



AMERICAN
PSYCHOLOGICAL
ASSOCIATION

Division of Clinical Neuropsychology Newsletter 40

Volume 27, Number 1

Winter/Spring 2009

Division 40 Executive Committee 2008 - 2009

Elected Officers

President	
Glenn Smith	2008-2009
President Elect	
Celiane Rey-Casserly	2008-2009
Past President	
Thomas Hammeke	2008-2009
Secretary	
Paula Shear	2003-2009
Treasurer	
Jacobus Donders	2006-2009

Members at Large

Deborah Koltai Attix	2008-2011
Kimberly Espy	2006-2009
Julie Bobholz	2007-2010

Council Representatives

Barbara Wilson	2005-2010
Linas Bieliauskas	2007-2010
Jennifer Manly	2006-2009
Joel Morgan	2006-2009

Chairs of Standing Committees

Membership	
Monica Rivera-Mindt	2006-2009
Fellows	
Ida Sue Baron	2007-2010
Program Chair	
Steven Paul Woods	2008-2009
Program Co-Chair	
Heather Belanger	2008-2009
Elections	
Tom Hammeke	2008-2009
Conflicts of Interest	
Erin Bigler	2005-2008

Chairs of Ad Hoc Committees

APA Relations	
Deborah Koltai Attix	2005-2008
Publications and Communication	
William Barr	2005-2011

Chairs of Umbrella Committees

Education Advisory	
Cindy Cimino	2008-2011
Scientific Advisory	
John Lucas	2005-2011
Practice Advisory	
Neil Pliskin	2002-2009
Public Interest Advisory	
Shelley Heaton	2008-2011
Awards Committee	
Laura Flashman	2008-2011
Early Career Psychologists	
Deborah Weber	2007-2010
ANST	
John Strang	2007-2010
Newsletter	
Michael McCrea	2008-2011

President's Message

Colleagues,

It is a great privilege to bring you this column. I want to first thank past-president, Dr. Thomas Hammeke for his great service to the Division in 2008. His leadership has left the Division stronger, more influential, and one of the few APA divisions that is growing. Thanks also to Paula Shear, our Secretary, and Jacques Donders, our Treasurer, and all the other members of the Division 40 Executive Committee (D40EC; www.div40.org/officers.html). These elected officers and appointees are really the engine of the Division. When next you have a chance, please give them each a pat on the back for their hard work.

Speaking of the growing influence of our division, hopefully you recently returned your apportionment ballot to APA with all 10 votes allocated to Division 40. Here are a few facts. All divisions and state/territorial associations are given 1 seat in the APA Council of Representatives, the legislature of APA. Additional seats are allocated based on the percentage of the total annual vote that is apportioned to the division and state/territorial associations. Many states and divisions are unlikely to gain seats because 'the base' is just not there in terms of the number of possible votes. But we have tremendous opportunity to add seats. And seats equal clout. Based on receiving 3.34% of the apportionment vote in 2007 we currently have 4 council seats (<http://www.apa.org/governance/elections/LY2009APPORTRESULTS.PDF>). If we were able to capture 150 more votes this year, we should be getting another seat. That's just 15 more people giving all 10 votes to us. And given that we have more than 3,500 voting members, we could easily have more than 10 seats if all the members would assign more than half their votes to D40. So if you simply pitched your apportionment ballot this year, please make one of your New Year's resolutions be to vote next year.

What an amazing time it is! As a nation we face great challenges and it is sure to be a time of great change. Some of the change affirms our highest ideals. Some of the change is frightening. But change is coming at break neck speed. Look, for example, at mental health parity. Years after our late great Senator Wellstone of Minnesota first was stonewalled on Mental Health parity, it suddenly passed as part of the financial bail-out. But it is unclear if parity within the current and future health care environment is a great victory. In this environment,

Continued on page 12

In This Issue

President’s Message	1
From The Editor	2
Don’t Miss The Future of Newsletter 40	3

Feature Articles:

Neurocognitive Effects of Cancer and Cancer Treatment in Adults	4
Neurocognitive Functioning in Childhood Cancer Survivors	9

New APA Division 40 Fellows Announced	15
2008 Division 40 Award Winners	16
Division 40 Launches Web-based Directory of Science Membership Research Expertise	17

Division 40 Committee Reports

Practice Advisory Committee	18
Science Advisory Committee	21
Early Career Psychologist Committee	22
Education Advisory Committee (EAC)	23

Past issues of the Division 40 Newsletter and Division 40 Executive Committee meeting minutes are now available online at the Division 40 Website. The URL address is: <http://www.div40.org/>.

From The Editor

I hope you will be as pleased as I am with the offerings in this issue of Newsletter 40. In the spirit of keeping our membership well-informed on new directions in our specialty, you will find this issue to contain several important updates on Division 40-lead initiatives vital to the future of clinical, scientific and academic neuropsychology. We are very fortunate to feature in this issue a pair of specialty articles from two highly-respected neuropsychologists who have lead the way for subspecialization in the neuropsychology of cancer. Christina Meyers, Ph.D. and Kevin Krull, Ph.D. have teamed up to provide us with terrific reviews of the literature on neurocognitive effects of cancer and cancer treatment in adults and children, respectively. Their work is a perfect example of the important contribution Division 40 neuropsychologists are making to advancing medicine and science, everyday.

I am also pleased to provide a sneak preview into the planned future for Newsletter 40. We are embarking on a plan to implement several improvements designed to enhance the Newsletter’s content, appearance and delivery to you. The most important change anticipated will involve transitioning Newsletter 40 from a traditional paper printed format to a web-based or PDF version that can be electronically distributed directly to our members. For your convenience, we anticipate the ability for members to print the full newsletter for portability and reading convenience. The move from our traditional to a new electronic platform will significantly reduce printing and mailing costs, make for a more environmentally-friendly product, and eliminate current constraints that limit our ability to enhance the overall appearance of the publication. Our first phase of this transition was to move the Division 40 Executive Committee meeting minutes from printed form in the newsletter to on-line access at www.div40.org, beginning with this issue.

Several steps need to fall into place to ensure the smoothest transition from old to new. The most important of these that involves you is making certain that we have your updated email address

where you would like us to send future newsletter notifications. Please see the special announcement posted below that contains instructions on how to update your email address and contact information in the APA database.

Also stay tuned for new content features in future issues of Newsletter 40. Thank you for your continued support of Division 40.

Sincerely,
Michael McCrea, Ph.D., ABPP-CN
Editor, Newsletter 40

Don't Miss the Future of Newsletter 40

Make Sure You Stay Connected to Important Happenings in Division 40

We anticipate that Newsletter 40 will transition from a traditional paper printed format to a web-based or electronically distributed (e.g., emailed PDF) publication in the near future.

To make certain that all Division 40 members are linked in to this change and receive future issues of Newsletter 40, we ask that you take a couple of minutes to complete the following steps:

1. Go to www.apa.org
2. Click on Association Information (on the left side of the orange banner)
3. Select Members Page
4. Log onto Members Account (this will require your 8-digit APA member number unless the member has previously changed their login; online assistance is provided if you experience difficulties with the login process).
5. On the top right, under myMembertools, select Update My Profile
6. Select Login Information
7. Select Email Address. Here you can enter a new email address or confirm your current email address.
8. At that point, you can also revise all your contact information in the main APA system, which will then be made available to Division 40.
9. Please be certain to make sure your email address is correct and current.

Thank you for your efforts in making this transition as smooth as possible. Please contact Michael McCrea, PhD, ABPP-CN, Newsletter 40 Editor, at michael.mccrea@phci.org with any questions.

Neurocognitive Effects of Cancer and Cancer Treatment in Adults

Christina A. Meyers, Ph.D., ABPP-CN
Professor and Chief, Section of Neuropsychology
Department of Neuro-Oncology
M.D. Anderson Cancer Center

Cancer patients experience numerous adverse symptoms, including cognitive dysfunction, fatigue, pain, sleep disturbance, and others. Interest in the pathogenesis, pattern of symptoms and interventions is growing both in the scientific literature, but also in lay publications. As cancer is now largely considered to be a chronic illness, the treatment of cancer-related symptoms is becoming more of a concern.

Cognitive dysfunction occurs in the majority of cancer patients on active therapy, and is not infrequently a symptom that heralds the diagnosis. In addition, it persists in a substantial number of patients long after treatment is discontinued. This experience of cognitive dysfunction is popularly termed “chemobrain” or “chemofog” although cognitive impairment can be due to a large number of factors, including (1) cancer in the central nervous system, (2) cancers outside of the CNS that have remote effects on brain function, (3) cancer treatment, (4) adjuvant medications, (5) co-existing neurologic or psychiatric disorders unrelated to cancer, and, very rarely (6) secondary gain.

