Title: There is a moderate level of evidence to support that exercise improves cognition and quality of life more than no treatment in adults receiving chemotherapy

---

Prepared by: Amie Kramp, OTS (kramp.amie@uwlax.edu)
Anthony Roberts, OTS (roberts.anth@uwlax.edu)

Date: December 7, 2013

CLINICAL SCENARIO:

Client Population: Adults diagnosed with cancer who are experiencing cognitive impairments secondary to chemotherapy treatment

Treatment Context: Exercise interventions were implemented in a hospital outpatient setting.

Problem/Condition: The effects of chemotherapy on the brain is a relatively new field of study. Many drugs used to treat chemotherapy can pass through the blood brain barrier (BBB) and have negative effects on brain matter which appear to impair cognitive ability. Cyclophosphamide and 5-fluorouracil are two of the chemicals used in chemotherapy that are able to pass through the BBB. Saykin et al., 2003 stated that these chemicals have been shown to cause decreases in gray matter of the brain and demyelination of white matter (as cited by Evens & Eschiti, 2009, p.662). The resulting cognitive impairments are commonly referred to as "chemo-brain."

Chemotherapy also negatively impacts a person's quality of life (QoL) which can decrease occupational performance and participation. Nausea, fatigue, cognitive impairments, and social participation all contribute to QoL and are negatively affected by chemotherapy. Although there are many assessments to measure QoL, it is often overlooked in the traditional medical model. Since QoL is often overlooked, these individuals may still be experiencing issues related to their treatment.

Incidence/Prevalence: Since problems with cognition are self-reported and difficult to measure objectively, the incidence of chemo-brain varies greatly. According to the American Cancer Society, the prevalence of cognitive deficits could be as high as 1 in 2 or as low as 1 in 6 in individuals receiving chemotherapy. (American Cancer Society, 2013).

Impact of the problem on activity/performance: Due to decreases in cognition, a person may have trouble performing a variety of occupations. It is common to see a decrease especially in performance of IADLs. Child care, home maintenance, and financial tasks all require a high level of cognitive processing in order to complete (E. Kaczmarowski, personal communication, September,18) . Work or scholastic performance may also suffer due to the decrease in cognitive ability or mental cloudiness that is associated with chemo-brain.

QoL is directly related to performance and participation in occupations. A compromise in physical, emotional, or social functioning may lead to a decrease in overall occupational performance. Poor performance in occupations may lead clients to end participation in those activities, thus giving up something that makes the client unique. If too many occupations are forfeited, the client may experience a further decline in QoL.

ICF level: This project focused on two outcomes: cognition and quality of life. According to the ICF, cognition in categorized as a body function, and quality of life is considered a participation outcome.

Intervention: Exercise has been widely studied and to examine to determine benefits on cognitive functioning and overall health for individuals diagnoses with cancer (Evens & Eschiti, 2009). This CAT focuses on two specific forms of exercise: medical Qigong & yoga.

Medical Qigong is a modified exercise program based on traditional Qigong practices. This program is designed to target the needs of cancer patients to control stress and emotions as well as improve physical function. Medical Qigong typically includes gentle stretching, body movement and postures both standing and seated, meditation, and breathing exercises. This type of exercise requires instruction and supervision from an experienced Qigong instructor. Medical Qigong can be practiced in group classes or in an individual home program (Oh et al., 2012).

Yoga has grown in popularity in recent years, and can be practiced in many different forms. Most types of yoga include stretching and strengthening exercises as well as focus on relaxation and breathing. There has been exploratory research done to support the use of an Iyengar-inspired yoga program with breast cancer survivors. These programs are designed for the particular needs and abilities of each participant, using props to ensure safe and precise positioning. The center focus of Iyengar yoga is stress management, body awareness, and relaxation, which is similar to other types of yoga. (Galantino et al., 2012).

