

Utilizing Response Time Assessments of Cognitive Function: The First Step in Understanding Cancer-Related Cognitive Impairment

UTSA

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Introduction to CRCI

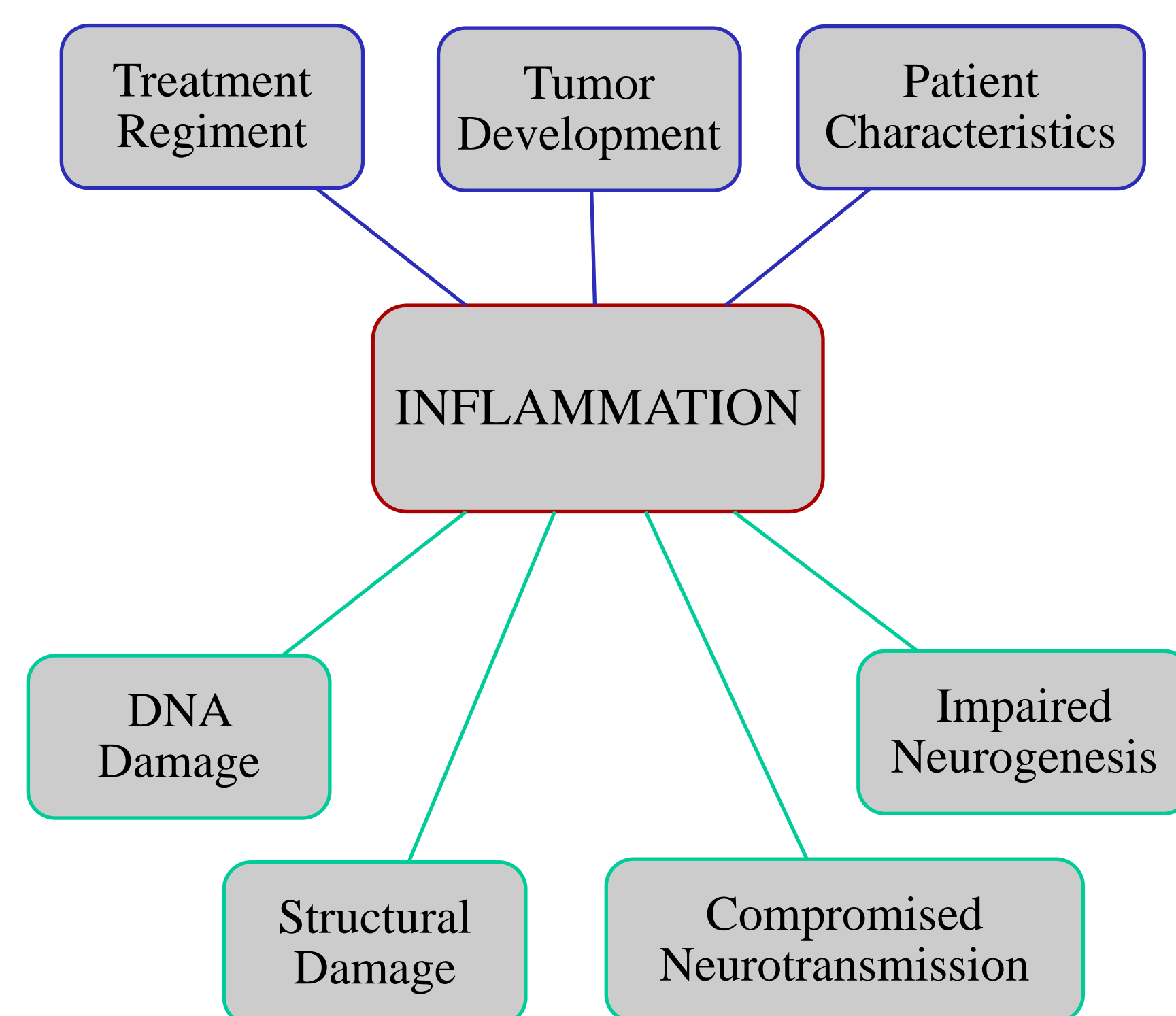
According to the World Cancer Research Fund International, there were 18.1 million *new* cancer cases diagnosed worldwide in 2020. At the same time, the average 5-year cancer survival rate has climbed to 68%. While the increases in survivability are encouraging, there is a growing need to address patient quality-of-life during and after cancer. One of the many symptoms impacting quality-of-life is **cancer-related cognitive impairment** (CRCI), commonly referred to as “chemo-brain.” This form of dysfunction can be debilitating, and patient experiences often include:

- Forgetting how to complete common tasks
- Getting lost on familiar routes and other directional difficulties
- Inability to multitask
- Forgetting words, or struggling with sentence formation

These symptoms often have deeper ramifications, including loss of social relationships, difficulties when returning to school or work, medication nonadherence, and lower survival rates. As these ripple effects can drastically impact a patient's quality-of-life, there has been a surge to understand what is causing CRCI, so we can create treatments (or even prevent) this dysfunction.

