The Use of Neurofeedback Training to Reduce Post-Cancer Cognitive Impairment in Women with Breast Cancer

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Goals of the Presentation

Goal 1
Define Post-cancer Cognitive Impairment

Goal 2
Discuss Cognitive Training and Neurofeedback

Goal 3
Describe Research Progress
Introduction

- Many cancer survivors have experienced a “mental cloudiness” that occurs after cancer treatment; a condition called chemo brain.
- A growing body of evidence suggests that “chemo brain” or postcancer cognitive impairment does exist.
- Cognitive issues can be resolved.
- Occupational therapists can address the symptoms and have a direct effect on neuroplasticity through participation in daily occupations.
Demographics

- 206,966 women and 2,039 men in the United States were diagnosed with breast cancer
- Approximately 232,670 new cases of invasive breast cancer diagnosed in women

(Center for Disease Control, 2013; American Cancer Society, 2013)
Research Process

- UCSF Mission Bay
- 2014 OTAC Annual Conference Poster Session
- Women’s Cancer Resource Center
- IRB Approval
- OTAC Spring Symposium Presentation
Types of Breast Cancer

**Noninvasive** (in situ) breast cancer: Cancerous cells remain in a particular location of the breast.

**Invasive** (infiltrating) breast cancer: Cancerous cells break through normal breast tissue barriers and spread to other parts of the body through the bloodstream and lymph nodes.
Wide Range of Chemotherapy
Side Effects of Chemotherapy

- Hair loss
- Mouth ulcers
- Nausea
- Diarrhea
- Lower number of white blood cells
Side Effects Chemotherapy

• One of the most feared side effects of cancer treatment is nausea.
• Neutropenia (Decreased White Blood Cells)
• Peripheral Neuropathy (Nerve Problems)
Problem

Many oncologists were not convinced that it existed because the data was collected from self reports.
Effect of Chemotherapy

Chemotherapy

Intelligence
Education
Genetics
Menopause

Cognitive Impairment
- Attention
- Concentration
- Memory
- Visuospatial
- Processing speed

Diminished Quality of life (Activities of daily living)

Anxiety
Depression
Fatigue

Journal of Oncology, New York, N.Y. 2003
What is Postcancer Cognitive Impairment?

- Forgetting and memory lapses
- Trouble concentrating; can’t focus
- Trouble remembering details, dates, telephone numbers
- Word finding problems
- Difficulty Multitasking
- Difficulty Performing ADL’s
Side Effects of Chemotherapy

- Chemotherapy causes physical and emotional side effects.
- Cognitive impairment can linger for years.
So... What is the Evidence?
What Causes “Chemo Brain?”

Post Cancer Cognitive Impairment is not well understood:
1. Blood Brain-Barrier vascular Injury?
2. Myelination changes?
3. Genetic Link?
4. Cancer Itself?
Breast Cancer survivors can experience significant decrease in cerebral blood flow of the Frontal, Cerebellar and Basal Ganglia regions 5-10 years after receiving chemotherapy. Silverman et.al (2007)
New Evidence

• Computed tomography and advanced imaging studies are finally beginning to reveal the causes of Chemo Brain.
Imaging Studies show that Chemotherapy Altered White Matter in a 60 year Monozygotic Twin Sister
Chemotherapy Affects Glial Cells
Delayed Myelin Destruction

5-Fluorouracil, a widely used chemotherapy agent, is toxic to oligodendrocytes (myelin sheath in CNS).

Meta-Analysis Study

- Analyzed 17 previous studies that included more than 800 breast cancer patients, concluding that verbal and visual-spatial abilities while on chemotherapy.

- Dr. Patricia Ganz- UCLA
Hierarchy of Evidence

Level 1
Level II
Level III
Level IV
Level V
Level VII

Meta Analysis of RCT’s

Systematic Reviews
Critically-Appraised Topics [Evidence Syntheses and Guidelines]
Critically-Appraised Individual Articles [Article Synopses]
Randomized Controlled Trials (RCTs)
Cohort Studies
Case-Controlled Studies
Case Series / Reports
Background Information / Expert Opinion

FILTERED INFORMATION
UNFILTERED INFORMATION
Meta-Analysis Study

- This study found a **statistically significant** association between neuropsychological test performance and **memory** complaints in women with post-treatment breast cancer.

- Dr. Patricia Ganz - UCLA
Combined PET and CT Scan

• Used positron emission to diagnose certain kinds of cancers.
• Better than MRI because PET/CT imaging, allows researchers to see how the brain is using energy.

Dr. Rachel A. Lagos
West Virginia University
This research correlated patient history, neurologic exam, and chemotherapy regimen with imaging for 128 patients diagnosed with breast cancer.

The women showed statistically significant decreases in regional brain metabolism.
New Evidence

- Statistically significant declines in glucose metabolism were observed in the superior medial prefrontal gyrus as a whole (P = .025), from left to right and in the temporal region (P = .036).
Frontal Lobe Changes
The amygdala recalls emotionally charged memories, such as a frightening situation.

