

Dealing with Cognitive Impairment in the Patient with Breast Cancer

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Sources of Funding

- Office of Cancer Survivorship, National Cancer Institute (CA23108, CA87845, CA116394)
- Chanel Foundation
- Martel Foundation
- Starr Consortium

Cognitive Impact of Cancer Therapies

- Cranial radiation +/- intrathecal chemo
- Cranial surgery
- Biological response modifiers
- High-dose chemotherapy
- Standard-dose chemotherapy
- Hormonal Therapies

Common Cognitive Problems Reported Post-Treatment

- Memory and Concentration
- Executive Function
- Ability to Learn New Material /Reading Comprehension
- Ability to Work with Numbers

Pattern of Cognitive Problems

- Not everyone is affected (15-20%)
- Problems may come and go (Good and bad days)
- Often worse when:
 - Multitasking
 - Under stress or deadline pressure
 - Fatigued / Poor sleep

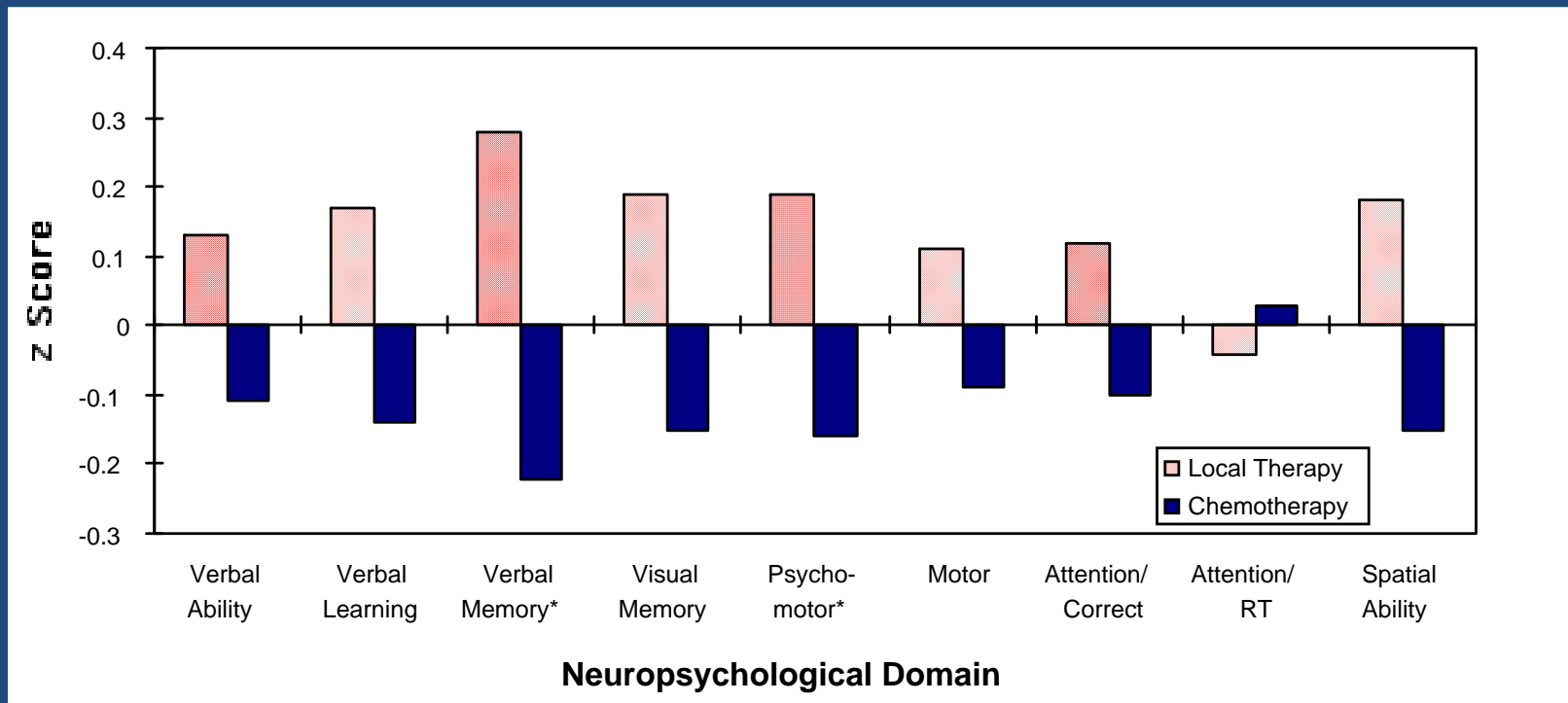
Factors Affecting Cognitive Functioning

- Fatigue / Sleep disorders
- Depression, anxiety, stress
- Pain and pain medications
- Other physical illnesses

