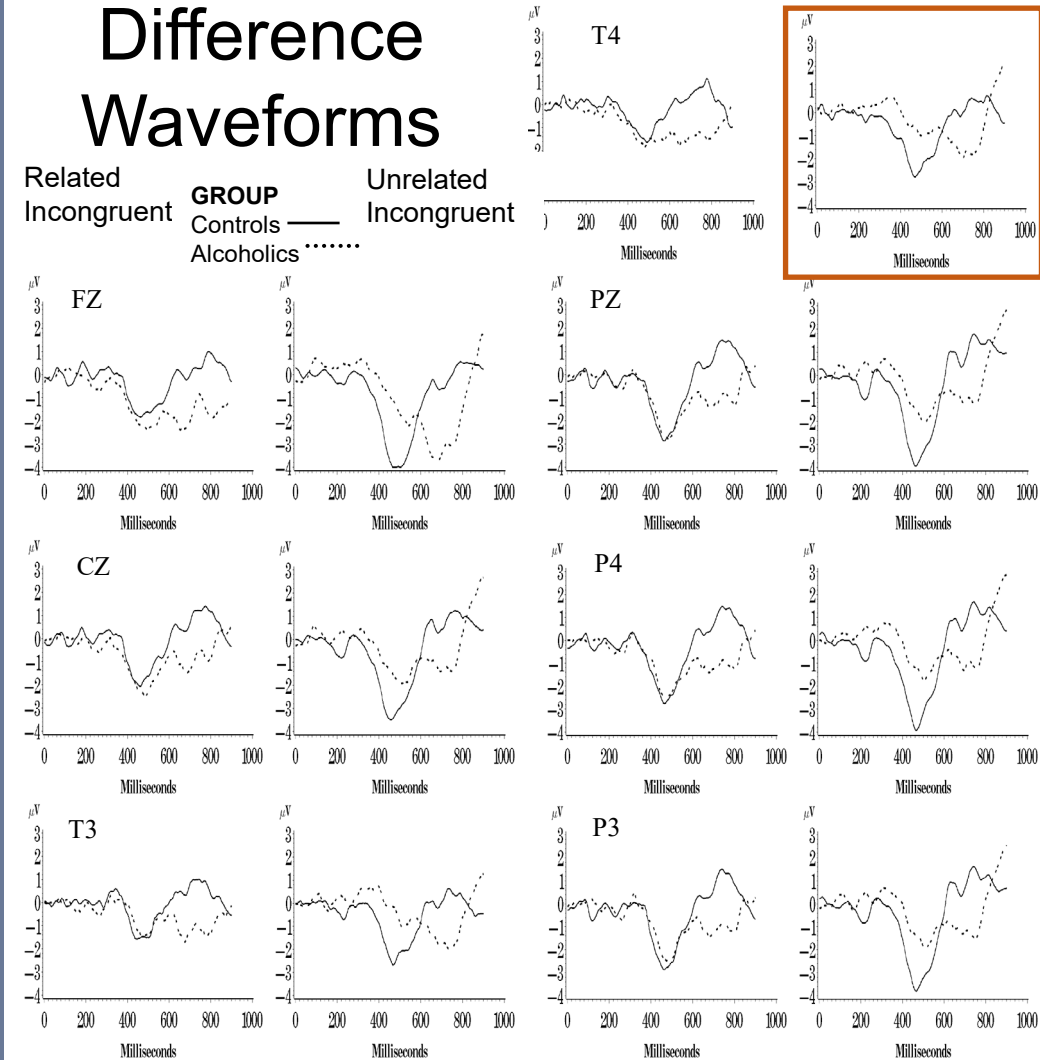


Bentin (1989) Lang
Speech, PMID: 2701178

Dysregulated
ERPs- purportedly
reflecting early &
later processes:
differentiating
relevant/irrelevant,
attention, working
memory, emotion
processing

Difference Waveforms

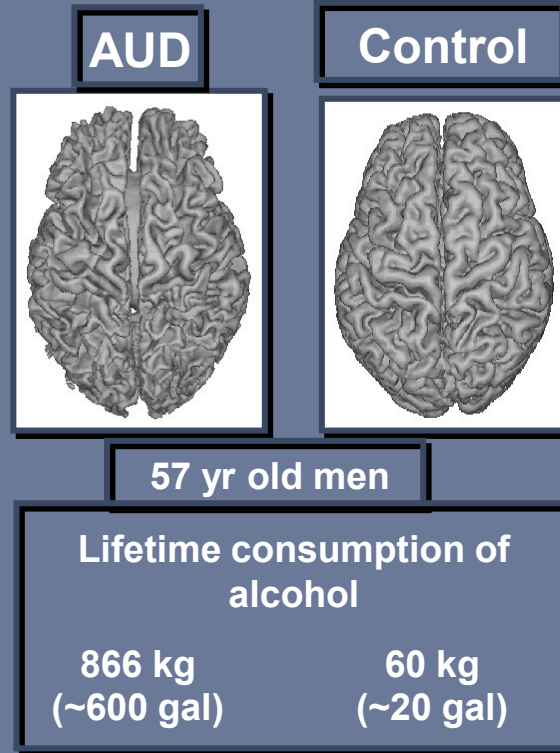
Related
Incongruent GROUP
Controls ———
Alcoholics Unrelated
Incongruent



Nixon, Tivis, Ceballos, Varner, Rohrbaugh (2002) Prog
Neuropsychopharmacol Biol Psychiatry
doi: 10.1016/s0278-5846(02)00206-3.

