

## A TAILORED OCCUPATIONAL THERAPY APPROACH TO COGNITIVE REHABILITATION OF CHEMOTHERAPY-RELATED COGNITIVE SIDE EFFECTS IN BREAST CANCER SURVIVORS: TWO CASE STUDIES OF PREMENOPAUSALLY AFFECTED WOMEN

UN ENFOQUE DE TERAPIA OCUPACIONAL ADAPTADA A LA REHABILITACIÓN COGNITIVA DE LOS EFECTOS COGNITIVOS COLATERALES ASOCIADOS A LA QUIMIOTERAPIA EN PACIENTES SUPERVIVIENTES DE CÁNCER DE MAMA: DOS ESTUDIOS DE MUJERES POSTMENOPÁUSICAS AFECTADAS

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### Abstract

This article describes a tailored occupational therapy program to rehabilitate chemotherapy-related cognitive side effects. A literature review of cognitive rehabilitation as well as pharmacological trials used to improve cognition in breast cancer patients is included. Two outpatient case studies of young women premenopausally affected with breast cancer (both BRCA-1 gene mutation carriers) are used to discuss the role of tailored occupational therapy techniques for developing compensatory strategies and for delivering cognitive remediation. Neuropsychological evaluation pre and post occupational therapy is used to document the result of tailored occupational therapy on cognitive performance. The case studies illustrate the neuropsychological profile of chemotherapy-related cognitive changes and the course of deficits over 7-9 months. For younger, educated patients who must return to competitive, fast-paced jobs, cognitive side-effects post-treatment are especially noxious as young adult patients are building their professional lives and are not necessarily provided time to wait for the usual trajectory of recovery to take its course.

**Keywords:** Breast cancer; adjuvant chemotherapy; cognitive dysfunction; rehabilitation; occupational therapy; survivorship.

### Resumen

En este artículo se describe un programa de terapia ocupacional adaptado para rehabilitar los efectos cognitivos secundarios asociados a la quimioterapia. Se incluye una revisión de la literatura de la rehabilitación cognitiva, así como de los ensayos farmacológicos utilizados para mejorar la cognición en pacientes de cáncer de mama. Se exponen dos estudios de caso ambulatorios de mujeres jóvenes premenopáusicas afectadas de cáncer de mama (ambas portadoras de mutaciones del gen BRCA-1) para examinar la función de técnicas de terapia ocupacional adaptadas para el desarrollo de estrategias compensatorias y para administrar rehabilitación cognitiva. La evaluación neuropsicológica antes y después de la terapia ocupacional se utiliza para documentar el resultado de la terapia ocupacional adaptada para el rendimiento cognitivo. Los estudios de casos ilustran el perfil neuropsicológico de los cambios asociados a la quimioterapia y el curso de los déficits durante 7-9 meses. En los pacientes jóvenes, con estudios que deben retornar a puestos de trabajo de ritmo rápido y competitivos, los efectos cognitivos secundarios postratamiento son especialmente nocivos, ya que los pacientes jóvenes adultos están construyendo sus vidas profesionales y no disponen del tiempo necesario de espera

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para que la trayectoria habitual de recuperación siga su curso.

**Palabras clave:** Cáncer de mama, quimioterapia adyuvante, disfunción cognitiva, rehabilitación, terapia ocupacional, supervivientes de cáncer.

## INTRODUCTION

The field of cognitive rehabilitation for non-CNS cancers is in its nascent stage. Both cognitive remediation, a structured set of therapeutic activities designed to restore an individual's ability to think, use judgment, and make decisions as well as compensatory strategies, tasks to augment an individual's abilities, are used jointly in cognitive rehabilitation to improve quality of life and ameliorate the ability to function in work, at home, and in the community.

Over the past decade, it has become evident that breast cancer and cancer treatment with adjuvant chemotherapy can result in cognitive dysfunction<sup>(1-7)</sup> and deficits can continue up to ten years post-chemotherapy<sup>(8)</sup>. Deficits associated with chemotherapy are typically subtle and involve the domains of working memory, executive function, memory, and processing speed<sup>(1,3,4,9-13)</sup>. A meta-analysis of mostly cross-sectional studies<sup>(14)</sup> found small to moderate effect sizes for difficulties in motor functions, executive functioning, learning and memory, spatial reasoning, and language functions.

For the majority of breast cancer survivors, cognitive side-effects ameliorate in 12-18 months<sup>(5)</sup>. While the potential for recovery is ultimately good news, how does this recovery trajectory impact the increasing population of young adult breast cancer survivors? This subset of the population usually cannot wait 12-18 months to recover their cognitive function in order to resume their occupational and domestic duties. In this article, we describe

the research to date on rehabilitation using cognitive, behavioral, and pharmacological interventions. We then provide clinical cases of young women impacted by cognitive side-effects and describe their course of tailored occupational therapy.

## REHABILITATION STUDIES

While research has primarily been focused on elucidating the profile of cognitive dysfunction post-chemotherapy, few studies have focused on treatment for these cognitive deficits. Behavioral interventions have included cognitive behavioral treatment<sup>(15,16)</sup>, an environmental intervention involving nature<sup>(17,18)</sup>, cognitive rehabilitation training and computerized training<sup>(19,20)</sup>, as well as cognitive remediation and compensatory strategies<sup>(21,22)</sup>.

Breast cancer survivors receiving cognitive behavioral treatment with Memory and Attention Adaptation Training (MAAT)<sup>(16)</sup> had significant improvement in verbal memory and spiritual well-being compared to controls. Improvements in other cognitive domains (i.e., executive functioning) or improvement in self-reported cognitive functioning or quality of life were not found. An environmental intervention designed to minimize attentional fatigue and restore attentional capacity in newly diagnosed stage I or II, breast-cancer patients status-post surgery patients included outdoor or leisurely activities that involved experiencing nature in some way (i.e., walking in a park, gardening, sitting by a pond, caring for pets) for three times a week for 20-30 minutes. Results

indicated that individuals who engaged in the restorative intervention had improved attentional capacity over time<sup>(17)</sup>. Patients who received high-dose chemotherapy and hematopoietic stem cell transplantation for systemic cancer were randomized to use either compensational strategies or an individualized, computer-based training software intervention to improve attention and memory or they were assigned to a control group. Training was implemented four times per week for one hour a day over the course of an inpatient stay. Significant improvements across all cognitive domains were found among the three study groups<sup>(19)</sup>. Poppelreuter and colleagues (2009)<sup>(20)</sup> replicated this study with stage I and II breast cancer patients. They found similar results as with the hematopoietic stem cell transplantation study in that there were no specific intervention effects and concluded that cognitive remediation is unnecessary for breast cancer patients after adjuvant chemotherapy as cognitive deficits were only a transient problem. Cognitive remedial and compensatory training using the Cognitive-Behavioral Model of Everyday Memory (CBMEM) which targeted health promotion instruction, memory strategies, and skill building in eight, 75-minute sessions conducted over four weeks was studied in a retirement community of individuals with chronic illness, eleven of which were identified as cancer survivors<sup>(21)</sup>. Cancer survivors showed significant improvements in short-term memory as well as subjective aspects of memory self-efficacy and meta-memory from pre-test to post-test. In a follow-up study, McDougall (2011)<sup>(22)</sup> found that cancer survivors (including breast, prostate, uterine, lymphoma and leukemia, throat, facial and/or basal cells on the nose) randomized to either CBMEM or a health training group that emphasized successful aging had improved memory after either intervention and improvement

maintained at 3 follow-up periods (6 months, 14 months, and 26 months). In this small group of cancer survivors, length of time from active cancer treatment was unknown. In addition to memory improvement, the CBMEM group also had moderate effects for group-by-time interactions for decreases in depression and trait anxiety. Additionally, the CBMEM group had a small increase in performance-based instrumental activities. They also had a significant increase in confidence about their everyday memory abilities, increased use of memory strategies, and less memory complaints. These gains were maintained at the fifteen month follow-up period.

Rehabilitative studies have typically had small samples<sup>(15-17,19-22)</sup> and not always required a cognitive complaint or a cognitive deficit<sup>(17,18,21,22)</sup>.

## **PHARMACOLOGICAL STUDIES**

There have been several clinical trials of stimulant medication as well as erythropoietin to improve cognitive side-effects as well as fatigue in cancer patients. To date, the studies of pharmacological agents have yielded inconclusive results.