Results of Post-treatment Studies

- Poorer cognitive performance for survivors treated with chemotherapy evaluated 6 months to 10 years post-treatment compared to survivors not exposed to chemotherapy
- Only a subgroup of survivors (17-35%) experienced persistent cognitive problems
- Cognitive problems not explained by depression, anxiety, or fatigue

Adjusted z-Transformed Domain Scores for the Chemotherapy vs. Local Therapy Groups



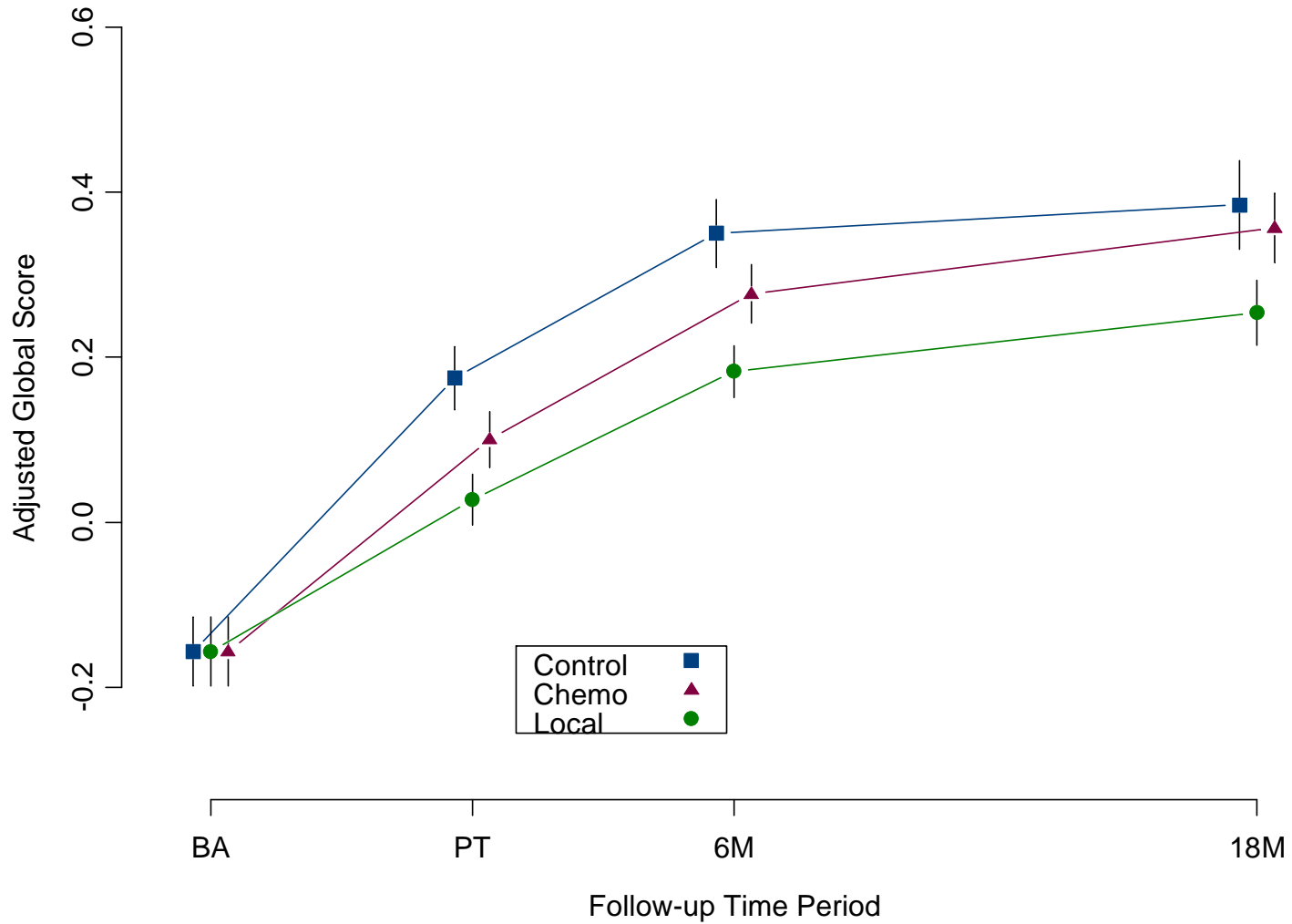
* $p < .05$, adjusted for age and education