The components of cognitive dysfunction will vary as a result of the specific etiology, but there are several core cognitive domains that appear to be differentially affected. Cancer patients with cognitive dysfunction often present with complaints of memory disturbance. However, objective testing of memory generally demonstrates a restriction of working memory capacity (e.g., the person is able to learn less information, and learning may be less efficient), and inefficient memory retrieval (e.g., spontaneous recall may be somewhat spotty). However, the ability to consolidate or store new information is generally intact, so that the memory disturbance observed in cancer patients is vastly different from that observed in neurodegenerative disorders such as Alzheimer’s disease, and is often subtle and relative to the individual’s pre-illness level of function. Additional common symptoms include periodic lapses of attention, distractibility, and slowed cognitive processing speed. In general, reasoning and intellectual functions are not affected in non-brain cancer patients, but patients often have difficulty performing their normal work due to these cognitive inefficiencies.

The effect of these symptoms on daily life can be quite profound, depending upon the demands present in the individual’s work and home life. Many patients observe that they can no longer multi-task, and that they may become overwhelmed when too much is happening at once. They are often easily distracted, and find that they may go from project to project without getting them done. Cognitive processing speed is generally diminished, so the person is slower to perform their usual activities. Finally, patients note that it takes increased mental effort to perform even routine tasks. This contributes to the fatigue that is often a co-existing symptom. In fact, cognitive impairment generally does not occur in isolation, but interacts in a negative way with fatigue, pain, sleep disturbance, etc.

The impact of cognitive dysfunction on cancer patients depends upon their developmental stage of life, type of work they do, and their pre-illness lifestyle. For instance, the symptoms described above may not significantly affect the quality of life of an older retired person who can take things at his or her own pace.

However, those symptoms may be disabling to an attorney in a court-room setting, and may necessitate changing jobs or going on disability.

Assessment of cognitive function in cancer patients is becoming more routine. For many patients, addressing cognitive problems that exist before treatment begins is important, and the underlying cause can be proactively addressed. In addition, cognitive testing is increasingly becoming an endpoint in clinical trials. In this way, the effect of new agents or treatments on brain function can be evaluated. New studies are incorporating advances in neuroimaging and biomarkers to help improve understanding of the mechanisms by which cognitive dysfunction and other symptoms develop. A number of possible mechanisms are being studied, including the inflammatory response [1, 2], autoimmune phenomena [3], hormonal influences [4], and direct neurotoxicity of specific agents [5,6]. These will guide the development of targeted interventions to minimize the impact of cognitive dysfunction on patients' lives.

CNS Cancers and Treatment

In adult patients with primary malignant brain cancer, presentation of neurocognitive deficits are associated with tumor location, tumor-related epilepsy, lesion type, lesion momentum (i.e. speed of tumor growth) and lesion volume. Although manifestations of the disease vary significantly across patients, Tucha et al. [7] assessed glioma patients with lesions in the temporal or frontal lobes before initiation of any treatment and reported neurocognitive dysfunction in 90% of patients. Executive functions were impaired in 78% and memory and attention were impaired in 60%. However, the specificity and severity of neurobehavioral impairments related to tumor site are often less pronounced than those observed with sudden-onset neurological conditions such as stroke due to the infiltrative nature of the lesions. [8] Individuals who present with low-grade tumors that have been present for many years may have no detectable changes in brain function because of cerebral plasticity and reorganization, [9] whereas those with fast growing tumors may have more widespread impairment because of the inability to

compensate for the rapidly expanding mass.

Brain metastases from other primary cancers is becoming increasingly prevalent due to the increased life expectancy, improvements in the treatment of the primary disease, and better imaging capabilities. [10] Approximately 24% of adult cancer patients will develop brain metastases, and cognitive dysfunction is exceedingly common in addition to neurologic signs and symptoms. Similar to the case of primary brain tumors, radiation to the brain continues to be the mainstay of treatment, and thus also may contribute to cognitive impairment. [10]

Neuropsychological studies of patients before and after radiation treatment document neurocognitive impairments that are consistent with frontal-subcortical dysfunction, including impaired information-processing speed, attention (e.g. working memory), mental flexibility, learning, memory, and frequently a decline in motor functioning, bilaterally, even in patients with no evidence of disease recurrence. [11, 12] One mechanism of the cognitive decline seen in patients treated with brain radiation is related to hippocampal dysfunction resulting from decreased hippocampal neurogenesis and proliferation, as well as increased cell death. [13] In addition, grafted stem cells that are implanted into radiated animal hippocampus have decreased differentiation into neurons, indicating that the microenvironment impacts neurogenesis. There is also an increase in activated microglia, indicating a chronic inflammatory response following cranial radiation exposure. These activated microglia secrete cytokines that negatively affect neural precursor cell proliferation and fate. [14]

Non-CNS Cancers and Treatment

Many studies have found that approximately one-third or more of cancer patients manifest cognitive dysfunction prior to beginning treatment. [1, 15, 16] However, the majority of patients experience declines on treatment and cognitive dysfunction may persist long after treatment is discontinued. [17]

The mechanisms by which chemotherapeutic agents that are not known to cross the blood brain barrier is only recently beginning to be understood.

For instance, methotrexate, 5-fluorouracil and cyclophosphamide induce impairments in spatial memory and other cognitive tasks in mice. [18, 19] Adriamycin has been demonstrated to increase oxidative stress in the brain, which may lead to cell dysfunction or cell death and thus contribute to the symptoms of “chemobrain”. [20] Long term exposure to 13-cis-retinoic acid is associated with decreased hippocampal neurogenesis and cell proliferation in the hippocampus and subventricular zone as well as impaired spatial learning and memory in young adult mice. [21] Dietrich et al. [22] also found that three widely used chemotherapy agents (carmustine, cisplatin and cytosine arabinoside) were more toxic to CNS progenitor cells and nondividing oligodendrocytes than multiple cancer cell lines in vitro, and that they caused increased cell death and decreased cell division in the subventricular zone, the dentate gyrus of the hippocampus and the corpus callosum in mice. These effects were observed for weeks after drug administration ended.

A recent study reported that therapeutic levels of 5-fluorouracil, an agent widely used in breast and colon cancers among others, is associated with delayed damage to myelin associated with altered transcriptional regulation in oligodendrocytes and extensive myelin pathology. In contrast, CNS inflammation and vascular damage was acute and did not appear to be related to the delayed effects on myelin. [23] In addition, myelin damage was associated with increased latency of the auditory brainstem response in vivo. These findings support the notion of delayed white matter injury due to chemotherapy exposure that is consistent with the clinical syndrome observed in patients. These findings are being supported by imaging and electrophysiologic studies in cancer survivors that reveal alterations in metabolism, gray and white matter volumes, and alterations of evoked potentials. [24]

Genetic Risk Factors for Developing Therapy-Induced Cognitive Dysfunction

Clinically, and in most research studies to date, cognitive dysfunction has been found to occur only in a subgroup of patients. This finding has provoked

interest in identifying potential genetic host risk factors that may underlie a given individual’s vulnerability to develop these side effects. Polymorphisms that alter the pharmacodynamics of chemotherapeutic agents may place individuals at greater risk via increased exposure of normal tissue to these agents secondary to reduced metabolism, decreased DNA repair capability, or increased permeability of agents across the blood brain barrier. [25, 26, 27] In children with leukemia treated with methotrexate containing regimens with or without cranial radiation, polymorphisms of genes modulating the folate pathway have been associated with diminished intelligence. [27, 28]

Interventions

Chemotherapy and immunotherapy are a necessary component to the management of many types of cancer. Although not all patients will experience treatment-related neurotoxicity, for a sub-population of patients cognitive symptoms are distressing and disruptive. Clearly, there is a need to explore therapies that may prevent negative side effects or minimize the impact and extent of symptoms that are already present. While determining the nature of the symptom is generally feasible, our understanding of the etiologic mechanisms underlying these symptoms is in its infancy.

In cases where a specific mechanism underlying the neurotoxicity has been characterized, targeted treatment strategies have been explored. For example, treatment with naltrexone (a μ -opioid receptor antagonist) was effective in relieving neurotoxic side effects in 7 of 9 patients undergoing interferon treatment for hematological malignancies. [29] Musselman et al. [30] demonstrated the benefit of pretreatment with paroxetine (e.g., selective serotonin reuptake inhibitor) in minimizing depression in melanoma patients receiving interferon treatment.

Stimulant therapies have proven effective in treating the cognitive dysfunction that is common in cancer patients, [31, 32, 33] and other pharmacologic interventions commonly used to treat other diseases affecting cognitive function are currently being explored. [10, 33] Cognitive and

behavioral intervention strategies that have been studied in the traditional rehabilitation literature with stroke and traumatic brain injury survivors are becoming increasingly common. [34, 35] These interventions often focus on compensatory strategy training, stress management, energy conservation and psychoeducation.

