

# Cognitive Change

To Lumosity or not to Lumosity?

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# Overview

- Background
  - Cognition: Are some patients more at risk than others for cognitive impairment following treatment?
- What cognitive changes commonly occur?
  - Cognitive complaints versus cognitive impairment
  - Multiple candidate mechanisms for cognitive impairment
- Research
  - Cognition, genetics, brain function and brain structure
- Interventions for cognitive complaints and impairment



# Background

- Each year, more than 1.6 million individuals are diagnosed with cancer in the US
- There are almost 14 million US cancer survivors and more than 25 million world wide
- Cognitive complaints are relatively common during and after treatment & may persist for many survivors
- Multiple candidate mechanisms proposed for these complaints and they are often associated with other post-treatment symptoms

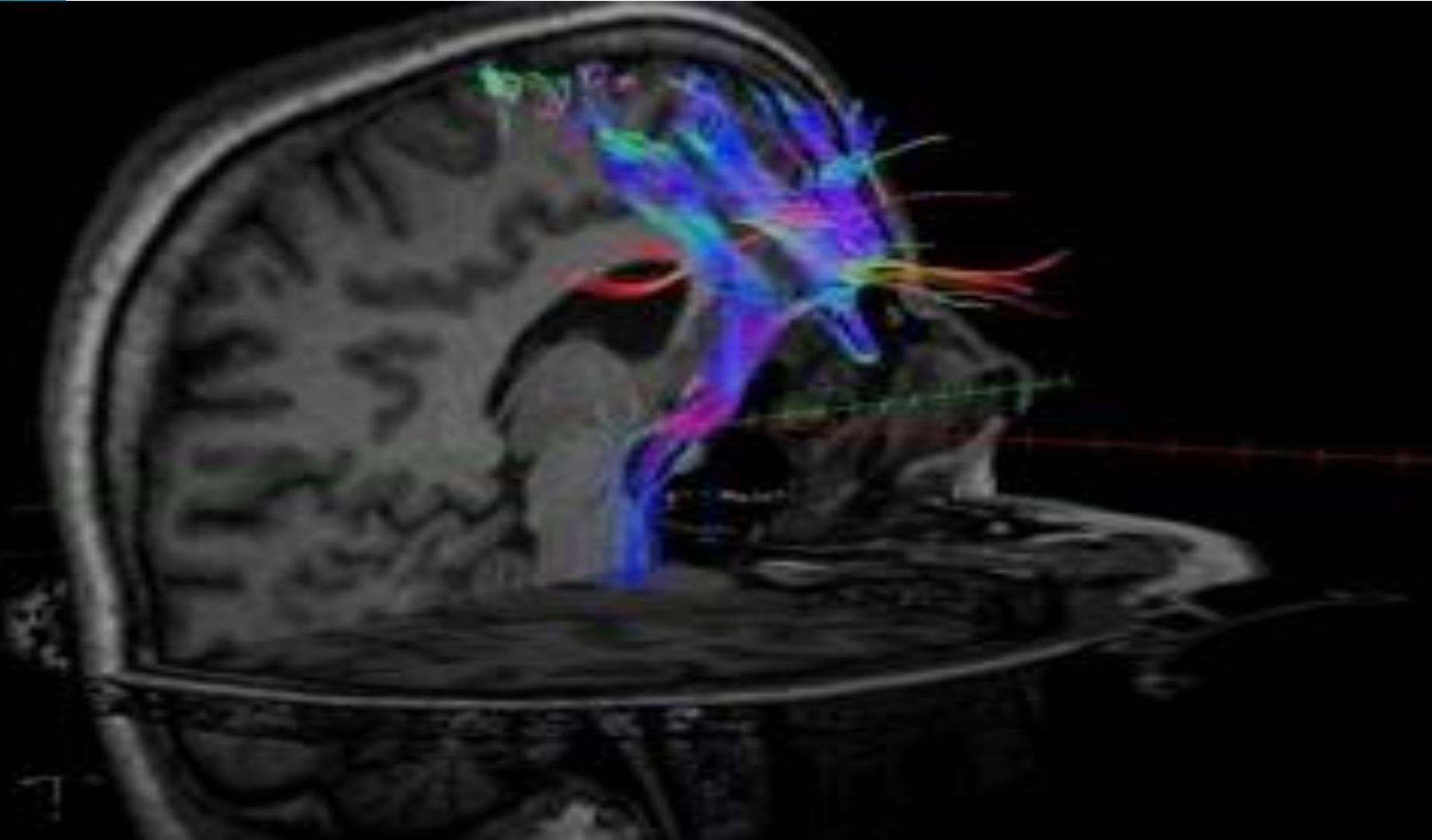


# Background

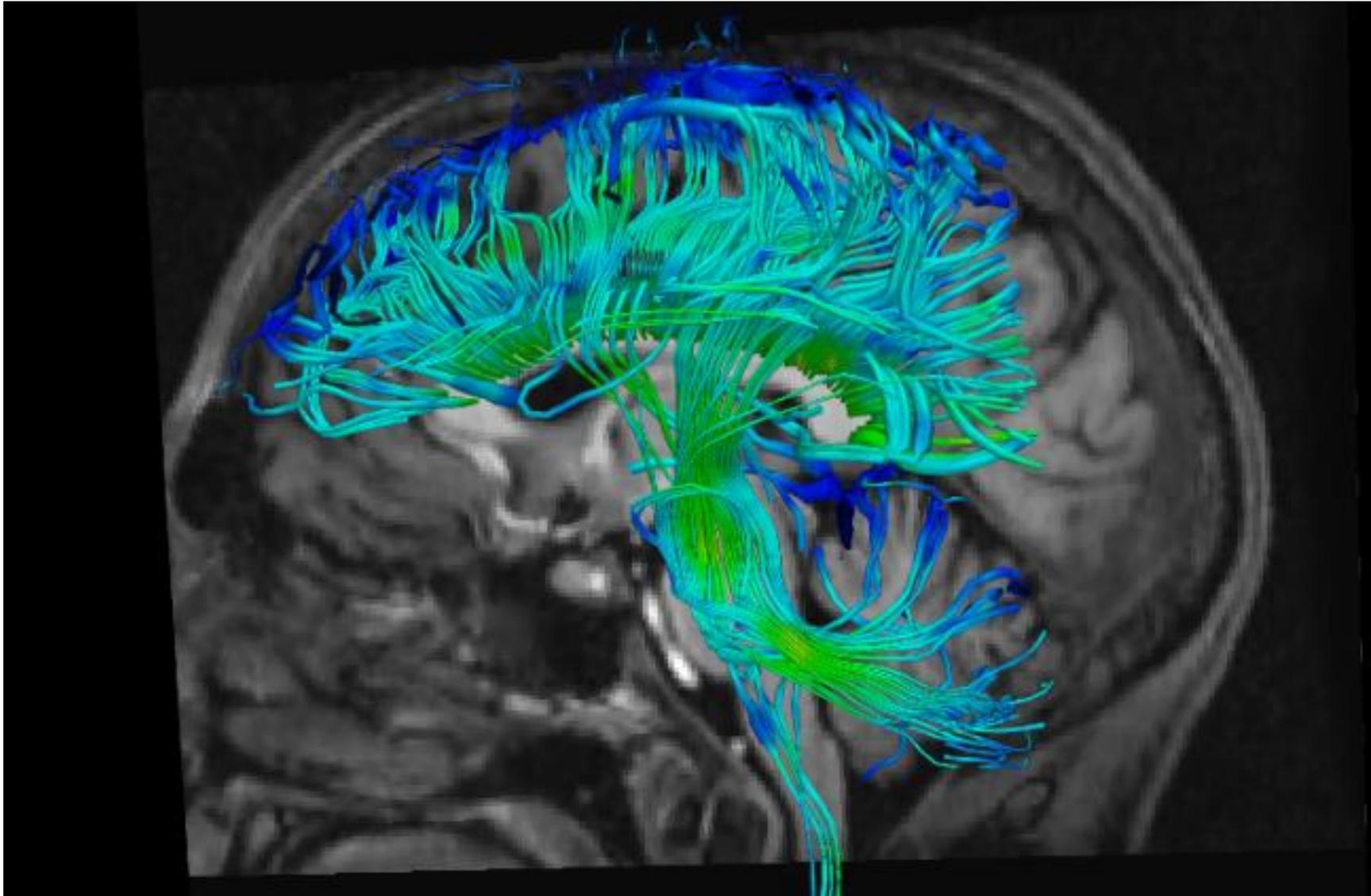
- Not Everyone has cognitive changes
- Treatment for cancer is important
- Should not avoid treatment only out of concerns for cognitive changes – should understand the risks and how to work to improve them.