Neuroimaging: Structure & Activation

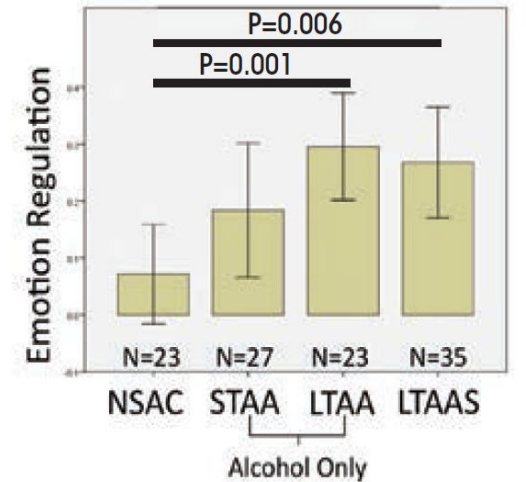
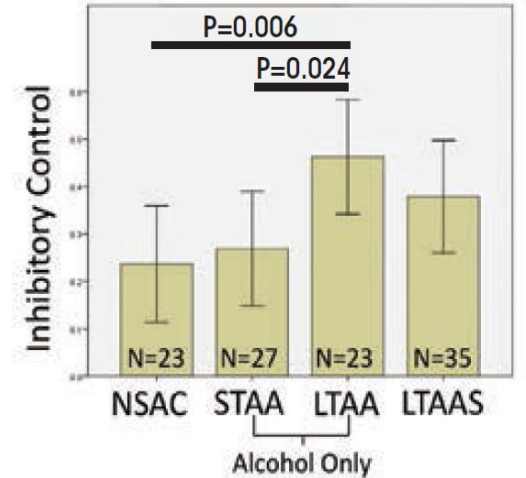
- Optimizing Spatial Dynamics
- Initially Descriptive
- Reflect differential volumetric loss atrophy/shrinkage
- Identify alcohol-related dysregulation within/across brain networks



Pfefferbaum et al 1997 IN: Oscar-Berman & Marinkovic, ARCR, 2003.



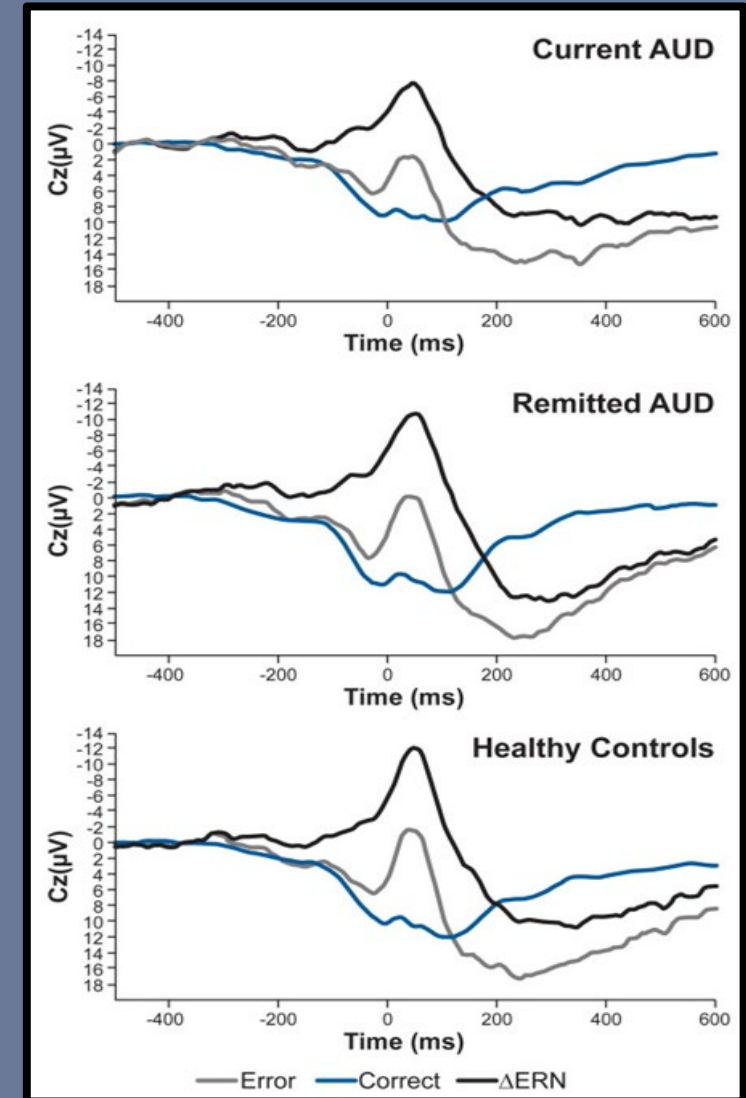
Reproduced in Zahr & Pfefferbaum (2017) Alcohol Res. PMID: 28988573