There is a need to develop effective intervention techniques and programs for cancer patients and establish their efficacy through clinical trials. The loss of productivity, societal/economic demands and psychological distress that are associated with cancer are highly significant. Advances in the treatment of cancer is being realized, and we must be ready to meet the needs of these survivors and their caregiving milieu. Effective and proactive assessment and treatment of cognitive dysfunction and other symptoms are a critical component throughout and following cancer treatment.

References

1. Meyers CA, Albitar M, Estey E. Cognitive impairment, fatigue, and cytokine levels in patients with acute myelogenous leukemia or myelodysplastic syndrome. *Cancer* 104:788-793, 2005.
2. Lee BN, Dantzer R, Langley KE, et al. A cytokine-based neuroimmunological mechanism of cancer-related symptoms. *Neuroimmunomodulation* 11:279-292, 2004.
3. Dropcho E. Paraneoplastic disorders. In Meyers CA & Perry JR (eds) *Cognition and Cancer*. Cambridge UK: Cambridge University Press, 2008.
4. Wefel JS, Lenzi R, Theriault RL, et al. The cognitive sequelae of standard dose adjuvant chemotherapy in women with breast cancer: Results of a prospective, randomized, longitudinal trial. *Cancer* 100:2292-2299, 2004.
5. Meyers CA, Kudelka AP, Conrad CA, et al. Neurotoxicity of CI-980, a novel mitotic inhibitor. *Clin Cancer Res* 3:419-422, 1997.
6. Scheibel RS, Valentine AD, O'Brien S, et al. Cognitive dysfunction and depression during treatment with interferon-alpha and chemotherapy. *J Neuropsychiat Clin Neurosci* 16: 185-191, 2004.
7. Tucha O, Smely C, Preier M, et al. Cognitive deficits before treatment among patients with brain tumors. *Neurosurgery* 2000; 47: 324-333.
8. Anderson, SW, Damasio H, Tranel D. Neuropsychological impairments associated with lesions caused by tumor or stroke. *Arch Neurol* 47:397-405, 1990.
9. Meyers CA, Berman SA, Hayman A, et al. Pathological left-handedness and preserved function associated with a slowly evolving brain tumor. *Dev Med Child Neurol* 34:1110-1117, 1992.
10. Khuntia D, Mathew BS, Meyers CA et al. Brain metastases. In Meyers CA & Perry JR (eds) *Cognition and Cancer*. Cambridge UK: Cambridge University Press, 2008.
11. Lee AW, Kwong DLW, Leung SF, et al. Factors affecting risk of symptomatic temporal lobe necrosis: significance of fractional dose and treatment time. *Int J Radiat Oncol Biol Phys* 53:75-85, 2002.
12. Shaw EG, Robbins ME. Biological bases of radiation injury to the brain. In Meyers CA & Perry JR (eds) *Cognition and Cancer*. Cambridge UK: Cambridge University Press, 2008.
13. Monje M L, Mizumatsu S, Fike J R, et al. Irradiation induces neural precursor-cell dysfunction. *Nat Med* 8: 955-962, 2002.
14. Monje M L, Toda H., et al. Inflammatory blockade restores adult hippocampal neurogenesis. *Science* 302(5651): 1760-1765, 2003.
15. Wefel JS, Lenzi R, Theriault R, et al. "Chemobrain" in breast cancer? A prologue. *Cancer* 101: 466-75, 2004.
16. Meyers CA, Byrne KS, Komaki R. Cognitive deficits in patients with small cell lung cancer before and after chemotherapy. *Lung Cancer* 12:231-235, 1995.
17. Wefel JS, Collins R, Kayl AE. Cognitive dysfunction related to chemotherapy and biological response modifiers. In Meyers CA & Perry JR (eds) *Cognition and Cancer*. Cambridge UK: Cambridge University Press, 2008.
18. Winocur G, Vardy J, Binns MA, et al. The effects

- of the anti-cancer drugs, methotrexate and 5-fluorouracil on cognitive function in mice. *Pharmacol Biochem Behav* 85:66-75, 2006.
19. Reiriz AB, Reolon GK, Preissler T, et al. Cancer chemotherapy and cognitive function in rodent models : memory impairment induced by cyclophosphamide in mice. [letter to the editor] *Clin Cancer Res* 12:5000, 2006.
 20. Joshi G, Sultana R, Tangpong J, et al. Free radical mediated oxidative stress and toxic side effects in brain induced by the anti cancer drug adriamycin: insight into chemobrain. *Free Radical Res* 39:1147-54, 2005.
 21. Crandall J, Sakai Y, Zhang J, et al. 13-cis-retinoic acid suppresses hippocampal cell division and hippocampal-dependent learning in mice. *PNAS* 101: 5111-16, 2004.
 22. Dietrich J, Han R, Yang Y, et al. CNS progenitor cells and oligodendrocytes are targets of chemotherapeutic agents in vitro and in vivo. *J Biol* 5:22, 2006.
 23. Han R, Yang YM, Dietrich J, et al. Systemic 5-fluorouracil treatment causes a syndrome of delayed myelin destruction in the CNS. *J Biol* 7:4, 2008.
 24. McDonald BC, Saykin AJ, Ahles TA. Brain imaging investigation of chemotherapy-induced neurocognitive changes. In Meyers CA & Perry JR (eds) *Cognition and Cancer*. Cambridge UK: Cambridge University Press, 2008.
 25. Largillier R, Etienne-Grimaldi MC, Formento JL, et al. Pharmacogenetics of capecitabine in advanced breast cancer patients. *Clin Cancer Res* 12:5496-502, 2006.
 26. Okcu MF, Selvan M, Wang L, et al. Glutathione S-transferase polymorphisms and survival in primary malignant glioma. *Clin Cancer Res* 10:2618-25, 2004.
 27. Barahmani N, Carpentieri S, Li XN, et al. Glutathione S-Transferase M1 and T1 polymorphisms may predict adverse effects after therapy in children with medulloblastoma. *Neuro Oncol* Oct 29, 2008 [Epub ahead of print].
 28. Krajcinovic M, Robaey P, Chiasson S, et al. Polymorphisms of genes controlling homocysteine levels and IQ score following treatment for childhood ALL. *Pharmacogenomics* 6:293-302, 2005.
 29. Valentine AD, Meyers CA, Talpaz M. Treatment of neurotoxic side effects of interferon-alpha with naltrexone. *Cancer Investig* 13:561-6, 1995.
 30. Musselman DL, Lawson DH, Gumnick JF, et al.. Paroxetine for the prevention of depression induced by high-dose interferon alpha. *New Engl J Med* 344:961-6, 2001.
 31. Meyers CA, Weitzner MA, Valentine AD, et al. Methylphenidate therapy improves cognition, mood, and function of brain tumor patients. *J Clin Oncol* 16:2522-7, 1998.
 31. Valentine A, Bruera E. Symptomatic therapies and supportive care issues. In Meyers CA & Perry JR (eds) *Cognition and Cancer*. Cambridge UK: Cambridge University Press, 2008.
 32. Shaw EG, Butler J, Case, LD, et al. Pharmacologic interventions for the treatment of radiation-induced brain injury. In Meyers CA & Perry JR (eds) *Cognition and Cancer*. Cambridge UK: Cambridge University Press, 2008.
 34. Locke DE, Cerhan JH, Malec JF. Behavioral strategies and rehabilitation. In Meyers CA & Perry JR (eds) *Cognition and Cancer*. Cambridge UK: Cambridge University Press, 2008.
 35. Guill B, Raynor RJ. Support services. In Meyers CA & Perry JR (eds) *Cognition and Cancer*. Cambridge UK: Cambridge University Press, 2008.

Neurocognitive Functioning in Childhood Cancer Survivors

Kevin R. Krull, Ph.D., ABPP-CN
Associate Professor
Department of Epidemiology and Cancer Control
St. Jude Children's Research Hospital

Acute Lymphoblastic Leukemia (ALL) and Central Nervous System (CNS) tumors are the two most common forms of cancer in childhood, with annual incidence rates of about 3,250 and 2,200 cases, respectively.[1] Improvements in the treatment of pediatric cancers over the past few decades have led to a remarkable increase in the survival rate, which currently exceeds 80% for ALL and is roughly 65% for CNS tumors.[1, 2] With these incidence and survival rates, it is estimated that 1 out of every 640 young adults will be a pediatric cancer survivor.[3] As many as two thirds of all pediatric cancer survivors experience one or more permanent side effects of their treatment, often referred to as “late effects” (i.e. persisting or developing five or more years following cancer diagnosis).[4] The late effects that commonly occur in survivors of pediatric cancer include neurocognitive impairment, fatigue, obesity, short stature, osteoporosis, osteonecrosis, and cardiac dysfunction.[5] The location of CNS tumors will often impact the type and extent of late effects experienced, though many of the long-term consequences of both cancer types appear related to the various treatment agents used.