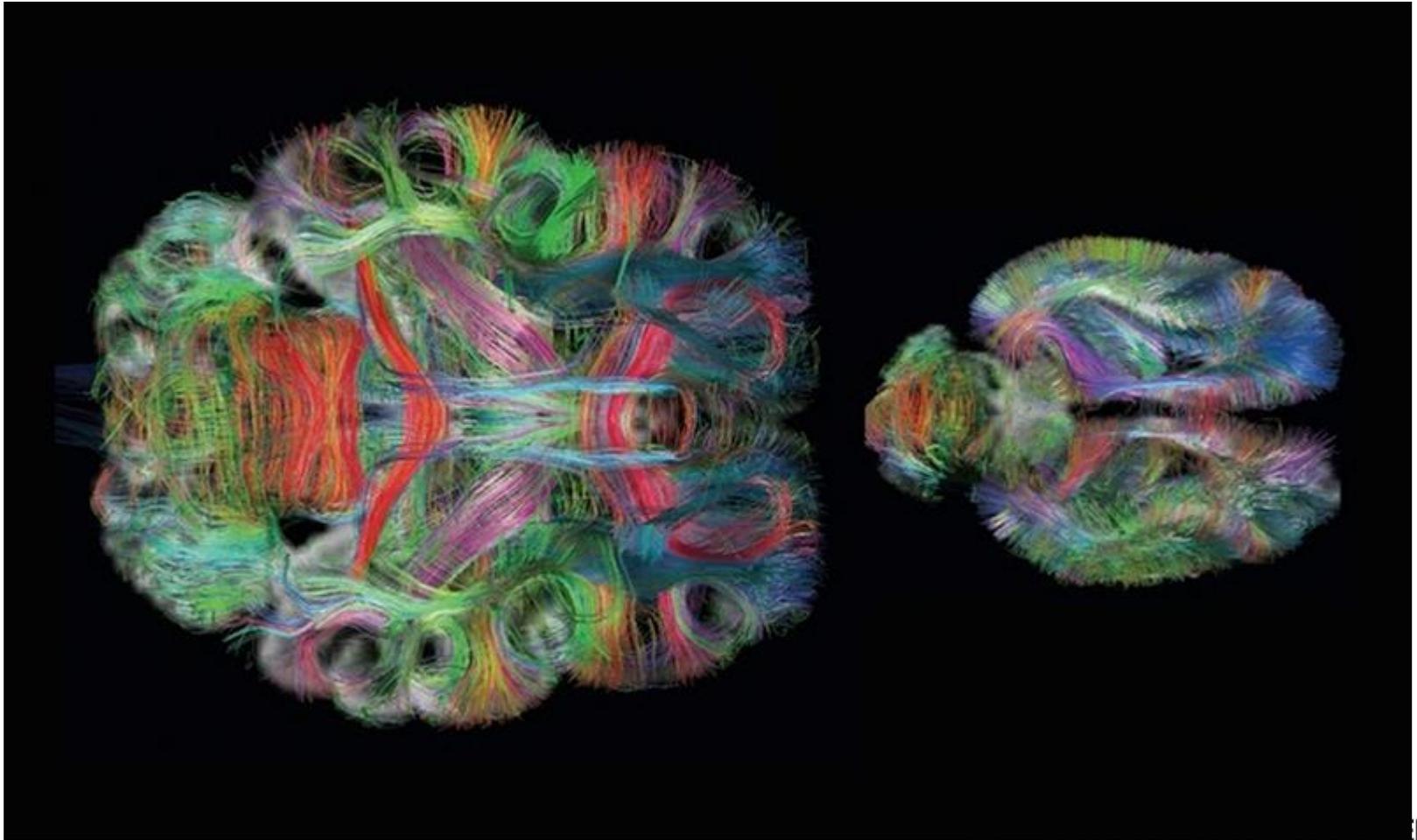
# The Amazing Human Brain

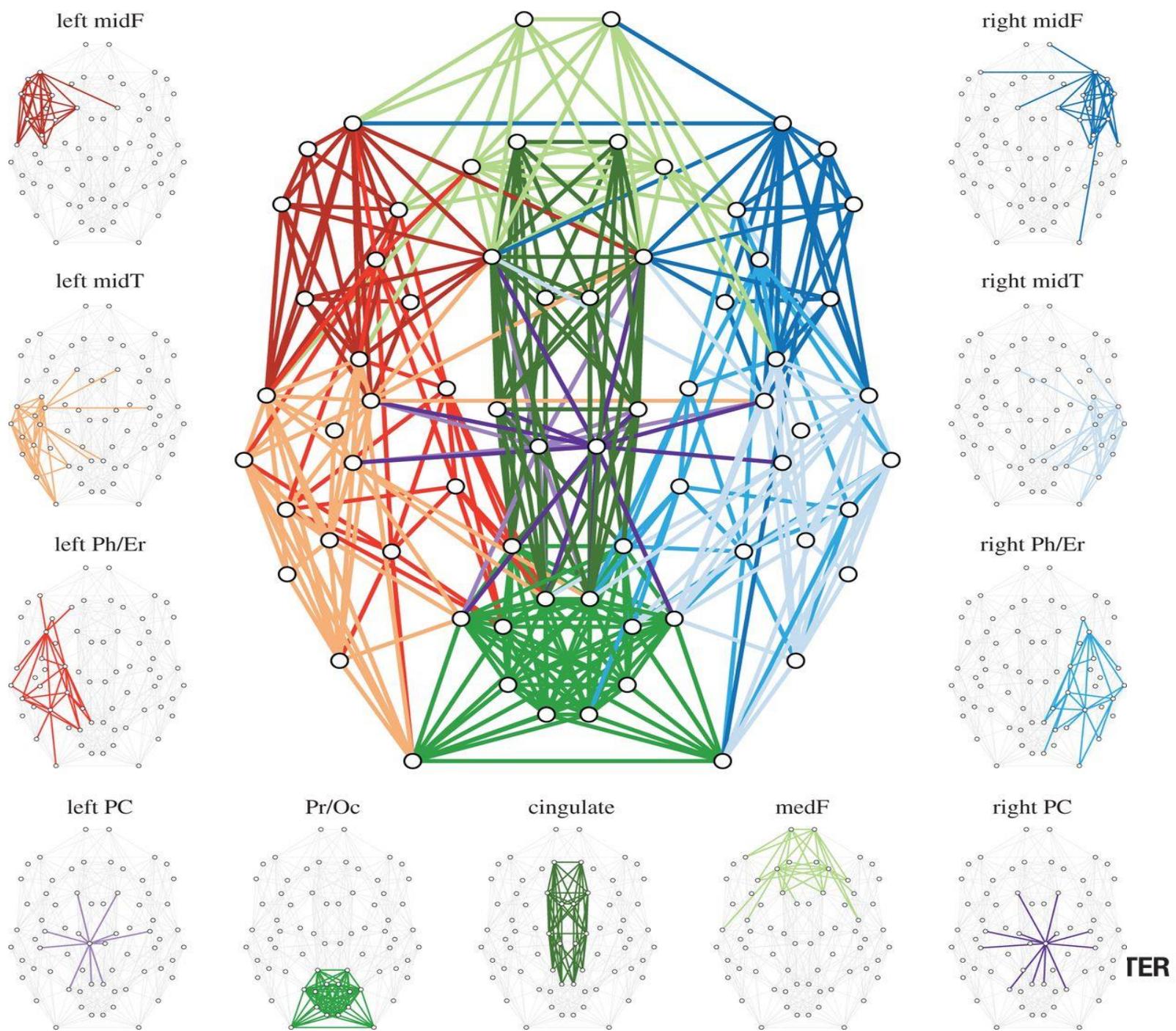


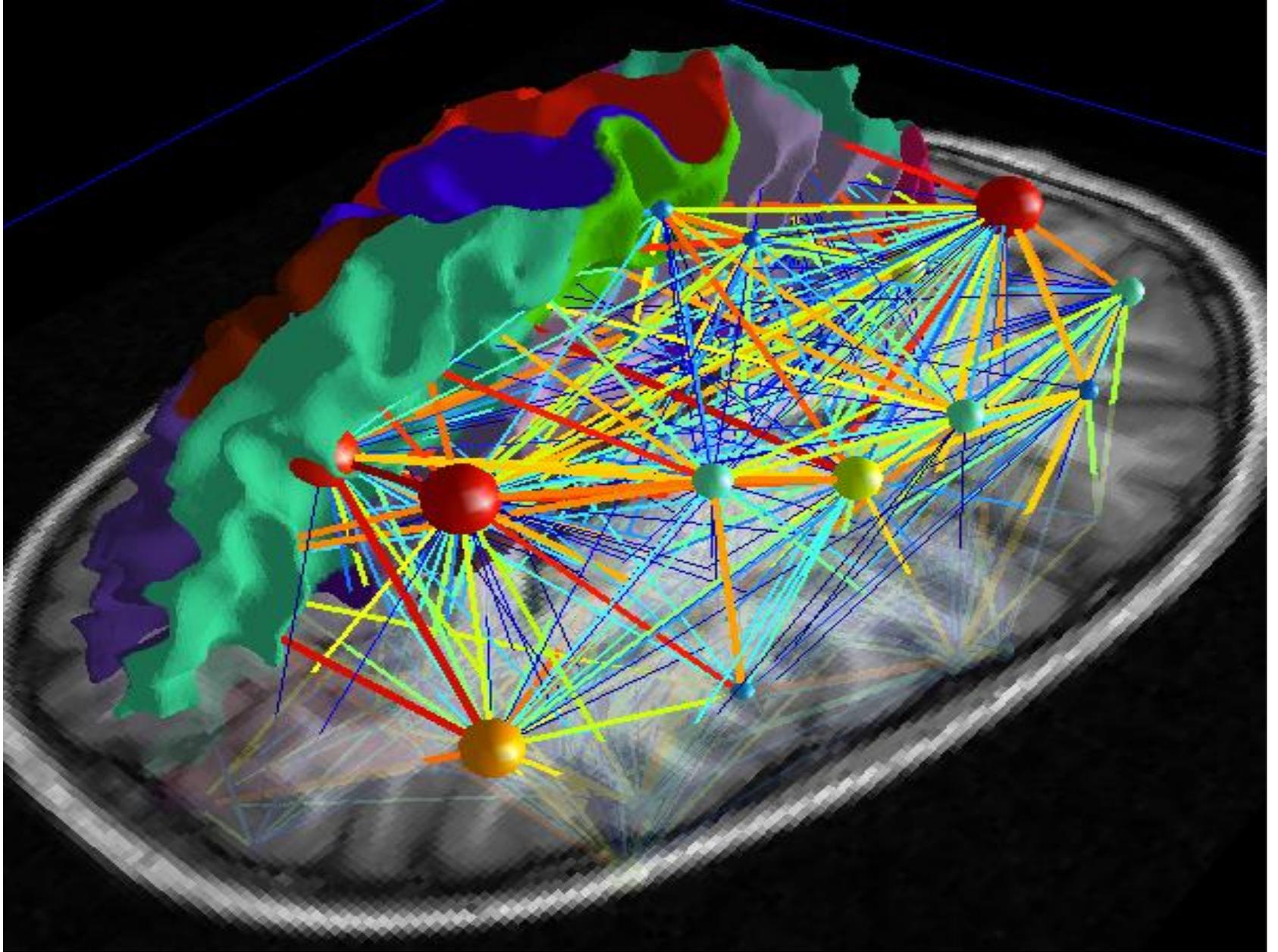
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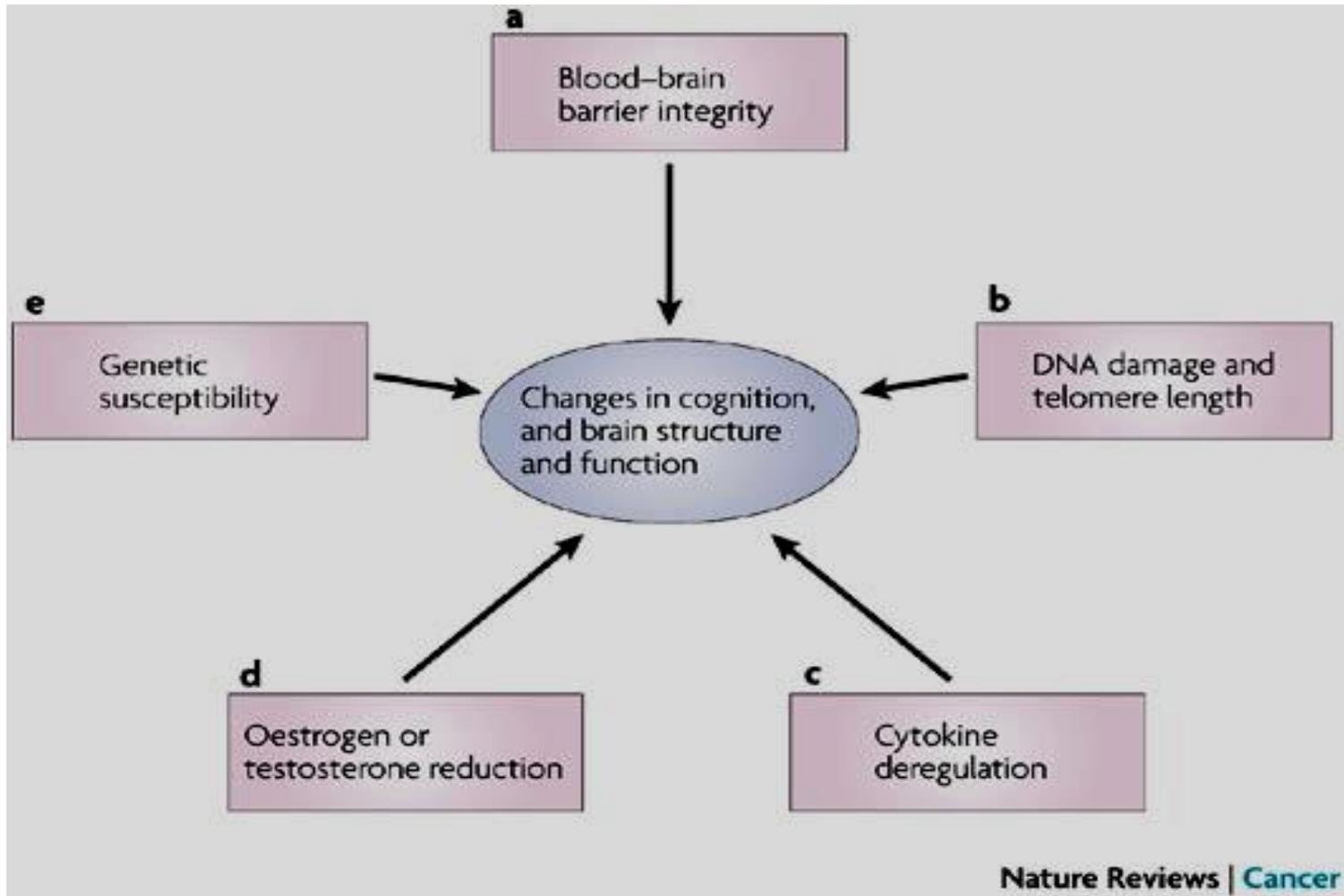






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# Candidate Mechanisms for Cognitive and Brain Changes



Ahles and Saykin *Nature Reviews Cancer* 7, 192–201 (March 2007) | doi:10.1038/nrc2073

# Risk Factors.....

- Age
- Cognitive reserve or vulnerability
- Age and medication interaction (e.g. Tamoxifen has stronger effects on cognition in older patients)
- Whole Brain Radiation
- Genetic predisposition/vulnerability to chemotherapy and/or cognitive impairment
  - APOE, COMT
  - poor DNA repair
- Menopause
- Hormonal therapy
- Anxiety, depression,
- Supportive care meds
- Comorbid medical conditions
- Surgery and anesthesia
- Sleep disturbance.
- Blood Brain Barrier Breakdown



# In Summary: There is likely a Multi-factorial Etiology

- Anxiety and depression
- 
- Pre-existing genetic factors
- Changes in estrogen levels
- Toxic effects of chemotherapy
- Proinflammatory cytokines influence on
- brain function



# What do the research studies tell us about specific cognitive changes?

- Few studies until about 20 years ago, when research began to increase
- Real consensus in 2003 regarding presence of cognitive change
- Initial cross-sectional designs in survivors
  - Poorer NP performance with chemotherapy exposure
  - No consistently identified domains
  - Self-reported cognitive complaints NOT usually associated with NP performance
  - Various chemotherapy regimens



# General Cognitive Findings During or Just Following Treatment (lots of “noise” in research, reflects cortical and subcortical changes)

## Attention

- Concentration
- Switching attention from one task to another
- Ignore distractions
- Attention to detail