Science behind intervention: Recently more studies have tried to determine the benefit exercise has on cognition. Hillman et al. concluded that after only 30 minutes of aerobic exercise there was an increased amplitude in the chemical P3, which indicates resources available for cognitive functioning (as cited by Hogan, Mata, Carstensen 2013). This suggests that exercise may increase attention, memory resources, and executive functioning. Colcombe and colleagues (as cited by Hogan, Mata, & Carstensen, 2013) examined the effect of exercising at least 30 minutes per day and found that vigorous aerobic exercise increased grey and white matter in the brain. This same study also found a moderate effect size for the influence of aerobic training on cognitive functions, especially executive functions including working memory, inhibiting processes and multitasking (as cited by Hogan, Mata, & Carstensen, 2013). Research done by Wilson et al. found that long term exercise reduced cytokine (inflammation producing cells) levels and converted them from pro to anti-inflammatory cells (as cited by Evens & Eschiti 2009). Nelson et al. found (as cited by Evens & Eschiti 2009) found aerobic exercise has been shown to increase oxygenation and blood flow to the brain. Hacker (as cited by Evens & Eschiti 2009) studied the effects of exercise on oncology patients and found that exercise can be used to prevent cognitive impairments and general health promotion. Therefore, exercise may be beneficial in preventing/remediating cognitive impairments related to chemotherapy drugs (Evens & Eschiti, 2009).

Why is this intervention appropriate for occupational therapy? This intervention is appropriate for use in OT because it is increasing the client's ability to engage in occupation. Exercise is classified as a preparatory intervention which is used to increase cognition in patients receiving chemotherapy. Increasing cognitive abilities, such as memory, may contribute to and increase in successful participation in IADL activities, such as home and financial management. Yoga and Qigong can be incorporated into a treatment session if the therapist is a certified instructor. Another option is to refer clients to community programs in addition to other therapy services.

Participation and functioning in occupations are greatly determined by QoL. To increase quality of life, we need to consider the physical, social, and emotional well-being, as well as role functioning. Yoga and Qigong address physical well-being through exercise, social well-being through group interaction, and emotional well-being through meditation and breathing exercises. When these three aspects are improved, clients may be more likely to participate in meaningful activities. This concept has recently been brought to the forefront of occupational therapy services, as rehabilitation facilities are becoming interested in participation outcomes as well as changes in client factors.

OT Theoretical Basis: The goal of this intervention is supported by the Model of Human Occupation. In this model, the person in broken down into three interrelated subsystems: volition, habituation, and performance. Improving cognition and quality of life for these individuals may enhance their volition, which means they could experience an increase in motivation to perform meaningful occupations. Exercise also has the potential to increase occupational competence for these individuals, meaning the feeling that "they are capable of engaging in productive and meaningful actions" (Cole & Tufano, 2008, p. 99). The volitional subsystem is frequently the focus area for motivation and change in this model, which is why it is a good fit for this intervention (Cole & Tufano, 2008).

FOCUSED CLINICAL QUESTION: Is exercise more effective than traditional therapy alone in improving cognition and quality of life in adults receiving chemotherapy treatment?

SUMMARY:

- Clinical Question: Is exercise more effective than traditional therapy alone in improving cognition and quality of life in adults receiving chemotherapy treatment?
- Search: Five data bases were searched, yielding eight articles related to our topic. Three relevant articles were selected for this critique: two randomized control trials and a case series (levels 1b, 2b, and 4 on the Canadian Levels of Evidence Scale). These were chosen because they had similar interventions and measured our specific outcomes.
- Across all three reviewed studies, yoga and medical Qigong programs resulted in improvements in both quality of life and perceived cognition for participants who were currently receiving, or recently completed, chemotherapy treatment.

CLINICAL BOTTOM LINE: There is a moderate level of evidence to support that exercise improves cognition and quality of life more than traditional treatment alone in adults receiving chemotherapy.

Limitation of this CAT: This critically appraised topic has been reviewed by occupational therapy graduate students and the course instructor.