Pathways to Damage

Over the last 20 years, research has shifted to a focus on how inflammation may be the underlying factor driving the multiple components causing CRCI.



Results have varied, as many biomarkers can serve as both pro- and anti-inflammatory agents, but the signaling proteins most frequently associated with increased CRCI are:

- interleukin (IL)-6, IL-2, IL-4, IL-10, IL-1 β
- interferon-alpha (IFN- α)
- tumor necrosis factor-alpha (TNF- α)
- brain-derived neurotrophic factor (BDNF)
- Possibly: amyloid beta and tau

Cognitive Domains

The experience often varies between patients, but common cognitive domains impacted by CRCI include:

Attention/ Orienting	Visuospatial Reasoning
Executive Control	Psychomotor Dexterity/ Speed
Working Memory	Verbal Fluency

So what's the problem?

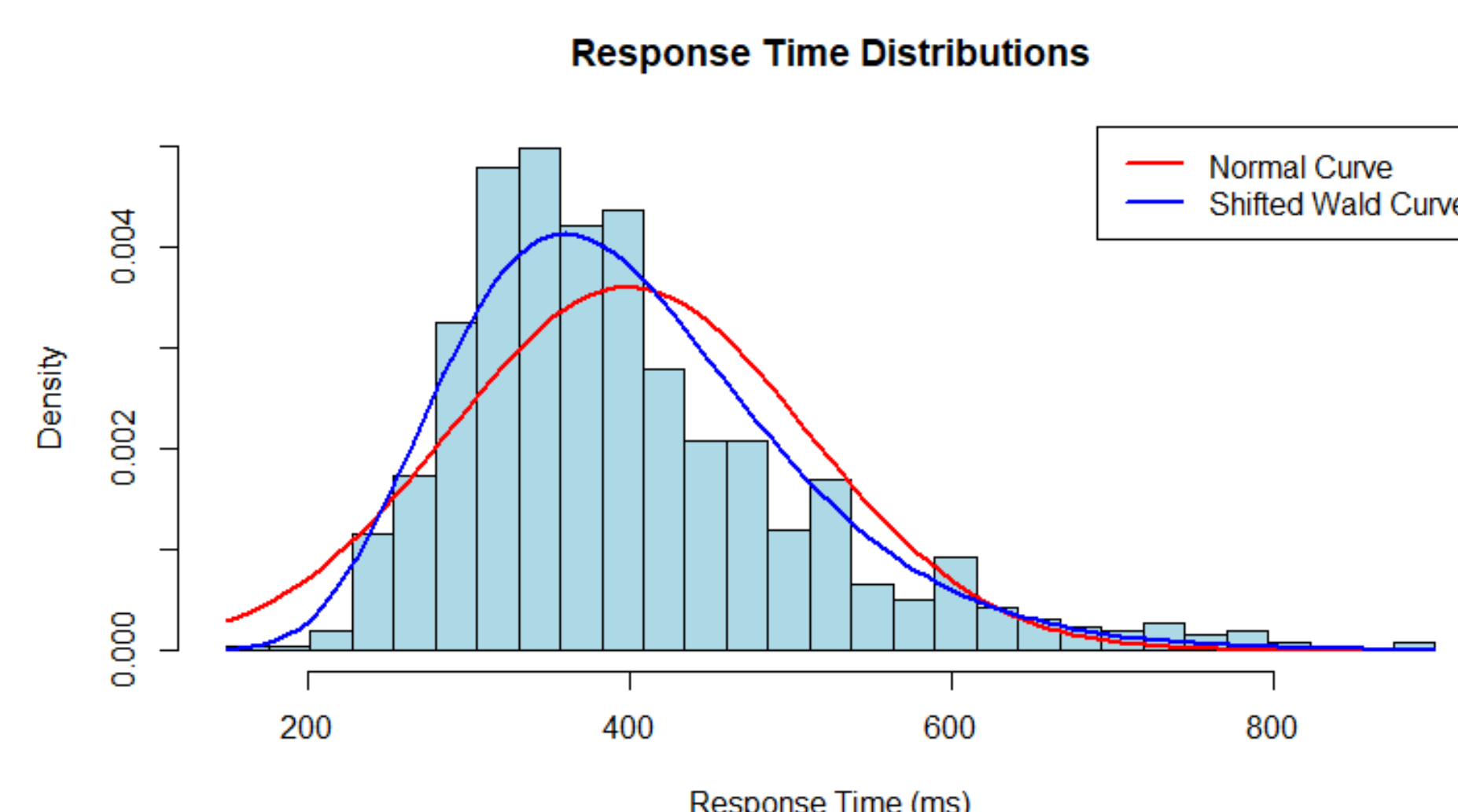
- Rate of CRCI incidence ranges from 15%-75%, depending on the study
- Qualitative and quantitative measures frequently lack correlation
- Across 34 articles, 61 different assessments were utilized, all meant to represent CRCI

Our measurements are not consistently capturing CRCI.