Fein & Cardenas, 2015. ARCR, PMID: 26259093

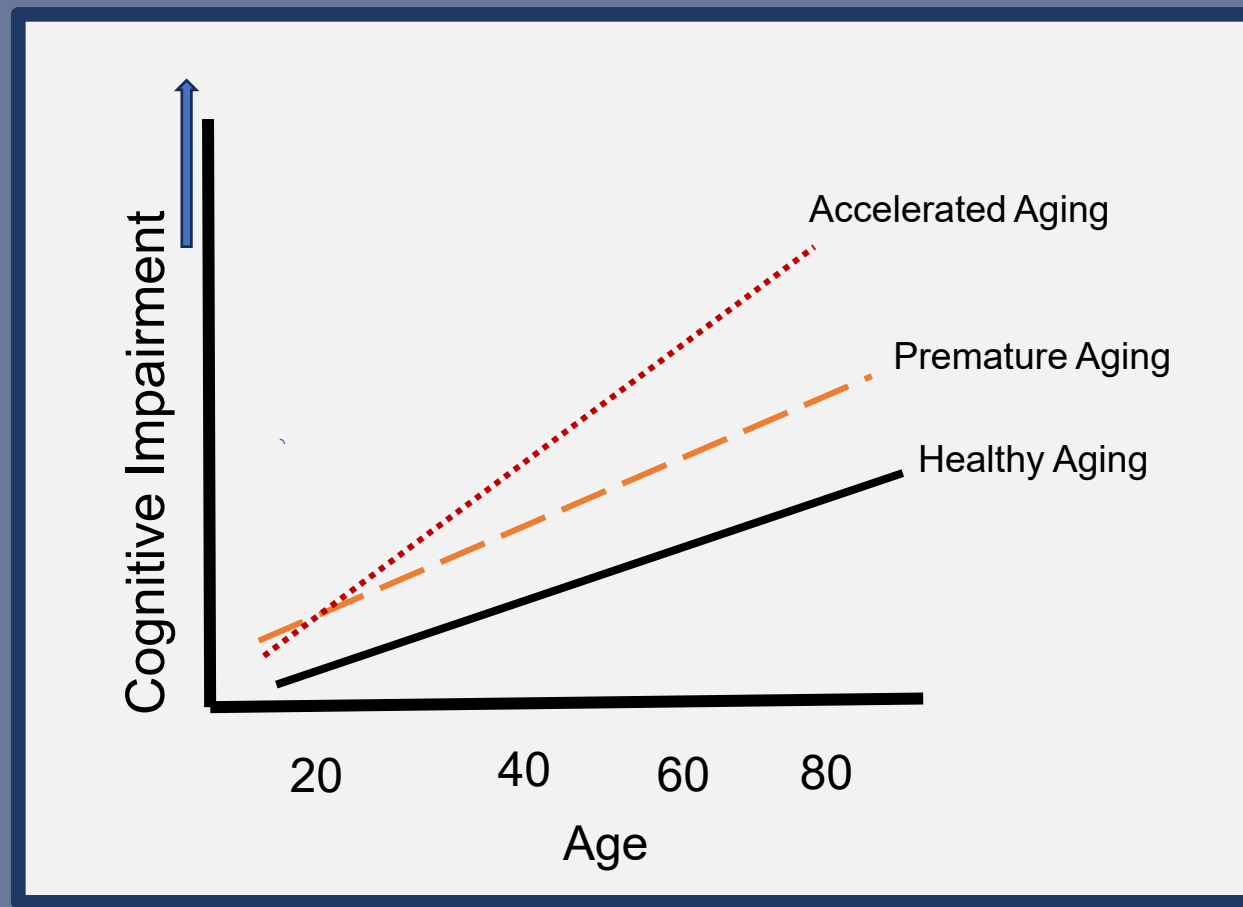
Recovery/Improvement with Abstinence/Reduction of Use

- Reduction in ventricular enlargement
- Volumetric improvement
- Early recovery in verbal processes
- Compensatory processes
- Improvement in complex cognitive processes more delayed & variable- including emotion processing and aspects of cognitive control
- Age Effects



Gorka, Lieberman, Kreutzer, et al. (2019), *Prog Neuropsychopharmacol Biol Psychiatry*, doi: 10.1016/j.pnpbp.2019.01.011. IN Nixon SJ, Lewis B. Brain Structure and Function in Recovery. *Alcohol Res.* 2020 Dec 3;40(3):04. doi: 10.35946/arcv.v40.3.04. PMID: 33282611; PMCID: PMC7703868. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7703868/>

Variable Trajectories: Age-Related Vulnerability



AGE & ALCOHOL IN THE ABSENCE OF AUD

Population Trends: NESARC

12-Month Use

	2001/2	2012/13	% Change
Overall	65.4 %	72.7 %	11.2 %
45-64	64.3 %	71.9 %	11.8 %
≥ 65	45.1 %	55.2 %	22.4 %

12-Month High Risk

	2001/2	2012/13	% Change
Overall	9.7 %	12.6 %	29.9 %
45-64	7.5 %	11.2 %	49.3 %
≥ 65	2.3 %	3.8 %	65.2 %

