Oral Qualifying Examination

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The Problem - Real-World Relevance

- Concurrent physical and cognitive demands are ubiquitous in daily life for older adults (carrying groceries while remembering a list, managing medication while gripping bottles, stabilizing objects during emergencies).
- <u>These everyday tasks become challenging with age.</u>

- **Significant Public Health Burden:**
  - Falls (nearly half potentially linked to attentional lapses during combined activities).
  - Medication errors (leading cause of emergency hospitalizations).

- Less research on *stationary force maintenance* (gripping, carrying) vs. mobility tasks, despite its prevalence.
- Understanding interactions across memory and perceptual domains is crucial for preserving independence and safety.

Why It Matters - The Scientific Question & Theories

- Why do older adults struggle with concurrent physical and cognitive demands?

- Tasks compete for the brain's finite processing resources.
    - **Resource Competition Theory**: Aging reduces overall resource capacity and flexibility, increasing interference.

- The brain's arousal system helps manage attention and processing efficiency.
    - **Neural Gain Theory**: The LC-NE system modulates neural gain (signal-to-noise). Aging impairs this, leading to inefficient processing under load.

These theories offer competing/complementary explanations: Is it simply running out of "brain power" (Resource Competition), or is the system that directs that power malfunctioning (Neural Gain)?

Literature Review - Prior Work

Previous research shows physical and cognitive effort can impact performance, but findings are mixed, especially in older adults.

Physical Effort (Isometric Handgrip):

- Younger adults: Moderate effort (20-40% MVC) often *enhances* cognitive performance (processing speed, executive function) - *consistent with optimal Neural Gain.* (Bachman et al., 2023; Zénon et al., 2014)
- Older adults: Similar moderate effort (e.g., 30% MVC) can *impair* working memory performance under high load - *suggesting exceeding limits* (Azer et al., 2023).

Cognitive Effort (Task Difficulty):

- High cognitive load consistently impairs memory (WM, LTM) and perceptual discrimination in older adults more than young adults - *consistent with reduced Resource Capacity and impaired Neural Gain.* (Gazzaley et al., 2005; Stark et al., 2013; Anderson et al., 2013)

Interactions: Evidence for how physical and cognitive effort *interact* in older adults is limited and inconsistent across tasks (Azer et al., 2023).

Literature Review - The Gap

Despite the real-world importance and theoretical relevance, critical gaps remain:

Limited understanding of *stationary* physical effort interactions: Most dual-task aging research focuses on mobility (walking). How does gripping/carrying interact with cognition across different domains (memory vs. perception)?

Conflicting theoretical accounts: Existing data doesn't clearly distinguish if dual-task costs in aging are primarily due to:

- Overall limits on processing capacity (**Resource Competition**)?
- Age-related failure in regulating attention/processing efficiency (**Neural Gain**)?

Lack of insight into protective factors: What *individual differences* (like cognitive reserve or arousal regulation ability) might buffer against these age-related declines under combined load?

Unclear if performance costs are domain-general (suggesting global limits) or domain-specific (suggesting localized bottlenecks), which has different theoretical implications.

My Plan - Specific Aims

To address this, my research has three specific aims:

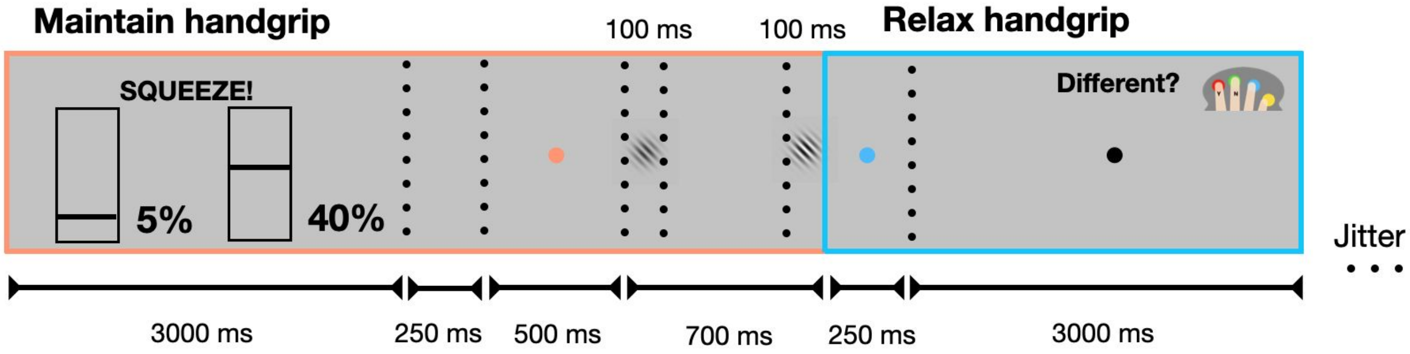
- **Aim 1**: Determine how concurrent physical and cognitive effort affects working and long-term memory performance in older adults.
  - *Hypothesis 1a* (CDT): Expect performance costs (accuracy, RT) with high effort, especially when combined. Replicate and extend previous work.
  - *Hypothesis 1b* (MST): Test if these effects generalize to long-term memory.
- **Aim 2**: Test whether these effects extend to perceptual performance (auditory and visual discrimination).
  - *Hypotheses 2a* (ADT) & *2b* (VDT): Expect similar patterns, testing if the problem is domain-general or specific to certain cognitive functions.
- **Aim 3**: Determine whether individual differences in cognitive reserve or arousal moderate the impact of these effort effects.
  - *Hypothesis 3a* (Cognitive Reserve): Higher reserve predicts better performance under high effort.
  - *Hypothesis 3b* (Arousal): Stronger arousal responses (pupil dilation) predict better performance under high effort.