### **Modafinil**

Modafinil has been studied to determine if it enhances cognitive functioning in patients with breast cancer<sup>(22)</sup>. Sixty-eight participants with breast cancer who completed treatment with chemotherapy and/or radiation >1 month prior to commencement of the study completed both the open-label phase of the study (Phase 1) as well as the randomization phase to continued treatment with modafinil or placebo (Phase 2). Neither cognitive complaints nor measured cognitive deficits were among the study's inclusion criteria. During Phase 1, all participants received 100mg/d of modafinil for the first three

days followed by 200mg/d of modafinil for four weeks. After four weeks, Phase 2 was initiated and participants were randomized to an additional four weeks of treatment with modafinil or placebo. Results indicated that 200mg/d of modafinil during Phase 1 significantly increased participants' ability to store, retain, and retrieve verbal and non-verbal information. These results were also found at the end of Phase 2 for individuals receiving continued treatment with modafinil. Further, increased sustained attention was also found at the end of Phase 2 for individuals receiving modafinil. Modafinil had no effect on working memory or brief attention in either phase.

In an advanced cancer patient population, modafinil's effect on cancer-related cognitive dysfunction has also been studied<sup>(24)</sup>. Twenty-eight patients with advanced cancer (breast, genitourinary, gastrointestinal, head/neck, hematologic, lung, other) participated in a double-blind, randomized, cross-over, single-dose trial of modafinil where patients were randomly assigned to receive a single dose of 200mg modafinil or placebo on day one and were crossed over to the alternative treatment on day four. Complaint or demonstration of cognitive dysfunction was not an inclusion criterion. Attention and psychomotor speed were assessed before tablet intake on each day and again four and a half hours after tablet intake on each day. Significant improvements were found in both finger tapping with the dominant hand and on a psychomotor speed, shifting task after treatment with modafinil compared with placebo. Taken together, these studies provide preliminary data regarding the potential efficacy of modafinil in improving cancer-related cognitive dysfunction.

Improved attention, psychomotor speed, and retention of information have been found with modafinil. However nei-

ther study required cognitive complaints nor measured cognitive deficits as inclusion criteria<sup>(23,24)</sup>.

### **Dexmethylphenidate (d-MPH)**

Dexmethylphenidate (d-MPH) was studied to determine whether or it could ameliorate cognitive dysfunction and fatigue in women undergoing adjuvant chemotherapy<sup>(25)</sup>. During chemotherapy for breast cancer women were randomized to d-MPH (N=29) or placebo (N=28) to see if it improved cognitive functioning, QOL, or fatigue. Participants were eligible for the study if they planned to receive at least four cycles of a standard regimen of chemotherapy for fully resected breast cancer. Complaints of fatigue or cognitive problems were not required inclusion criteria. Women were recruited after one cycle of chemotherapy. They started on 5 mg bid of placebo for one cycle of chemotherapy. If they demonstrated compliance with the placebo, they were randomized to d-MPH 5 mg bid or to matched placebo. If this regimen was well tolerated, the dose was increased to 10 mg bid one week later. If 10 mg bid was not well-tolerated, a decrease to 5 mg bid was made. Patients took either 5 mg bid or 10 mg bid (whichever they tolerated) until the end of their final cycle of chemotherapy. There were no significant differences in cognitive functioning, QOL, or fatigue at any of the assessments. In the d-MPH group, patients classified as having moderate to severe cognitive dysfunction decreased from 3.6% at baseline to 0% at the end of chemotherapy. Rate of impairment was stable at 11% in the placebo group. However, a correction factor applied for practice effects at the follow-up assessments led to 11% with moderate to severe impairment in the d-MPH group and 22% in the placebo group. Twelve of the patients had grade

3 toxicity during treatment. Four patients had an adverse event suspected to be related to study medication. Eight patients in each arm required dose adjustment of their study drug due to presumed toxicity. A total of 18 patients discontinued the study medication before the end of the study (12 in the d-MPH group and 6 in the placebo group). Some withdrew study consent, some participants stopped their chemotherapy, some had neurotoxicity presumed secondary to the study drug, two had presumed study drug toxicities, and two withdrew for other reasons. Only 20% of patients in either group were interested in continuing the study drug were they given this option. The major study limitation was that women were reluctant to take medication and thus, the accrual goal was not met and the study was underpowered.

In another study, Lower et al. (2005)<sup>(26)</sup> conducted a randomized placebo control trial of d-MPH as a treatment for cognitive dysfunction and fatigue in non-anemic breast and ovarian cancer patients. Patients were eligible if they were treated with  $\geq$  4 cycles of chemotherapy and had completed chemotherapy at least 2 months prior to study entry. Patients who completed a single-blind placebo period without symptomatic improvement were randomized to an 8 week double blind phase. Placebo or d-MPH was adjusted from 10-50 mg per day and maintained for  $\geq$  2 weeks. One hundred fifty two patients (76% breast cancer and 13.6% ovarian cancer) were randomized to placebo (N=75) or d-MPH (N=77). Significant improvement in memory and fatigue was observed in the d-MPH group. The mean highest dose of d-MPH was 27.5 mg/day. The d-MPH was well tolerated in breast and ovarian cancer patients.

Thus, the results from these two studies reveal that the efficacy of d-MPH in treating cancer-related cognitive side-effects is

inconclusive but better results were found when using d-MPH post-chemotherapy<sup>(26)</sup>.

## Erythropoietin

While studies of epoetin-alpha with breast cancer patients undergoing chemotherapy have been mixed<sup>(27,28)</sup>, since these studies were published Bohlius et al. (2009)<sup>(29)</sup> completed a meta-analysis of nearly 14,000 patients (including breast cancer patients) from 53 trials conducted worldwide and found increased on-study mortality and worsened overall survival in cancer patients receiving erythropoiesis-stimulating agents (including epoetin-alpha).

## CLINICAL CASES

As the review of published treatments shows there is a lack of evidence based treatments for chemotherapy-related cognitive deficits. Thus, we present two cases of premenopausal young women each with a positive BRCA-1 gene mutation who complained of cognitive side-effects following chemotherapy. Their medical course, neuropsychological functioning (pre and post cognitive rehabilitation), and an Occupational Therapy intervention tailored to treat their deficits is reviewed. One patient was also unsuccessfully treated with methylphenidate following her Occupational Therapy treatment.

### Patient 1

Patient 1 was a 24-year-old woman, with no significant medical history when she presented to her gynecologist because of a suspicious mass she discovered on self-examination in her right breast. Breast ultrasound revealed a suspicious mass at the 9 o'clock area measuring 3.0 X 1.7 X 2.9cm. Patient 1 underwent a right breast core biopsy, which revealed a poorly dif-

differentiated invasive ductal carcinoma with focal micropapillary features that was estrogen receptor (ER) and progesterone receptor (PR) positive and negative for the human epidermal growth factor receptor-2. A FDG PET scan was conducted and negative for any distant metastases. A bilateral mammogram revealed a 3cm nodularity in the posterior portion of the right breast and a bilateral breast MRI performed on the same day revealed a 1.8 X 2.2 X 2.7cm enhancing mass in the posterolateral right breast. The left breast was unremarkable. A fine needle aspiration of the right axillary lymph node was negative. Patient 1's stage was T2N0M0 (Stage IIA).

After genetic testing revealed that Patient 1 was positive for the BRCA-1 gene mutation, she decided to undergo bilateral mastectomy with immediate expander reconstruction. Right mastectomy revealed T2N0M0 invasive ductal carcinoma, moderately to poorly differentiated, measuring 2.4cm with lymphovascular invasion present with ER and PR levels of 98 and 95 respectively. Right sentinel lymph node biopsy revealed five negative lymph nodes on H&E and cytokeratin. The left mastectomy specimen was unrevealing.

Patient 1's postoperative clinical course was unremarkable as she continued to undergo expansion. Oncotype DX testing revealed a score of 29, suggesting a 20% chance of distant recurrence. CA125 was 200 and systemic therapy was recommended. Prior to starting chemotherapy she underwent ovarian egg retrieval where 24 oocytes were retrieved after which she was diagnosed with ovarian hyper-stimulation syndrome and put on Oxycodone. Following the resolution of her ovarian hyper-stimulation syndrome she started and completed an adjuvant chemotherapy regimen which consisted of 4 cycles of doxorubicin and cyclophosphamide followed by 4 cycles of paclitaxel. After her ACT chemotherapy

treatment, she complained of cognitive delays and memory problems. Two months after finishing chemotherapy she began Tamoxifen. She declined radiation therapy.

Patient 1 denied ever having a head injury, loss of consciousness, seizure or any neurological disorder. Family neurologic history includes temporal lobe epilepsy, in her mother. She denied any history of toxic chemical exposure. She also denied that her mother experienced any perinatal problems or difficulties with labor and delivery of Patient 1. Patient 1 denied tobacco use and drinks alcohol socially, one drink a week. She denied using illicit drugs.

Her neuropsychological evaluation took place one month from finishing adjuvant chemotherapy as she had returned to work and was having difficulty performing her job.