**Moderate Drinking Lifestyles
are Punctuated by Acute
Drinking Bouts**

Cognitive Aging

Neuropsychological Decline

- Working Memory

- Attentional Control

- Behavioral inhibition

Neurobiological Change/Dysregulation

- Brain Structure

- Connectivity

- Neurophysiology

Acute Alcohol Effects

Neurocognitive/Behavioral Processes

- Directed/selective attention

- Dual-task processing

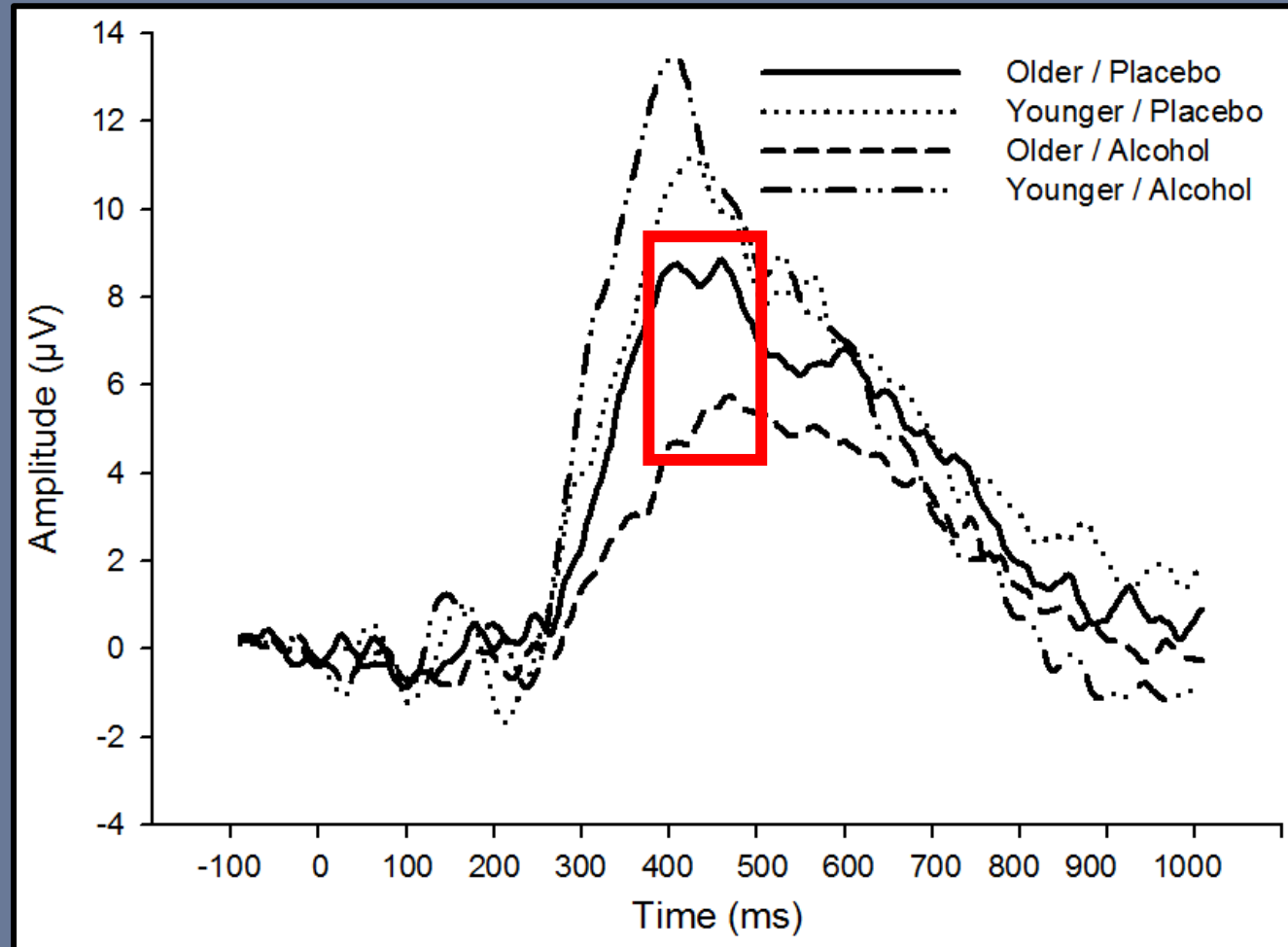
- Aspects of memory processing

Neural Activation

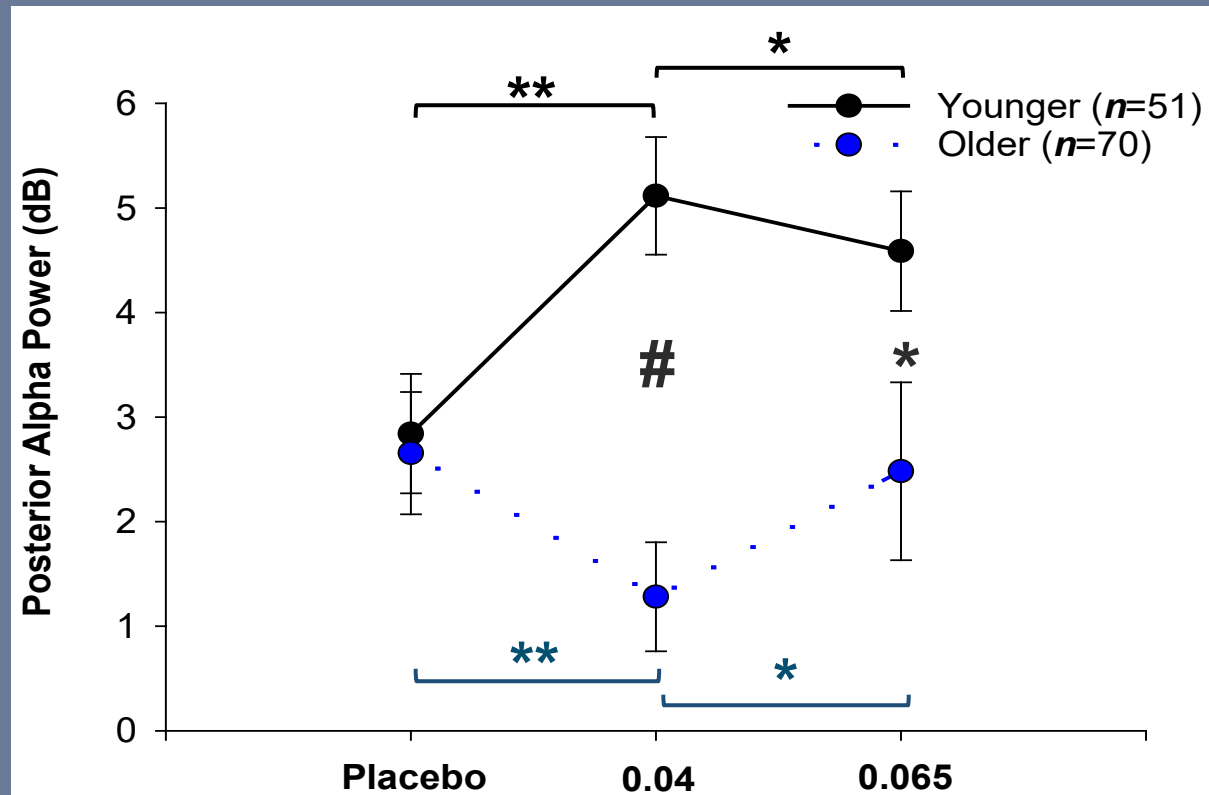
Reviews by Holloway (1994, DOT/FAA/AM-94/24) and Fillmore (2007, Int J Disabil Hum Dev 6(2):115-125)