How I'll Do It - Participants

- **Sample:** 50 healthy older adults (60-90 years) recruited from the local community.

- **Key Inclusion Criteria:**
    - Normal or corrected-to-normal vision and hearing
    - Cognitively healthy, as screened by the telephone Montreal Cognitive Assessment (T-MoCA > 17)

How I'll Do It - A VDT Example



An Example Using the Visual Discrimination (VDT)

- **Physical Effort:** On each trial, participants maintain an isometric handgrip at either 5% MVC (Low Effort) or 40% MVC (High Effort).
- **Cognitive Effort:** They must discriminate between two Gabor patches with varying contrast levels. The four levels of contrast difference are grouped to create a Low vs. High Cognitive Effort comparison.

How I'll Do It - The Tasks (Memory)

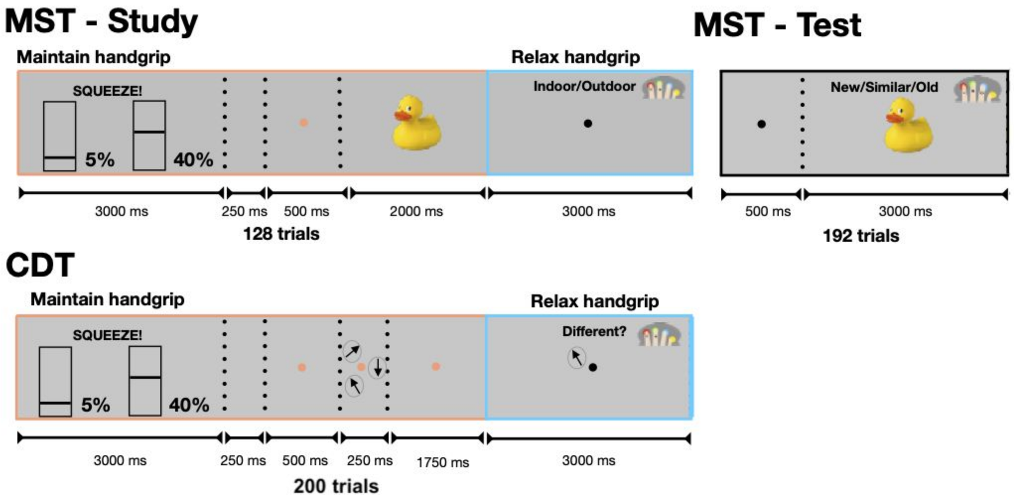
Participants perform cognitive tasks *while* maintaining handgrip.

Visual Working Memory (CDT):

- Remember orientation of arrows.
- Cognitive Effort: Manipulated by how much the probe arrow rotates (small vs. large rotation = high vs. low similarity).

Long-Term Memory (MST):

- Study objects (indoor/outdoor classification).
- Test: Recognize items as Old, Similar (Lure), or New.
- Cognitive Effort: Manipulated by how similar the "lure" items are to studied items (high vs. low similarity).



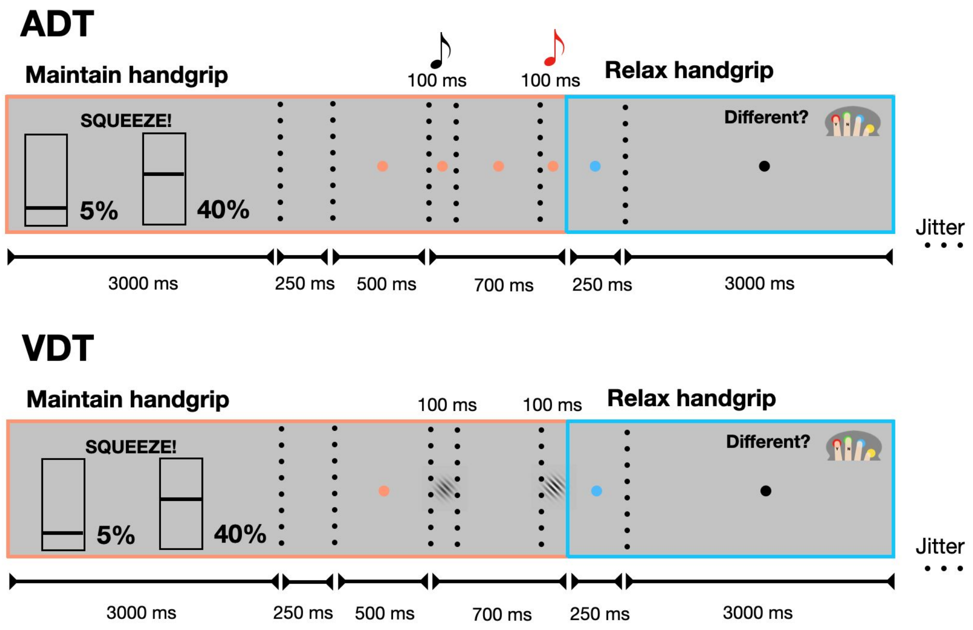
How I'll Do It - The Tasks (Perception)