*Chief Complaint:* "I can't focus. My mind drifts. I can accomplish simple tasks at work. I can't sleep." She also complained of word-finding difficulties and said she uses a lot of "filler" words. Patient 1 reported trying to write a personal statement for graduate school applications but could only write 3-4 sentences and then her mind would drift.

*Psychiatric History:* Patient 1 was seen for psychiatric consultation as requested by her oncologist. The consultation was precipitated by Patient 1's mother calling the oncologist and reporting that Patient 1 cried for hours each day, declined to leave her room, and stayed up all night searching the internet for information on the BRCA mutation. Patient 1 was seen by psychiatry during her adjuvant chemotherapy treatment. Patient 1 had no past psychiatric history, and her family psychiatric history was negative. Her psychiatric diagnosis was Adjustment Disorder with Mixed Anxiety and Depressed Mood, rule out of Mild Major Depressive Episode. The psychiatrist noted that Patient 1 presented as very well defended and appeared to

be making a visible effort to “hold it together.” Patient 1 was offered the option of starting antidepressant therapy, but she declined. She preferred to have psychotherapy with her social worker with whom she was familiar. Patient 1 was prescribed lorazepam prn by her oncologist. Patient 1 met with her social worker a couple of times during her chemotherapy treatment. Patient 1 stated that she was fine 90% of the time and when she was not fine, it was not her scheduled appointment time so, she stopped therapy. At the time of the neuropsychological evaluation, she described her mood as “not bad. I’m a pretty happy person overall. There’s a difficult situation in my life now but what can you do?” Patient 1 stated she was angry that she had agreed to chemotherapy and said she would “rather die in 10 years than be stupider for having had chemotherapy.” Despite this statement, Patient 1 denied suicidal ideation.

Patient 1 complained of insomnia with delayed sleep phase and interrupted sleep. She reported trying diphenhydramine HCl to help her sleep. She stopped taking it three days prior to her initial neuropsychological evaluation. She reported her insomnia has worsened since she finished chemotherapy. She denied feeling anxious and reported

taking lorazepam only three times. Once she took it at her doctor’s urging, and twice to sleep. However, it did not help her sleep.

*Psychosocial/Occupational/Academic Functioning:* Patient 1 was single and lived alone. She worked as a trade analyst for the French government and was primarily responsible for trade promotion. Her job duties required a great deal of translating, writing the monthly newsletter, and maintaining the website. She reported that her employer was very supportive of her and very flexible in letting her take time to go to medical appointments. Prior to her diagnosis, Patient 1 intended to start a graduate school program at a top tier school. Instead she deferred admission and began her cancer treatment.

Patient 1 had always been in excellent student. She received in a full scholarship to a competitive college. She was in the Honors program at college and graduated with an “A” average. In college, she majored in social science and French. She reported that her admission test for business school was in the 99<sup>th</sup> percentile. She is fluent in French and is conversant in Spanish and German. She denied ever being diagnosed with a learning disability or attention deficit disorder. Patient 1 reported having a good support system with her family and

**Table 1. Neuropsychological Assessment Tests Used**

Neuropsychological tests administered: Advanced Practice Solutions subtest: Reliable Digit Span<sup>(38)</sup>; Beck Depression Inventory – Fast Screen (BDI-Fast Screen)<sup>(39)</sup>; Boston Naming Test<sup>(40)</sup>; California Verbal Learning Test-Second Edition (CVLT-II)<sup>(41)</sup>; Continuous Performance Test-II (CPT-II)<sup>(42)</sup>; Controlled Oral Word Association Test<sup>(43,40)</sup>; Delis Kaplan Executive Function System (DKEFS) Selected Subtests: Color Word Interference Test, Category Fluency<sup>(44)</sup>; North American Adult Reading (NAART)<sup>(45)</sup>; Paced Auditory Serial Addition Test (PASAT)<sup>(46)</sup>; Personality Assessment Inventory<sup>(30,34)</sup>; Rey Complex Figure Test<sup>(35)</sup>; Test of Memory Malingering (TOMM)<sup>(47)</sup>; Trail Making Test, Part A and B<sup>(40)</sup>; Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV) Selected Subtests: Arithmetic; Digit Span, Coding, Symbol Search<sup>(48)</sup>; Wechsler Memory Scale-Fourth Edition (WMS-IV) Selected Subtests: Logical Memory I&II, Recognition<sup>(49)</sup>; Wide Range Achievement Test IV - Reading subtest<sup>(50)</sup>; Wisconsin Card Sorting Test<sup>(37)</sup>.

Table 2. **Patient 1: First Neuropsychological Evaluation (1 month post-chemotherapy)**

Test	Score	Percentile	Interpretation	Norms/Reference
<b>Motivation</b>				
CPT-II			Valid	Conners, 2004 <sup>(42)</sup>
Reliable Digit Span	<u>Raw=8</u>	>25	Above cut-off	Pearson, 2009 <sup>(38)</sup>
CVLT-II Forced Choice	Raw=16/16		Valid	Delis et al. 2000 <sup>(41)</sup>
<u>PAI</u>	<u>T-Score</u>			Morey, 2009 <sup>(34)</sup>
Inconsistency	52			
Infrequency	55			
Negative Impression Management	47			
Positive Impression Management	52			
<b>Premorbid IQ Estimate</b>				
North American Adult Reading Test	<u>Standard Score</u>	<u>Percentile</u>		Blair & Spreen, 1989 <sup>(45)</sup>
Estimated FSIQ	118	88	High Average	
<b>Attention</b>				
<u>WAIS-IV</u>	<u>Standard Score</u>	<u>Percentile</u>		Wechsler, 2008 <sup>(48)</sup>
Working Memory Index	108	70	High Average	
<u>Working Memory Subtests</u>	<u>Scaled Score</u>	<u>Percentile</u>		
Arithmetic	9	63	Average	
Digit Span	14	91	Superior	
Digit Span Forward	10	50	Average	
Digit Span Backward	16	98	Very Superior	
Digit Span Sequencing	14	91	Superior	
Reliable Digit Span		>25	Above cut-off	
<u>Continuous Performance Test-II</u>	<u>T-Score*</u>	<u>Percentile</u>		Conners, 2004 <sup>(42)</sup>
Omissions	57	76	Within Normal	
Commissions	71	98	Markedly Atypical	
Hit RT	40	18	A little fast	
Hit RT SE	68	97	Markedly Atypical	
Variability	76	99	Markedly Atypical	
Detectability	62	89	Mildly Atypical	
Response Style	46	35	Within Normal	
Perseverations	47	41	Within Normal	
Hit RT Block Change	49	49	Within Normal	
Hit SE Block Change	69	97	Markedly Atypical	
Hit RT ISI Change	60	85	Mildly Atypical	
Hit SE ISI Change	84	99	Markedly Atypical	
*Scores are reversed scored				



Test	Score	Percentile	Interpretation	Norms/Reference
<u>Paced Auditory Serial Addition Test (PASAT)</u>	<u>z-score</u>	<u>Percentile</u>		Rao et al. 1991 <sup>(46)</sup>
3 seconds	0.06	52	Average	
2 seconds	0.94	83	High Average	
<b>Information Processing Speed</b>				
<u>WAIS-IV</u>	<u>Standard Score</u>	<u>Percentile</u>		Wechsler, 2008 <sup>(48)</sup>
Processing Speed Index	114	82	High Average	
<u>Processing Speed Subtests</u>	<u>Scaled Score</u>	<u>Percentile</u>		
Coding	13	84	High Average	
Symbol Search	12	75	High Average	
<u>Trail Making</u>	<u>T-Score</u>	<u>Percentile</u>		Heaton et al. 2004 <sup>(40)</sup>
Trails A	71	98	Very Superior	
<b>Language Functioning</b>				
<u>Verbal Fluency</u>	<u>Scaled Score</u>	<u>Percentile</u>		
Letter Fluency	T=52	58	Average	Heaton et al. 2004 <sup>(40)</sup>
Category Fluency	13	84	High Average	Delis et al. 2001 <sup>(44)</sup>
	T score			
Boston Naming Test	56	73	Average	Heaton et al. 2004 <sup>(40)</sup>
<b>Visual Spatial</b>				
<u>Rey Complex Figure Test</u>	<u>Raw Score</u>	<u>Percentile</u>		Meyers & Meyers, 1995 <sup>(35)</sup>
Copy	35	>16	Average	
<b>Executive Functioning</b>				
<u>Trail Making</u>	<u>T-Score</u>	<u>Percentile</u>		Heaton et al. 2004 <sup>(40)</sup>
Trails B	51	54	Average	
<u>Color Word Interference</u>	<u>Scaled Score</u>	<u>Percentile</u>		Delis et al. 2001 <sup>(44)</sup>
Color Naming	9	37	Average	
Word Reading	11	63	Average	
Inhibition	9	37	Average	
Inhibition/Switching	1	<1	Impaired	
<b>Memory</b>				
<u>WMS-IV</u>	<u>Scaled Score</u>	<u>Percentile</u>		Wechsler, 2009 <sup>(49)</sup>
Logical Memory I	11	63	Average	
Logical Memory II	11	63	Average	