## Mental Processing speed

- How quickly one can think, respond

## Motor

- Dexterity, coordination, speed

## Memory

- Short- and Long-term memory
- Learn and recall words, stories
- Remember events versus facts
- Remember designs, faces

## Executive function

- Organizing, planning and carrying out a plan
- Problem solving
- Reasoning
- Multi-tasking

## Working memory

- Mentally manipulate information

## Visuospatial functioning

- Copying, use blocks to make 3-D designs, map reading, hand-eye coordination

## Language

- Naming
- Word retrieval



# Self-Reported Complaints (often related to slowed processing speed and variable attention)

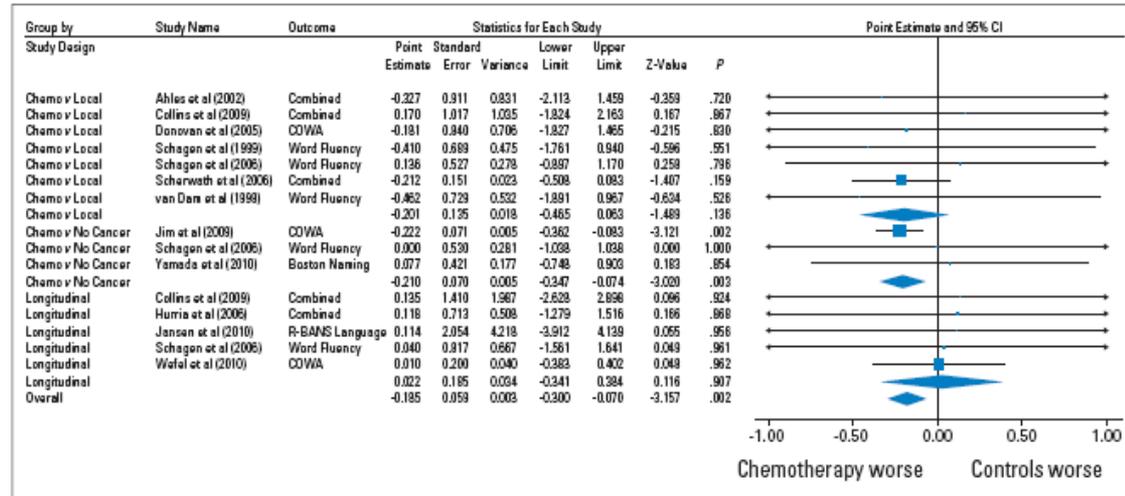
- Difficulty finishing something started
- Inefficient at doing well-known tasks
- Problems planning and carrying out a plan
- Problems multi-tasking; difficulty managing complex tasks
- Difficulty learning and remembering new things



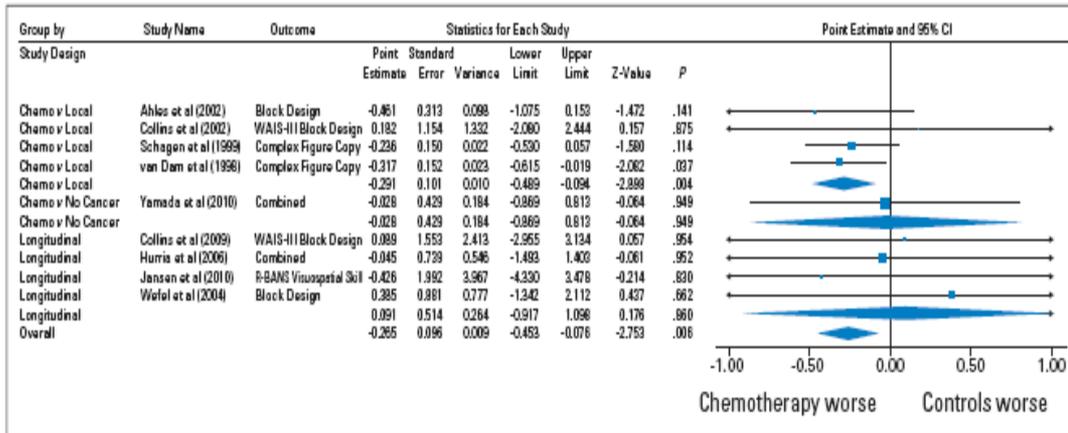
## Meta-Analysis of Cognitive Functioning in Breast Cancer Survivors Previously Treated With Standard-Dose Chemotherapy

Heather S.L. Jim, Kristin M. Phillips, Sari Chait, Leigh Anne Faul, Mihaela A. Popa, Yun-Hsiang Lee, Mallory G. Hussin, Paul B. Jacobsen, and Brent J. Small

Verbal Ability—word generation, naming



Visuospatial ability  
Figure copy, block designs



On average, across all studies, **over time** cognitive deficits are limited to these two domains in breast cancer survivors treated with chemotherapy.

# Specific Example of Course of Cognitive Symptoms in Breast Cancer Patients Over Time

- Anxiety and depression are common, and associated with cognitive complaints
- Impaired NP test performance found prior to chemotherapy treatment
- Decline in NP function during treatment that recovers by a year
- Symptoms and decrements in quality of life (QOL) are common at end of primary treatment and **resolve** over time in most patients
- A subset of breast cancer problems have **persistent** cognitive complaints and poor QOL.