Auditory Discrimination (ADT):

- Listen to two tones.
- Cognitive Effort: Manipulated by how much the second tone's frequency differs from the first (small vs. large frequency offset).
- Indicate if tones are same or different.

Visual Discrimination (VDT):

- Look at two visual patterns (Gabors).
- Cognitive Effort: Manipulated by how much the second pattern's contrast differs from the first (small vs. large contrast offset).
- Indicate if patterns are same or different.



Analyzing the Results - Effort Interactions (Aims 1 & 2)

- **Statistical Approach:** A 2 (Physical Effort) x 2 (Cognitive Effort) mixed-effects ANOVA on accuracy and RT per task.

- **What We'll Look For (For Each Task):**
  - Main effects of Physical Effort and Cognitive Effort.
  - The crucial **Physical x Cognitive Effort interaction**: Is the performance cost of high physical effort exacerbated by high cognitive load?

- **Interpreting the Pattern (Across Tasks):**
  - A consistent pattern of interactions across memory and perceptual tasks would be interpreted as evidence for **domain-general** limiting factors (e.g., central resource depletion).
  - A pattern where interactions are strong in some domains but absent in others would suggest **domain-specific** mechanisms play a more prominent role.

Analyzing the Results – Moderation (Aim 3)

- **Statistical Approach:** Linear Mixed-Effects Models (LMEMs) on trial-level performance.

- **What we'll look for:** Do cognitive reserve or arousal predict the *magnitude* of the effort effect?
  - **To Test for Cognitive Reserve's Role (H3a)**: We are looking for a significant three-way interaction (PE x CE x LEQ Score).
    - *This would indicate*: The performance cost under high dual-task load is <u>smaller</u> for individuals with higher Cognitive Reserve .
  - **To Test for Arousal's Role (H3b)**: We are looking for a significant three-way interaction (PE x CE x Pupil Dilation).
    - *This would indicate*: The performance cost under high dual-task load is <u>smaller</u> for individuals with more robust phasic arousal responses .

Expected Impact and Innovation

Expected Advancements:

- Provide critical evidence to differentiate between Resource Competition and Neural Gain theories in aging.
- Characterize *when* and *where* (which tasks/effort levels) impairments are worst.
- Identify *who* is most resilient (cognitive reserve, arousal responsivity).

Innovation:

- First unified protocol across *four* cognitive domains testing these interactions.
- Using ecologically relevant effort levels (40% MVC).
- Integrating pupillometry as a real-time biomarker of neural gain.
- Linking reserve measures to dual-task performance.

Ultimate Goal: Advance cognitive aging models and provide a scientific basis for interventions to preserve independence and quality of life.

Thank you!
Questions

Theoretical Framework

Resource Competition Theory

Core Principle: The brain has a limited capacity for information processing, and when concurrent tasks demand the same finite resources, performance suffers due to interference.

Evolution of the Model:

- Early models, like that of **Kahneman (1973)**, proposed a single, undifferentiated "pool" of mental effort. This view suggests that any two demanding tasks will compete.
- More advanced models, notably the **Multiple Resource Theory by Wickens (2008)**, argue for several distinct resource pools based on specific processing dimensions.

Key Dimensions of a Multiple Resource Model (Wickens, 2008):

- **Processing Stages:** Perception/Cognition resources are separate from those for Response Selection/Execution.
- **Processing Codes:** Spatial processing resources are distinct from Verbal (linguistic) resources.
- **Input Modalities:** Visual and Auditory perceptual resources are largely separate.

Key Prediction for This Study: A pattern of dual-task costs (especially if it differs between auditory and visual tasks) would provide evidence for competition within specific resource pools, rather than just a single general pool.

Neural Gain Theory (NGT)

- **Core Principle:** Performance is determined not just by resource capacity, but by the efficiency of neural processing, which is modulated by the Locus Coeruleus-Norepinephrine (LC-NE) arousal system.
- **Arousal-Performance Relationship:** NGT provides a mechanistic basis for the classic Yerkes-Dodson inverted-U curve.
    - **Low Arousal:** Under-performance.
    - **Moderate Arousal:** Optimal performance due to high "neural gain" (an improved signal-to-noise ratio in relevant neural circuits).
    - **High Arousal:** Performance declines due to a noisy, dysregulated system.