The hippocampus located in the temporal lobe and has a central role in processing memory of language, autobiography & episodic memory.
Neuroplasticity

- Neuroplasticity can be facilitated with purposeful cognitive and behavioral activities.
Compensatory Rehabilitation Does Little to Promote Neuroplasticity

- **Compensation** such as for following routines, focusing on one thing at a time, using a daily planner to track appointments.

- **Remediation** such as mental tasks which involve computer assisted cognitive remediation programs are supported by the neuroscience literature.
So...What have we Learned?

1. Post Cancer Cognitive Impairment does exist; it is measurable.

2. Chemotherapy appears to affect oxygen and glucose metabolism in the frontal and temporal regions of the brain.

3. It makes sense that people who have had chemotherapy will need remediation to recover.

- 6 month Prospective study with control
- 23 female breast cancer survivors
- TX 3Xs at week for 10-weeks
- Significant results ($P < .001$) on 4 cognitive measures.
Study Design

Inclusion Criteria
1. Breast cancer survivors
2. Age 40 years or older
3. Post Chemotherapy
4. Self-reported Cognitive Impairment

Pretest and posttests:
• FACT-Cognitive Function – Version 3
• Test for Variables of Attention (TOVA)
• Basic Neuropsychological and Cognitive exam
• NeurOptimal Data
Using Brain HQ and NeurOptimal® training, there will be measurable changes in executive functions in processing speed, attention, and memory, after participating for 33.5 minutes, 2 times a week for 10 weeks.
Recruitment Methods

- Participants
  - Inclusion and exclusion criteria
  - Small sample size of 6 participants
  - Single Subject multiple baseline design
  - Convenience sample from the Women’s Cancer Resource Center and various other agencies
Instruments: Functional Assessment of Cancer Therapy (FACT-Cog)

FACT-Cognitive Function (Version 3)

Below is a list of statements that other people with your condition have said are important. Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

<table>
<thead>
<tr>
<th>PERCEIVED COGNITIVE IMPAIRMENTS</th>
<th>Never</th>
<th>About once a week</th>
<th>Two to three times a week</th>
<th>Nearly every day</th>
<th>Several times a day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cap13 I have had trouble forming thoughts</td>
<td>0 1 2 3 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cap14 My thinking has been slow</td>
<td>0 1 2 3 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cap15 I have had trouble concentrating</td>
<td>0 1 2 3 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cap16 I have had trouble finding my way to a familiar place</td>
<td>0 1 2 3 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cap17 I have had trouble remembering where I put things, like my keys or my wallet</td>
<td>0 1 2 3 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cap18 I have had trouble remembering new information, like phone numbers or simple instructions</td>
<td>0 1 2 3 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cap19 I have had trouble recalling the name of an object while talking to someone</td>
<td>0 1 2 3 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cap20 I have had trouble finding the right word(s) to express myself</td>
<td>0 1 2 3 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cap21 I have used the wrong word when I referred to an object</td>
<td>0 1 2 3 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cap22 I have had trouble saying what I mean in conversations with others</td>
<td>0 1 2 3 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cap23 I have walked into a room and forgotten what I meant to get or do there</td>
<td>0 1 2 3 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cap24 I have had to work really hard to pay attention or I would make a mistake</td>
<td>0 1 2 3 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cap25 I have forgotten names of people soon after being introduced</td>
<td>0 1 2 3 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Test for Variables of Attention (TOVA)

- Continuous Performance Test
- Provides objective measures of client’s performance on visual attention tasks over time (21.6 minutes).
- Measures response time on an electron micro switch in milliseconds.
Brief Neuropsychological Cognitive Evaluation (BNCE)

• A short (approximately 30 minute) evaluation
• Has ten subtests assessing:
  – Working memory
  – Language
  – Orientation
  – Attention
  – Executive functions

(Tonkonogy, 1997)
Computer-assisted Cognitive Remediation - Brain HQ

Evidence shows it improves Attention & Visual Processing
Computer-assisted Cognitive Remediation - Brain HQ

https://play.brainhq.com/play/brainhq
Brain HQ and Working Memory
Visual Speed Processing Training Reduces Cognitive Impairment

- Randomized control study used **10 hours** of visual speed processing on N=620 adults.
- Improved on standard cognitive function tests.
- Improved health related quality of life measures.

