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”

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Cancer and cancer-therapy related cognitive dysfunction: an international perspective from the Venice cognitive workshop

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Recent Commentaries

UCLA Jonsson Cancer Center
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

Castellon et al. 2004
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

Castellon et al. 2004
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—e.g., 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
• 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).

Silverman et al., 2007
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](http://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