- **Key Mechanisms (Aston-Jones & Cohen, 2005):**
    - **Phasic LC Activity:** Brief, event-related bursts of LC firing are associated with focused, task-engaged performance ("exploitation") and are thought to drive optimal neural gain.
    - **Tonic LC Activity:** High baseline LC firing is associated with distractibility and scanning for alternative behaviors ("exploration"), leading to poor performance on a focused task.

- **Relevance to Aging:** The LC-NE system is known to degrade with age. This leads to the hypothesis that the inverted-U curve **compresses and shifts leftward**, making older adults more susceptible to the detrimental effects of high arousal .

A Deeper Mechanism: The GANE Model

GANE = Glutamate Amplifies Noradrenergic Effects (Mather et al., 2016).

Core Problem Solved: How can a global arousal signal (norepinephrine) selectively enhance *important* information while suppressing *unimportant* information?

The "NE Hotspot" Mechanism:

- High-priority information is represented by high local levels of the neurotransmitter **glutamate** .
- During arousal, this high glutamate level triggers a positive feedback loop, causing even more **norepinephrine (NE)** to be released locally .
- This creates a "hotspot" of intense, self-amplifying activity only at the site of the important information.

The "Winner-Take-More, Loser-Take-Less" Effect:

- **Enhancement:** Inside the hotspot, high NE levels activate excitatory β-adrenoreceptors, amplifying the "winner" signal.
- **Suppression:** Away from the hotspot, lower ambient NE levels activate inhibitory α-2 adrenergic receptors, suppressing the "loser" signals (background noise).

A Unifying Theme: Failure of Inhibitory Control in Aging

Core Idea: a central theme emerging from the literature is that dual-task costs, especially in aging, often stem from a breakdown in the ability to suppress irrelevant information.

Evidence in Aging:

- Classic work by **Gazzaley et al., (2005)** demonstrated that a key aspect of age-related working memory decline is a deficit in suppressing task-irrelevant distractors.

Evidence Under Arousal (The NGT Link):

- The GANE model posits that a key function of the LC-NE system is to amplify inhibition of less-active representations .
- Critically, the study by **Lee et al. (2018)** provides direct evidence for an age-related failure in this process. They found that under arousal, younger adults successfully enhanced salient information AND suppressed non-salient information.
- However, older adults showed **intact enhancement but a failure of suppression**; for them, arousal indiscriminately amplified <u>*both*</u> salient and non-salient stimuli, increasing the potential for distraction .

Implication for My Study: This "failure of inhibition" provides a powerful, unifying lens. I hypothesize that the high concurrent load in my paradigm will overwhelm the aging brain's already compromised inhibitory control systems, leading to the predicted performance decrements.

Methodological Justification

Advantages of Isometric Handgrip for This Study

1. Precise Experimental Control:

- Allows for precise and continuous control of effort relative to each individual's Maximum Voluntary Contraction (MVC).

2. Minimization of Artifacts:

- Crucially, the static nature of the task minimizes head and body movements, which is essential for collecting high-quality, low-noise pupillometry data.

3. Controlled Physiological Response:

- IHE reliably increases sympathetic nervous system activity and norepinephrine release in a more localized and predictable manner than whole-body exercise (Zénon et al., 2014).

Conclusion: While having lower ecological validity, the high degree of experimental control and compatibility with pupillometry makes IHE the ideal tool to isolate the specific mechanisms under investigation.

5% MVC: A "Minimal Effort" Active Control

Premise: 5% MVC is not "no effort." It is a carefully chosen **active control condition**.

Rationale 1: Isolates the Variable of Interest.

- By comparing 40% MVC to 5% MVC, we can isolate the effect of the *level* of physiological exertion, not just the effect of performing a secondary motor task.

Rationale 2: Equates Procedural Demands.

- In both conditions, participants perform the same actions: holding the dynamometer, attending to cues, and maintaining a contraction. The only difference is the force required.

Rationale 3: Follows Precedent.

- This approach is standard in the literature (e.g., Azer et al., 2023) for creating a clean and rigorous comparison.

Rationale for 40% MVC as the High-Effort Condition

- **A Strong Test of Neural Gain Theory (NGT):**
  - The 40% MVC level is specifically chosen to robustly test the hypothesis that older adults have a compressed or left-shifted arousal-performance curve .
  - This higher level provides a sufficient physiological challenge to push participants past their optimal arousal point and onto the detrimental "descending limb" of the inverted-U curve, where NGT predicts performance should decline .
- **A Robust Probe of Resource Competition (RC):**
  - To fairly test RC theory, the physical task must be demanding enough to consume a significant portion of the shared resource pool.
  - The 40% MVC level ensures we are probing for significant resource depletion, providing a strong context to observe potential interference effects .
- **Building on Prior Work:**
  - This choice builds on, rather than just replicates, prior work that found detrimental effects around 30% MVC (e.g., Azer et al., 2023). By using a slightly higher level, we can more effectively test the theoretical boundaries of these effort effects.