SEARCH STRATEGY:

Table 1: Search Strategy

Databases Searched	Search Terms	Limits used	Inclusion and Exclusion Criteria
Journals @ OVID	chemotherapy cognition intervention		Include Related Terms
Health Professions Database (EBSCO)	chemotherapy and cognition	2000 - 2013	Full Text only
Cochrane Collection Plus (EBSCOhost)	cognitive interventions used in chemotherapy		Full Text Only
Alt Health Watch	Chemotherapy and cognition interventions		
Health Professions Database (EBSCO)	Chemotherapy exercise		
OT Seeker	exercise cognition	2000-2013	Full Text only

RESULTS OF SEARCH:

Table 2: Summary of Study Designs of Articles Retrieved

Level	Study Design/ Methodology of Articles Retrieved	Total Number Located	Data Base Source	Citation (Name, Year)
Level 1a	Systematic Reviews or Metanalysis of Randomized Control Trials	1	CINAHL Plus with Full Text	Vearncombe & Pachana, 2009
Level 1b	Individualized Randomized Control Trials	2	CINAHL Plus with Full Text	Poppelreuter, Weis, & Bartsch, 2009
			Academic Search Complete	Oh, et al., 2012
Level 2a	Systematic reviews of cohort studies			
Level 2b	Individualized cohort studies and low quality RCT's (PEDro < 6)	1	OTseeker	Culos-Reed, et al., 2006
Level 3a	Systematic review of case-control studies	1	MEDLINE with Full Text	Biegler, Chaoul, & Cohen, 2009
Level 3b	Case-control studies and non-randomized controlled trials	2	Consumer Health Complete - EBSCOhost	Myers, 2012

			MEDLINE with full text	Fardell, Vardy, Shah, & Johnston, 2012
Level 4	Case-series and poor quality cohort and case-control studies	1	MEDLINE	Galantino, et al., 2012
Level 5	Expert Opinion			

STUDIES INCLUDED:

Table 3: Summary of Included Studies

	Galantino, et al. (2012)	Culos-Reed, et al. (2006)	Oh, et al. (2012)
Design	Case Series	RCT	RCT
Level of Evidence	4	2b	1b
PEDro score (only for RCT)	N/A	4/10	6/10
Population	- 4 Caucasian women - Ages: 44-65 (mean = 54.75) - All four participants were diagnosed with stage II breast cancer - All were receiving chemotherapy during intervention <u>Inclusion Criteria:</u> - Over the age of 18 - Female - Diagnosed with stage I, II, or III breast cancer - Scheduled to receive chemotherapy <u>Exclusion Criteria:</u> - Receiving neoadjuvant therapy - History of past chemotherapy, chronic anemia, or chronic fatigue - History of a major psychiatric disorder with psychotic features - Current major medical comorbidities	- 38 participants - Age: approximately 50 years old - Most participants were female - Majority diagnosed with breast cancer <u>Inclusion Criteria:</u> - Over the age of 18 - Minimum 3 months post-chemotherapy - Cleared to participate in physical activity <u>Exclusion Criteria:</u> - No other health concerns	- 81 participants - Ages: 34-86 (mean = 62) - Majority diagnosed with breast or colorectal cancer - 48 participants post-chemotherapy; 28 currently receiving chemotherapy - No significant differences between control and experimental group at the start of study. <u>Inclusion Criteria:</u> - Over the age of 18 - Diagnosed with a malignant tumor who received or is receiving chemotherapy - Expected to live more than 12 months <u>Exclusion Criteria:</u> - Major medical or psychiatric disorder - History of epilepsy, brain metastasis, delirium, or dementia