# Brain Function: Effects of Chemotherapy on the Brain in Cancer Discordant Twins

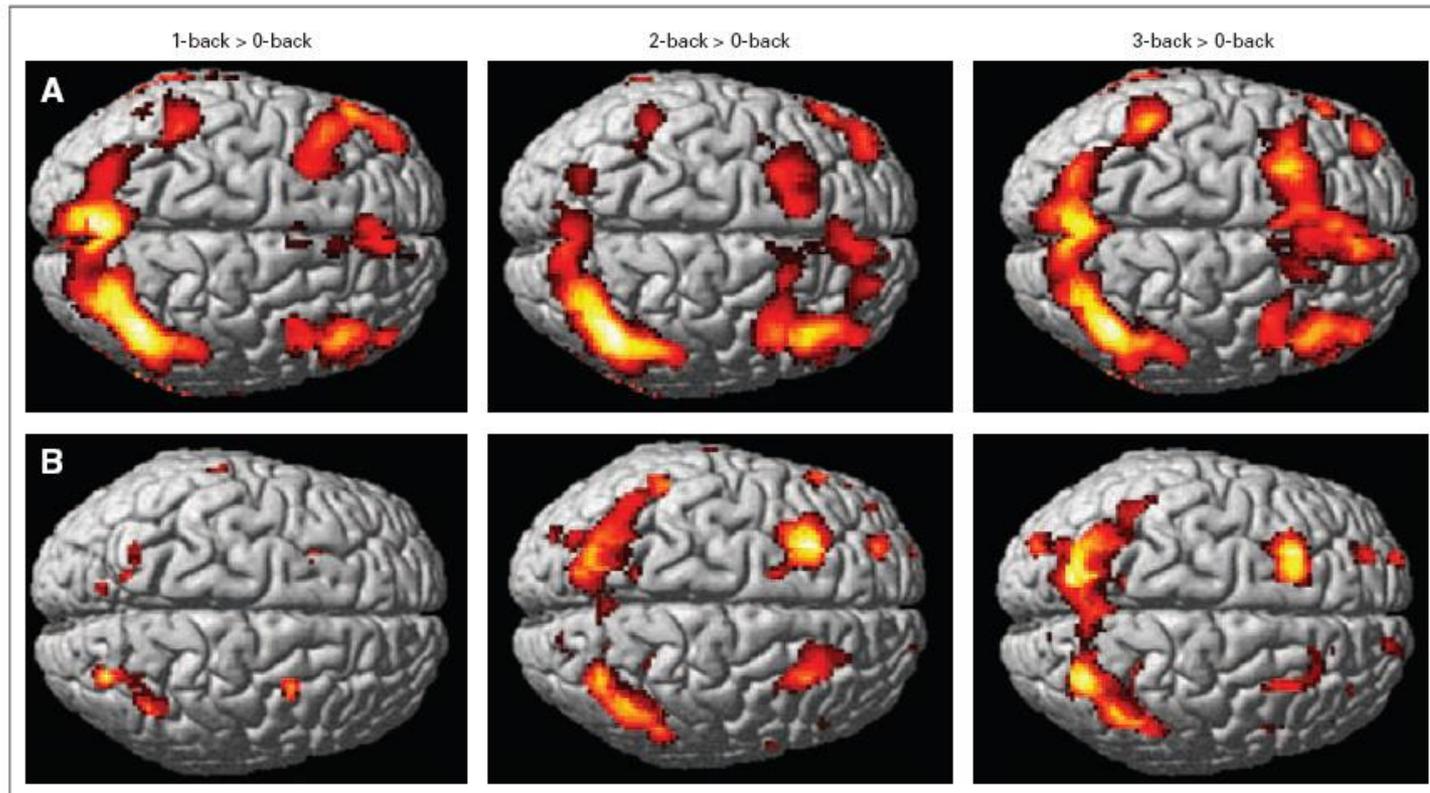


Fig 2. Functional magnetic resonance images of 60-year-old identical twins during a working memory task with incrementally increasing levels of difficulty (left to right). Colored regions denote increased brain activation during working memory relative to a simple vigilance task. (A) Twin treated with chemotherapy; (B) twin who did not receive chemotherapy. Note the expanded spatial extent of cortical activation in the chemotherapy-treated twin.

*Twin Study:* A is patient with breast ca and B is her identical twin without breast ca.

**Chemotherapy exposed brains may have to work harder to compensate for damage to neural networks**      Ferguson et al. JCO 2007



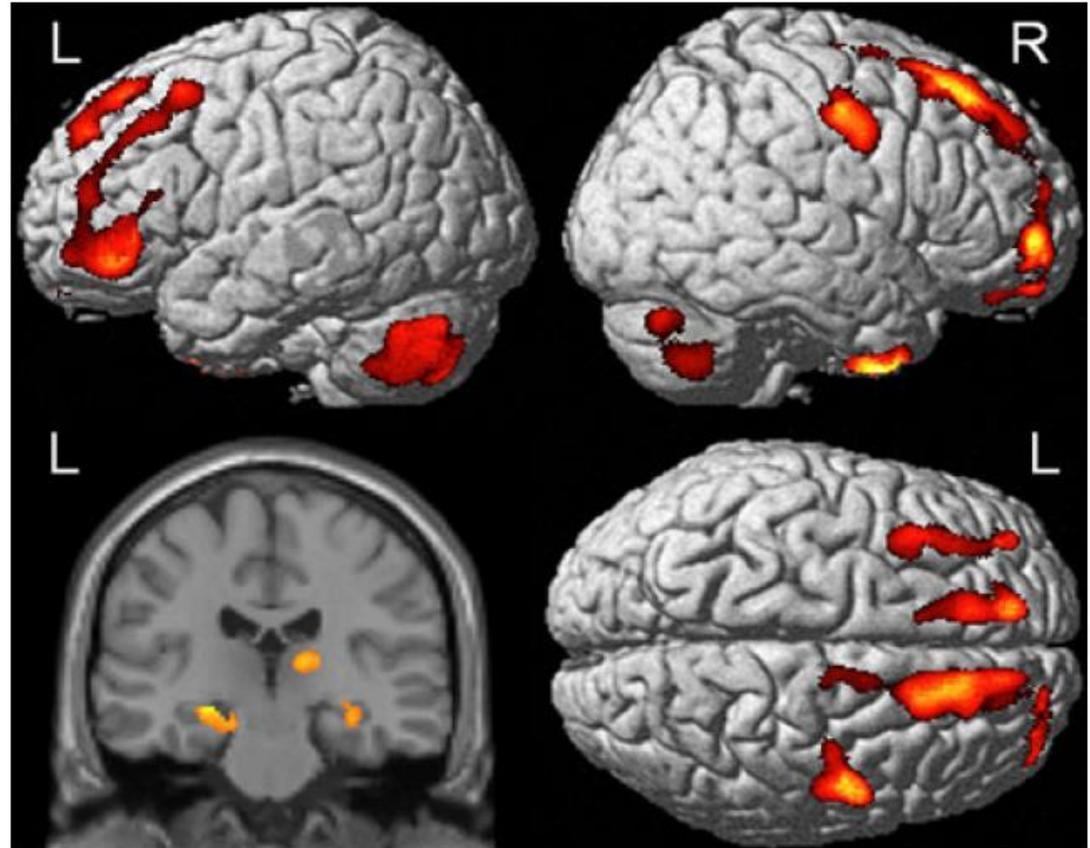
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## Gray matter reduction associated with systemic chemotherapy for breast cancer: a prospective MRI study

Brenna C. McDonald · Susan K. Conroy ·  
Tim A. Ahles · John D. West · Andrew J. Saykin