Rationale for Analyzing Two vs. Four Cognitive Effort Levels

1. To Maximize Statistical Power for the Primary Question

- Our core hypotheses for Aims 1 and 2 test for an **interaction** between Physical Effort and Cognitive Effort.
- Analyzing cognitive effort as a two-level factor (Low vs. High) provides the most direct and powerful test of this primary interaction effect within our planned 2x2 mixed-effects ANOVAs.
- Distributing trials across four separate cognitive effort levels in the main ANOVA would reduce the number of trials per cell, potentially leaving us underpowered to detect the crucial interaction.

2. The Four Levels Serve as a "Difficulty Gradient"

- We designed the tasks with four distinct similarity levels to ensure we successfully created a range of difficulty that spans from relatively easy to challenging for our older adult sample. This granular design helps prevent floor or ceiling effects.
- Conceptually, the levels represent a gradient (e.g., Easy, Medium, Hard, Very Hard). The analysis plan groups the two easier levels and the two harder levels to create a robust and meaningful **"High vs. Low Cognitive Effort"** comparison that aligns with our theoretical framework.

3. We Will Not Ignore the Granular Data

- **Exploratory Analysis:** While not our primary analysis, we plan to conduct exploratory analyses to examine the dose-response relationship between all four cognitive effort levels and performance.

Pupillometry: A Validated, Non-Invasive Window into LC-NE Activity

- **Why Pupillometry?**
  - **Validity:** Pupil dilation is a well-established surrogate for LC activity, correlating with LC firing in animal models and LC structural integrity in humans. It is sensitive to cognitive changes in aging and preclinical AD (Granholm et al., 2017).
  - **Feasibility:** Unlike fMRI, it is temporally sensitive and dynamic. Unlike EEG, it is less susceptible to motion artifacts from handgrip exertion.
- **Isolating Cognitive Effort from Physical Effort**
  - **Baseline Correction:** Task-evoked pupil dilation is expressed as a percentage change from the pre-stimulus baseline on each trial, normalizing for tonic shifts in arousal caused by physical exertion.
  - **Analysis:** We can statistically model the main effect of physical effort on pupil size and then examine the *additional* dilation related to cognitive events.
- **Connection to Imaging :**
  - In the broader project, LC integrity can be measured with neuromelanin-sensitive MRI. We can (in exploratory analyses) correlate individuals' MRI-based LC integrity with their pupillary responses to validate the mechanism in our sample (Dahl et al., 2019; Clewett et al., 2016).

Managing and Measuring Individual Differences

Screening and Inclusion:

- We use strict inclusion/exclusion criteria to create a well-defined "healthy" sample.
- Cognitive screening (T-MoCA > 17) is used to exclude individuals with likely MCI, addressing the confound of incipient dementia.

Measuring, Not Just Controlling For, Heterogeneity:

- **Cognitive Reserve:** This is a key variable of interest. We measure it with the LEQ to test its role as a *moderator* in Aim 3.
- **Baseline Fitness:** While not a primary moderator, we can measure baseline physical activity levels (e.g., via a questionnaire) and MVC as a proxy for strength. These can be included as covariates in exploratory analyses to see if they account for variance in performance.
- **Benefit:** By measuring these sources of variance, we can statistically account for them and also explore how they contribute to resilience against dual-task costs.

Detecting and Interpreting Task Management Strategies

Instructional Control: Participants are explicitly instructed to give equal priority to both the handgrip and cognitive tasks.

Preventing "Pre-crastination":

- The cognitive tasks are designed to require continuous engagement (e.g., stimuli are presented throughout the grip maintenance period), preventing participants from simply "getting the cognitive task done" early.

Analyzing Trade-Offs:

- We will calculate dual-task costs for both the physical task (e.g., increased variability in force output) and the cognitive task (e.g., reduced accuracy).
- We can plot these costs against each other to identify individuals who exhibit asymmetric performance—sacrificing one task to preserve the other (e.g., a "posture-first" strategy). These strategic differences can be explored as an interesting source of individual variation
    a. Additionally, in a separate project, we have been plotting a “Cohen’s d” for separability of grip forces to assess their adherence to the instruction

Alternative Experiment: Testing Neural Gain with Cardiovascular Measures

- **The Flaw:** Assume pupillometry is an unreliable index of central arousal in older adults.
- **The Goal:** Find an alternative, non-ocular proxy for arousal responsivity to test the core hypothesis of Aim 3.
- **Alternative Design:**
  - **Keep the Paradigm:** The 2x2 behavioral design remains the same.
  - **Replace the Measure:** Instead of pupillometry, continuously record electrocardiogram (ECG) data.
  - **New Arousal Proxy:** Derive **Heart Rate (HR)** and **Heart Rate Variability (HRV)** from the ECG. A robust arousal response could be indexed by the magnitude of the task-evoked increase in HR.
  - **New Hypothesis:** The three-way interaction (PE x CE x ΔHR) will be significant, such that individuals with a larger, more robust cardiovascular response to effort will show a smaller decline in cognitive performance.
- **Conclusion:** This provides a feasible alternative for testing the core principles of NGT without relying on the pupil.

