Treating Chemobrain: Rehabilitation Therapies Emerge

By Caroline McNeil

Cancer patients had been reporting problems with cognitive function for years. And for years, clinicians had been stumped about how to handle a problem that has come to be known as chemobrain.

But now, more cancer centers have begun testing interventions for chemobrain, including, most notably, cognitive behavioral therapy (CBT). Major cancer centers in the U.S. and Australia, among others, are now recruiting patients for randomized controlled trials of CBT; five of the trials have 2012 launch dates (see sidebar).

The growing number of trials reflects accumulating data and changing attitudes. Patricia Ganz, M.D., at UCLA’s Jonsson Comprehensive Cancer Center, traces several stages in the evolution of thinking about cancer and cognition. At first, everyone believed that the blood–brain barrier protected patients from chemotherapy, so patient reports were not taken seriously.

As chemotherapy became more common and rigorous, complaints multiplied and researchers began paying attention. Now, more sophisticated imaging methods and animal models have begun to show evidence of brain changes associated with cancer and to suggest mechanisms that could make chemotherapy one of the culprits.

“We are chipping away at getting a scientific database to persuade people,” Ganz said.

One addition to that database came in March, with the publication of a small controlled study showing that impaired cognitive function after chemotherapy is associated with longitudinal changes in the brain’s white matter. Sabine Deprez, M.D., of Belgium’s University Hospital Gasthuisberg, and colleagues showed that changes in the white matter associated with neuropsychological test results and with the patients’ own reports of specific problems, such as word retrieval. The study appeared in the Journal of Clinical Oncology.

Subjective Versus Objective Cognition

Many chemobrain studies have found no association between patient reports of cognitive problems—“subjective cognition” in psychologists’ terms—and the findings of test results, or “objective cognition.” But Deprez’s study found that structural changes in the brain associated with both subjective and objective cognition.

This was “one of the first studies to show that what patients are saying is backed up by test abnormalities,” Ganz said. “It shows we have to believe the patient.”

Heather Green, Ph.D., an Australian investigator, agrees: “The so-called objective tests have their limitations,” she wrote in an e-mail from Griffith University in Southeast Queensland. “In a number of circumstances, patients’ self-reports of their everyday experiences may be more accurate and more sensitive than what can be detected by our current objective assessment methods.”

Green and others say that whether cancer-related cognitive dysfunction is based on standardized test performance or patient reports of dysfunction, it needs to be treated.

Interventions

Treatment research has included some pharmacologic studies, but the drugs tried so far (e.g., modafinil, methylphenidate, donepezil) had mixed results, and studies of cognitive rehabilitation have become more prominent. The first single-arm studies at the beginning of the 2000s were followed by larger trials with waitlist controls (subjects randomized to a waitlist to receive the same intervention later). Studies with active controls (subjects who receive an alternative intervention, such as counseling) are now under way in a few places. The five trials opening this year have estimated enrollments of 40–180, and two have active control groups.

“I would say, compared with even 3 years ago, treatment research is expanding,” said Tim Ahles, Ph.D., at Memorial Sloan–Kettering Cancer Center in New York. Ahles is one of the leaders of the International Cancer and Cognition Task Force, which began as “25 of us around a table” 6 or 7 years ago. The task force held its second full-scale conference this year in March, attracting 140–150 investigators. Its agenda included many studies focused on chemobrain mechanisms and risk factors, as well as two treatment studies—both completed CBT trials.

One of those trials, led by Green and Alana Schuurs, Ph.D., tested group sessions focused on thinking and memory skills, including compensatory and enhancement strategies. Compared with waitlist controls, participants had improved overall cognitive function, memory, and visual and spatial skills. A larger randomized trial based on the same intervention opened this year.

Also reported at the task force was a trial at the University of Washington in Seattle, led by Monique Cherrier, Ph.D. Participants learned assistive techniques,
such as using a calendar, as well as memory
and other cognitive skills. Compared with
waitlist controls, subjects had a statistically
significant improvement in working
memory/attention. A larger randomized
trial of the same intervention with ovarian
cancer patients at Fred Hutchinson Cancer
Research Center should open in the fall.

At Eastern Maine Medical Center in
Bangor, a waitlist-controlled trial of an
intervention called MAAT (Memory and
Attention Adaptation Training), published in
February in *Psycho-Oncology*, has been
followed by a larger randomized trial with
an active control group that receives sup-
portive counseling. Both interventions
are through a videoconference network.
Maine’s Robert Ferguson, Ph.D., said that
an additional multisite trial is now being
planned in partnership with Moffitt Cancer
Center in Tampa, Fla.

As the number of cognitive behavioral
interventions expands, researchers hope
to learn more about what models and
components are most effective. “There
are so many questions out there,” said
Cherrier. “There’s the optimal duration
and frequency of the intervention, [and] the
method—should it be individual- or group-
based, computerized or in-person?”

And then there are broader issues, such
as which cancer patients are likely to need
treatment. Seventeen to 75% of adult can-
cer patients with solid tumors, not including
brain tumors, may be affected, according to
one often-quoted estimate. But little is
known about how many are substantially
affected or for how long or, most impor-
tant, who is at greatest risk.

“This is a wide-open question,” Ferguson
said.

**SIDEBAR:**
**Chemobrain Intervention Trials Now
Recruiting**

Following pilot studies, research centers
have begun to launch larger randomized
trials of therapies for cancer-related cogni-
tive dysfunction.

**Fred Hutchinson Cancer Research
Center/University of Washington Cancer
Consortium,** Seattle: Memory and
Thinking Skills Workshop in Improving
Cognitive Rehabilitation in Ovarian
Cancer Survivors; participants randomized
to group therapy or no therapy (waitlist);
launched 2012; estimated enrollment 80,
completion March 2013.

**Griffith University,** Southeast Queensland,
Australia: Group Cognitive Rehabilitation
for Cancer Survivors; participants rand-
omized to group therapy of no therapy (wait-
list); launched 2012; estimated enrollment
40, completion 2013.

**Eastern Maine Medical Center,** Bangor:
Videoconference CBT for Rural Breast
Cancer Survivors with Cognitive Complai-
ts; participants randomized to videoconference
group session with either CBT or supportive
counseling; launched 2011; estimated enroll-
ment 48, completion December 2013.

**Memorial Sloan–Kettering Cancer Center,**
New York: Rehabilitation of Cognitive
Changes in Breast Cancer Survivors; par-
ticipants randomized to one of two versions
of CogMed, a software training program;
launched 2010; estimated enrollment 52,
completion August 2013.

**Stanford University,** Palo Alto: Intel-
lectual Impairment in Women With Breast
Cancer; participants randomized to neuro-
feedback training or cognitive rehabili-
tation; launched 2012; estimated enrollment
180, estimated completion August 2014

**UCLA Jonsson Cancer Center,** Los
Angeles: Breast Cancer Cognitive Rehabi-
litation Study; participants randomized
to group therapy or no therapy (waitlist);
launched 2012; estimated enrollment 60,
completion June 2014

**University of Sydney,** Australia:
1. Cognitive Rehabilitation for Breast
Cancer Survivors with Perceived
Cognitive Impairment; participants
randomized to one of two rehabili-
tation groups or observation; to be
activated October 2012; estimated
enrollment 160, completion 2015.
2. Evaluation of Insight, a Web-based
Cognitive Rehabilitation Program, in
Cancer Survivors with Self-Reported
Cognitive Impairment; participants
randomized to the Web-based Insight
or observation; launched 2009; esti-
mated enrollment 264, completion
December 2014.