Might socially relevant alcohol doses, consistent with moderate drinking lifestyles, acutely compromise vulnerable processes in older drinkers?

Alcohol & Older Adults - Neurophysiology



WM Maintenance: Spectral Power



$p < .001$ ** $p < .01$ * $p < .05$

Boissoneault, Frazier, Lewis, Nixon (2016) ACER, PMC5009001

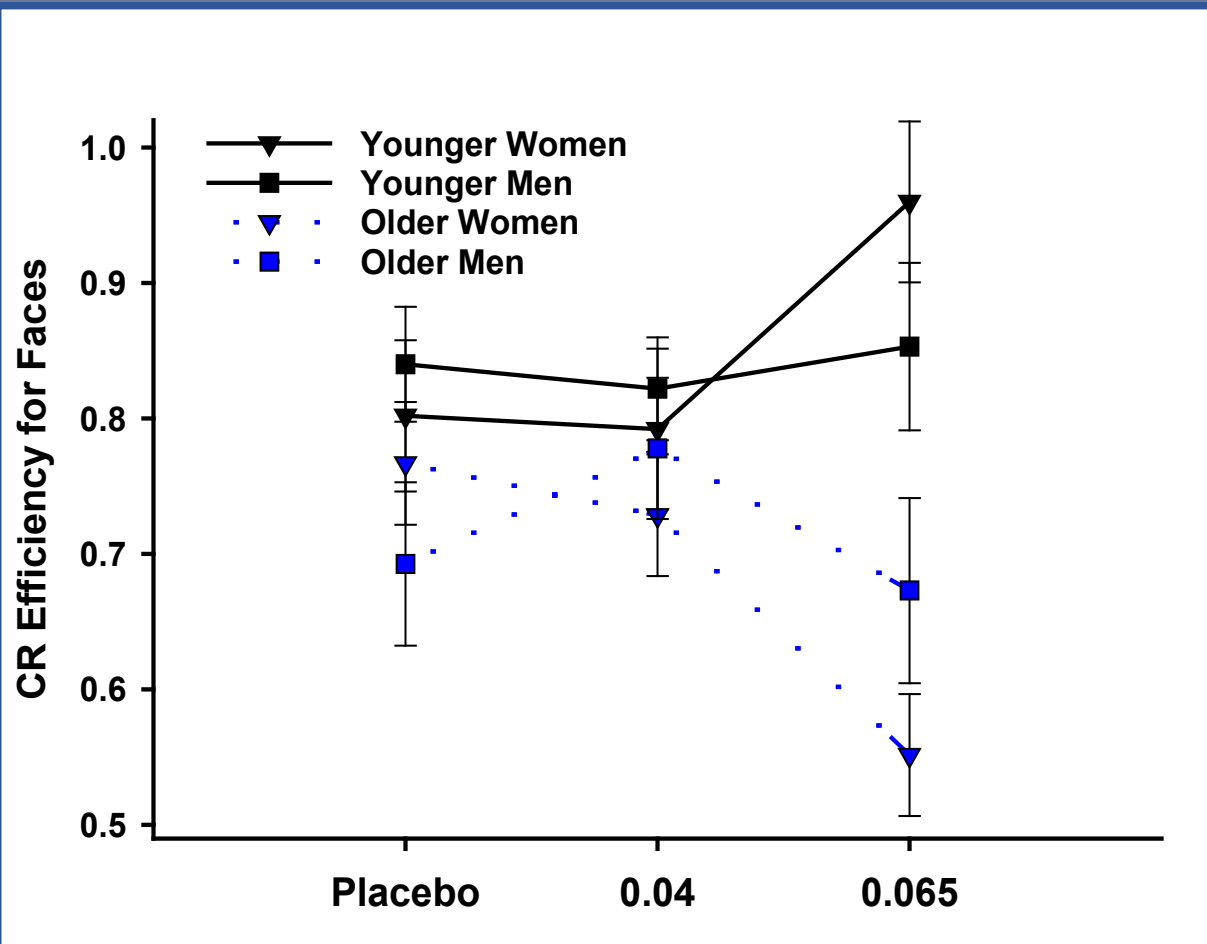
WM: Correct Rejection: Attend to Faces (Novel Face)