Response Time Modeling

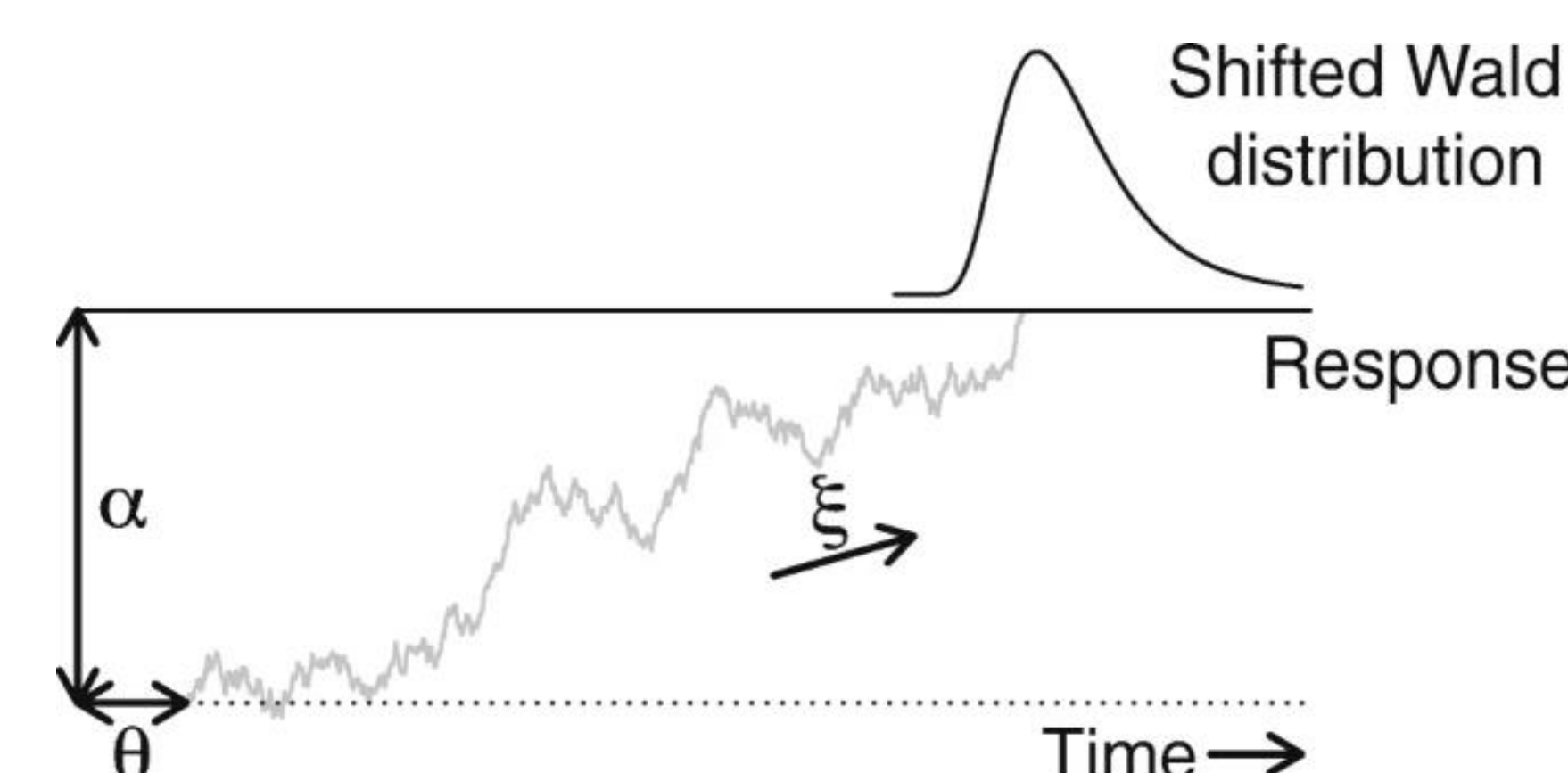
While neurocognitive tasks in CRCI research commonly measure response times, past analyses have relied on mean-based assessments. As Schwarz (2001) explained, “the decision to initiate and execute a specific overt response does not arise holistically, in an all-or-none fashion, but is rather preceded by a stage during which response-related information gradually accumulates over time.” How could assessing this accumulation of information improve our understanding of CRCI? By utilizing accumulator models to analyze the distribution of response times, we can gain more information than available when relying on averages.