Results of Longitudinal Studies

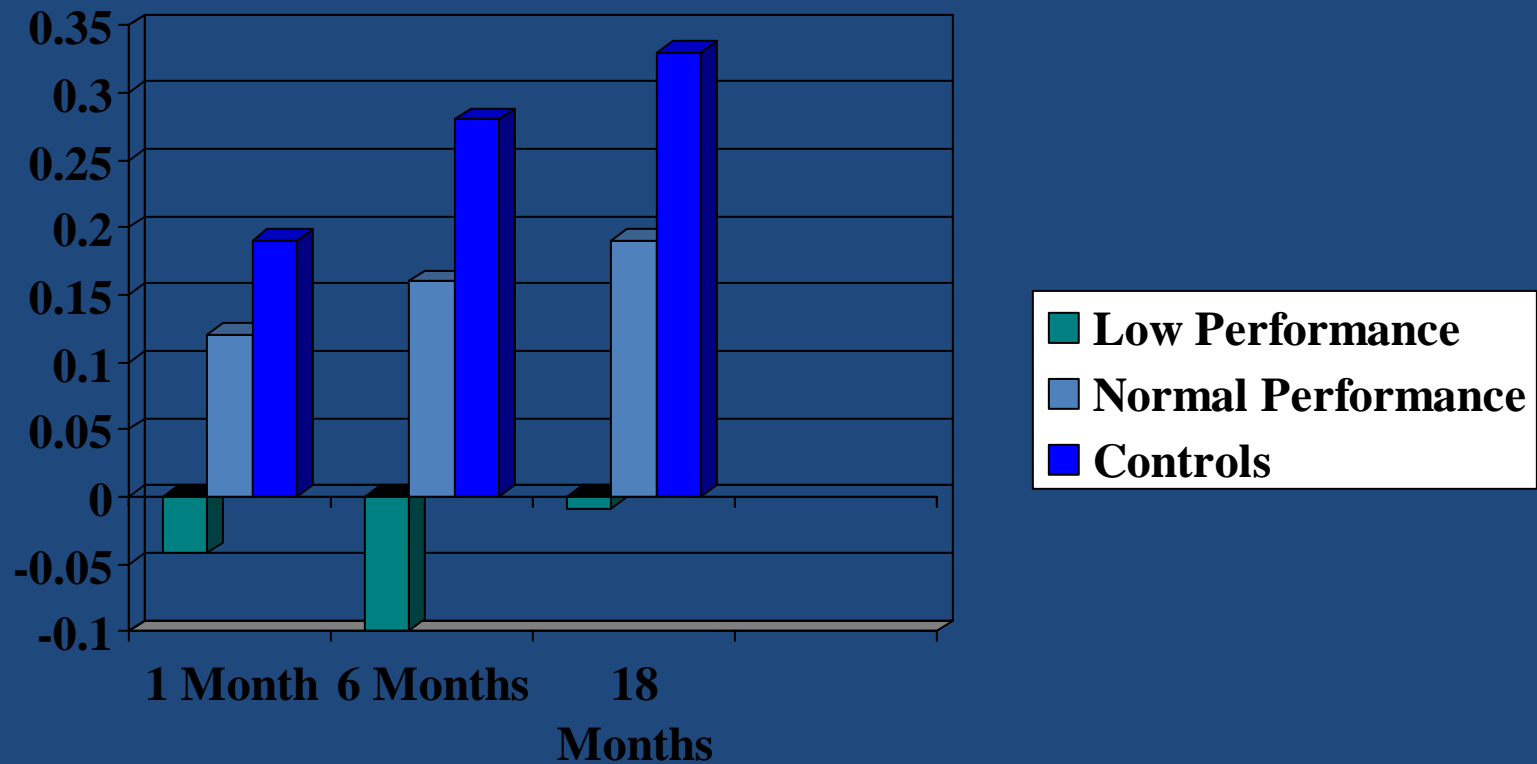
- 20-30% of breast cancer patients demonstrate lower than expected cognitive performance prior to adjuvant treatment which is not related to depression, anxiety or fatigue
- Patients treated with chemotherapy and patients treated with non-chemotherapy-based regimens performed more poorly than matched healthy controls

Global

(Adjusted for age, education, and baseline)



