

Cognitive Changes after Cancer Treatment

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Overview

- How common are cognitive complaints?
- Who is at risk?
- What do the research studies show us?
- What should we do in the clinic?



Does “Chemobrain” Exist?

- Patients often report changes in thinking and memory while on chemotherapy
- Some patients report persistent difficulties with memory and concentration long after treatment ends
- May also be associated with chemotherapy-induced menopause —*not all post-treatment cognitive complaints are from chemotherapy*
- *Cognitive complaints are not just related to chemotherapy exposure—whole brain irradiation and endocrine therapy may also be associated*



Who is definitely at risk?

- Children and adults treated for brain tumors
- Children & adults treated with whole brain radiation
- Leukemia and lymphoma survivors receiving certain intraspinal chemotherapy



Questions Arising from Research Findings

- Self-reported complaints don't always match objective performance on NP testing
- Some studies document NP test deficits that pre-exist cancer treatment and they do not worsen with treatment
- True incidence of treatment associated cognitive decline is uncertain



COMMENTARY

Renaming “Chemobrain”

Arti Hurria, M.D.,¹ George Somlo, M.D.,¹ and Tim Ahles, Ph.D.²

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review

Annals of Oncology 19: 623–629, 2008
doi:10.1093/annonc/mdm500
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Cancer and cancer-therapy related cognitive dysfunction: an international perspective from the Venice cognitive workshop

J. Vardy¹, J. S. Wefel², T. Ahles³, I. F. Tannock⁴ & S. B. Schagen^{5*}

Recent Commentaries



Cognitive complaints: Why Important?

- Growing number of cancer survivors potentially affected
- Impact on quality of life among long-term survivors suggested by early research
- Need for more accurate information to provide more informed treatment decisions and/or modifying current treatment recommendations



Who is at risk?

- **Example patient A:**
 - 45 year old professional woman (e.g. ICU nurse, elementary school teacher, lawyer) is diagnosed with breast cancer
 - Stops menstruating with chemotherapy and is placed on tamoxifen
 - Has two school age children and works full-time



Patient A: symptoms & cognitive complaints

- 6 mos after completion of chemotherapy, trouble multi-tasking and doing routine chores; forgets to pick up children at school
- Reports anxiety about risk for cancer recurrence
- Sleeping poorly with hot flashes, night sweats

What's happening?



Who is at risk?

- **Example patient B:**
 - 70 year old retired male physician who is widowed
 - History of TIAs and some memory problems
 - Treated for non-Hodgkin lymphoma with CHOP chemotherapy and Rituxan