The primary treatments that have been associated with neurocognitive problems in pediatric cancer survivors include cranial radiation therapy (CRT) and antimetabolite chemotherapy. In addition to the type of cancer diagnosed, these treatments are applied in varying intensities dependent upon the risk of relapse, age at diagnosis and, in some circumstances, the sex of the child.

CRT is associated with physiological late effects including growth suppression, obesity, and endocrine dysfunction.[6] Steno-occlusive disease of large and small cerebral vessels, abnormal vascular collateralization, aneurysms, and vascular malformations are a particularly morbid complication of CRT because of increased risk for ischemic stroke and intraparenchymal hemorrhage.[7, 8] Higher cumulative doses of cranial radiation and young age at the time of treatment are associated with general intellectual dysfunction and reduced academic performance.[9] Initially, children diagnosed with ALL were treated prophylactically with 2,400 cGy whole brain radiation therapy, though current use is typically reserved for high risk protocols and is limited to 1,800 cGy. Children treated with 2,400 cGy have been reported to display lower IQ's than children treated with 1,800 cGy.[10] Still, 1,800 cGy CRT has been associated with reduced processing speed and attention problems.[11, 12] CNS tumors involve doses as high as 5,500 cGy, though this intensity is typically local and focused at the tumor site.[13]

Many CNS tumors also undergo surgical removal, which can have different effects dependent upon the location of the tumor. For example, surgery in region of the posterior fossa results in cerebellar mutism in roughly 25% of survivors.[14] Although the mutism typically resolves within several weeks, naming and fluency deficits may remain. Antimetabolite chemotherapeutic agents including methotrexate (MTX), 6-mercaptopurine (6-MP), and cytarabine (Ara-C) are commonly used for the treatment of pediatric leukemia, as well as some forms of lymphoma and solid tumors. MTX is administered intrathecally (IT; i.e., directly into the cerebrospinal fluid through the spinal canal) and/or through high dose intravenous (IV) administration.[15] MTX administered through IV readily crosses the blood-brain barrier and, thus, both

routes of administration lead to direct CNS exposure. MTX treatment in children has been linked to attention problems, reduced intelligence, visual-motor decline, and academic problems, particularly in mathematics.[16, 17] The amount or intensity of MTX has been correlated with the degree of neurocognitive problems.[18] Furthermore, intensive MTX therapy has been associated with white matter changes in the frontal lobes.[19]

Glucocorticoids (i.e. prednisone, prednisolone, dexamethasone) are also used for the cancer treatment in children. These agents inhibit glucose utilization by neurons and glia and subsequently increase concentration of glutamate, particularly in the hippocampus, which causes excitotoxic neuronal death as a result of overstimulation.[20] Dexamethasone has been shown to be a potent cytotoxic agent, with higher rates of CNS penetrance than prednisone and prednisolone.[21] Memory problems and reduced visual-spatial organization have been reported in children with ALL treated with dexamethasone compared with prednisone.[22]

There are many other chemotherapeutic agents that are often used in conjunction with CRT and antimetabolite treatment, though their impact on neurocognitive functions has not been well-researched. Common agents that are potentially associated with cognitive or behavioral dysfunction include anthracyclines (e.g., adriamycin, daunomycin, doxorubicin), vinca alkaloids (e.g., vincristine and vinblastine), and bacterial enzymes (e.g. asparaginase). Anthracyclines are often associated with cardiovascular toxicity, though direct cerebrovascular impact has not yet been demonstrated.[23] Vinca alkaloids have been associated with acute peripheral neuropathy.[24] Asparaginase is associated with cerebrovascular complications including venous thrombosis and cerebral hemorrhage.[25]

Pediatric ALL and CNS tumor survivors may suffer from neurocognitive impairment on a transient (i.e., acute) or lasting (i.e., late effects) basis. Impairment may occur in one or more domains that impede learning new information along with maintaining previously learned information, ultimately leading to declines in intelligence and

academic and vocational success, as well as lowered self-esteem and behavioral disorders.

Children diagnosed with ALL demonstrate acute changes in neurocognitive functions during the first two years of chemotherapeutic treatment, with those treated with higher doses of IV MTX demonstrating larger declines.[18] Initial problems in processing speed assessed shortly after treatment initiation has also been correlated to declines visual-motor integration and perceptual problem solving one and two years following diagnosis.[26]

Neurocognitive impairment is one of the most common late effects in long-term survivors of pediatric cancer (i.e. ? 5 years post diagnosis), with 20% to 40% of all patients demonstrating deficits in one or more domains of function.[27, 28] Long-term survivors of pediatric cancer are more likely to need special education services and are rated lower on academic skills when compared with referenced controls.[29] Deficits in mathematics calculation and applied arithmetic problem solving are frequently noted, though reading difficulties have also been reported.[17] Reading problems are reported as particularly problematic in survivors of medulloblastoma.[30] This impact on academics, as well as global cognitive abilities, may not fully emerge until at least five years after diagnosis, with a steady decline in functions over time.[31] In fact, the decline in intelligence test performance after cranial radiation continues progressively for at least six years.[30]

In addition to intellectual functioning and academics, abnormalities in specific neurocognitive skills are reported, particularly processing speed, attention, and memory functions. Behavioral attention problems are also common, and these problems correspond to reduced school performance and teacher rated math difficulties.[32, 33] In a recent survey of 2,979 parents of adolescent survivors, both children with ALL and CNS tumors were identified as having significantly higher rates of attention problems compared to sibling controls.[34]

Long-term survivors of pediatric cancer appear to be at increased risk for brain abnormalities. In a large retrospective multicenter study, pathological brain magnetic resonance imaging (MRI) scans were

reported in 52% of ALL survivors.[35] Although rates of MRI abnormality were higher in children who received cranial irradiation, 39% of the children who received only chemotherapy also displayed abnormal MRI. Abnormal brain imaging has been associated with neurocognitive problems, particularly for the occurrence of white matter abnormalities.[12] Patients treated with CRT display reduced development of academic functions, including mathematics and reading skills, as well as problems with sustained attention, while patients treated with chemotherapy only display attention problems. Furthermore, in both groups, smaller white-matter volumes were significantly associated with impaired sustained attention. Intracerebral calcifications are also correlated with problems in attention, memory, and visual motor skills.[36]

The impact of chemotherapeutic agents on neurocognitive function is not universal, and most investigations have found significant individual variability in outcomes.[28, 37, 38] These differences in outcome studies raise questions of sample representation and individual variability. Samples of clinical convenience may be influenced by motivation for follow-up care or family resources, and may not reflect functioning in the population of survivors.

Age at diagnosis has the potential to influence outcomes due both to maturational difference in brain development, as well as the fact that age impacts risk classification and, thus, treatment intensity. Infants and children older than 10 at diagnosis are at higher risk for disease severity and treatment adjustments are made accordingly.[15] In general, children treated at younger ages are at higher risk for poor neurocognitive outcomes. For chemotherapy treatment, attention problems are more prevalent in children treated at younger ages,[39] while for CRT younger age at treatment is associated with multiple areas of impairment.[9]

Sex of the patient has also been identified as a potential moderator of late effects and neurocognitive outcomes. Boys are reported to display worse event-free survival at two and five years following diagnosis, and higher rates of hematologic relapse.[40, 41] However, females are reported to be at increased risk for adverse

neurocognitive outcomes following chemotherapy,[42, 43] as well as CRT,[44] Differences in neurocognitive outcome may be related to varied sexual dimorphism in male and female brains. During childhood, females have a lower white to gray matter ratios than males, particularly in frontal brain regions.[45] This difference may predispose females to neurocognitive deficits associated with treatments that differential affect white matter integrity.

Advances in treatment of pediatric cancer are associated with a recent trend in evaluating genetic contributions to individual treatment response factors. Genetic characteristics may influence treatment approaches as well as neurocognitive outcomes. For example, genetic polymorphisms in the folate pathway (e.g. 5,10-methylenetetrahydrofolate reductase; MTHFR) have recently been associated with differential functional outcomes in long-term survivors of pediatric leukemia.[33]

Other factors that may have mediating/moderating effects on treatment intensity and/or outcome include neurotoxicity (i.e., leukoencephalopathy), cardiovascular toxicity, and hepatic toxicity. Chemotherapeutic agents are cytotoxic and often result in secondary adverse systemic toxicities to organ systems. MTX has been associated with acute leukoencephalopathy and hepatic toxicity, while anthracyclines have been associated with cardiotoxicity.[46] If these toxicities become overly troublesome, modifications to the treatment regimens may be made. Neurocognitive impairment secondary to organ system toxicities warrants further consideration.

