Chemobrain

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Terminology

- Chemotherapy-associated cognitive dysfunction
- Post-chemotherapy cognitive impairment
- Cancer treatment-associated cognitive changes

What is chemobrain?

- Subjectively reported problems with concentration and thinking following chemotherapy treatment
- Objectively measured changes in cognition following chemotherapy
- May consist of concentration or memory difficulties during or after chemotherapy

Common Issues

- Difficulty with attention and multitasking
- Leaving tasks incomplete
- Difficulty finding words
- Difficulty remembering things
- Greater need for reminders
- Slower thinking
- Concerns with effect on job performance

Chemotherapy for Cancer

- Improves prospects for long-term survival
- May have long-term side effects
- Approximately 14% of cancer survivors report memory problems compared with 8% in those without a cancer history*
- Cancer survivors who received chemotherapy are more likely to have changes on objective cognitive tests

*Jean-Pierre et al. J Oncol Pract. 2011

Is it the chemotherapy or is it other factors related to cancer treatment?

- Some studies show cognitive dysfunction in people newly diagnosed with cancer even prior to receiving chemotherapy
- Surgery and anesthesia may contribute to cognitive changes
  - Particularly in older patients, those with cardiovascular disease, those with extensive surgical procedures and/or complications
  - Should resolve in days to months

Other Contributing Factors

- Other medications
- Menopause, hormonal changes
- Depression/anxiety
- Pain
- Fatigue
- Sleep problems
- Other medical problems
- Alcohol, sedatives
- Normal aging

Anxiety and Depression

- Common with a new diagnosis of cancer
- Mood changes may affect sleep and other physiologic functions
- In a study of breast cancer patients "worry" prior to treatment was associated with alterations in brain function by functional MRI studies*
- Other studies have shown anxiety/distress correlated with self-perceived but not objective cognitive changes

*Berman et al. Health Psychology 2014

Hormonal Factors

- Going through menopause as a result of chemotherapy and/or receiving anti-estrogen treatments (part of breast cancer treatment) associated with fatigue and sleep difficulty as well as some changes in cognitive function

Study in NHL patients

- Lymphoma survivors (> 5 years out from treatment) who had prior chemotherapy scored somewhat worse on cognitive testing than those who had local therapy only (radiation).
  - Deficits were subtle
  - Those receiving chemotherapy generally had higher stage lymphoma
  - Most survivors scored within the normal range

Ahles TA, et al. J Clin Oncol 20:485-493

Effects differ by chemotherapy regimen

- R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone) compared to BR (bendamustine and rituximab)
- Within 3 months of completing chemotherapy, participants receiving BR experienced more changes in cognitive testing performance than the R-CHOP group and a control group
- R-CHOP patients reported more subjective changes in cognitive function

Zimmer et al. Leukemia & Lymphoma Feb 2015; 56(2):347-352

What about high-dose chemotherapy and stem cell transplant?

- Patients with CML or MDS were evaluated at 3 time points: baseline (prior to transplant or soon after diagnosis), approximately 1 year and approximately 18 months later
  - Overall, cognitive performance improved over the three time periods
  - Transplant patients performed worse on motor function testing but similarly to non-transplant patients on other neuropsychological tests
  - Transplant patients were younger on average

Chang G et al. Cancer 2009 October 1;115(19):4625-4635

How is cognitive function assessed?

- For research purposes, assessments usually include a battery of standardized neuropsychologic tests
- Patient reports of cognitive concerns do not necessarily correlate with a decline in performance on the neuropsychologic testing
  - Testing of memory impairment tends to correlate better than other cognitive domains (such as learning, processing, and executive function)

MRI and other radiology tests

- No routine role for neuroimaging in evaluating "chemobrain" in the absence of specific neurologic symptoms
- May have a role in evaluating for vascular problems or other causes of cognitive changes
- Functional MRI has been used in the research setting

Patient-reported measures

- By definition subjective and, therefore, difficult to use for research purposes
- Probably the most important measure in clinical practice
- Subjective concerns are more likely to impact quality of life than objectively measured changes
- No standard diagnostic criteria for chemotherapy associated cognitive dsfucntion

Factors influencing cognitive function prior to cancer diagnosis

- Age
- Education
- Intelligence
- Medical conditions
  - Diabetes
  - Cardiovascular disease

Non-chemotherapy factors related to the cancer diagnosis

- Cancer type and stage
- Pain
- Surgery/anesthesia
- Anxiety/psychosocial stress
- Sleep difficulties
- All of the baseline factors