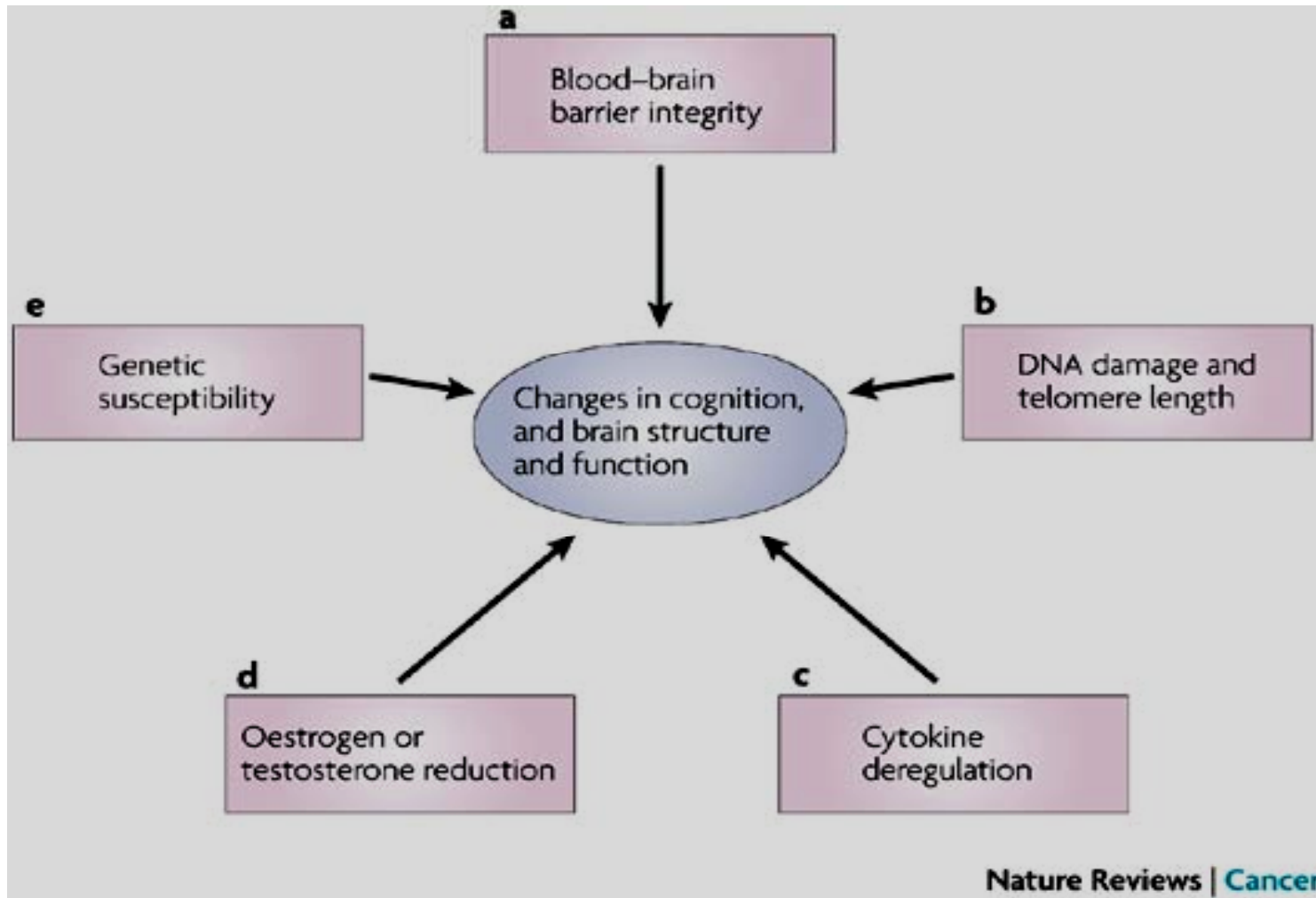
Patient B: symptoms & cognitive complaints

- 6 months after completion of chemotherapy: reports increased fatigue and difficulty sleeping
- Needs more assistance with activities of daily living, including shopping and balancing his check book

What's happening?



Candidate Mechanisms



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

Multi-factorial Etiology

- Anxiety and depression
- Pre-existing genetic factors
- Changes in estrogen levels
- Toxic effects of chemotherapy
- Proinflammatory cytokines influence on brain function
- *High functioning individuals may be more likely to notice subtle changes*