Neurofeedback Training

- Neurofeedback is concerned with assessment and training of brain wave frequencies using electrodes (sensors) applied to the scalp.
Neurofeedback Training

1. Sensors are placed on the scalp & ears to read the brain's electrical activity

2. Brainwaves are displayed on the therapist's computer and goals are set

3. When the brainwave activity meets the set goals, the client gets positive feedback (visual & auditory) to guide their success with the game

http://www.neurofeedbackholiday.com/neurofb.shtml
EEG Neurofeedback

• How does the brain generate measurable electrical signals?
The Neurofeedback Signal is derived from Assemblies of Pyramidal Cells Located on the Outer Surface of the Cortex (Electrical Potentials)

Figure 19.3
The generation of very small electrical fields by synaptic currents in pyramidal cells. In this case, the synapse is on the upper part of the dendrite. When the afferent axon fires, the presynaptic terminal releases glutamate, which opens numerous cation channels. Positive current flows into the dendrite, leaving a slight negativity in the extracellular fluid. Current spreads down the dendrite and escapes out of its deeper parts, leaving the extracellular fluid slightly positive at those sites. The EEG electrode, which is referred to a second electrode some distance away, measures this scene through thick layers of tissue. Only if thousands of cells contribute their small voltage does the signal become strong enough to see at the surface of the scalp. (The convention in EEG work is to plot the signals with negativity upward.)

Amplifier EEG

EEG electrode

Scalp
Skull

Dura mater
Arachnoid
Subarachnoid space
Pia mater

Active synapses
Afferent axon
Effereent axon

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Hypoperfusion of the Frontal Lobe
Neurofeedback Training

Vascular Coupling
Beta Waves are Associated with States of Arousal

Research has found that boosting beta brain waves, raises arousal levels.
Neurofeedback Promotes Self-Regulation & Relaxation
NeurOptimal® Personal Trainer

Price: $5,500.00 (USD)
Zengar Company, Canada
NeurOptimal®
International Electrode Placement
Hook up Methods

- Procedure
  - 2 times a week for ten weeks
    - NeurOptimal 33.5 min
    - Brain HQ ~33.5 min
  - 3 participants will use Brain HQ
  - 3 participants will use NeurOptimal
C3 & C4 are Associated with Sensorimotor Rhythm (Mu)

Mu wave – (7.5 – 12.5 Hz);
SMR wave – (12.5 – 15.5 Hz)
NeurOptimal®

• NeurOptimal® monitors brainwaves and alerts the central nervous system when it is not functioning coherently.
NeurOptimal®

- NeurOptimal® automatically adjusts with each person and lends itself well to single subject design.
- Simultaneously targets sixteen sets of frequencies in the same manner for all users.
NeurOptimal®

• NeurOptimal® provides moment to moment feedback on the brain’s activity. The brain makes adjustments using real time feedback across a wide spectrum of frequencies meant to increase overall mental fitness.

• NeurOptimal® does not push the brain- it simply offers information and the brain adjusts itself naturally.
Visual and Sound discrimination are critical for modulating brain circuits.
Visual Images
Visual Images on the Screen Sends Signals to the Visual Cortex.
Visual Streams

- The ventral stream (or "vision-for-perception" pathway) is mainly involved in recognition and discrimination of visual shapes and objects,
- The dorsal stream (or "vision-for-action" pathway) has been primarily associated with visually guided reaching and grasping based on the spatial location, shape, and orientation of objects.
Causes of Cognitive Impairment

- Reduction in grey matter
  (Lepage, Smith, Moreau, barlow-Krelina, Wallis, Collins, MacKenzie, & Scherling, 2014)

- Reduction in white matter
  (Han, Yang, Dietrich, Luebke, Mayer-Pröschel, & Noble, 2008)

Corpus Callosum; Superior Longitudinal Fasciculus- connecting the frontal and parietal cortices.
Pathway for Reception and Expression of Language
Effects of Music

Neuroimaging studies have demonstrated that musical experience leads to functional alterations in language processing.
Music Scored by Jeff Bova

- Music is processed Globally
- Affects brain regions that are related to emotion.
- Reduces Stress
- Improves Physical Rehabilitation
- Stimulates Theta and Alpha Brain waves
Nucleus Basalis of Meynert

- Major **cholinergic** neurons in the brain.
- Major source of **acetylcholine** to support memory, attention and learning.
- Stimulated by tones and music.
How NeurOptimal® Works

• When brain activity shows signs of dysregulation, the music within the NeurOptimal® neurofeedback software is **momentarily interrupted**.

• The music stops momentarily and this subtle cue alerts the brain that it is operating inefficiently.

• This repeated stimulus allows the brain to “reset” itself and self-regulate more smoothly.

• The tones of the music, the subtle cues and the visual stimuli occur in regions of the cortex and subcortical structures outside of conscious awareness.
One aim of occupational therapy in oncology is to help clients cope with the anxiety, despair and fatigue as they are undergoing cognitive changes in their Daily Living Skills.
NeurOptimal may also help build brain resilience, or an increase in the central nervous system’s ability to “recover” from a negative event.

Individuals with a more regulated brain report feeling happier and exhibit a more profound sense of relaxation.
Eight Occupations to Improve Executive (Cognitive) Functioning

1. Computer Assisted Cognitive Remediation & Neurofeedback training (Dopamine)
2. Prescriptive exercise program (Endorphin)
3. Sleep Hygiene (Melatonin)
4. Light and Diet (Serotonin)
5. Stress Management (Mindfulness Meditation)
6. Communication (Social Support)
7. Learn New Activities (Hippocampus)
8. Incorporate Music in Daily Life (ACh)
Questions?