Test	Score	Percentile	Interpretation	Norms/Reference
Recognition	Raw=25	26-50%	Average	
<u>Rey Complex Figure Test</u>	<u>T-Score</u>	<u>Percentile</u>		Meyers & Meyers, 1995 <sup>(35)</sup>
Immediate Recall	16.5	2	Impaired	
Delayed Recall	15.5	1	Impaired	
Recognition	23	82	High Average	
<u>CVLT-II</u>	<u>z-Score</u>	<u>Percentile</u>		Delis et al. 2000 <sup>(41)</sup>
Learning Slope	1	84	High Average	
Trials 1-5 Total	T=49	46	Average	
SDFR	0	50	Average	
SDCR	0.5	69	Average	
LDFR	0	50	Average	
LDCR	0.5	69	Average	
Recognition	-0.5	31	Average	
False Positives	-0.5	31	Average	
<b>Behavioral and Emotional Functioning</b>				
<u>PAI</u>	<u>Score</u>			Morey, 2009 <sup>(34)</sup>
Inconsistency	52			
Infrequency	55			
Negative Impression Management	47			
Positive Impression Management	52			
Somatic Complaints	58			
Anxiety	48			
Anxiety-Related Disorders	51			
Depression	60			
Mania	56			
Paranoia	45			
Schizophrenia	53			
Borderline Features	51			
Antisocial Features	53			
Alcohol Problems	49			
Drug Problems	54			
Aggression	40			
Suicidal Ideation	49			
Stress	50			
Nonsupport	39			
Treatment Rejection	53			
Dominance	54			
Warmth	54			

friends from college that she sees every 4-5 days. She texts and speaks often with her boyfriend.

*Behavioral Observations:* Patient 1 was unaccompanied to the appointment. She was oriented in all spheres. Patient 1's gait appeared normal. No extraneous movements were observed. Her speech was fluent and of normal rate and volume. Patient 1 was personable, friendly, and made good eye-contact. Her attitude toward testing was positive, and she exerted good effort. Mood was euthymic. Patient 1 was slightly tangential in her thought process. There was no evidence of hallucinations, delusions, or compulsions. Patient 1 was anxious about her cognitive difficulties and angry that she had agreed to chemotherapy as she said she "knew it would make her stupid." Following the assessment, Patient 1 became tearful when discussing her current cognitive difficulties.

*Neuropsychological Assessment:* (see Table 1 for the various neuropsychological tests used in the case studies presented). Table 2 presents the individual neuropsychological tests used with Patient 1. Tests that were 1.5 standard deviations below the premorbid IQ estimate were considered lower than expected.

At the time of the evaluation, Patient 1 described herself as a pretty happy person overall (but had been seen by a psychiatrist during adjuvant chemotherapy and was prescribed lorazepam, which she took 3 times). Her responses on the Personality Assessment Inventory (30) revealed mild or transient depressive symptomatology. She denied suicidal ideation. Patient 1 was very independent and had a tendency to present herself in a positive light such that she would deny problems. For instance, she reported having a stress level comparable to that of normal adults which was inconsistent with her life situation at the time of the evaluation. However, she also reported having a large social network that

she could turn to for support. Consistent with her reluctance to engage in psychiatric treatment or supportive counseling, her profile revealed that her motivation for treatment is substantially lower than most adults. Her responses suggested that she was satisfied with herself as she was and that she was not exhibiting significant psychopathology. Thus, she saw little need for changes in her behavior.

The cognitive assessment revealed adequate motivation to perform her best. Significant attentional difficulties were revealed. On a continuous performance task, Patient 1 had problems quickly and efficiently processing stimuli. Her responses were more erratic when inter-stimulus intervals slowed. Also, her responses were less consistent as the test progressed. Patient 1 exhibited variability in her learning and working memory, which is consistent with attentional lapses. Testing of the limits on mental arithmetic by allowing her to use pencil and paper, improved her score. Her recognition for a word list was lower than expected for her premorbid IQ estimate as were her making two false positive errors on recognition. Her immediate and delayed visual memory was deficient largely due to the haphazard and unorganized manner in encoding a previously seen figure. On executive functioning, she had impaired set shifting when shifting between inhibiting and not inhibiting a response. Her performance on reciprocal inhibition was lower than expected (given her premorbid IQ estimate). She also had a very mild dysnomia. Notably, her processing speed was an area of strength. Verbal memory (word list retrieval and narrative retrieval) was within normal limits.

The results of the evaluation were consistent with Patient 1's complaints of inattention, distractibility and to a lesser extent, word finding problems. Her daily life was impacted by her cognitive difficulties. She reported being unable to

complete graduate school applications and had decreased job performance. Without a premorbid neuropsychological assessment (conducted prior to her cancer or its treatment), it is impossible to determine the exact causation of Patient 1's attentional difficulties. However, her negative premorbid history for cognitive problems, her neuropsychological profile, and her subjective complaints are consistent with chemotherapy-related cognitive side-effects. Patient 1 was assessed only 1 month post-chemotherapy and thus, it was likely her cognitive side-effects would gradually resolve. However, she was impatient to have her cognition return to her usual high functioning state as she planned to attend a graduate school program in 8-9 months. Since her insomnia could be contributing to her cognitive she was prescribed zolpidem to help restore her circadian rhythm. After a two week course of zolpidem Patient 1's sleep was restored, and she was referred for cognitive rehabilitation.

### **Occupational Therapy**

Patient 1 presented to Occupational Therapy for evaluation and treatment of impaired cognition/attention. She was managing all basic and instrumental activities of daily living without reporting any difficulty and no safety concerns were identified during the initial evaluation or course of treatment. She completed the Montreal Cognitive Assessment (MOCA)<sup>(31)</sup> with a score of 30/30. This patient reported her most significant impairments are noted during work tasks. She reported difficulty initiating and attending to Power Point slide presentations she created, often finding she stared blankly at the computer screen. She also reported difficulty with reading 100 pages of a document and recalling all information read, as well as synthesizing it into another format, such as conversation or written communication.

At the time of evaluation, it was determined that Patient 1 would attend one Occupational Therapy treatment session each week for the following 4 weeks. The frequency of once per week was determined in order to allow the patient time to implement the personalized strategies learned in session. This schedule facilitates time to practice these interventions and provide personalized feedback to the clinician regarding effectiveness and frequency of strategy use. The patient and clinician together can then modify the strategies or choose new ones to implement. The duration of 4 weeks was determined to allow sufficient time to implement learned strategies and allow these to develop into habits. At the completion of 4 weeks' time, the plan was for re-evaluation to assess for any changes in functional status. Areas of deficit to be addressed included time management, organizational strategies for daily planning of work tasks, shifting between tasks at work, and reading comprehension with superior encoding and retrieval of information.

Of note, upon completion of the evaluation, the clinician provided several simple strategies for easy and quick implementation at work in order to improve daily task management and flow. Strategies included use of a computerized calendar (such as Outlook or other comparable software) to provide time reminders to transition between tasks, as well creating a daily schedule in the morning to provide structure and organization to daily tasks and responsibilities. The patient stated that she would try implementing these strategies, however verbalized a desire for more sophisticated ways of improving her cognitive skills.

Patient 1 completed 3 treatment sessions in addition to the initial evaluation, with approximately 2 weeks between sessions, due to patient's schedule. The first session

focused on strategies to implement in order to maintain attention to task during free writing or Power-Point presentation composition at work. The patient was provided with a 5 step process<sup>(32)</sup> to check whether she was staying on task, as well as strategies such as imagery/visualization, using external cues and completing self-checks throughout a task. The 5 step process to focus her attention included the following: Stop (think, "what am I doing? What is my objective?"), Define (the main task), List (the steps), Learn (the steps and repeat them so they become automatic/easily retrieved), and Check ("Am I doing what I planned to do?"). The patient verbalized understanding of these strategies and said she would try implementing them during the week.

The second and third treatment sessions focused on reading comprehension and synthesizing information read into a written summary. The patient read a self-selected article from New York Times, using a highlighter and was given verbal cues to stop every 3-4 paragraphs to summarize aloud what she had read. The patient was able to verbally summarize the article content every few paragraphs however, she demonstrated difficulty with a written summary of the salient article points upon completing the article. When asked 2 detailed questions taken from content in the article, the patient needed to reference the article to provide the proper answer.

Throughout the New York Times article activity, the patient stated that reading items of this nature was not as challenging as required readings for her anticipated graduate studies. Despite her statement, the patient was observed to have mild difficulty with this activity. Additionally, the patient reported that she was having more difficulty with this type of activity when the reading material was in French. In order to address this perceived deficit, the clinician structured a similar activity

in French in order to better simulate the patient's work tasks.