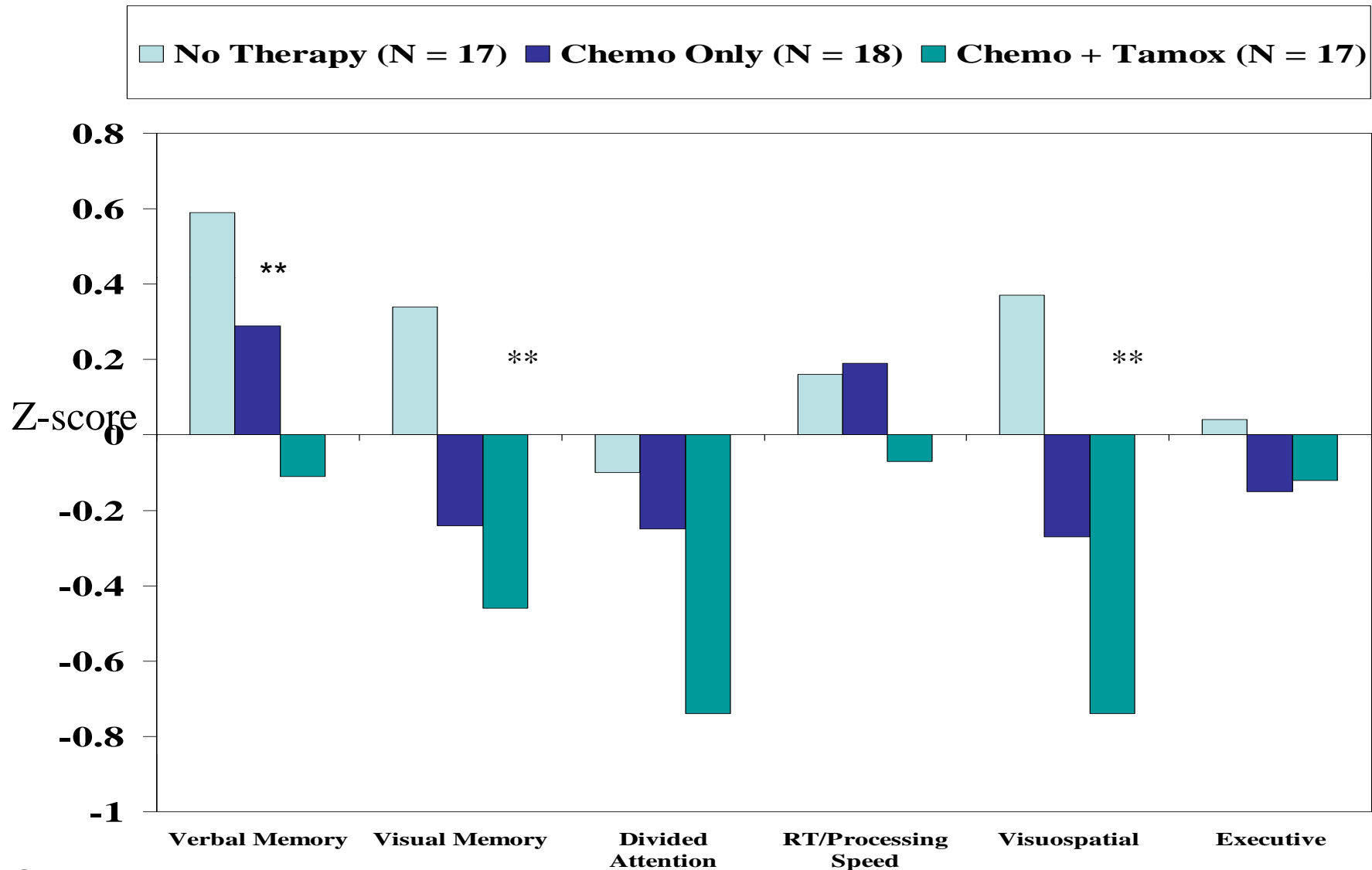


What do the research studies tell us?

- Few studies until a decade ago
- Initial cross-sectional designs in survivors
 - Poorer NP performance with chemotherapy exposure
 - No consistently identified domains
 - Self-reported cognitive complaints not consistently associated with NP performance
 - Various chemotherapy regimens