Processing Speed: Change Scores from Baseline



Potential Explanations for Pretreatment Differences

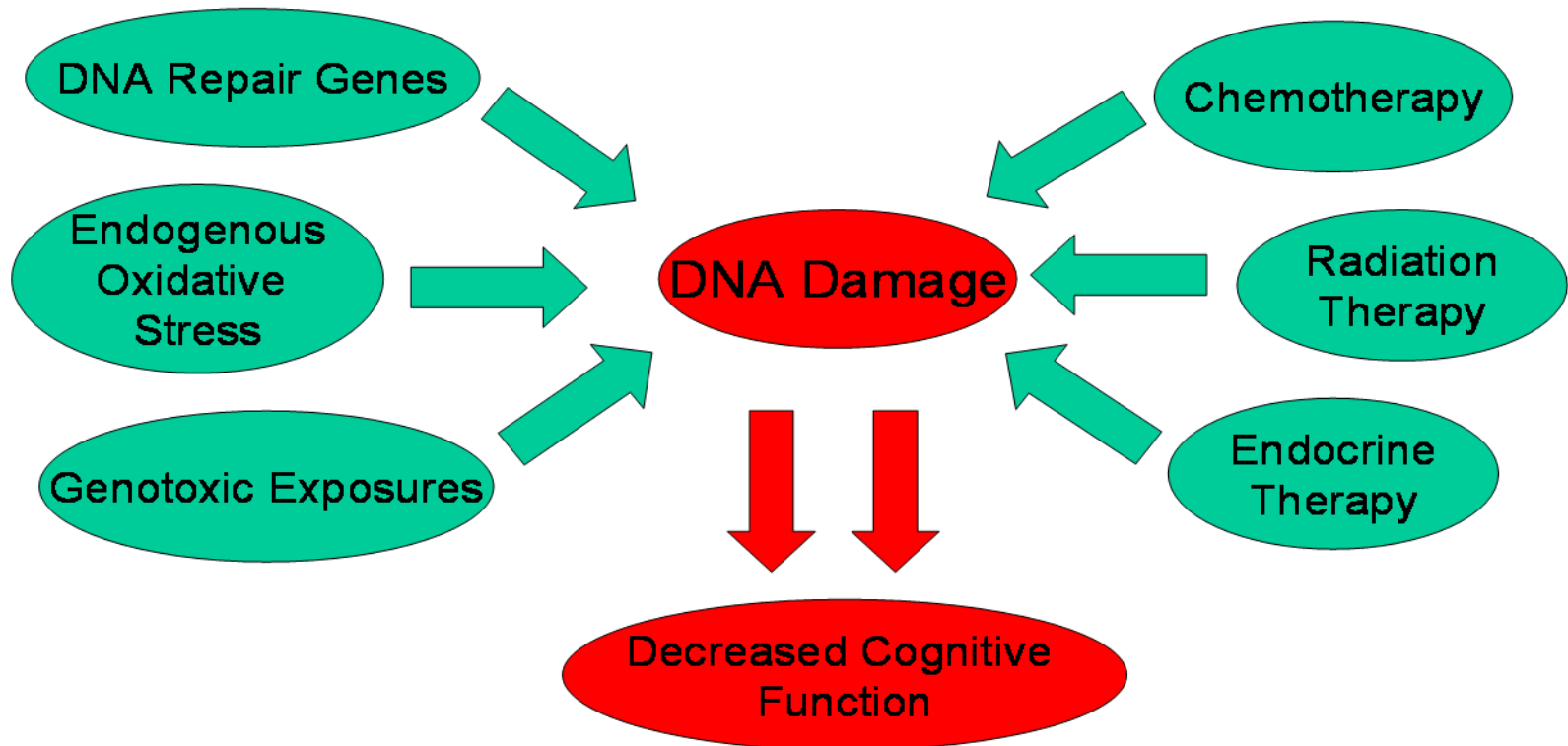
- Shared risk factors for development of cancer and mild cognitive decline
- Potential role of DNA damage and the genetics of DNA repair

DNA Damage Hypothesis

- DNA damage is associated with risk for cancer and risk for neurodegenerative disorders / cognitive changes with aging
- Chemotherapy, as well as other aspects of cancer treatments, are DNA damaging

Pre-Cancer Diagnosis

Cancer Treatments



Potential Explanations for Post-Treatment Results

- Potential role of endocrine treatments (Tamoxifen and Aromatase Inhibitors)
- Role of chemotherapy-induced menopause
- Estrogen reduction may be associated with cognitive change

Renaming “Chemobrain”

- Cancer or cancer-associated cognitive change
- “if you have Tim's e-mail address, maybe contact him and say if he expects his favorite project to resonate with the general public, he'd better leave the name as is because "chemobrain" slips off the tongue quite willingly, while the proposed new name is a gnarly mouthful!”