During this patient's third session, the Occupational Therapist<sup>(33)</sup> (as well as another clinician who is fluent in French) was present. The patient again selected an article to read, this time from *Le Parisien*, a French newspaper. The patient read this article, using a highlighter as needed, with verbal cues to stop and summarize content every few paragraphs. All follow-up questions were written by GM, shown to the French speaking therapist, and then read aloud in French. The patient was able to respond to the questions and explain answers in French, with minimally increased time. This clinician then asked the patient to write a synopsis of the article in French. The patient was able to do this, writing one paragraph in approximately 10 minutes. The patient reported that this activity was moderately challenging. Plans were made to review patient-written synopsis and continue to address areas of deficit at the next treatment session.

After completion of this third session, GM reviewed the patient-written synopsis with the French-speaking clinician. Several grammatical and gender errors were noted with this written synopsis in the patient's second language, French. This feedback was not given to the patient though, because she did not return for next scheduled appointment. Patient 1 did not respond to further attempts to schedule Occupational Therapy and complete her course of treatment.

## **Reflection**

Patient 1 initially stated that she functions at a very high cognitive level, and will be attending an intense academic graduate program. While the Occupational Therapist<sup>(33)</sup> explained that Occupational Therapy approaches include both remediation and compensatory strategies, this patient

**Table 3. Patient 1: Comparison of Neuropsychological Scores on Selective Tests Found to be Impaired or Lower than Expected**

Premorbid IQ Estimate						
	Standard Score		Percentile	Interpretation		
North American Adult Reading Test	118		88	High Average		
Test	Baseline (1 Month Post-Chemotherapy)			Re-Evaluation after OT (7.5 Months Post-Chemotherapy)		
	Score	%	Interpretation	Score	%	Interpretation
<b>Attention</b>						
<u>WAIS-IV</u>	<u>Scaled</u>	<u>%</u>		<u>Scaled</u>	<u>%</u>	
Arithmetic	9	37	Average	12 (13)*	75 (84)	High Average
<u>Continuous Performance Test-II</u>	<u>T-Score*</u>	<u>%</u>		<u>T-Score*</u>	<u>%</u>	
Omissions	57	76	Within Normal	47	39	Within Normal
Commissions	71	98	Markedly Atypical	66	96	Markedly Atypical
Hit RT	40	18	A little fast	47	40	Within Normal
Hit RT SE	68	97	Markedly Atypical	38	12	Good performance
Variability	76	99	Markedly Atypical	43	26	Good performance
Detectability	62	89	Mildly Atypical	67	96	Markedly Atypical
Response Style	46	35	Within Normal	48	45	Within Normal
Perseverations	47	41	Within Normal	47	41	Within Normal
Hit RT Block Change	49	49	Within Normal	67	96	Markedly Atypical
Hit SE Block Change	69	97	Markedly Atypical	63	91	Mildly Atypical
Hit RT ISI Change	60	85	Mildly Atypical	40	17	Good performance
Hit SE ISI Change	84	99	Markedly Atypical	47	36	Within Normal
*Scores are reversed scored						
<b>Executive Functioning</b>						
<u>Color Word Interference</u>	<u>Scaled</u>	<u>%</u>		<u>Scaled</u>	<u>%</u>	
Color Naming	9	37	Average	8	25	Low Average
Word Reading	11	63	Average	14	91	Superior
Inhibition	9	37	Average	11	63	Average
Inhibition/Switching	1	<1	Impaired	13	84	High Average
<b>Language</b>						
<u>Boston Naming Test</u>	<u>T Score</u>	<u>%</u>		<u>T Score</u>	<u>%</u>	
	56	54	Average	67	92	Superior
<b>Memory</b>						
<u>Wechsler Memory Scale-IV</u>	<u>Scaled</u>	<u>%</u>		<u>Scaled</u>	<u>%</u>	
Logical Memory I	11	63	Average	15	95	Superior
Logical Memory II	11	63	Average	14	91	Superior
Recognition	Raw=25/30	26-50%	Average	Raw=28/30	>75%	Within Normal

California Verbal Learning Test-II (CVLT-II)	z Score	%		z Score	%	
Learning Slope	1	84	High Average	-0.5	31	Average
Trials 1-5 Total	49=T	46	Average	54=T	66	Average
SDFR	0	50	Average	0	50	Average
SDCR	0.5	69	Average	0.5	69	Average
LDFR	0	50	Average	0	50	Average
LDCR	0.5	69	Average	0	50	Average
Recognition	-0.5	31	Average	0	50	Average
False Positives	-0.5	31	Average	0.5	69	Average
Rey Complex Figure Test	T Score	%		T Score	%	
Copy	35	>16	Within Normal	32	2-5	Mildly Impaired
Immediate Recall	29	2	Impaired	48	42	Average
Delayed Recall	27	1	Impaired	44	27	Average
Recognition	59	82	High Average	60	84	High Average

demonstrated resistance to implementing compensatory strategies. Patient 1 wanted her cognitive function to be restored to her premorbid level, without implementing new strategies to facilitate her previous high level of functioning. It appeared that Patient 1 did not complete Occupational Therapy due to the challenging nature of the last activity. Patient 1 may not have wanted to confront the fact that there were errors in her simple written paragraph, and thus did not return to therapy.

The largest barrier to treatment success with Patient 1 was her lack of engagement in the therapy process. From the initiation of Occupational Therapy, Patient 1 verbalized that she wanted her cognitive function to be restored to its prior level, without having to change how she performs her work tasks or implement compensatory strategies. Throughout the course of Occupational Therapy treatment, it was reinforced to Patient 1 that in order to achieve a successful outcome with both work tasks and future enrollment in an academically intense graduate program, she may have to implement compensatory or “study” strategies. This patient was resistant to this concept throughout treatment, creating a

barrier to both a successful Occupational Therapy outcome and improved cognitive functional performance in her daily life. The patient terminated Occupational Therapy by avoiding further contact with her Occupational Therapist, thus there was no closure to her course of Occupational Therapy treatment. Her behavior was also borne out in her Personality Assessment Inventory<sup>(33)</sup>, where she indicated a reluctance to engage in psychiatric treatment or supportive counseling. Her profile revealed that her motivation for treatment is substantially lower than most adults. Thus, there is a defensive personality style that makes it difficult for her to confront deficits and actively engage in working on difficulties.

Following her course of Occupational Therapy treatment, two weeks later she was started on methylphenidate 5 mg. She reported taking methylphenidate only a few times but it made her hyperactive so, she discontinued it. She was prescribed modafinil but her insurance company refused to authorize its use for cognitive problems.

*Neuropsychological Re-Evaluation:* Table 3 presents the individual neuropsychological

logical tests used in Patient 1's re-evaluation. Tasks that Patient 1 exhibited difficulty with were repeated (see Table 1 for all neuropsychological tests). Tests that were 1.5 standard deviations below the premorbid IQ estimate were considered lower than expected.

Patient 1 was re-evaluated three months after her course of Occupational Therapy treatment and 7.5 months post-chemotherapy. At the time of her re-evaluation, she was taking tamoxifen 20 mg. She reported problems with attention / concentration, problem solving, and memory. Her complaints were not as severe as at her initial evaluation and she indicated she was less "foggy" and tasks were less frustrating for her.

Results of the re-evaluation indicated a significant improvement in Patient 1's memory, cognitive flexibility, and word finding. Her visual memory both immediately and at delayed recall, improved from the impaired to the average range. Her memory for narratives improved from average to superior. Recognition for a word list and overall list learning (Trials 1-5) improved as well. She also exhibited improved confrontation naming (average to superior). Thus, there is no longer any evidence of a mild dysnomia. Lower than expected performance on reciprocal inhibition improved and shifting between inhibiting and not inhibiting a response improved from impaired to high average. Mental arithmetic also improved. Results on a sustained attention task suggested improvement in her reaction time as well as less variability and better consistency in her reaction time over the course of the task. Despite these improvements, inattention and poor vigilance were still apparent. Inattention to details on her copy of the Rey Complex Figure<sup>(35)</sup> was also seen however, as stated above, her recall (of the figure) improved.

Patient 1 appeared to be demonstrating the typical trajectory of improvement in

cognitive functioning post-chemotherapy. Attention and vigilance appeared to continue to be deficits. Despite taking tamoxifen, she did not report noticing any decrement in her cognitive functioning, and her neuropsychological re-evaluation shows overall improvement. She was encouraged to use academic support services when she began her graduate studies.