			- Medical contraindications for exercise - Already practicing Qigong therapy
Intervention Investigated	12 week Iyengar-inspired yoga program adapted to the needs of each participant - Small group met 70 min 2x/wk for first 6 wks, then 1x/wk for final 6 wks - Home program 3x/wk (total 15 min/day) <u>Yoga program:</u> - Combination of static and active stretches - Isometric and dynamic strengthening postures - Breathing exercises - Relaxation/meditation - Use of props to adapt to participants' ability level	7 week yoga therapy program made up of 75 minute sessions <u>Yoga program:</u> - 10 mins gentle breathing - 50 mins modified yoga asanas (gentle stretching and strengthening exercises) - 15 mins shevesana (relaxation, paying attention to breathing and body sensations)	10 week medical Qigong program plus "usual care" -90 min. Qigong sessions offered 2x/week, participants required to attend 1x/wk <u>Qigong program:</u> -15 mins discussion of health issues -30 mins of gentle stretching and body movements in standing postures to stimulate energy channels -15 mins of seated postures -30 min of meditation and breathing exercises
Comparison Intervention	Baseline scores of each participant	Wait-list for intervention	Usual care: appropriate medical interventions without offering complementary or alternative medicine resources
Dependent Variables	- Cognition - Functional outcomes - Quality of Life	- Fitness - Stress symptoms - Mood states - Quality of Life	- Cognitive functioning (CF) - Systemic inflammation - Quality of Life (QoL)
Outcome Measures	Measurements taken at baseline, 6 & 12 weeks during chemotherapy, and 1 & 3 months after intervention - CogState - Perceived Cognition Questionnaire (PCQ) - FACT-B - Profile of Mood States	Measurements taken before starting yoga program, and immediately after completing the program - Psychological questionnaire - POMS - Symptoms of Stress Inventory (SOSI)	Measurements taken before starting Qigong therapy and immediately after completion of the program. - EORTC QLQ-30 - Functional assessment of cancer therapy- Cognitive

	(POMS) - Sit and Reach (SR) - Functional Reach (FR) - Qualitative questionnaire	- European Organization for Research and Treatment of Cancer (EORTC QLQ-C30) - Leisure Score Index (LSI) - Canadian Physical Activity, Fitness, and Lifestyle Appraisal (CPA-FLA)	function (FACT-Cog) - Functional Assessment of Cancer therapy-General Inflammation: blood collected and CRP (inflammation) was measured
Results	P1: improved QoL (FACT-8), improved speed, decreased accuracy, & fewer errors (CogState), improvements on PCQ P2: perceived cognition had no change (PCQ), increased QoL during intervention (decreased back to baseline at follow up), no changes in accuracy, fewer errors, & increased speed at follow up (CogState) P3: improved speed, decreased accuracy, & fewer errors (CogState); improved perception of cognition, improved QoL at follow up P4: decreased CogState scores at 3 month follow-up; improved QoL at 3 month follow-up, no change in perceived cognition	EORTC: greater increase in QoL ($p<0.01$) and emotional function ($p<0.05$) for intervention group SOSI: greater decrease in emotional irritability ($p< 0.10$) and cognitive disorganization ($p<0.10$) for intervention group (not statistically significant) POMS: improvements in total mood disturbance, tension, depression, and confusion ($p<0.10$) CPA-FLA: both groups changed significantly over time	-CF measured by EORTC QLQ-C30 increased significantly ($p=.014$) -CF measured by FACT-COG improved significantly ($p=.029$) -QoL measured by FACT-G improved significantly ($p<.001$) -Systemic inflammation measured by CRP decreased significantly ($p=.042$)
Effect Size	N/A	- QoL (EORTC): d=1.03 - Cognitive disorganization (SOSI): d=0.37 - Concentration (POMS): d=0.57	-Cognition (EORTC QLC-C30): d=0.29 -Cognition (FACT-COG): d=0.24 -Global quality of life (FACT-G): d=0.72 - Inflammation (CRP): d=0.72

Conclusion	Yoga may impact some aspects of cognition during and after chemotherapy	Yoga has potential as a beneficial physical activity for cancer survivors.	Qigong interventions may have a positive influence on QoL, perceived cognition, and systemic inflammation in cancer survivors.