Data Analysis & Interpretation

Power Analysis & Sample Size Justification

Overall Goal: To determine the sample size required for **80% statistical power** at an alpha level of 0.05, which is the standard in the field.

For Aims 1 & 2 (PE x CE Interactions):

- **Analysis:** A priori power analysis for a within-subjects repeated-measures ANOVA (conducted using G*Power).
- **Target Effect Size:** A medium effect of $\eta_p^2=0.12$.
- **Required N:** 38 participants.

For Aim 3 (Moderation by CR & Arousal):

- **Analysis:** Power simulations for Linear Mixed-Effects Models (LMEMs) (conducted using the 'simr' package in R).
- **Target Effect Size:** A medium-sized three-way interaction of $f^2 \sim 0.15$.
- **Required N:** 45-50 participants.

Final Target Sample Size: N = 50

- This sample size provides >80% power for all primary analyses.
- It also builds in a buffer to account for potential attrition (~10-15%) and loss of pupillometry data due to artifacts, ensuring a final N of at least 45 for robust analyses.

Justification of Anticipated Effect Sizes

Guiding Principle: The targeted effect sizes are not arbitrary but are informed by direct precedent, the existing literature, and strong theoretical considerations.

Justification for Aims 1 & 2 Interaction (eta_p^2~0.12):

- **Direct Precedent:** This effect size is based on the directly comparable findings of **Azer et al. 2023** who investigated a similar concurrent physical and working memory task in older adults and found an interaction of this magnitude.

Justification for Cognitive Reserve Moderation (f^2~0.15):

- **Literature Support:** This is supported by studies showing that CR proxies account for a significant portion of the variance in dual-task performance in older adults (e.g., Vallesi, 2016).
- **Theoretical Rationale:** While direct correlations can be smaller, CR's theoretical role is to enhance resilience *under challenge*. Therefore, a medium effect size for *moderation* in a demanding dual-task context is a plausible and well-reasoned expectation .

Justification for Pupillometry (Arousal) Moderation (f^2~0.15):

- **Literature Support:** The literature shows that in demanding tasks, task-evoked pupil dilation is strongly correlated with performance, with some studies showing it can account for up to 25% of the variance in error rates (e.g., Rondeel et al., 2015).
- **Theoretical Rationale:** If arousal responsivity (our pupil measure) explains such a substantial portion of performance on its own, it is highly reasonable to expect it to also significantly *modulate* the effects of other manipulated load factors. Therefore, targeting a medium effect size for this three-way interaction is a justifiable estimate .

LMEM for Moderation Analysis

Conceptual Model: An LMEM is a flexible regression that accounts for the fact that trials are nested within participants. It estimates the main effects for the whole group while also modeling each person's unique baseline.

Fixed Effects (The Main Question):

- Physical Effort (PE), Cognitive Effort (CE), Moderator (LEQ or Pupil), and all their interactions.
- **Hypothesis Test:** A significant three-way interaction (PE x CE x Moderator) indicates that the moderator changes the relationship between concurrent effort and performance.

Random Effects (Accounting for Individual Differences):

- **Random Intercept for Participant:** This is the key. It allows the model's starting point, or baseline performance, to be different for each person. This accounts for the fact that some people are just faster or more accurate overall, leading to a more powerful and precise test of the fixed effects.

Distinguishing Theories Based on the Pattern of Interaction

- **Scenario 1: Evidence for Resource Competition**
  - **Pattern:** A gradual, additive-like decline in performance as total load increases.
  - **Interpretation:** Suggests a linear depletion of a fixed capacity resource pool.
  - **(Sketch of a bar graph showing a stepwise decline across the four conditions)**
- **Scenario 2: Evidence for Supra-Optimal Arousal (NGT)**
  - **Pattern:** A sharp, "cliff-edge" drop in performance that only occurs under the highest combined load condition.
  - **Interpretation:** Suggests a non-linear state change, consistent with crossing a threshold into a dysfunctional, over-aroused state.
  - **(Sketch of a bar graph showing stable performance for the first three conditions and a sharp drop for the fourth)**

Distinguishing a True Interaction from a Floor Effect Artifact

- **The Challenge:** A floor effect (performance at or near chance level) in a difficult condition can create a statistical pattern that *mimics* a true synergistic interaction, making interpretation difficult.