### Short-term effects of chemotherapy on brain structure

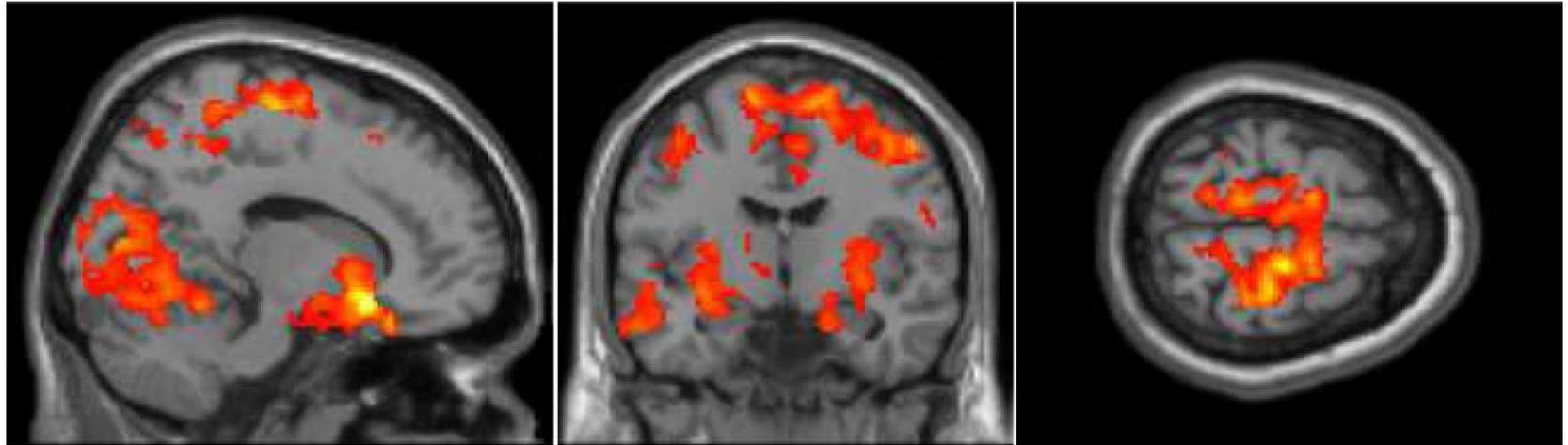
Areas in red indicate gray matter density declines in chemotherapy patients 1 month after treatment.



**Fig. 2** Regional gray matter density declines in chemotherapy-treated breast cancer patients from baseline to 1 month after chemotherapy

## Chemotherapy Altered Brain Functional Connectivity in Women with Breast Cancer: A Pilot Study

Julie A. Dumas<sup>1,\*</sup>, Jenna Makarewicz<sup>1</sup>, Geoffrey J. Schaubhut<sup>1</sup>, Robert Devins<sup>1</sup>, Kimberly Albert<sup>1,2</sup>, Kim Dittus<sup>3</sup>, and Paul A. Newhouse<sup>1,2</sup>



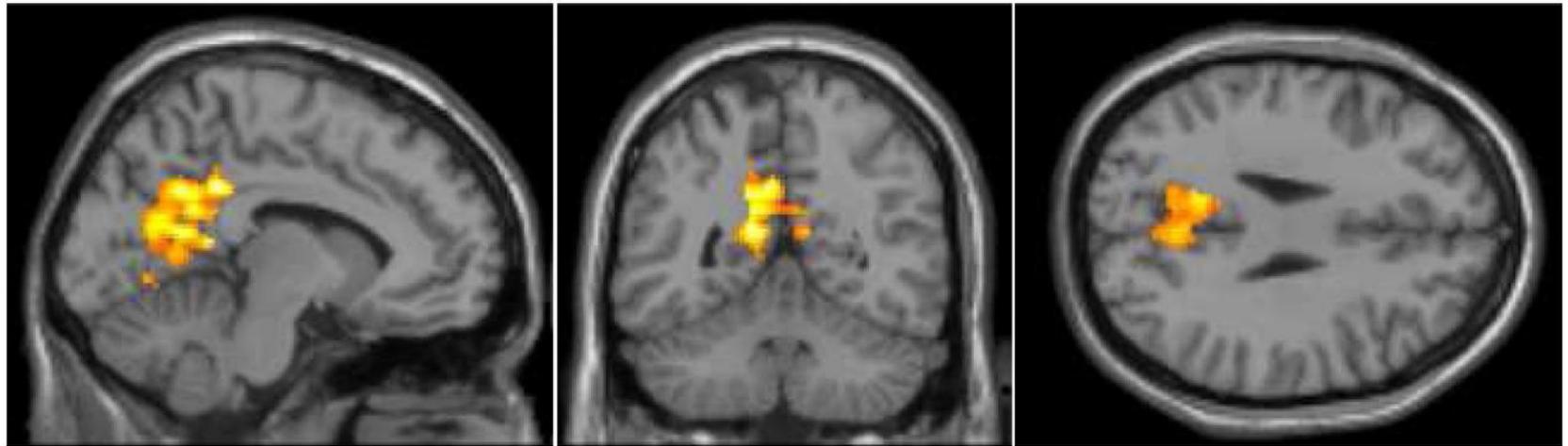
**Figure 1.**

Functional connectivity in the dorsal attention network ( $p < .05$ ;  $k = 1000$ ) that decreased at one month and recovered one year after chemotherapy treatment.



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Julie A. Dumas<sup>1,\*</sup>, Jenna Makarewicz<sup>1</sup>, Geoffrey J. Schaubhut<sup>1</sup>, Robert Devins<sup>1</sup>, Kimberly Albert<sup>1,2</sup>, Kim Dittus<sup>3</sup>, and Paul A. Newhouse<sup>1,2</sup>



**Figure 2.**

Functional connectivity in the default mode network ( $p < .05$ ;  $k = 1000$ ) that decreased one



# Potential Treatments

- First, address untreated depression, pain, and anxiety
- Ensure adequate sleep
- Focus on management of fatigue
- If complaints persist, obtain consultation from a trained neuropsychologist familiar with cancer treatment
- Role of pharmacological agents



# The Effect of Modafinil on Cognitive Function in Breast Cancer Survivors

Sadhna Kohli, PhD, MPH<sup>1</sup>; Susan G. Fisher, PhD<sup>2</sup>; Yolande Tra, PhD<sup>3</sup>; M. Jacob Adams, MD, MPH<sup>2</sup>; Mark E. Mapstone, PhD<sup>4</sup>; Keith A. Wesnes, PhD<sup>5</sup>; Joseph A. Roscoe, PhD<sup>6</sup>, and Gary R. Morrow, PhD, MS<sup>6</sup>

Cancer 2009;115:2605-16. © 2009 American Cancer Society.