## Patient 2

Patient 2 was a 36-year-old woman who presented to her gynecologist with a noted mass in her right breast with a past medical history that was significant for a sinus infection and a heart murmur. She also had a history of uterine fibroids and ovarian cysts. Six years prior she discovered a different mass in her left breast that was biopsied and found to be benign. PET imaging showed two adjacent nodules in the upper central right breast spanning 2.7 cm. One nodule was 1.2cm, the other 0.7cm. Subsequent core biopsies showed a poorly differentiated invasive ductal carcinoma that was estrogen receptor (ER) and progesterone receptor (PR) negative and negative for the human epidermal growth factor receptor-2. Patient 2's stage was T2N0M0 (Stage IIA).

A breast MRI was performed pre-operatively to determine her anatomy and revealed a 2.2cm lesion at the 10 o'clock position in her right breast consistent with two lesions close together. One lesion measured 8mm and the other appeared to be 1.5cm away. Patient 2 then underwent MRI needle localization followed by a partial mastectomy and sentinel lymph node biopsy. Pathology showed three sentinel lymph nodes that were all free of cancer and a 2.5mm grade III, poorly differentiated invasive ductal carcinoma. The medial margin did show a second focus of cancer measuring 9mm. Genetic testing revealed that Patient 2 was positive for the BRCA-1 gene mutation, but she decided against



pursuing a prophylactic mastectomy. Prior to starting chemotherapy, she underwent ovarian egg retrieval where 6 oocytes were retrieved for fertility preservation.

She completed four cycles of taxotere and cyclophosphamide (TC) chemotherapy which was followed by radiation therapy. She experienced a chemotherapy extravasation which resulted in left thumb/wrist and forearm pain. She was seen by Occupational Therapy and was treated with a splint to immobilize her wrist and thumb. Following the completion of her adjuvant chemotherapy, she experienced hot flashes and mild sensorimotor polyneuropathy which presented as numbness in her fingers and plantar fasciitis. She was treated with pregabalin at 100 mg. She reported of cognitive decline following chemotherapy. She had a course of radiation was referred for a neuropsychological evaluation.

Patient 2 denied ever having a head injury, loss of consciousness, seizure or any neurological disorder. She denied any history of toxic chemical exposure. She also denied that her mother experienced any perinatal problems or difficulties with labor and delivery of Patient 2. Patient 2 denied tobacco use and drinks alcohol socially (1-2 drinks). She denied using illicit drugs. Her neuropsychological evaluation took place 3 months after her chemotherapy ended.

*Chief Complaint:* Patient 2 complained that her thoughts were “fuzzy” and that she forgets what she is going to say. She also reported memory difficulties including forgetting things she has been asked her to do, and forgetting well-know things (i.e., the name of a computer system that she previously used every day at work).

*Psychiatric History:* Patient 2 saw a social worker sporadically for cognitive behavioral therapy and psychoeducation during her cancer treatment. She had no prior psychiatric history. During her cancer treatment, she received mindfulness meditation to help her with stress reduction.

Patient 2 had insomnia post-treatment and tried meditation to help her relax.

*Psychosocial/Occupational/Academic Functioning:* Patient 2 was single and worked as an account supervisor at an advertising agency. She was on short-term disability for 7 months prior to the neuropsychological evaluation. Patient 2 had concerns about being able to keep up with the details of managing accounts when she eventually returned to work. She did well in school and reported receiving mostly A's and B's in high school. She denied ever being diagnosed with a learning disability or attention deficit disorder. She was in gifted classes when she was younger and in high school, took accelerated classes in English and Math. Patient 2 had a Bachelor's degree in business and a Master's degree in marketing and communications from a competitive university. Patient 2 reported having a good support system with her family and boyfriend as well as friends from the schools she attended. Prior to her diagnosis, she enjoyed dancing and was regularly involved in this activity.

*Behavioral Observations:* Patient 2 was alert and oriented in all spheres. Patient 2's gait appeared stiff. No extraneous movements were observed. She had reported limited mobility in her nondominant, left hand. Her speech was fluent and of normal rate and volume. Patient 2 was very personable, friendly, and made good eye-contact. Her attitude toward testing was positive, and she exerted good effort working diligently on all tasks presented. Mood was euthymic. Patient 2 demonstrated a logical and organized thought process. There was no evidence of hallucinations, delusions, or compulsions. Patient 2 appeared to have insight into her cognitive problems. Judgment was intact. The assessment appeared to be an accurate representation of her current cognitive functioning.

*Neuropsychological Assessment* (see Table 1 for the various neuropsychological

Table 4. **Patient 2: First Neuropsychological Evaluation (3 months post-chemotherapy)**

Test	Score	Percentile	Interpretation	Norms/Reference
<b>Motivation</b>				
<u>TOMM</u>				Tombaugh, 1996 <sup>(47)</sup>
Trial 1	48/50		Valid	
Trial 2	49/50		Valid	
CPT-II			Valid	Conners, 2004 <sup>(42)</sup>
Reliable Digit Span	Raw=8	>25	Above cut-off	Pearson, 2009 <sup>(38)</sup>
CVLT-II Forced Choice	Raw=16/16		Valid	Delis, et al. 2000 <sup>(41)</sup>
<u>PAI</u>	<u>T-Score</u>			Morey, 2009 <sup>(34)</sup>
Inconsistency	37			
Infrequency	44			
Negative Impression Management	44			
Positive Impression Management	50		Slightly Elevated	
<b>Premorbid IQ Estimate</b>				
<u>WRAT-4</u>	<u>Standard Score</u>	<u>Percentile</u>		Wilkinson, 2006 <sup>(50)</sup>
Word Reading	108	70	Average	
<b>Attention</b>				
<u>WAIS-IV</u>	<u>Standard Score</u>	<u>Percentile</u>		Wechsler, 2008 <sup>(48)</sup>
Working Memory Index	92	30	Average	
<u>Working Memory Subtests</u>	<u>Scaled Score</u>	<u>Percentile</u>		
Arithmetic	8	25	Low Average	
Digit Span	9	37	Average	
Digit Span Forward	9	37	Average	
Digit Span Backward	8	25	Low Average	
Digit Span Sequencing	10	50	Average	
<u>Continuous Performance Test-II</u>	<u>T-Score*</u>	<u>Percentile</u>		Conners, 2004 <sup>(42)</sup>
Omissions	275	99	Markedly Atypical	
Commissions	49	49	Within Normal	
Hit RT	67	96	Atypically Slow	
Hit RT SE	86	99	Markedly Atypical	
Variability	82	99	Markedly Atypical	
Detectability	58	79	Mildly Atypical	
Response Style	42	23	Mildly Atypical	
Perseverations	85	99	Markedly Atypical	
Hit RT Block Change	73	99	Markedly Atypical	
Hit SE Block Change	87	99	Markedly Atypical	
Hit RT ISI Change	62	90	Mildly Atypical	
Hit SE ISI Change	80	99	Markedly Atypical	

\*Scores are reversed scored

<b>Information Processing Speed</b>				
<u>WAIS-IV</u>	<u>Standard Score</u>	<u>Percentile</u>		Wechsler, 2008 <sup>(48)</sup>
Processing Speed Index	108	70	Average	
<u>Processing Speed Subtests</u>	<u>Scaled Score</u>	<u>Percentile</u>		
Coding	15	95	Superior	
Symbol Search	8	25	Low Average	
<u>Trail Making</u>	<u>T-Score</u>	<u>Percentile</u>		Heaton et al. 2004 <sup>(40)</sup>
Trails A	53	62	Average	
<b>Language Functioning</b>				
<u>Boston Naming Test</u>	<u>Raw Score</u>	<u>Percentile</u>		Heaton et al. 2004 <sup>(40)</sup>
Spontaneously Correct	57/60	66	Average	
<u>Verbal Fluency</u>	<u>Scaled Score</u>	<u>Percentile</u>		
Letter Fluency	T=48	42	Average	Heaton et al. 2004 <sup>(40)</sup>
Category Fluency	14	91	Superior	Delis et al. 2001 <sup>(44)</sup>
<b>Visual Spatial</b>				
<u>Rey Complex Figure Test</u>	<u>Raw Score</u>	<u>Percentile</u>		Meyers & Meyers, 1995 <sup>(35)</sup>
Copy	36	>16	Within Normal	
<b>Executive Functioning</b>				
<u>Trail Making</u>	<u>T-Score</u>	<u>Percentile</u>		Heaton et al. 2004 <sup>(40)</sup>
Trails B	56	73	Average	
<u>Color Word Interference</u>	<u>Scaled Score</u>	<u>Percentile</u>		Delis et al. 2001 <sup>(44)</sup>
Color Naming	13	84	High Average	
Word Reading	15	95	Superior	
Inhibition	11	63	Average	
Inhibition Total Errors	7	16	Low Average	
Inhibition/Switching	10	50	Average	
Inhibition/Switching Total Errors	11	63	Average	
<u>Wisconsin Card Sorting Test</u>	<u>T-Score</u>	<u>Percentile</u>		Heaton, 2005 <sup>(37)</sup>
Categories	Raw=6	>16	Within Normal	
Trials to First Category	Raw=18	6-10%	Mildly Impaired	
PSV Responses	T=40	16	Low Average	
PSV Errors	T=41	18	Low Average	
% Conceptual Level Responses	T=42	24	Low Average	
Failure to Maintain Set	Raw=0	>16	Within Normal	
Learning to Learn	Raw=7.78	>16	Within Normal	
<b>Memory</b>				
<u>Wechsler Memory Scale-IV</u>	<u>Scaled Score</u>	<u>Percentile</u>		Wechsler, 2009 <sup>(49)</sup>
Logical Memory I	7	16	Low Average	
Logical Memory II	6	9	Mildly Impaired	
Recognition	Raw=21/30	10-16	Low Average	