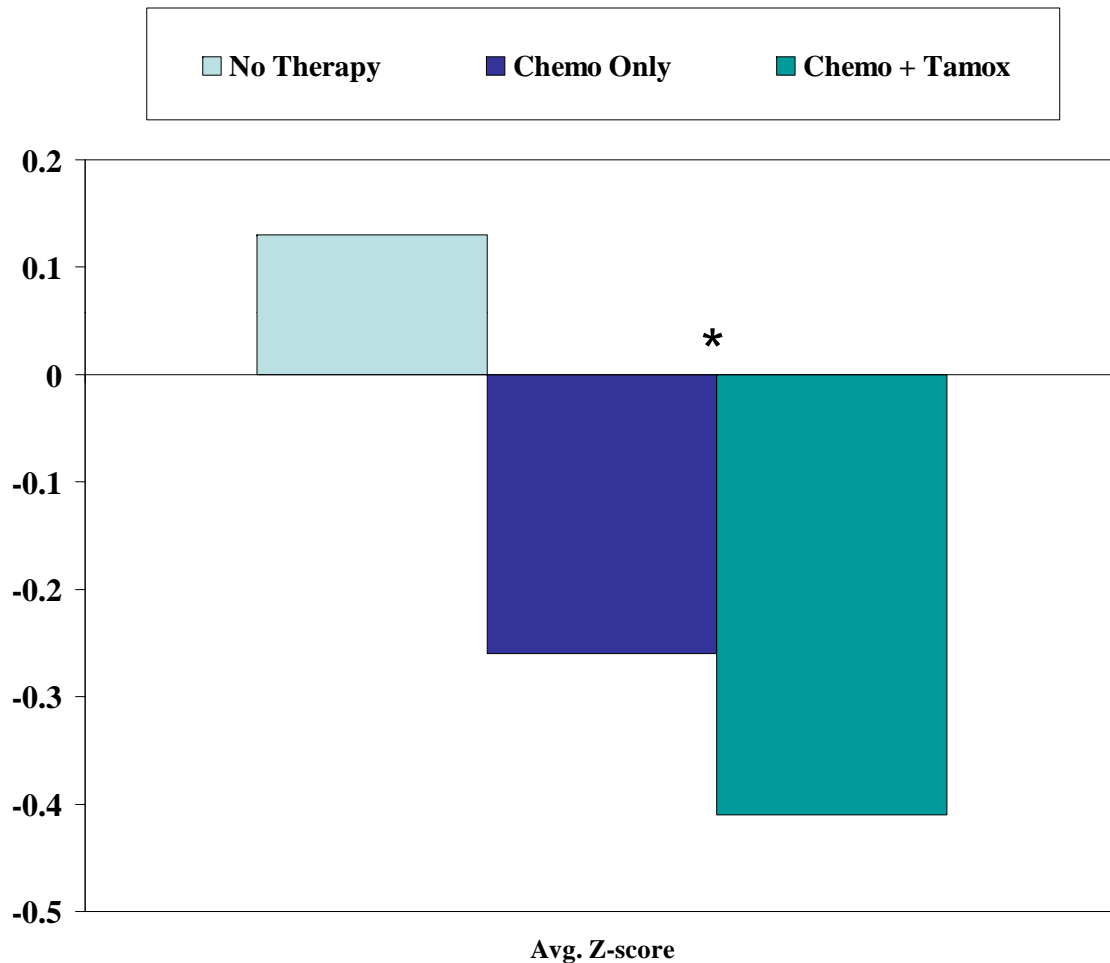


Neurocognitive Performance in BC Groups Relative to Non-Cancer Controls

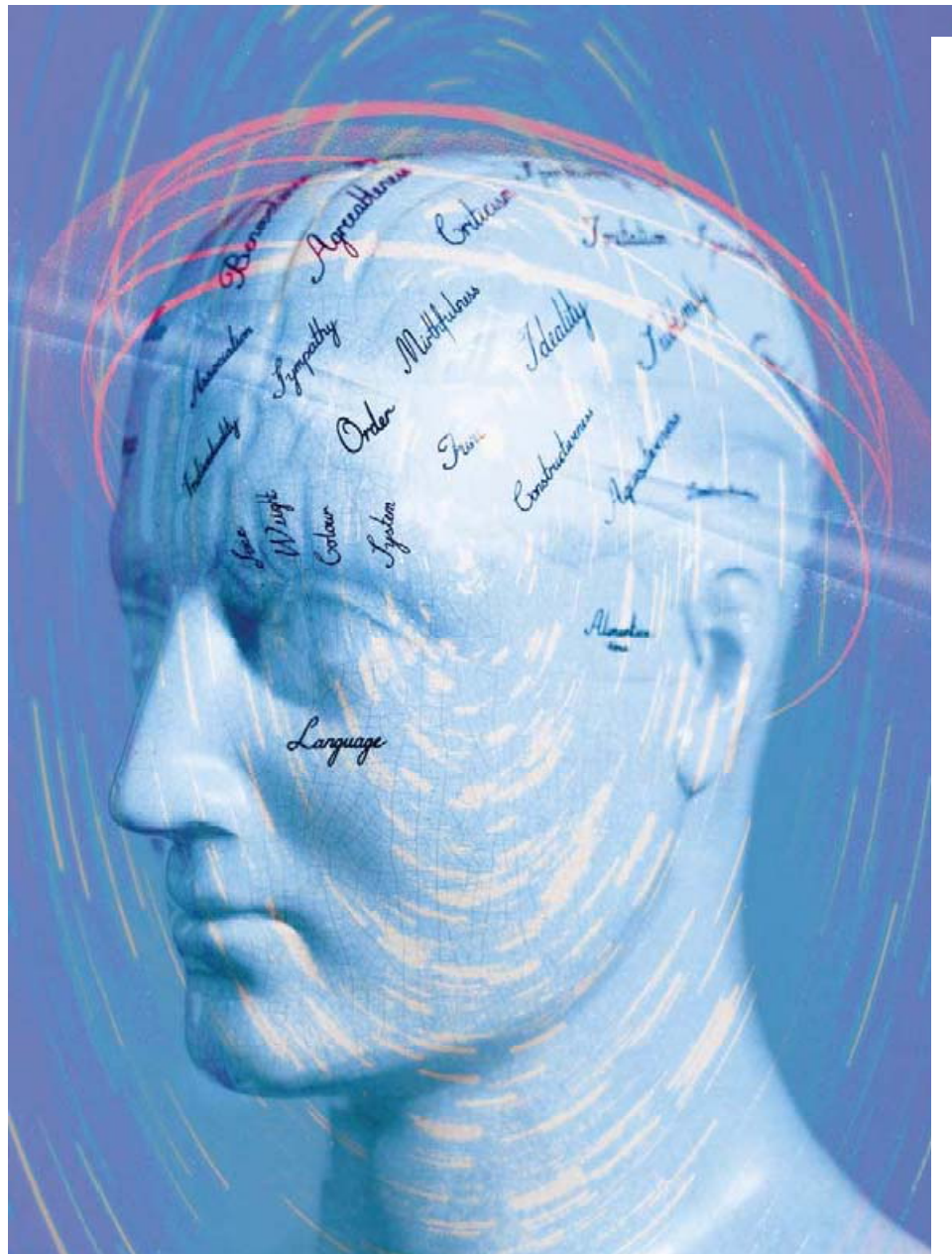


General Neurocognitive Performance Index

Average of all z-scores across each of 8 cognitive domains, relative to matched, non-BCS comparison group.



* $P < .05$ for no therapy vs. chemotherapy



Panel: Major issues to be addressed to improve the quality of future research

Minimum sets of core cognitive domains for neuropsychological examinations

Encourage standardisation in test selection and minimum requirements for tests, regarding reliability, validity, and reproducibility

Consensus on criteria by which to classify patients as cognitively impaired, and, in the case of prospective studies, to define what will constitute a significant change in cognitive function

Accountability of repeated testing effects in the analysis when establishing cognitive change in longitudinal studies

Comparison of performance of patients with an appropriate control group, for which demographic information, and basic performance measures, should be reported

Listing of specified outcome statistics—eg, effect size outcomes—in published manuscripts to allow for independent meta-analyses

Chemobrain is poorly understood...Lancet Oncology Oct 2007

Other Supportive Findings

- Provocative results from animal studies--- short and long-term neural injury from some chemotherapy drugs
- Poor memory function after chemo exposure in some animal studies
- Brain imaging studies in women with breast cancer show need to recruit additional brain areas in response to a memory task