IMPLICATIONS FOR PRACTICE, EDUCATION and FUTURE RESEARCH (Synthesis Section)

Overall Conclusions:

Cognition Results: Cognitive abilities encompass a wide range of skills and abilities. Within the reviewed articles, several cognitive functions were assessed. Each study measured cognition differently. Galantino, et al. (2012) evaluated the speed, accuracy, and errors committed when completing a task using the CogState and Perceived Cognition Questionnaire (PCQ). Oh et al. (2012) used the Functional Assessment of Cancer Therapy-Cognitive Function (FACT-Cog) to measure perceived cognitive impairments and abilities, and how cognitive impairments affect QoL. Oh et al. also used 2 cognitive subtests from the European Organization for Research and Treatment of Cancer (EORTC QLC 30). Culos-Reed, Carlson, Daroux, & Hately-Aldous (2006) measured cognitive disorganization and concentration using the Symptoms of Stress Inventory (SOSI) and Profile of Mood States (POMS).

Overall, there was an increase in client reported cognitive functioning across all three articles. Oh, et al. (2012) and Culos-Reed et al. (2006) reported changes in perceived cognition with small effect sizes. Only the results from Oh et al. (2012) were statistically significant. Galantino, et al. also reported increases in cognition, but effect sizes and significance were not calculated.

Quality of Life Results: Each study used different assessments to evaluate QoL in patients with cancer. Galantino et al (2012) used the FACIT and FACT-B to assess social, emotional, physical, and functional wellbeing. Culos-Reed et al (2006) used the EORTC QLC 30 to measure QoL. Areas assessed by the EORTC QLC 30 include physical, emotional, social, cognitive, and role functioning. Oh et al (2011) evaluated the participants using the Functional Assessment of Cancer Therapy-General (FACT-G) which measured physical, social emotional, and functional well-being.

Oh et al. (2012) and Culos-Reed et al. (2006) found statistically significant results, with medium to large effect sizes respectively, in four areas of QoL including emotional, social, physical, and functional well-being. Galantino et al. (2012) found a slight increase in overall QoL, but it was not found to be significant.

Analysis of differences: There were two different types of exercises used in the studies we investigated; Qigong and yoga. Galantino et al. (2012) and Culos-Reed used yoga as their intervention. Galantino et al. conducted the yoga class twice per week for 70 minutes for six weeks. After the first six weeks, participants only went to yoga once per week for the final six weeks. At the six week mark, a home exercise program was administered and prescribed three times per week for 15 minutes for the final six weeks (25.5 hours of treatment). Culos-Reed et al. (2006) had participants engage in a group yoga class for 75 minutes once per week for seven weeks (8.75 hours of treatment). There was no home program to accompany therapy. The participants in Oh et al. (2012) completed Qigong therapy up to two times per week for 90 minutes over ten weeks, however the participants only needed to attend one session per week. A home based exercise program was prescribed to be completed every day which took approximately 30 minutes (50-65 hours of therapy).

Each intervention incorporated gentle breathing exercises, gentle stretching, and some sort of meditation or mindfulness training. Oh et al. (2012) differed in treatment intervention by incorporating time in their therapy session to partake in a question and answer session regarding overall health. Another difference between the studies are the participants in the intervention. Galantino et al. (2012) and Oh et al. (2012) recruited participants who were undergoing or already received chemotherapy whereas Culos-Reed et al. (2006) only tested individuals who survived cancer, completing chemotherapy more than three months ago.

In conclusion, there is a moderate level of evidence to support that physical activity improves cognition and QoL more than no treatment in adults receiving chemotherapy.

Boundaries: The total number of participants in these three studies was 123, with ages ranging from 34 to 86 years old. The majority of participants were females diagnosed with breast cancer. Most participants were undergoing chemotherapy at the time of intervention. However, one study did require that all participants completed chemotherapy at least three months before entering the study. It was common in this population to have both chemotherapy and radiation treatment instead of chemotherapy alone, but this was not a requirement of the studies. Across all three studies, participants were excluded if they had any other medical concerns or psychiatric disorders.