Young Men: No alcohol effect on ignoring faces

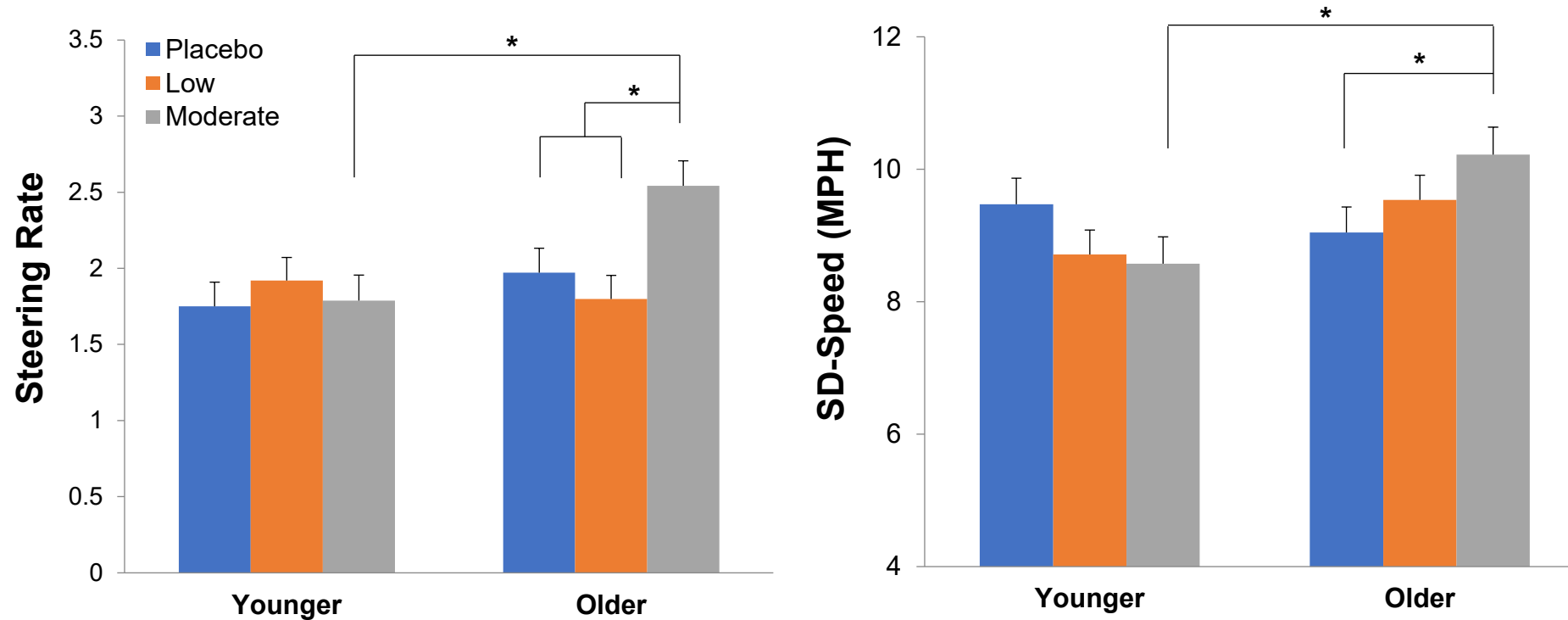
Older Men: Better with a little alcohol

Younger Women: No effect of low dose: *Mod dose group: Most efficient*

Older Women: Slight ns decline at low dose: Exceptionally poor at moderate dose



Driving Precision



*p< .05

Section Conclusion

Age-specific strategies under acute alcohol: Effects seen in laboratory & “real-world” tasks. How can these findings inform public health initiatives?

Disadvantageous outcomes may be long-lived, alcohol-related injury, financial/legal loss, interpersonal conflict.

Age-related vulnerability to acute alcohol constitutes a significant public health concern due, 1st, to its direct effects, and 2nd, its indirect/secondary costs to individuals and society .

Neurobiobehavioral Health Outcomes & “Moderate” Drinking Lifestyles

Straightforward question: “Does a moderate drinking lifestyle benefit (i.e., delay/offset) age-related cognitive decline?”

DEPENDS ON THE SOURCE

Some studies suggest no harm, if not benefit for Drks/Day = ~3 (women) and 4 (men). Others say NO level of drinking lends benefit with even low levels contributing to impairment/decline