Recent attempts at intervention for neurocognitive consequences of cancer therapy have focused on psychostimulant medication (i.e., methylphenidate). Initial studies demonstrated promise in the treatment of primary attention problems, based on performance on the Conners' Continuous Performance Test (CPT).[47] Similar improvement has been noted on parent and teacher rating scales.[48] However, none of these trials to date have demonstrated long-term efficacy or an impact on higher level cognitive skills.

Direct cognitive rehabilitation of deficits in long-term survivors has also been conducted. Intensive

President's Message
Continued from page 1

Psychology must be prepared to advocate for our profession in the health care debate to come. This appears to be part of the reason APA president James Bray is organizing a Future of Professional Practice (FPP) summit to be held next year. The D40EC voted to contribute money and send delegates to the FPP summit. We must be active at all levels in advocating for our discipline in the future of health care.

Finally, part of the future is likely to be doing more with less. And in this regard let me direct your attention to the Editor's column in this Newsletter. Mike McCrea took the helm this year and is doing a great job with the Newsletter. He and Bill Barr (Chair of the Publications and Communications committee) brought forward a plan to make the Newsletter more accessible and to save a whole bunch of green (trees) and Green (\$\$\$). He has proposed to bring the Newsletter into the digital age. We will produce an online version, disseminated via e-mail and available on the website as a pdf in case you still want to print a paper copy. This will save the organization an estimated several thousand dollars a year, yet make copies of the Newsletter available to all with access to an internet connection. The D40EC heartily supported this proposal. So, be prepared to find an upcoming Newsletter in your e-mail inbox instead of your mail box. I look forward to reading mine on my phone. What an amazing time it is!!

Glenn Smith PhD ABPP-CN
President

attention training has recently been reported to improve primary attention skills in pediatric cancer survivors experiencing attention problems,[49] including reported improvement on parent rating scales.[50] However, no improvement in higher-level cognitive abilities has been demonstrated and no indication has been given that improvement occurs in daily school performance.

In summary, long-term sequelae of pediatric cancer, commonly referred to as late effects, can be particularly problematic and may vary in severity, duration, and manifestation over time. The pattern of problems may be specific at onset (i.e. sustained attention or processing speed), though may evolve into more expansive deficits (i.e. academic learning, executive functioning) as the child ages. Although many children may escape cancer therapy with relatively few problems, a subset of children appears to be particularly affected. Relevant risk factors for neurocognitive late effects include the specific type and intensity of treatment, age at treatment, sex, genetic predispositions, and health of organ systems. As further progress is made in tailoring treatments to individuals or targeting treatments to specific groups (e.g., based on risk or genetic polymorphisms), it will be important to continue to evaluate neurocognitive and psychosocial outcomes with the goal of developing rehabilitative strategies for these survivors to achieve educational and vocational success and to promote the best quality of life possible. Given the gradual onset of significant impairment, treatment approaches should encompass preventative strategies, particularly when increased risk has been determined.

The Children's Oncology Group (COG) is a multi-disciplinary organization funded by the National Cancer Institute to organize and implement clinical trials in pediatric cancer. COG has established guidelines for the standard of care in monitoring the late effects of long-term survivors of pediatric cancer (www.survivorshipguidelines.org).[51] These guidelines call for neurocognitive evaluation of all patients treated with CRT or antimetabolite chemotherapy. A recent extension to this recommendation calls for such testing to include assessment of intellectual, academic, and specific neurocognitive processes.[52] It was further

recommended that such testing occur as a baseline when the patient enters the phase of long-term follow-up, with re-evaluations conducted at times of life transition and when academic difficulties occur.

References

1. Ries, L.A.G., et al., *SEER Cancer Statistics Review, 1975-2004*. 2007, National Cancer Institute: Bethesda, MD. p. http://seer.cancer.gov/csr/1975_2004/.
2. Pui, C.H. and W.E. Evans, *Treatment of acute lymphoblastic leukemia*. *N Engl J Med*, 2006. **354**(2): p. 166-78.
3. Jemal, A., et al., *Cancer statistics, 2006*. *CA Cancer J Clin*, 2006. **56**(2): p. 106-30.
4. Oeffinger, K.C. and M.M. Hudson, *Long-term complications following childhood and adolescent cancer: foundations for providing risk-based health care for survivors*. *CA Cancer J Clin*, 2004. **54**(4): p. 208-36.
5. Hewitt, M., S.L. Weiner, and J.V. Simone, *Childhood Cancer Survivorship: Improving Care and Quality of Life*, ed. N.R. Council. 2003, Washington, D.C.: National Academy of Sciences. 224.
6. Geenen, M.M., et al., *Medical assessment of adverse health outcomes in long-term survivors of childhood cancer*. *Jama*, 2007. **297**(24): p. 2705-15.
7. Kondoh, T., et al., *Moyamoya syndrome after prophylactic cranial irradiation for acute lymphocytic leukemia*. *Pediatr Neurosurg*, 2003. **39**(5): p. 264-9.
8. Duhem, R., et al., *Cavernous malformations after cerebral irradiation during childhood: report of nine cases*. *Childs Nerv Syst*, 2005. **21**(10): p. 922-5.
9. Hoppe-Hirsch, E., et al., *Malignant hemispheric tumors in childhood*. *Childs Nerv Syst*, 1993. **9**(3): p. 131-5.
10. Moore, I.M., et al., *Cognitive function in children with leukemia. Effect of radiation dose and time since irradiation*. *Cancer*, 1991. **68**(9): p. 1913-7.
11. Waber, D.P., et al., *Neuropsychological outcomes from a randomized trial of triple intrathecal chemotherapy compared with 18 Gy cranial radiation as CNS treatment in acute lymphoblastic leukemia: findings from Dana-Farber Cancer Institute ALL Consortium Protocol 95-01*. *J Clin Oncol*, 2007. **25**(31): p. 4914-21.
12. Reddick, W.E., et al., *Smaller white-matter volumes are associated with larger deficits in attention and learning among long-term survivors of acute lymphoblastic leukemia*. *Cancer*, 2006. **106**(4): p. 941-9.
13. Merchant, T.E., *Current management of childhood ependymoma*. *Oncology (Williston Park)*, 2002. **16**(5): p. 629-42, 644; discussion 645-6, 648.
14. Robertson, P.L., et al., *Incidence and severity of postoperative cerebellar mutism syndrome in children with medulloblastoma: a prospective study by the Children's Oncology Group*. *J Neurosurg*, 2006. **105**(6 Suppl): p. 444-51.
15. Pui, C.H., L.L. Robison, and A.T. Look, *Acute lymphoblastic leukaemia*. *Lancet*, 2008. **371**(9617): p. 1030-43.
16. Montour-Proulx, I., et al., *Cognitive changes in children treated for acute lymphoblastic leukemia with chemotherapy only according to the Pediatric Oncology Group 9605 protocol*. *J Child Neurol*, 2005. **20**(2): p. 129-33.
17. Peterson, C.C., et al., *A meta-analysis of the neuropsychological sequelae of chemotherapy-only treatment for pediatric acute lymphoblastic leukemia*. *Pediatr Blood Cancer*, 2008.
18. Carey, M.E., et al., *Brief report: effect of intravenous methotrexate dose and infusion rate on neuropsychological function one year after diagnosis of acute lymphoblastic leukemia*. *J Pediatr Psychol*, 2007. **32**(2): p. 189-93.
19. Reddick, W.E., et al., *Quantitative morphologic evaluation of magnetic resonance imaging during and after treatment of childhood leukemia*. *Neuroradiology*, 2007. **49**(11): p. 889-904.
20. Sapolsky, R.M., *The possibility of neurotoxicity in the hippocampus in major depression: a primer on neuron death*. *Biol Psychiatry*, 2000. **48**(8): p. 755-65.
21. Mitchell, C.D., et al., *Benefit of dexamethasone compared with prednisolone for childhood acute*