- **The Analytical Check:**
  - The key is to examine performance in the **High Cognitive Effort / Low Physical Effort** condition.
  - **If performance here is well above chance:** The design has enough "room" to detect a further drop. A significant interaction is likely a true synergistic effect.
  - **If performance here is already at chance:** The design is "at floor." A lack of further decline is uninterpretable, and the interaction cannot be trusted.

Interpreting the Nature of Performance Costs: Speed vs. Accuracy

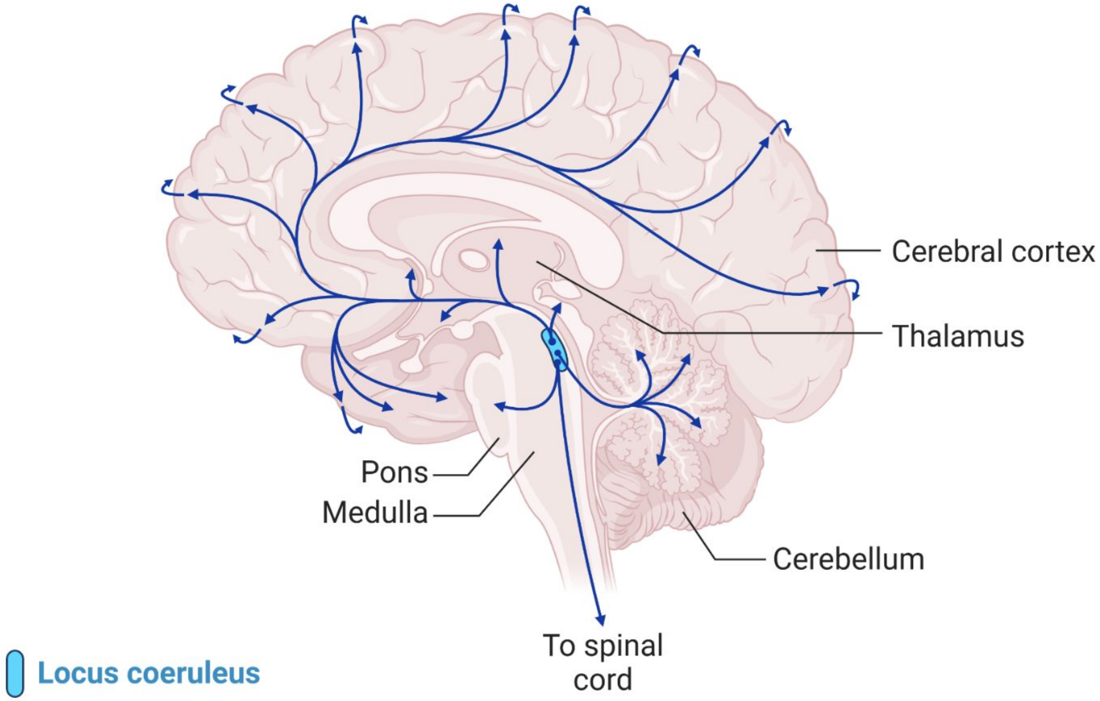
Scenario 1: Interaction in Reaction Time ONLY

- **What it looks like:** Accuracy remains high and stable, but participants become disproportionately slower only in the high PE / high CE condition.
- **Interpretation:** This suggests a failure of **processing efficiency**.
- **Theoretical Meaning:**
  - **RC View:** Participants are compensating for high resource demand by allocating more *time* to the task, preserving accuracy.
  - **NGT View:** The neuromodulatory system is less efficient, requiring a longer period of evidence accumulation to achieve a clear signal, resulting in a slower but still correct response.

Scenario 2: Interaction in Accuracy ONLY

- **What it looks like:** Participants respond just as quickly, but their error rate increases sharply only in the high PE / high CE condition.
- **Interpretation:** This suggests a more fundamental breakdown in the **quality and fidelity of the mental representation**.
- **Theoretical Meaning:**
  - **RC View:** The resource demand has exceeded a critical threshold, preventing the information from being fully processed, no matter how much time is taken.
  - **NGT View:** The neural gain system is dysfunctional; the signal-to-noise ratio is so poor that the correct information is corrupted or lost, making an accurate response impossible (consistent with **Lee et al., 2018**).