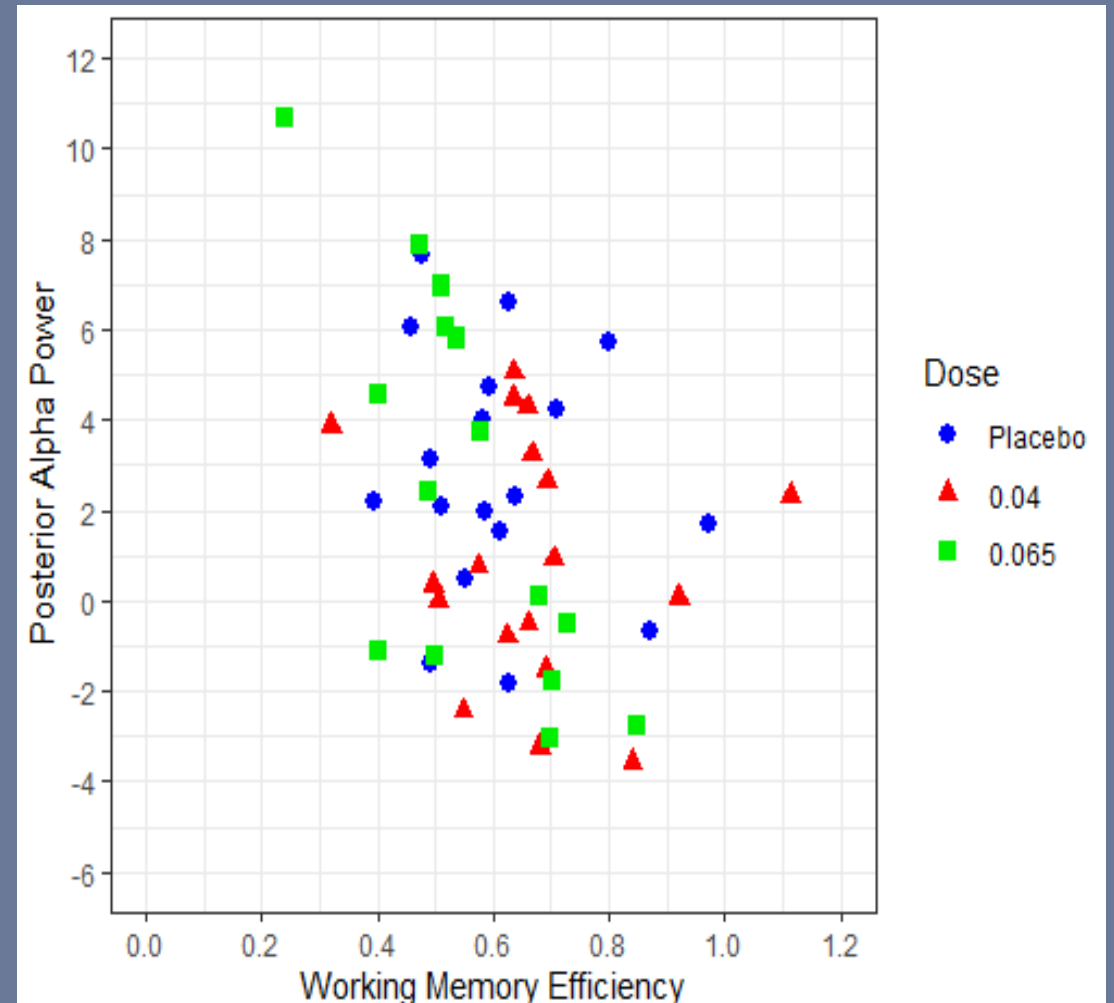
Challenges to Generalization Include

- Operational Definitions & Comparison Groups
 - Abstainers vs Quitters
 - Low/occasional vs “moderate”
 - Moderate vs Heavy
 - Cross-Sectional vs Longitudinal Assessments
- Constrained by number /timing of drinking pattern assessments
- Range of Drinking Patterns

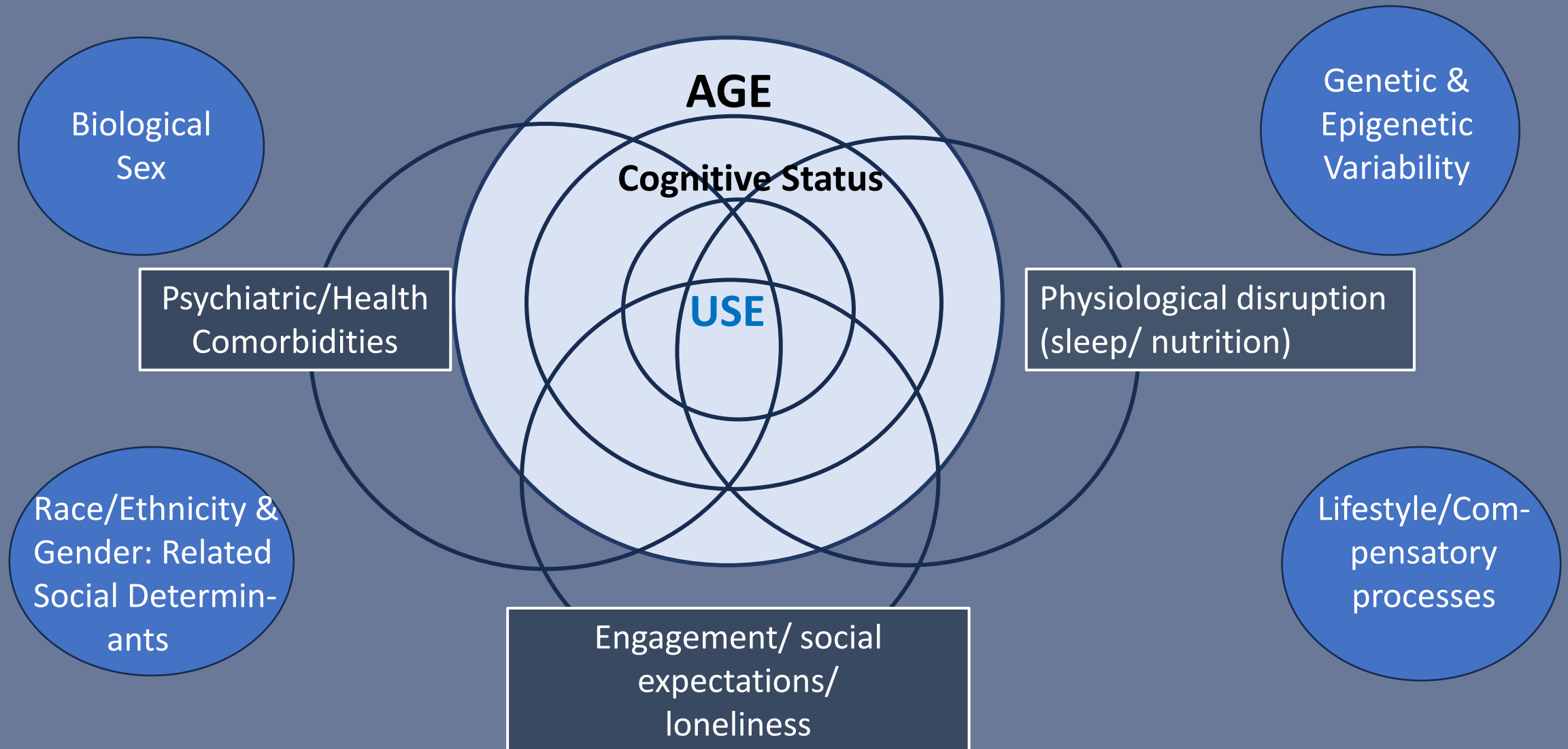
Contributing to Inconsistent Conclusions: Inattention to Within Group Vulnerability