- lymphoblastic leukaemia: results of the UK Medical Research Council ALL97 randomized trial.* Br J Haematol, 2005. **129**(6): p. 734-45.
22. Waber, D.P., et al., *Cognitive sequelae in children treated for acute lymphoblastic leukemia with dexamethasone or prednisone.* J Pediatr Hematol Oncol, 2000. **22**(3): p. 206-13.
23. Kremer, L.C., et al., *Frequency and risk factors of subclinical cardiotoxicity after anthracycline therapy in children: a systematic review.* Ann Oncol, 2002. **13**(6): p. 819-29.
24. Reinders-Messelink, H.A., et al., *Analysis of handwriting of children during treatment for acute lymphoblastic leukemia.* Med Pediatr Oncol, 2001. **37**(4): p. 393-9.
25. Kieslich, M., et al., *Cerebrovascular complications of L-asparaginase in the therapy of acute lymphoblastic leukemia.* J Pediatr Hematol Oncol, 2003. **25**(6): p. 484-7.
26. Hockenberry, M., et al., *Longitudinal evaluation of fine motor skills in children with leukemia.* J Pediatr Hematol Oncol, 2007. **29**(8): p. 535-9.
27. Moleski, M., *Neuropsychological, neuroanatomical, and neurophysiological consequences of CNS chemotherapy for acute lymphoblastic leukemia.* Arch Clin Neuropsychol, 2000. **15**(7): p. 603-30.
28. Krull, K.R., et al., *Screening for neurocognitive impairment in pediatric cancer long-term survivors.* J Clin Oncol, 2008. **26**(25): p. 4138-43.
29. Christie, D., et al., *Intellectual performance after presymptomatic cranial radiotherapy for leukaemia: effects of age and sex.* Arch Dis Child, 1995. **73**(2): p. 136-40.
30. Mulhern, R.K., et al., *Neurocognitive consequences of risk-adapted therapy for childhood medulloblastoma.* J Clin Oncol, 2005. **23**(24): p. 5511-9.
31. Brown, R.T. and A. Madan-Swain, *Cognitive, neuropsychological, and academic sequelae in children with leukemia.* J Learn Disabil, 1993. **26**(2): p. 74-90.
32. Buizer, A.I., et al., *Behavioral and educational limitations after chemotherapy for childhood acute lymphoblastic leukemia or Wilms tumor.* Cancer, 2006. **106**(9): p. 2067-75.
33. Krull, K.R., et al., *Folate pathway genetic polymorphisms are related to attention disorders in childhood leukemia survivors.* J Pediatr, 2008. **152**(1): p. 101-5.
34. Schultz, K.A., et al., *Behavioral and social outcomes in adolescent survivors of childhood cancer: a report from the childhood cancer survivor study.* J Clin Oncol, 2007. **25**(24): p. 3649-56.
35. Hertzberg, H., et al., *CNS late effects after ALL therapy in childhood. Part I: Neuroradiological findings in long-term survivors of childhood ALL--an evaluation of the interferences between morphology and neuropsychological performance. The German Late Effects Working Group.* Med Pediatr Oncol, 1997. **28**(6): p. 387-400.
36. Iuvone, L., et al., *Long-term cognitive outcome, brain computed tomography scan, and magnetic resonance imaging in children cured for acute lymphoblastic leukemia.* Cancer, 2002. **95**(12): p. 2562-70.
37. Kingma, A., et al., *No major cognitive impairment in young children with acute lymphoblastic leukemia using chemotherapy only: a prospective longitudinal study.* J Pediatr Hematol Oncol, 2002. **24**(2): p. 106-14.
38. Spiegler, B.J., et al., *Comparison of long-term neurocognitive outcomes in young children with acute lymphoblastic leukemia treated with cranial radiation or high-dose or very high-dose intravenous methotrexate.* J Clin Oncol, 2006. **24**(24): p. 3858-64.
39. Buizer, A.I., et al., *Chemotherapy and attentional dysfunction in survivors of childhood acute lymphoblastic leukemia: effect of treatment intensity.* Pediatr Blood Cancer, 2005. **45**(3): p. 281-90.
40. Shuster, J.J., et al., *Prognostic significance of sex in childhood B-precursor acute lymphoblastic leukemia: a Pediatric Oncology Group Study.* J Clin Oncol, 1998. **16**(8): p. 2854-63.
41. Margolin, J.F., C.P. Steuber, and D.G. Poplack, *Acute Lymphoblastic Leukemia*, in *Principles and Practice of Pediatric Oncology*, P.A. Pizzo and D.G. Poplack, Editors. 2006, Lippincott, Williams, & Wilkins: Philadelphia, PA. p. 538-

- 590.
42. Buizer, A.I., et al., *Visuomotor control in survivors of childhood acute lymphoblastic leukemia treated with chemotherapy only*. J Int Neuropsychol Soc, 2005. **11**(5): p. 554-65.
 43. Langer, T., et al., *CNS late-effects after ALL therapy in childhood. Part III: neuropsychological performance in long-term survivors of childhood ALL: impairments of concentration, attention, and memory*. Med Pediatr Oncol, 2002. **38**(5): p. 320-8.
 44. Waber, D.P., et al., *Sex differences in cognitive processing in children treated with CNS prophylaxis for acute lymphoblastic leukemia*. J Pediatr Psychol, 1990. **15**(1): p. 105-22.
 45. Cosgrove, K.P., C.M. Mazure, and J.K. Staley, *Evolving knowledge of sex differences in brain structure, function, and chemistry*. Biol Psychiatry, 2007. **62**(8): p. 847-55.
 46. Adamson, P.C., et al., *General Principles of Chemotherapy*, in *Principles and Practice of Pediatric Oncology*, P.A. Pizzo and D.G. Poplack, Editors. 2006, Lippincott, Williams, & Wilkins: Philadelphia, PA. p. 290-365.
 47. Thompson, S.J., et al., *Immediate neurocognitive effects of methylphenidate on learning-impaired survivors of childhood cancer*. J Clin Oncol, 2001. **19**(6): p. 1802-8.
 48. Mulhern, R.K., et al., *Short-term efficacy of methylphenidate: a randomized, double-blind, placebo-controlled trial among survivors of childhood cancer*. J Clin Oncol, 2004. **22**(23): p. 4795-803.
 49. Butler, R.W. and D.R. Copeland, *Attentional processes and their remediation in children treated for cancer: a literature review and the development of a therapeutic approach*. J Int Neuropsychol Soc, 2002. **8**(1): p. 115-24.
 50. Butler, R.W., et al., *A multicenter, randomized clinical trial of a cognitive remediation program for childhood survivors of a pediatric malignancy*. J Consult Clin Psychol, 2008. **76**(3): p. 367-78.
 51. Group, C.s.O. *Long-term follow-up guidelines*. 2006 [cited 2008; Available from: www.survivorshipguidelines.org].
 52. Nathan, P.C., et al., *Guidelines for identification*

of, advocacy for, and intervention in neurocognitive problems in survivors of childhood cancer: a report from the Children's Oncology Group. Arch Pediatr Adolesc Med, 2007. **161**(8): p. 798-806.

Congratulations to New APA Division 40 Fellows

APA Fellow status is an honor that recognizes evidence of unusual and outstanding contribution to or performance in the field of psychology that has had impact beyond a local, state, or regional level. We in Division 40 view election of a Fellow as an honor not only for the individual but for the Division as well. We are delighted to formally acknowledge and congratulate these individuals who recently joined the ranks of APA Fellow in Division 40:

William B. Barr
 Kyle Brauer Boone
 Manfred F. Greiffenstein
 H. Julia Hannay
 Ronald M. Lazar
 Tatia Lee
 Cheryl Silver
 Edith V. Sullivan
 Mieke Verfaellie
 Michael Westerveld

Questions regarding the Fellow nomination process can be addressed to Ida Sue Baron Ph.D., ABPP; Chair, Division 40 Fellows Committee at ida@isbaron.com.

2008 Division 40 Award Winners

The Awards Subcommittee of the Div 40 Science Advisory Committee is pleased to announce the recipients of this year's Benton-Meier Scholarships, Junior Investigator Pilot Grants, and Student Travel Awards.

Benton-Meier Scholarship

Two annual \$2,500 **Benton-Meier scholarships** are funded by the American Psychological Foundation to support neuropsychology graduate students with a record of achievement indicating a promising career in neuropsychological research. Information regarding this annual award can be found at <http://www.apa.org/apf/hecaen.html> . Deadline for the next round of applications is June 1, 2009.

Congratulations to the 2008 recipients:

Ania Mikos
Department of Clinical & Health Psychology
University of Florida

Ida Kellison
Department of Clinical & Health Psychology
University of Florida

Junior Investigator Pilot Grant

Division 40 funds a \$10,000 **Junior Investigator Pilot Grant**, the purpose of which is to support early career members who are collecting preliminary data for the purpose of securing subsequent extramural funding for neuropsychological research. The next cycle of grant applications (due September 1, 2009) will be announced in Spring 2009. Congratulations to this cycle's grant recipients:

Heather Belanger, PhD
University of South Florida
Title: *Intervention for Postconcussion Symptoms in Active Duty, Veteran, and Civilian Participants with a History of mTBI*

Farzin Irani, PhD
University of Pennsylvania
Title: *Neural Correlates of Familiar Face Recognition in Schizophrenia*

2008 Student Travel Grant

Division 40 funds a \$2,500 **Student Travel Grant** program for neuropsychology graduate students or first-year postdoctoral residents to offset costs for attendance of the annual APA convention. The next cycle of grant applications will be announced in Spring 2009. Congratulations to this cycle's travel grant recipients:

Lisa Jacola
University of Cincinnati

Melissa Castro
Ponce School of Medicine

Announcement

Division 40 Launches Web-based Directory of Science Membership Research Expertise

To promote the interests of neuropsychological science within APA, Division 40 has developed a web-based science membership directory/database. All members engaged in scholarly inquiry are invited to log on and register their research expertise and funding experiences. By doing so, you will help guide the Division's efforts in advocating for neuropsychological science. In addition, members will have an opportunity to indicate their interest in becoming more active in advancing the neuropsychology science agenda within APA by serving on advisory panels, attending interdivisional summits, reviewing policy statements, etc. when Division input on topics related to their area of research expertise is sought.