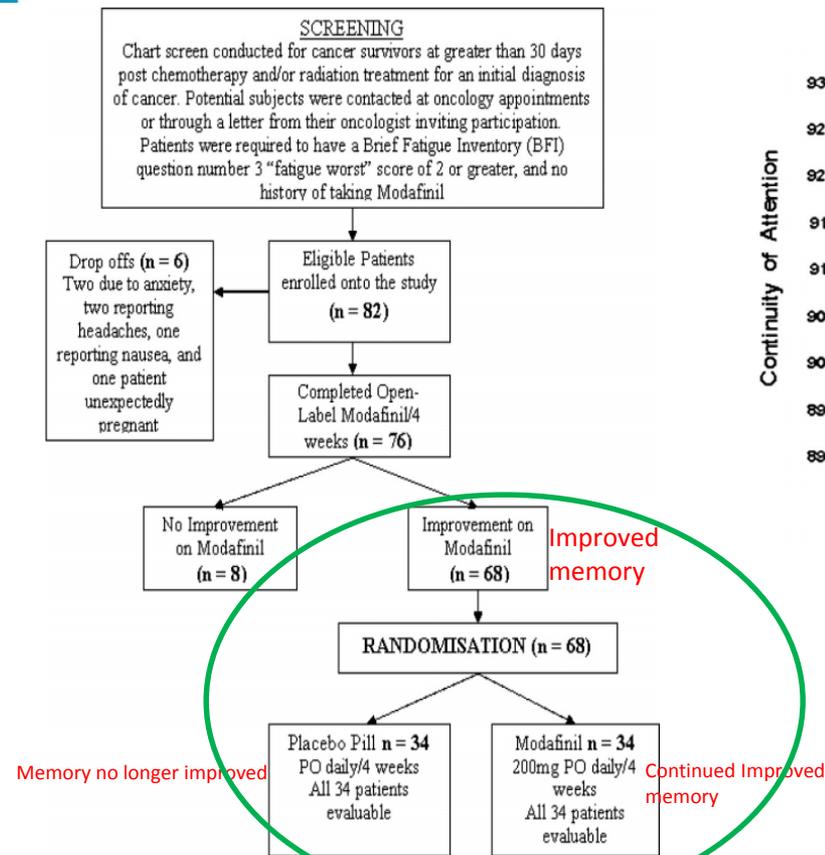
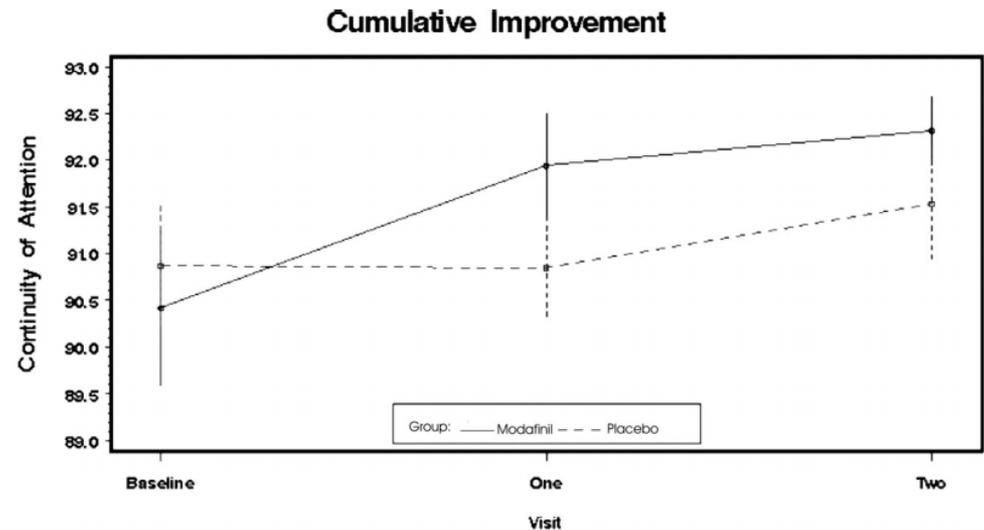


FIGURE 2. Patients who completed study at each time-point.



Treatment with modafinil embedded within a fatigue study, increase wakefulness also see better memory



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Research says.....



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The power of play: The effects of Portal 2 and Lumosity on cognitive and noncognitive skills



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# So, what can I do?

- Cognitive Rehabilitation: individualized treatment, to address ***personal, relevant functional goals*** – less emphasis on particular cognitive functions.
- Compensatory Strategies: ways to “work around” or adapt to cognitive weaknesses
- Restorative: retraining of cognitive skills after a loss of function.



# Cognitive Rehabilitation Techniques

Determine what is important to you.

The brain thrives on structure/routine, but seeks novelty and learning.

A lot of the recommendations for cognitive rehabilitation are things you're already doing – to improve automaticity.



# Cognitive Rehabilitation: Routine/Structure

- Keep the same sleep/wake schedule every day
  - Sleep hygiene
- Keep a daily planner or calendar. Get into the routine of using it *everyday* for *every activity*.
  - The use of alarms
  - The use of emojis
- Establish a daily schedule at the beginning of your day
- Complete tasks one at a time.
- Environmental Modifications
  - White board in a highly visibly place
  - Things you want to remember together, place together.
- In the beginning, allow yourself some extra time.



# Cognitive Rehabilitation: Novelty and Learning

- Change tasks frequently (according to your daily schedule).
  - Take breaks - working while tired will NOT be helpful to anyone!
- Least interesting tasks (or hardest task) when you're at your "cognitive best"
- Keep your brain and body active!
  - Engage in physical activity daily
  - Seek out cognitive stimulation: reading, problem solving, social interactions, listening to the news, volunteering, employment
  - Find things you find interesting, and do them!
- Get in touch with a therapist or counselor



# Memory Specific Rehabilitation Techniques:

- Identify the information to be remembered
  - Say it back
- Minimize the amount of information to be remembered
  - Write it down
  - Chunk similar things together
- Structure the information to learn, make this as meaningful as possible
  - Visual imagery, relate it to a story, etc
- Define a cue to retrieving the information
  - Visual or verbal
- Rehearse what needs to be remembered.
  - Practice!





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