Influences on cognitive function during chemotherapy

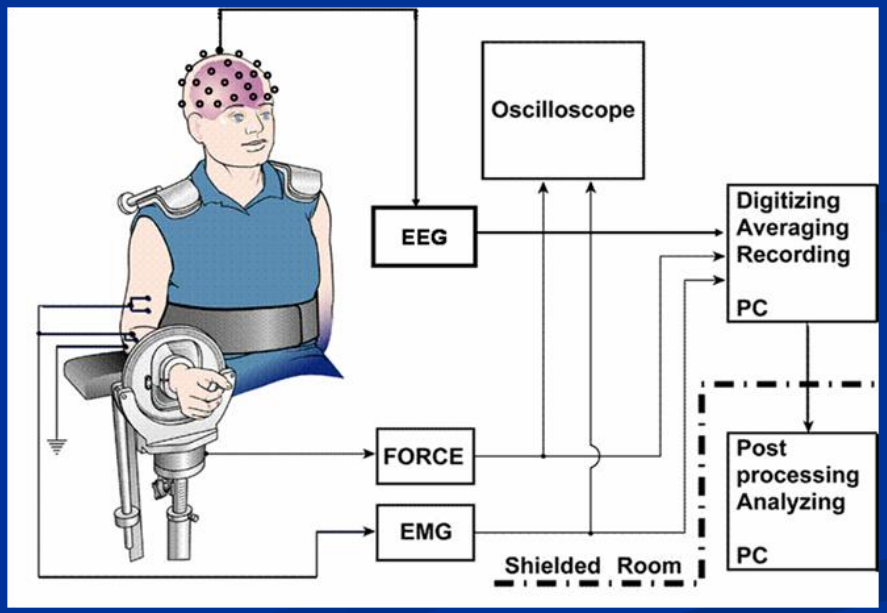
- Central nervous system effects of chemotherapy
  - Possibly mediated through proinflammatory cytokines
- Peripheral neuropathy
- Fatigue
- Anemia
- Supportive medication
- Plus baseline and other post-diagnosis factors

Long-term influences on cognitive function

- Normal aging
- Hormonal changes or hormonal treatments
- Other medical issues
- Psychosocial factors
- Baseline factors
- Degree of resolution of diagnosis and treatment related factors

Cleveland Clinic Study: Physiology of Chemotherapy Related Fatigue and Cognitive Function

- Women undergoing chemotherapy for breast cancer and a control group assessed at time points prior to, during and after chemotherapy
- Physical and cognitive tasks, fatigue inventory, depression screen and neurophysiologic measurements



Moore et al. Support Care Cancer (2014) 22:2127–2131

Chemobrain study findings

- Physical fatigue was subjectively greater in cancer patients than controls prior to chemotherapy, worsened with chemotherapy and persisted at 1 year
  - Objective physical endurance testing did not differ in patients or controls at the different time points
- Perceived cognitive function was adversely affected during treatment only for patients (improving by 1 year)
  - Cognitive function testing did not identify change in processing speed index associated with chemotherapy.
- EEG activity was increased in patients relative to controls during chemotherapy treatment and demonstrated a greater increase in response to the mental and physical tasks. These changes did not persist at one year.

Moore et al. Support Care Cancer (2014) 22:2127–2131

Cognitive Compensation

- May help explain discrepancies between correlative tests, subjective concerns, and formal objective testing results
- Individuals with sufficient "cognitive reserve" may be able to increase activity in some parts of the brain to maintain testing performance, although these individuals may perceive the tasks as more difficult
- Supported by a finding that patients with lower baseline "cognitive reserve" and those who were older were more likely to experience objective cognitive changes prior to chemotherapy.

Moore et al. Support Care Cancer (2014) 22:2127–2131

Management

- Improve cognitive reserve by addressing outside factors that may affect cognitive function
  - Address anxiety, sleep, fatigue, depression, contributing medications
- Use notes, calendars, other reminders
- Avoid multitasking when fatigued

Other Interventions

- Exercise has beneficial effects on cognitive function, perhaps through an increase in blood flow to the brain or through reduction in inflammation
- Biofeedback and cognitive behavioral therapy appear to improve both objective and subjective as well as quality of life measures
  - Cleveland Clinic speech therapy department provides cognitive rehabilitation services

Options For Some

- Crossword puzzles, brain teasers
  - Unproven but no harm
- Improve nutrition
  - Not well studied for this purpose but important for overall health
- Stimulant medications
  - Mixed results in clinical trials
  - More likely to improve fatigue than cognitive function

Reassurances

- Cognitive changes are common during and after cancer treatment
- Chemotherapy related cognitive changes usually improve with time

Community Resources

- The Gathering Place
- American Cancer Society
- Education Resource Center at your Cancer Center

Summary

- Chemotherapy may affect both objective and subjective measures of cognition
  - Most chemotherapy effects will subside with time
  - A subset of individuals may experience longer-term concerns
- Objective and subjective measures of cognitive changes do not always correlate, perhaps due in part to cognitive compensation
- Cognitive rehabilitation, exercise and modification of other contributing factors can improve “chemobrain”