Brain Function in Cancer Discordant Twins

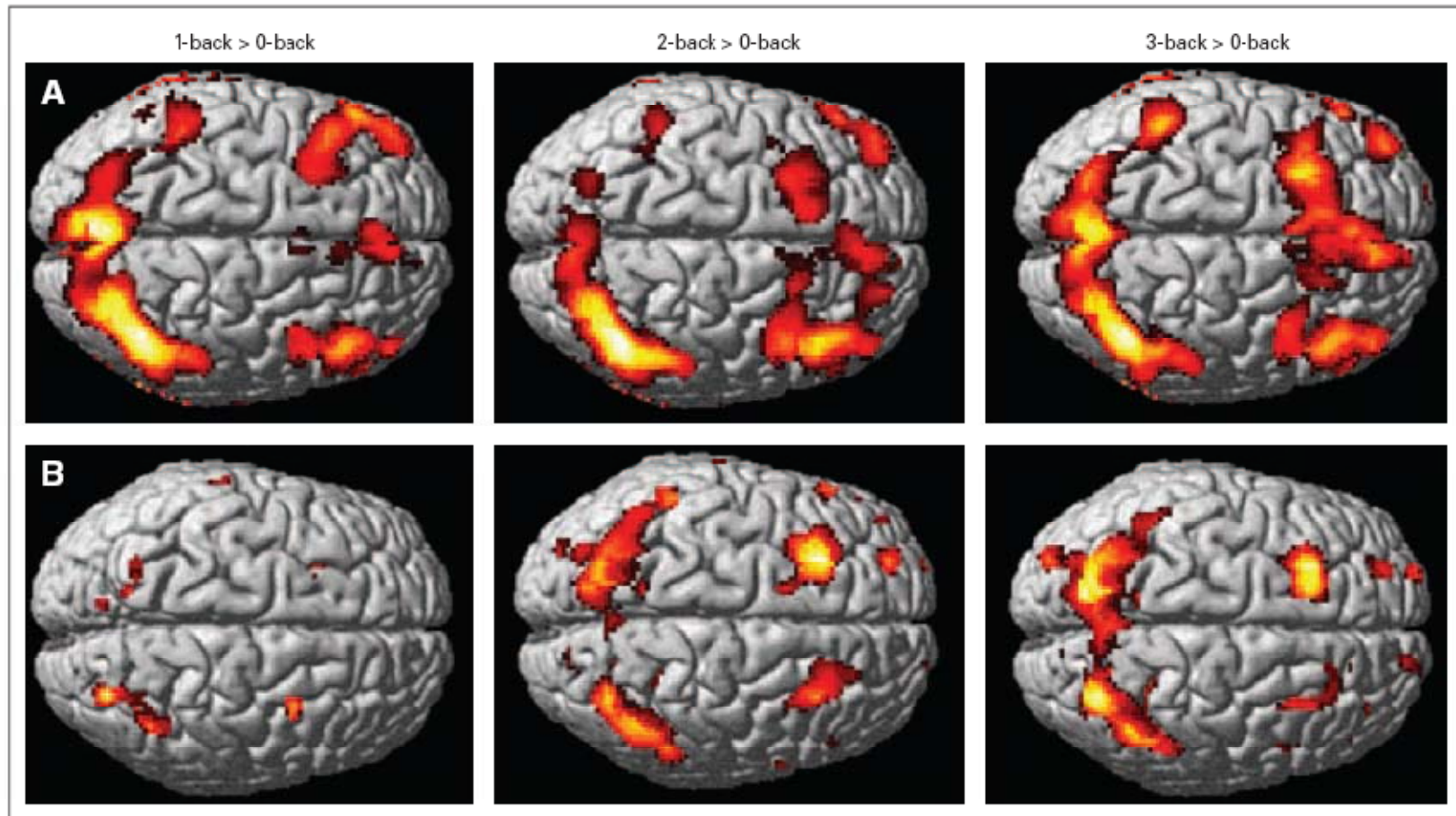


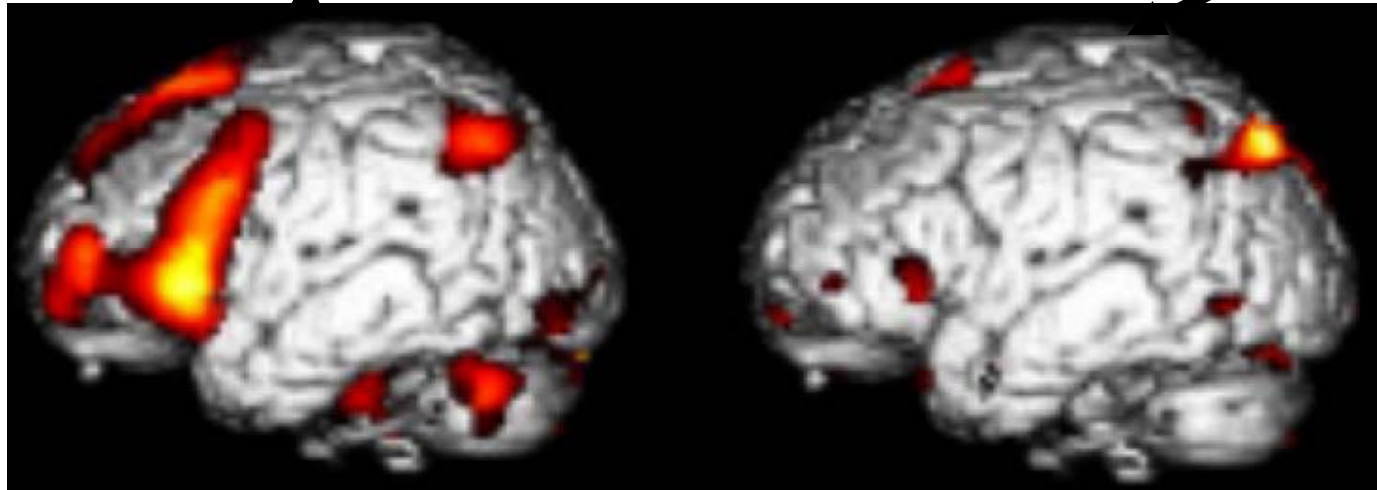
Fig 2. Functional magnetic resonance images of 60-year-old identical twins during a working memory task with incrementally increasing levels of difficulty (left to right). Colored regions denote increased brain activation during working memory relative to a simple vigilance task. (A) Twin treated with 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.