Many sources of individual differences accounted for in epidemiological studies. Yet inconsistent findings remain.

We anticipate that individual differences in response to alcohol's acute effects may portend differential vulnerability to the interaction of the cumulative neurobiological effects of alcohol and cognitive aging processes- with processes underlying variables such as inhibition and cognitive control being differentially vulnerable.



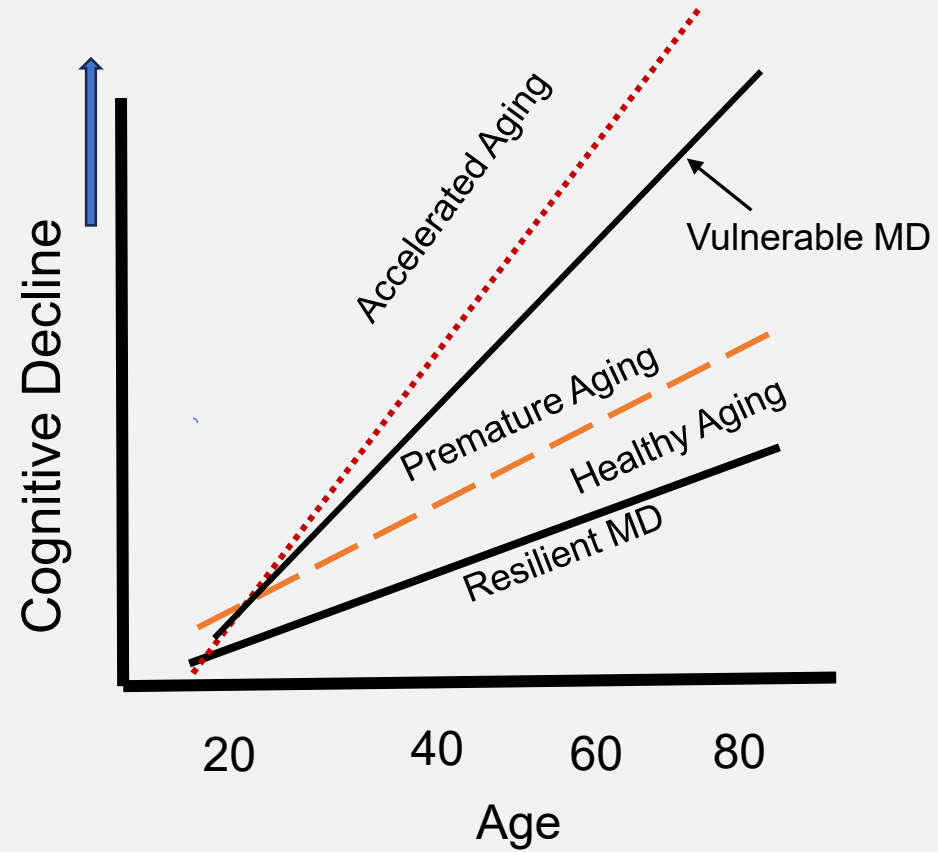
Modulators: Chronic Alcohol Effects & Dementia



Modulators: Chronic Alcohol Effects & Dementia

Differential *vulnerability* to the interaction of *Alcohol's Neurobiologic Effects* and Cognitive Aging Processes heighten risk for alcohol-related cognitive decline/impairment. With continued drinking, differential sensitivity to alcohol's acute effects interacts with processes underlying cognitive aging, enhancing vulnerability to alcohol-related cognitive impairment/decline.

Variable Trajectories: Alcohol-related Decline With Age



Future Considerations

- Individual projects insufficient to address complexity
- Laboratory studies probing trajectories- inform underlying processes
- Leverage heterogeneity – differential vulnerability/resiliency
- Relevance of Biopsychosocial Approaches
- Practical considerations
 - Variable designs are appropriate
 - Age ranges responsive to study objective and feasibility
 - Limitations of recruitment/retention/attrition
- **Sustained programmatic support**

Acknowledgements



Support for these projects

- NIAAA R03 AA014039
- NIAAA R01 AA019802
- NIAAA F31 (Boissoneault, Sponsor, SJN)
- NIAAA F30 (Sklar, Sponsor, SJN)
- MBI Dissertation Support (RG)
- UF CARE Dissertation Support (CCG)

Special Thank You to our Participants

Jeff Boissoneault, PhD
Mark Fillmore, PhD
Ian Frazier, PhD
Christian Garcia, PhD
Rebecca Gilbertson, PhD
Lauren Hoffman, PhD
Ben Lewis, PhD

Layla Lincoln, BS
Robert Prather, BA
Julianne Price, PhD
Alfredo Sklar, MD-PhD
Meagan Sullivan, MPH