Neuropsychological Testing

- Primarily designed to assess people with significant brain damage (stroke, head injury) or disease (Alzheimer's)
- Problem: Many cancer survivors score well within the normal range even though they report having cognitive problems

Results of MRI, PET and EEG Studies

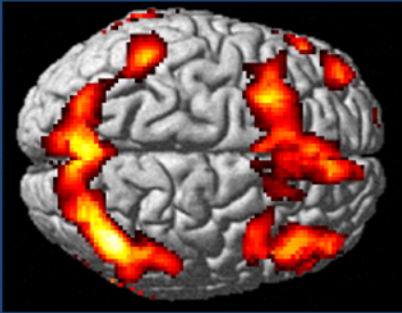
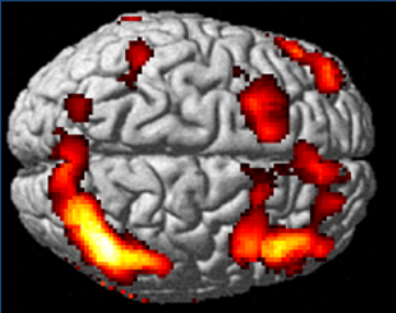
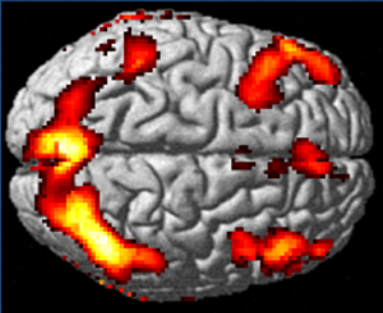
- MRI and PET studies suggest that there are changes in brain structure and function associated with chemotherapy
- EEG studies suggest changes in measures of information processing (P300) associated with chemotherapy

fMRI Activation Pattern for Identical Twins Discordant for Breast Cancer

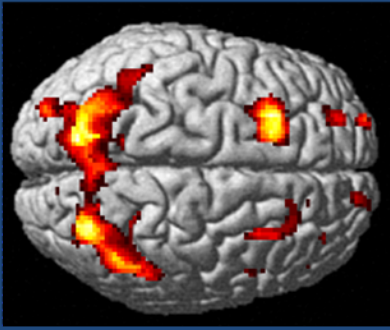
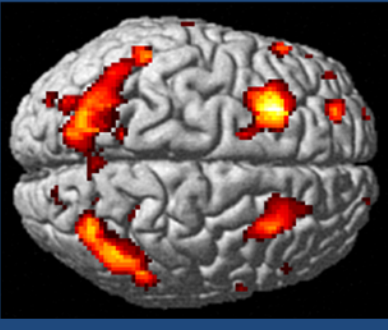
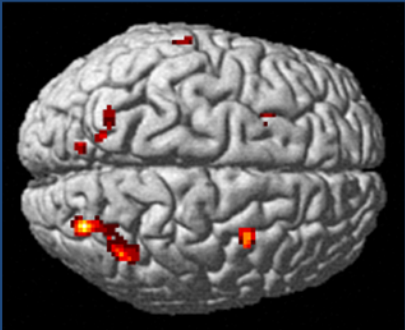
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Chemotherapy-treated Twin-Twin A



Non-cancer Twin-Twin B

Genetic Factors

- Repair of nerves and blood vessels (APOE)
 - DNA repair
 - Inflammatory response
 - Blood brain barrier
-
- Understanding genetic risk factors may lead to tailored treatments which avoid toxicities like cognitive problems

Interventions

- Pharmacologic Interventions
 - psychostimulants
 - cholinesterase inhibitors
 - gingko biloba
- Cognitive Rehabilitation



NORRIS COTTON CANCER CENTER
DARTMOUTH-HITCHCOCK MEDICAL CENTER

Memory and Attention Training:

A Brief Behavioral Skills Program for Cancer Survivors with Attention and Memory Problems Associated with Chemotherapy

Robert J. Ferguson, Ph.D.*

Behavioral Medicine Section

Dartmouth Medical School

RUNNING HEAD: Memory and Attention Training

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Memory and Attention Training

- Education
 - Common cognitive errors
 - Different types of memory and attention

Memory and Attention Training

- Compensatory Strategies
 - Lists, calendars, palm pilots
 - Self-instructional training
 - Scheduling / Time management
 - Sleep hygiene / Fatigue management

Memory and Attention Training

- Relaxation Training
 - Progressive Muscle Relaxation
 - Breathing exercises

Memory and Attention Training

- Problem-Solving
 - A structured approach to applying the skills in everyday life

Summary

- Cognitive problems experienced by cancer patients are likely not exclusively associated with chemotherapy
- Pretreatment cognitive problems suggest that there may be common risk factors for development of cancer and cognitive problems
- Imaging techniques will be important to understanding cognitive changes associated with breast cancer treatments
- Genetic factors are likely important in increasing vulnerability for long-term cognitive problems
- Medication and cognitive rehabilitation interventions are being evaluated