To access the science membership directory/database website, please visit www.div40.org/sacsid or follow the link from the Division 40 home page (www.div40.org). **Registering your information will take approx. 10 minutes.**

John A. Lucas, Ph.D., ABPP/CN
Chair, Division 40 Science Advisory Committee

Glenn E. Smith, Ph.D., ABPP/CN
President, Division 40

Practice Advisory Committee

Neil Pliskin, Ph.D., ABPP-CN, Chair

Your Practice Advisory Committee has been monitoring and working on the following issues during the past 6 months:

CPT Test Coding Update

There have been positive developments in the summer of 2008 which may finally clarify and address many of the reimbursement issues that our members have had with using the CPT Test Codes. On June 19, 2008 the Centers for Medicare and Medicaid Services (CMS) posted on the agency's website questions and answers (Q&As) that clarify how the CPT codes for psychological and neuropsychological testing should be used. APA requested this information after a CMS transmittal issued in September 2006 resulted in confusion about Medicare's rules for billing multiple codes when testing is administered by a technician or computer. The Q&As clarify when the professional codes for psychological and neuropsychological testing, 96101 and 96118 respectively, can be used to account for the integrative interpretation and comprehensive report writing for services administered by a technician or computer.

As has been the case for almost two years, the Division 40 Practice Advisory Committee has worked closely with the APA Practice Directorate, the National Academy of Neuropsychology and the Society of Personality Assessment to address the confusion created by the 2006 CMS transmittal. After months of work by APA and CMS, the CPT Editorial Panel agreed in February 2007 to add language to the *CPT 2008* manual stating that codes 96101 and 96118 can be used for time spent integrating other sources of clinical data, including previously completed and reported technician and computer-administered tests.

Despite the new CPT language, psychologists and facility compliance officers still have had reservations about the proper use of the codes based on the 2006 CMS transmittal. Knowing that only a statement from CMS would address those concerns, APA sought to have the agency take further action. In June 2007, CMS agreed to consider publishing a series of Q&As that APA drafted about the codes' usage. While this was a very unusual step for CMS to take, it recognized the need to resolve the confusion arising from the 2006 transmittal. After making some slight revisions and undergoing a very long clearance process, CMS has now posted the Q&As

(https://questions.cms.hhs.gov/cgi-bin/cmshhs.cfg/php/enduser/print_alp.php?faq_array=9177,9179,9176,9180,9181,9182,9183,9178) which are also reprinted below:

Frequently Asked Questions and Answers on CPT Testing Codes

Question **What are the supervision requirements for diagnostic psychological and neuropsychological tests?**

Answers: Under the diagnostic test provision as authorized under Medicare law at section 1861(s)(3) of the Social Security Act (the Act) and interpreted under regulations at 42 CFR 410.32, all diagnostic tests are assigned a certain level of supervision. Generally, regulations governing the provision of diagnostic tests require a physician to provide the appropriate level of supervision for such tests. That is, the physician must either provide general, direct, or personal supervision. However, for diagnostic psychological and neuropsychological tests (96101-96120), there is a regulatory exception at 42 CFR 410.32(b)(2)(iii) that allows either a clinical psychologist (CP) or a physician to provide the required general supervision for diagnostic psychological and neuropsychological tests. Moreover, nonphysician practitioners (NPPs) such

as nurse practitioners (NPs) and clinical nurse specialists (CNSs) under 42 CFR 410.32(b)(2)(B)(v), and physician assistants (PAs) under 42 CFR 410.32(b)(3) who personally perform diagnostic psychological and neuropsychological tests are excluded from the supervision requirements for diagnostic tests. However, they must meet the collaboration and physician supervision practice requirements under their respective benefits.

Question Are expenses for diagnostic psychological and neuropsychological tests subject to the payment limitation for outpatient mental health treatment services?

Answers: In most cases, expenses for diagnostic psychological tests and neuropsychological tests are not subject to the payment limitation on certain outpatient mental health treatment services. The outpatient mental health treatment limitation (the limitation) is the payment limitation on treatment services for mental, psychoneurotic and personality disorders as authorized under section 1833(c) of the Social Security Act. However, the limitation does apply to diagnostic psychological and neuropsychological tests when these tests are performed to evaluate a patient's progress during treatment rather than to establish or confirm the patient's diagnosis. (See section 210.1, Chapter 12 of the Medicare Claims Processing Manual, Pub.100-04).

Question Do Current Procedural Terminology (CPT) codes for psychological and neuropsychological tests include tests performed by technicians and computers?

Answers: Yes. Effective January 1, 2006, CPT codes for psychological and neuropsychological tests include tests performed by technicians and computers (CPT codes 96102, 96103, 96119 and 96120) in addition to tests performed by physicians, clinical psychologists (CPs), independently practicing psychologists (IPPs) and other qualified nonphysician practitioners (NPPs). The payment amounts for tests performed by a technician or a computer are adjusted depending upon whether the service was performed in a facility or non-facility setting.

Question Can more than one CPT code for psychological or neuropsychological testing be billed on the same date of service for the same patient?

Answers: Yes. If several different, clinically appropriate tests are administered on the same date to the same patient (whether by a physician/psychologist, technician or by computer), then the appropriate testing codes for psychological testing or neuropsychological testing can be billed together. More than one code can also be billed when several distinct tests are administered to the same patient on the same date of service via technician (96102/96119) or computer (96103/96120), and the physician/psychologist needs to integrate the separate interpretations and written reports for each of these tests into a comprehensive report.

Question Can more than one CPT code for psychological or neuropsychological testing be billed together on the same date of service for the same patient if all of the testing is administered by a technician and/or computer?

Answers: Yes. The technician-administered code (96102/96119) is billed based on the number of hours that the technician spends face-to-face with the patient. The computer-administered testing code (96103/96120) is billed once regardless of the time spent completing the tests. Note, however, that when testing is administered by a technician or a computer, the time that the physician/psychologist spends interpreting and reporting the results of each individual test is already included in each of these codes.

Question Can more than one CPT code for psychological or neuropsychological testing be billed together for services rendered to the same patient but on different dates?

Answers: The physician/psychologist is expected to bill for the work he/she performed on that date of service. If all of the testing is conducted by a physician/psychologist, then the professional code should be billed for the time spent on test administration, interpretation and report preparation, as well as integration of previously interpreted test results into a comprehensive report (96101 or

96118). Only the appropriate technician administered or computer administered codes can be billed on the actual date of service if a physician/psychologist interprets and writes a report on individual tests administered by a technician (96102 or 96119) or computer (96103 or 96120). The interpretation and reporting of the individual test results by the physician/psychologist which may sometimes occur on a different date than the testing date are already captured in the payment for the technician and computer-administered codes.

Question Should I bill the CPT code for computer-administered psychological (96103) or neuropsychological testing (96120) if my patient takes a paper-and-pencil test, and I use a computer to score it?

Answers: The computer codes (96103 and 96120) can only be billed when a computer is used to administer tests. The codes cannot be billed if the computer is used only to score tests. For paper-and-pencil tests, the physician/psychologist should bill appropriately for any other service provided.

Question Who is authorized by Medicare to bill for CPT code 96125 (that was added under CPT effective January 1, 2008)?

Answers: CPT code 96125 (standardized cognitive performance testing (eg, Ross Information Processing Assessment) per hour of a qualified health care professional's time, both face-to-face time administering tests to the patient and time interpreting these test results and preparing the report) is designated under Medicare as an "always therapy" code. Physical therapists (PTs), occupational therapists (OTs), and speech language pathologists (SLPs) may bill this code for patients only when the patient is under a therapy plan of care. (Please note that CPT Changes: An Insider's View 2008 suggests that when testing like that performed under 96125 is performed by a physician or a psychologist, a code from the 96101-96103 or 96118-96120 series should be reported.)

The Division 40 PAC will continue to monitor this situation closely.