Distribution of Norepinephrine Neurotransmitters in the Human Brain



Broader Context & Future Directions

Anticipated Challenges & Mitigation Strategies

- **Challenge 1: Muscle Fatigue as a Confound**
  - **Mitigation:**
    1. **Individualized Baselines:** Re-measure Maximum Voluntary Contraction (MVC) at the start of every session to account for daily variability.
    2. **Real-Time Monitoring:** Continuously monitor grip force during trials for significant declines or increased variability indicative of fatigue.
    3. **Analytical Control:** Include block number as a factor in statistical analyses to model performance decrements over time.
    4. **Exclusion Criteria:** Pre-define criteria to exclude trials or participants showing excessive force decline (e.g., >15% drop).
- **Challenge 2: Task Order & Practice Effects**
  - **Mitigation:**
    1. **Williams Design:** Use a robust counterbalancing design to ensure every task precedes and follows every other task an equal number of times, balancing for first-order carryover effects.
    2. **Practice Trials:** Begin each session with practice trials to stabilize performance before data collection.
    3. **Statistical Control:** Include task sequence as a covariate in mixed-effects models to account for any residual order effects.
- **Challenge 3: Pupillometry Artifacts & Confounds**
  - **Mitigation:**
    1. **Light Reflex:** Use luminance-matched stimuli and apply a trial-by-trial pre-stimulus baseline correction to isolate the cognitive/arousal response.
    2. **Medication Effects:** Screen for and exclude participants on specific psychotropic medications. Track other common medications (e.g., beta-blockers) and include them as covariates in statistical models.
    3. **Data Quality:** Employ rigorous data cleaning algorithms to remove blinks and other artifacts.
- **Challenge 4: Difficulty Levels (Floor/Ceiling Effects)**
  - **Mitigation:**
    1. **Pilot Testing:** Use pilot data from older adults to inform the selection of stimulus similarity levels.
    2. **Analytical Checks:** Before interpreting interactions, I will explicitly test for floor effects (i.e., performance at or near chance) in the most difficult conditions.
    3. **Exclusion Criteria:** Exclude participants whose performance indicates a misunderstanding of the task (e.g., at-chance performance in easy conditions).

Prelim Data & Proof of Concept

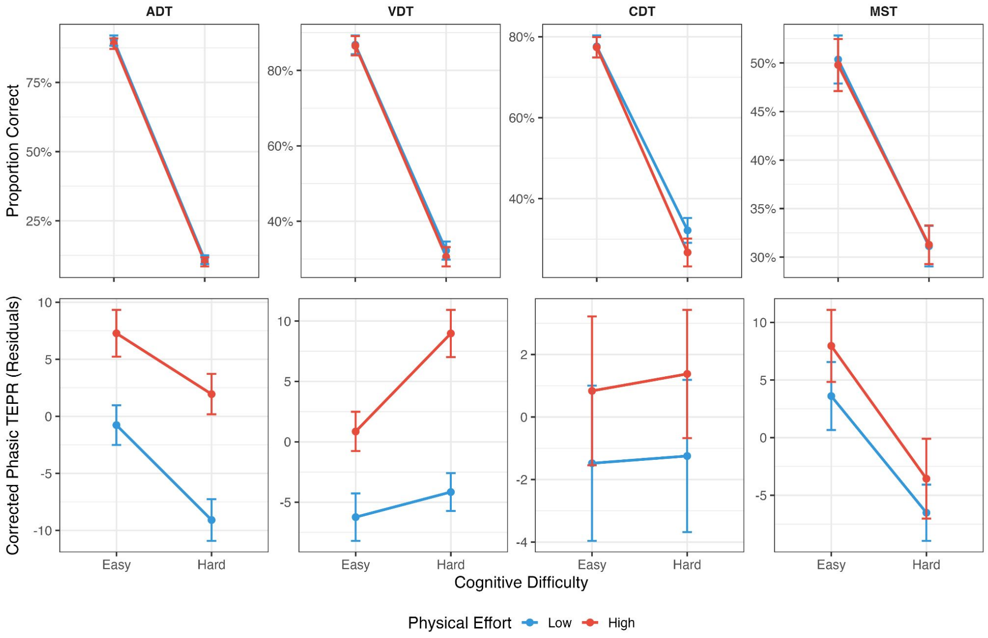
Prelim Data (SYP): Younger Adults Show Performance Resilience Despite Arousal Cost

Key Finding 1 (Behavior): In 38 younger adults, high physical effort (40% MVC) **did not significantly impair accuracy** on any of the four tasks. Performance was highly resilient.

Key Finding 2 (Physiology): However, the high physical effort condition **did** elicit a significantly larger pupillary response, indicating a greater allocation of physiological arousal or effort.

Conclusion: This dissociation shows that younger adults can successfully compensate for high physical demands to maintain performance, but it comes at a physiological cost.

Bridge to Quals Proposal: This provides a strong baseline and raises the critical question for my proposal: Will older adults, with their potentially less efficient neuromodulatory systems, show this same resilience, or will their performance decline under high effort?



Prelim Data (SYP): Task-Evoked Pupillary Responses Across Tasks

Key Finding 1 (Reliability): Across all four distinct cognitive tasks, we observed a reliable, time-locked, task-evoked pupillary response. This confirms the tasks are effective at engaging cognitive processing.

Key Finding 2 (Sensitivity): The magnitude of the pupil dilation was sensitive to our manipulation of Cognitive Effort, with high-effort trials generally eliciting a larger response than low-effort trials.

Conclusion: This demonstrates that pupillometry is a robust and sensitive index of cognitive engagement in this paradigm.

Bridge to Quals Proposal: These results validate the use of task-evoked pupil dilation as the primary physiological measure for Aim 3, where I will test if the strength of this response moderates dual-task performance in older adults.