Implications for practice: All three studies demonstrated positive results from 7-12 weeklong exercise programs. Exercise occurred in group classes as well as individual home programs. The length of the program and setting did not appear to have any effects on the outcomes measured. The interventions produced positive outcomes for participants currently going through chemotherapy as well as shortly after completing treatment. Individuals still experiencing decreases in cognition and quality of life longer after completing treatment may not have the same results as noted in this review.

The majority of participants in these studies were women diagnosed with breast cancer, so it is unclear if exercise would have the same results in males, or in people with other types of cancer. Additionally, the three studies reviewed were limited to a similar type of exercise intervention. It is not known if other types of exercise, such as walking or other aerobic activities, would be as effective.

All three studies reported greater changes in QoL scores than in the cognitive functioning measures. However, we speculate that exercise may not have been the only aspect that impacted change in QoL. Social participation and support involved with group interventions may have contributed to the increase in QoL. Additionally, mindfulness and meditation were part of the yoga and Qigong programs, which could have impacted QoL.

REFERENCES:

Articles Reviewed

Culos-Reed, S., Carlson, L., Daroux, L., & Hately-Aldous, S. (2006). A pilot study of yoga for breast cancer survivors: Physical and psychological benefits. *Psycho-Oncology, 15*, 891-897.

Galantino, M., Greene, L., Daniels, L., Dooley, B., Muscatello, L., & O'Donnell, L. (2012). Longitudinal impact of yoga on chemotherapy-related cognitive impairment and quality of life in women with early stage breast cancer: A case series. *EXPLORE, 8*(2), 127-135.

Oh, B., Butow, P., Mullan, B., Clarke, S., Beale, P., Pavlakis, N., Lee, M., Rosenthal, D., Larkey, L., & Vardy, J. (2012). Effect of medical qigong on cognitive function, quality of life, and a biomarker of inflammation in cancer patients: A randomized controlled trial. *Support Care Cancer, 20,* 1235-1242.

Related Articles (not individually appraised)

Biegler, K., Chaoul, M., & Cohen, L. (2009). Cancer, cognitive impairment, and meditation. *Acta Oncologica (Stockholm, Sweden)*, *48*(1), 18-26.

Fardell, J., Vardy, J., Shah, J., & Johnston, I. (2012). Cognitive impairments caused by oxaliplatin and 5-fluorouracil chemotherapy are ameliorated by physical activity. *Psychopharmacology*, *220*(1), 183-193.

Myers, J. S. (2012). Chemotherapy-Related Cognitive Impairment: The Breast Cancer Experience. *Oncology Nursing Forum*, *39*(1), E31-E40.

Poppelreuter, M., Weis, J., & Bartsch, H. (2009). Effects of specific neuropsychological training programs for breast cancer patients after adjuvant chemotherapy. *Journal of Psychosocial Oncology*, *27*(2), 274-296.

Vearncombe, K., & Pachana, N. (2009). Impact of health, treatment and psychological factors on cognitive functioning after chemotherapy for early breast cancer. *Australian Psychologist*, *44*(4), 235-247.

Additional Resources

American Cancer Society (2013, May 17). *Chemo brain*. Retrieved from http://www.cancer.org/treatment/treatmentsandsideeffects/physicalsideeffects/chemotherapyeffects/chemo-brain

Cole, M. B., & Tufano, R. (2008). Applied theories in occupational therapy: A practical approach. Thorofare, NJ: SLACK Incorporated.

Evens, K., & Eschiti, V. (2009). Cognitive effects of cancer treatment: "chemo brain" explained. *Clinical Journal of Oncology Nursing, 13*(6), 661-666.

Hogan, C., Mata, J., & Carstensen, L. (2013). Exercise holds immediate benefits for affect and cognition in younger and older adults. *Psychology & Aging*, *28*(2), 587-594.