Better Representation of Data



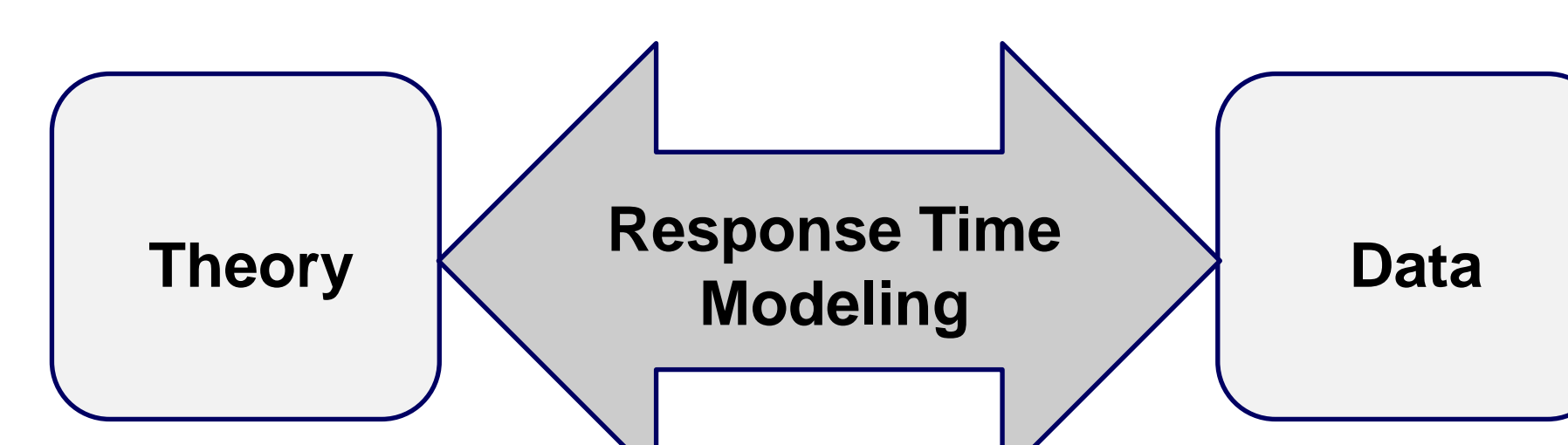
Meaningful Parameters

In one example, the shifted-Wald model, each of the three parameters (shift, drift rate, and response threshold) are informative of unique, underlying cognitive processes.



Why It Matters

Utilizing a response time modeling approach is not the only step we will need to take to understand CRCI, but it is still an important step. It removes the vagueness of a change in average response time, and provides a way to map theory onto empirical data.



We can do better, so we should do better.

The Planned Study

In a collaboration with the HEAL team at UT-Health San Antonio, we plan to evaluate CRCI throughout a 6-month holistic, therapeutic yoga intervention. This project will be split between San Antonio and Laredo, Texas, with 35 Latino and 35 non-Latino breast cancer survivors. Throughout this study, the cancer survivors will receive dietary counseling and daily psychosocial support. At intervals throughout the 6-months, multiple facets of cancer survivor quality-of-life will be measured, including spiritual health, cognition, FitBit activity, physical functioning, body image, stress, motivation, social support, dietary choices, and inflammation biomarkers. This holistic approach is designed to evaluate the efficacy of a culturally-sensitive intervention, while assessing the multi-dimensional changes in survivor quality-of-life.



The Cognitive Assessments

Attention Network Test (ANT)

- Fan et al. (2002)
- Evaluates three areas of attention (alerting, orientation, and executive control)

Dual-N-Back Task

- Heathcote et al. (2015)
- Provides a measure for workload capacity

Open-Source Anticipated Response Inhibition (OSARI) Task

- He et al. (2022)
- An alternative to stop-signal delay tasks for measuring executive control

PROMIS Functional Assessment of Cancer Therapy-Cognitive Function (FACT-Cog) Short Form

- Henneghan et al. (2023)
- One of the most commonly used self-report measures of CRCI
- Associated with changes in multiple biomarkers, including IL-6, IL-4, and IL-1 β

The UTSA team will utilize response time modeling to longitudinally assess changes on the three response time tasks for each participant. Our focus is to evaluate the effectiveness of the intervention on cognitive outcomes while developing our understanding of the relationship between CRCI and inflammation.

Considerations

Response time modeling approach provides a crucial avenue to improve CRCI assessment analysis. Future studies can focus on many components of implementing this approach, including:

- Developing a reference point for this population
- Establishing any differences for current cancer patients
- Assessing how individuals vary in cognitive abilities before an intervention
- Evaluating which CRCI tasks can be most benefited by a modeling approach
- Determine the impact of compensation tactics on evaluating CRCI

Though challenging, there is great potential for improving CRCI measures by changing our approach.

For references, contact information, and more, please see QR code. Questions, concerns, or ideas are welcome.