Ferguson et al. JCO 2007

Chemotherapy

No chemotherapy



- Activation associated with short-term recall in chemotherapy-treated (left) and untreated (right) subjects
- Color scale corresponds to voxels with significant activation ($p < 0.01$).
- Peak activation occurring in the inferior frontal gyrus (bright yellow area in left image), was highly significant ($p < 0.0005$) in treated patients
- Untreated patients showed more significant activation in the parietal cortex (bright yellow area in right image).

What should we do in the clinic?

- For patients who are worried that chemotherapy can cause cognitive problems...
 - Re-assure that cognitive problems are infrequent and not necessarily caused by chemotherapy
 - Use chemotherapy judiciously & only when benefits outweigh potential risks, especially in early stage favorable tumors



What should we do in the clinic?

- When patients complain that they are having trouble concentrating and remembering things...
 - Treat anxiety, depression, menopausal symptoms and insomnia
 - Acknowledge concerns, and if no improvement obtain NP consultation
 - Counsel on managing daily activities, limit distractions, organize schedule

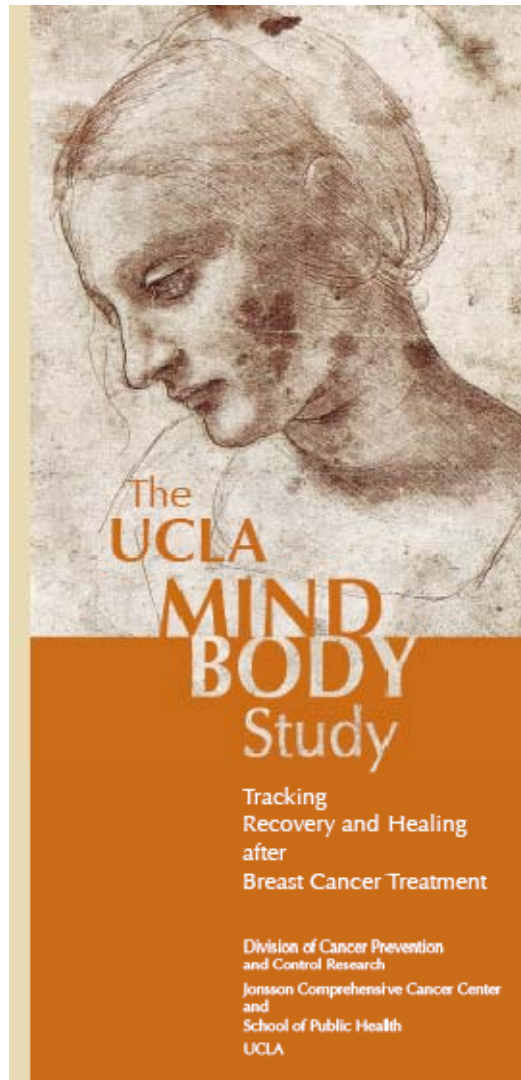


What do we have available at UCLA?

- New cognitive rehabilitation study for breast cancer survivors—contact my research coordinator—Barbara Kahn at 310-825-2520 or bkahnmills@mednet.ucla.edu
 - For post-treatment patients, within 5 years of diagnosis
 - 21-75 years of age
 - willing and able to attend 6 weekly group sessions and participate in pre and post-evaluation



What do we have available at UCLA?



- Comprehensive study of physical, emotional and cognitive outcomes in the year after breast cancer dx
- Newly diagnosed patients only, age 21-65 years
- Must enter prior to starting endocrine therapy
- Contact Amy Oppenheim at 310-267-0959

What do we have available at UCLA?

- Comprehensive survivorship consultations, to evaluate potential causes of cognitive complaints and make recommendations for further assessments
- *Survivors of all types of cancer*



www.vita.mednet.ucla.edu

Or call

Erin Hahn at 310-825-9781



Conclusions

- Cognitive complaints are common in healthy people as they age
- Cancer and its treatments may exacerbate these complaints, especially in high functioning individuals



Conclusions

- Causes of cognitive complaints are multifactorial, with pre-existing changes in some individuals
- Ongoing research will help to refine knowledge about who is at risk, what treatments are problematic, and how to help those who develop cognitive complaints