<u>CVLT-II</u>	<u>z-Score</u>	<u>Percentile</u>		Delis, et al. 2000 <sup>(41)</sup>
Learning Slope	0	50	Average	
Trials 1-5 Total	T=57	76	High Average	
SDFR	0.5	69	Average	
SDCR	0.5	69	Average	
LDFR	0.5	69	Average	
LDCR	0	50	Average	
Recognition	0	50	Average	
False Positives	-0.5	31	Average	
<u> Rey Complex Figure Test</u>	<u>T-Score</u>	<u>Percentile</u>		Meyers & Meyers, 1995 <sup>(35)</sup>
Immediate Recall	59	82	High Average	
Delayed Recall	56	73	Average	
Recognition	20/24	>16	Within Normal	
<b>Behavioral and Emotional Functioning</b>				
<u>BDI-Fast Screen</u>	<u>Raw Score</u>			
Total Depression Score	4/21		Mild Symptoms	Beck, 2000 <sup>(39)</sup>
<u>PAI</u>	<u>T Score</u>			Morey, 2009 <sup>(34)</sup>
Inconsistency	37			
Infrequency	44			
Negative Impression Management	44			
Positive Impression Management	50		Slightly Elevated	
Somatic Complaints	57			
Anxiety	52			
Anxiety-Related Disorders	51			
Depression	54			
Mania	56			
Paranoia	41			
Schizophrenia	49			
Borderline Features	54			
Antisocial Features	48			
Alcohol Problems	45			
Drug Problems	42			
Aggression	54			
Suicidal Ideation	43			
Stress	55			
Nonsupport	39			
Treatment Rejection	46			
Dominance	60			
Warmth	65		Elevated	

tests used in the case studies presented). Table 4 presents the individual neuropsychological tests used with Patient 2. Tests that were 1.5 standard deviations below the premorbid IQ estimate were considered lower than expected.

Tests of motivation indicated that Patient 2 put forth her best effort on the neuropsychological tasks. On a personality inventory, she had a slight tendency to present herself favorably, free of common shortcomings. Patient 2's neuropsychological profile is indicative of deficits in attention and executive functioning. On a continuous performance test, she produced a strikingly atypical profile marked by extremely poor attentional capacity and vigilance deficits. Though her commission error rate was within normal limits, she made substantially more omission errors than same aged peers, and she produced significantly more omission errors as the test advanced. Her performance was inconsistent, erratic, and her reaction time was slow, particularly as the test progressed and as the tempo of the stimuli presentation slowed. In addition, Patient 2 had difficulty detecting the stimuli from the non-stimuli. On an executive functioning task measuring reciprocal inhibition, her errors were low average, a performance which was lower than expected for her (given her premorbid IQ estimate). On a measure of concept formation and problem solving, she generally performed within normal limits but it took her longer than same-aged peers to consistently implement a strategy (mildly impaired). Overall her memory functioning was adequate with the exception of narrative recall. While story memory is usually better than word list retrieval, her fluctuating attention may have impacted her recall of narratives. Her memory for narratives was lower than expected (given her premorbid IQ estimate) at the immediate recall and mildly impaired after

a half-hour delay. Patient 2 also appeared to be exhibiting some mild depression and posttraumatic anxiety related to her cancer and fears of recurrence (based on her individual responses to a few items about post-traumatic stress). However, her mild depression and anxiety was not wholly responsible for her cognitive deficits. Without a premorbid neuropsychological assessment (conducted prior to her cancer and its treatment), it is impossible to determine the exact causation of Patient 2's cognitive difficulties. However, her negative premorbid history for cognitive problems, her neuropsychological profile, and her subjective complaints are consistent with chemotherapy-related cognitive side-effects. Patient 2 was not interested in medication for her attentional problems. Cognitive rehabilitation was recommended to ameliorate her attention and executive functioning deficits with the eventual goal of being able to return to her former occupation and perform at her previous high-level of functioning.

### **Occupational Therapy**

Patient 2 presented to Occupational Therapy for evaluation and treatment of cognitive deficits after her neuropsychological evaluation. Of note, she had previously been seen by Occupational Therapy for left hand fine motor deficits secondary to her chemotherapy extravasation. For the purpose of this paper, we will describe the Occupational Therapy interventions targeted at addressing her cognitive deficits. Patient 2 reported no difficulty managing her basic or instrumental activities of daily living due to cognitive deficits. No safety concerns were identified during initial evaluation or throughout the course of treatment. Patient 2 completed the Montreal Cognitive Assessment (MOCA)<sup>(31)</sup> with a score of 27/30. Areas of deficit were identified to include attention/

calculation and memory. Patient 2 was able to complete 2/5 correct calculations during Serial 7's, and able to successfully recall 3/5 novel items. The additional 2 items she was able to recall with category cues. She reported that 2 weeks prior to initiating Occupational Therapy, she felt as though she was "pushing through a fog" to think. At the time of evaluation, she stated she "just feel[s] blank." She reported word-finding difficulties during conversation and was anxious about returning to work in the near future.

At the time of the evaluation, it was determined that Patient 2 would attend one Occupational Therapy treatment session each week for 8 weeks. Again, the frequency was determined in order to allow time for strategy implementation between sessions. The duration of 8 weeks of therapy intervention was determined by the level of Patient 2's deficits as well as the additional goal of transitioning back to work. At the completion of the 8 weeks of Occupational Therapy intervention, re-evaluation was performed, and Patient 2 was scheduled for an additional 6 treatment sessions. It is important to note that the additional treatment sessions were primarily to address limited thumb mobility and strength due to a previous chemotherapy extravasation, however any ongoing cognitive issues were also addressed.

Patient 2 completed a total of 14 treatment sessions, mostly addressing cognitive deficits. Interventions included in treatment sessions addressed memory (with content presented both visually and aurally), organizational strategies, functional organization and communication of information, relaxation/visualization techniques and remediation of divided attention and set-shifting. A wide range of activities were implemented to address these deficits. Patient 2 typed a self- and clinician-generated compensatory

strategies sheet for improving functional memory during work meetings. This sheet including such tasks such as taking notes, using post-its, marking or highlighting items to which she should return. Contextual strategies for working memory and delayed recall included creating a sentence or short story linking items to be remembered. Office computer software programs such as Power-Point and Excel were used to synthesize and communicate provided information, in order to simulate the work task of preparing presentations. Computer-based games were used to improve ability with divided attention and set-shifting.

Patient 2 reported difficulty with getting adequate rest at night due to rumination and difficulty relaxing. She felt fatigue was impacting her performance at work, specifically impacting her attention and memory. Patient 2 was taught relaxation techniques to improve nighttime rest, including counting backwards, progressive muscle relaxation, and visualization. Of note, during the treatment session where the patient was instructed with these techniques, she was yawning after practicing these techniques, and reported she will try to implement them consistently at home.

After 8 Occupational Therapy sessions, Patient 2 was re-evaluated. The Mini-Mental State Exam (MMSE)<sup>(36)</sup> was administered at the re-evaluation, with the patient scoring 30/30. While she completed 4/5 Serial 7 calculations correctly, she was able to spell the word, "world," backward, receiving full credit for the attention/calculation component of this assessment. By this time, she had returned to work part-time. She stated she had ongoing difficulty with organizing the flow of work presentations and remembering connections between topics, however, she found that rehearsing her presentations was helpful. Notably, this was a strategy that she had not needed to implement prior to her chemotherapy treatment.

Additional treatment sessions were focused on developing and practicing compensatory strategies to assist with organization and flow of work-related presentations. Activity-based intervention to address these difficulties included asking Patient 2 to read a self-selected New York Times article and start creating a Power-Point presentation summarizing the salient features of the article. She required increased time with this task, stating the task demonstrated exactly what she has difficulty doing at work. Strategies such as highlighting items to be included in the presentation as well as creating an initial outline were discussed, with Patient 2 reporting that she would try implementing such strategies at work.

Upon discharge from Occupational Therapy, Patient 2 continued to work part-time. The Montreal Cognitive Assessment (MOCA)<sup>(31)</sup> was administered at this time, with Patient 2 scoring 28/30. Improvements were noted with attention/calculation component of Serial 7's in comparison to initial administration on evaluation. Upon discharge, the patient miscalculated the first subtraction, however all subsequent subtractions were correct based on that miscalculation. Thus, Patient 2 received full credit for this component. The area in which she continued to demonstrate deficit was in delayed recall, again recalling 3/5 items and requiring cuing for the additional 2 items. However, this type of task is one that is easily compensated for during daily activity through either note-taking or utilizing a contextual strategy. Upon completion of Occupational Therapy treatment, Patient 2 demonstrated understanding of these strategies.

## **Reflection**

Patient 2 was engaged and consistent with the therapy process. She was open to learning and implementing compensatory strategies to improve success at work,

while working towards remediating deficits in her attention and memory. Part of this engagement in the therapy process may be due to meeting her Occupational Therapist<sup>(33)</sup> prior to initiating Occupational Therapy to address her cognitive deficits. GM initially met Patient 2 at the time of her chemotherapy extravasation. Patient 2 was referred for orthotic fabrication to immobilize her thumb and wrist after the extravasation. It is possible that due to rapport developed during those 2-3 visits, the patient felt more comfortable with her Occupational Therapist<sup>(33)</sup> and was thus more engaged in the therapeutic process.

The most significant barrier to Patient 2's success regarding her return to work full-time was the intensity of her work environment. Patient 2 worked in an extremely fast-paced, high-demand setting with multiple teams and varied leadership. Part of her role within this structure was to facilitate communication between these different parties, leading to very detailed and high-demand work. Patient 2 was often required to meet immediate deadlines and work 14-16 hour days. Despite working part-time upon completing Occupational Therapy, Patient 2 was still putting in extra hours at home in order to complete her required work. Additional barriers to successful outcomes included Patient 2's external stressors (financial, familial -- elderly parents who lived 120 miles away) as well as her inadequate nightly rest.

*Neuropsychological Re-Evaluation:* Table 5 presents the individual neuropsychological tests used in Patient 2's re-evaluation. Tasks that Patient 2 had difficulty with were repeated (see Table 1 for all neuropsychological tests). Tests that were 1.5 standard deviations below the premorbid IQ estimate were considered lower than expected.

Patient 2 was re-evaluated 2 weeks after her course of Occupational Therapy treatment and 9 months post-chemotherapy.

**Table 5. Patient 2: Comparison of Neuropsychological Scores on Selective Tests Found to be Impaired or Lower than Expected**

Premorbid IQ Estimate						
WRAT-4 Word Reading	Standard Score 108		Percentile 70		Interpretation Average	
Test	Baseline (3 Months Post-Chemotherapy)			Re-Evaluation after OT (9 Months Post-Chemotherapy)		
	Score	%	Interpretation	Score	%	Interpretation
<b>Attention</b>						
<u>WAIS-IV</u>	<u>Standard</u>	<u>%</u>		<u>Standard</u>	<u>%</u>	
Working Memory Index	92	30	Average	92	30	Average
<u>Working Memory Subtests</u>	<u>Scaled</u>	<u>%</u>		<u>Scaled</u>	<u>%</u>	
Arithmetic	8	25	Low Average	8 (10 ) <sup>^</sup>	25	Low Average
<sup>^</sup> Test the Limits						
Digit Span	9	37	Average	9	37	Average
Digit Span Forward	9	37	Average	10	50	Average
Digit Span Backward	8	25	Low Average	8	25	Low Average
Digit Span Sequencing	10	50	Average	8	25	Low Average
<u>Continuous Performance Test-II</u>	<u>T Score*</u>	<u>%</u>		<u>T-Score*</u>	<u>%</u>	
Omissions	27.5	99	Markedly Atypical	62	90	Mildly Atypical
Commissions	49	49	Within Normal	56	74	Within Normal
Hit RT	67	96	Atypically Slow	47	42	Within Normal
Hit RT SE	86	99	Markedly Atypical	54	66	Within Normal
Variability	82	99	Markedly Atypical	54	68	Within Normal
Detectability	58	79	Mildly Atypical	62	90	Mildly Atypical
Response Style	42	23	Mildly Atypical	42	23	Mildly Atypical
Perseverations	85	99	Markedly Atypical	46	38	Within Normal
Hit RT Block Change	73	99	Markedly Atypical	49	47	Within Normal
Hit SE Block Change	87	99	Markedly Atypical	62	90	Mildly Atypical
Hit RT ISI Change	62	90	Mildly Atypical	57	77	Within Normal
Hit SE ISI Change	80	99	Markedly Atypical	66	95	Markedly Atypical
*Scores are reversed scored						
<b>Executive Functioning</b>						
<u>Color Word Interference</u>	<u>Scaled</u>	<u>%</u>		<u>Scaled</u>	<u>%</u>	
Color Naming	13	84	High Average	11	63	Average
Word Reading	15	95	Superior	11	63	Average
Inhibition	11	63	Average	11	63	Average
Inhibition Total Errors	7	16	Low Average	9	37	Average
Inhibition/Switching	10	50	Average	10	50	Average
Inhibition Switching Errors	11	63	Average	12	75	High Average



Wisconsin Card Sorting Test	T Score	%		T-Score	%	
Categories	Raw=6	>16	Within Normal	Raw=5	11-16	Low Average
Trials to First Category	Raw=18	6-10	Borderline	Raw=11	>16	Low Average
PSV Responses	T=40	16	Low Average	30	2	Impaired
PSV Errors	T=41	18	Low Average	32	4	Borderline
% Conceptual Level Responses	T=42	24	Low Average	42	21	Low Average
Failure to Maintain Set	Raw=0	>16	Within Normal	Raw=5	≤1	Impaired
Learning to Learn	Raw=7.78	>16	Within Normal	Raw=-4.85	6-10	Borderline
<b>Memory</b>						
Wechsler Memory Scale-IV	Scaled	%		Scaled	%	
Logical Memory I	7	16	Low Average	11	63	Average
Logical Memory II	6	9	Mildly Impaired	11	63	Average
Recognition	Raw=21/30	10-16	Low Average	Raw=21/30	10-16	Low Average

Her neuropsychological profile revealed some improvements but in some areas she continued to have difficulty. She improved in verbal memory for narratives. Her total errors on reciprocal inhibition also improved. However, Patient 2’s performance indicated continued attentional difficulties and executive dysfunction, consistent with chemotherapy-related cognitive side effects. While her performance on a continuous performance test was improved, Patient 2 continued to demonstrate problems maintaining attention and a significant decrement in her ability to maintain a problem-solving strategy. Her difficulty on the Wisconsin Card Sorting Test<sup>(37)</sup> was particularly notable as this test has such a pronounced practice effect.

**CONCLUSION**

As demonstrated by these cases, a tailored Occupational Therapy intervention tends to be better at helping patients compensate for difficulties rather than completely restoring premorbid cognitive functioning. While chemotherapy-related cognitive deficits typically resolve within 12-18 months<sup>(5)</sup>, it still begs the question: What is a person to do and how can

she improve her daily functioning during that time? This quandary is highlighted in these case studies of young women who are working and having difficulty in fast-paced, multi-tasking work environments. The primary role of Occupational Therapy in this population is to facilitate improved daily functioning.

It is important to note that working in conjunction with neuropsychology, a better delineation of a patient’s cognitive difficulties can be made than solely relying on screening measures such as the MOCA<sup>(31)</sup> or the MMSE<sup>(36)</sup>. For Patient 1, her pre-therapy MOCA score of 30/30 was inconsistent with her perception of self-functioning that was below her premorbid level of cognitive functioning. This perception was validated by her deficits on neuropsychological testing. Tailoring remediation and compensatory strategies to the patient in order to address both demonstrated and reported deficits is crucial. However, neuropsychological evaluation occurs in an environment free from distractions which diminishes its ecological validity. Occupational Therapy intervention requires understanding the impact of the patient’s deficits in their daily life, whether the challenges are at

one's job or managing one's household. Working to document in descriptive terms the quality of the patient's performance on tasks helps contextualize her deficits in environments outside of the therapy and also assists in measuring improvement in the quality of the patient's functional performance over the course of treatment. Improving a half a standard deviation on a neuropsychological test is meaningless without such descriptive information.

### Future directions

Future directions for research include using advances in technology to delineate the neural mechanisms underlying cognitive rehabilitation. Using structural and functional neuroimaging may help determine whether a tailored Occupational Therapy intervention changes brain structure and function and/or affects compensatory mechanisms.

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