Training Issue

In its September 2006 transmittal, the Centers for Medicare and Medicaid Services reiterated the long held rule that Medicare Part B funds cannot be used to support the clinical time for trainees. As the proper use of the new testing codes becomes less of an issue, it is anticipated that Medicare will begin to focus more efforts towards enforcement of this trainee rule. This means that individual practitioners and programs who utilize trainees could eventually be audited to insure that no trainees's time is billed to Medicare. Therefore, the trainee issue continues to be a huge potential crisis looming for practice and education in neuropsychology.

The situation we find ourselves in is that according to the federal government we are not classified as Physicians while many other specialties (see podiatrists for example) are. As such, we cannot qualify for Graduate Medical Education (GME) funds but can't bill Medicare because of GME.

The PAC has been working on raising awareness of this issue for over a year by involving APPIC, the Education Directorate and the Practice Directorate. While other interim solutions are being considered, it will take an act of Congress to get Psychology included in the GME program, which is the only viable long-term fix. With the successes of the legislative agenda this year (i.e., mental health parity, Medicare reimbursement; see Federal Advocacy Coordinator report below), the PAC will continue to advocate to make the GME issue a high priority for the new legislative year.

New York Technician Issue

As described in my last report, the New York State Psychological Association (NYSPA) Council voted 25 to 8 on 11/9/2007 to support Legislative Draft #11, which would enable neuropsychologists in New York State to return to the use of technicians when providing assessment services. Unfortunately there has been little progress since this last report. Although neuropsychologists in NY (through their trade organization NYSAN) now have the NYSPA backing to move forward on the technician legislation, the technician bill is clearly not at the top

of NYSPA's agenda and they do not have the experienced personnel necessary for moving it through the legislature. Hence there is a need for NYSAN to employ its own lobbyist with the support of national organizations such as the American Psychological Association and the Division of Clinical Neuropsychology. The next main goal is to arrange a summit meeting between members of NYSAN and NYSPA in preparation for a formal meeting with members of the State Education Department, high-level NYSPA officials, and national leaders in neuropsychology and APA. Such a meeting would be the first time that all key members needed for advancing the technician bill would be assembled, in the hopes of arriving at language that would facilitate finding a legislative sponsor. The PAC will continue to work closely with NY colleagues in NYSPA and NYSAN to achieve these goals.

Science Advisory Committee

John A. Lucas, Ph.D., ABPP-CN, Chair

The Science Advisory Committee (SAC) facilitates the scientific mission of Division 40 by communicating and promoting the integration of scientific goals within the Division, within APA, and across professions. Recent activities include:

The APA Science Leadership Conference was held in October 2008. Division 40 members in attendance included Robert Bilder (Div40 representative), Jennifer Manly (Board of Scientific Affairs member), Deborah Weber (Div40 Early Career chair), and Paul Craig (APA Treasurer). The theme of the meeting was innovations in dissemination of psychological science. Dr. Bilder discerned two broad areas of interest where Div40 could make important contributions. First, Div40 can take the lead in elaborating neuropsychology concepts within a broader effort to define formally the concepts and measurements used widely in psychology. The goal of this overarching effort will be to represent existing knowledge, reflect both consensus and disagreements, and facilitate links to other emerging repositories of biological knowledge, possibly

through modifications to the APA PsycInfo database. A second effort is the plan to develop a national assessment knowledgebase through various means such as the aggregation of summary psychometric data from the published literature. We will continue to follow these developments and advocate for continued Div40 representation as these and other projects evolve.

A Science Membership Database has been created to facilitate the promotion of neuropsychological science within the division and within APA. Div40 members engaged in research are encouraged to access the database and enter information regarding their area(s) of research expertise and funding sources. Members will also be given an opportunity to indicate whether they would be willing to assist Div40 and/or APA in committee work or policy development that would benefit from their specific expertise. To access the science membership directory/database website, please visit www.div40.org/sacsid or follow the link from the Division 40 home page (www.div40.org).

Committee Members

The following members ended their committee service at the conclusion of the August 2008 APA convention: Drs. Mark Aloia, William Barr, Desiree Byrd, Tanis Ferman, Bonny Forrest, Tessa Hart, David Loring (Awards Subcommittee Chair), Mary Machulda, Otto Pedraza, Laurie Rilling, Kathie Welsh-Bohmer. Their service to the SAC and Division 40 has been greatly appreciated.

Current SAC members include: Adam Brickman, Dean Beebe, Corwin Boake, Meryl Butters, Jessica Chapin, Jovier Evans, Philip Fastenau, Laura Flashman (Awards Subcommittee Chair), Amy Heffelfinger, Ramona Hopkins, Sterling Johnson, Liza Kozora (Transdisciplinary Research Subcommittee Chair), Christina Meyers, Sid O'Bryant, Robert Paul, Beth Rush, Alex Troster, Jennifer Vasterling

Early Career Psychologist Committee

Deborah Weber, Ph.D., Chair

Early Career Psychologist (ECP) Survey

Early Career Psychologists – we need your input! To find out more about Division 40 ECPs the Division 40 ECP Committee is conducting a needs assessment survey. By conducting a needs assessment survey we want to identify and prioritize the needs and issues relevant to ECPs in neuropsychology in order to assist/guide the Committee in creating and supporting opportunities that further professional development and provide informational resources and services for ECPs. We hope this survey will help us identify areas to focus on (ex: types of convention programming, mentoring activities, resources needed, major issues/obstacles, etc).

The survey is being sent to over 450 Division 40 ECPs who have email address on file. If you are an ECP (within seven years of receiving your doctorate) and you did not receive an email about the survey and would like to participate send an email to deb_weber@yahoo.com with “D40 ECP Survey” in the subject line.

ECP Social at INS

Join us at INS for an ECP social hour. The social hour will be on Thursday, February 12th after INS programming. The time of this event is to be announced, so please check the message board when you arrive at the INS meeting.

Congratulations Dr. Steven Woods – Early Career Award Winner

Dr. Steven Woods is the 2008 Robert A. & Phyllis Levitt Early Career Award Winner.

Dr. Wood is an Assistant Professor (in residence) in the Department of Psychology at the University of California, San Diego. He earned his B.S. in psychology in 1994 from Portland State University in Portland, Oregon. In 2000, he received his Psy.D. in clinical psychology (neuropsychology track) from the Virginia Consortium, which is a joint doctoral program comprised of The College of William & Mary, Eastern Virginia Medical School, Norfolk

State University, and Old Dominion University. Dr. Woods’ completed his internship in clinical neuropsychology at the VA Connecticut Healthcare System (West Haven). His postdoctoral fellowship was conducted under the mentorship of Dr. Alexander I. Tröster at the University of Washington School of Medicine. Dr. Woods’ research focuses on the application of cognitive models of language (e.g., verb generation) and memory (e.g., prospective memory) to the study of neuroAIDS and substance abuse. For example, he is currently the Principal Investigator on an NIMH-funded R01 award to study the cognitive mechanisms and functional consequences (e.g., medication nonadherence) of prospective memory impairment in older adults with HIV infection.

APA EARLY CAREER NEWS

The APA Committee on Early Career Psychologists (CECP) recently conducted a survey of more than 2, 475 ECPs (both APA and non-APA members). Several key findings emerged from the survey. Overall, debt amounts continue to increase and are a major challenge for ECPs. Over 75 percent of ECPs participating in the survey had education-related debt upon receipt of their doctoral degree with ethnic minorities having slightly higher debt levels than non-ethnic minorities. PsyDs had almost double the mean debt levels when compared to PhDs and EdDs. Individuals under 30 had the highest level of debt with those who were divorced having the second highest debt level. Additionally, over a third of participants identified finances, family, and caregiver responsibilities (especially for women) as factors negatively impacting their career. One finding from the survey particularly relevant to Division 40 members is that ECPs who are neuropsychologists are reporting a high debt load after completing their training (over \$70,000) compared to other specialties/subfields in the field of psychology. For more results of the survey go to: http://www.apa.org/earlycareer/pdf/2007_Early_Career_Psychologists_Survey_Report.pdf

The Early Career Psychologist Financial Planning Brochure is now available to APA members at: http://members1.apa.org/earlycareer/Financial_Handbook.pdf

List serve:

You can join the CECP Early Career Listserv, a forum dedicated to the needs of early career psychologists that includes ECPs from across APA Divisions and the State and Provincial Psychological Associations. To subscribe to the list, send an email to listserv@lists.apa.org with the following text in the body of the message: **SUBSCRIBE EARLYCAREER** (example: SUBSCRIBE EARLYCAREER Robert Smith).

Education Advisory Committee (EAC)

Cindy Cimino, Ph.D., Chair

Continuing Members: Cindy Cimino (Chair), Rus Bauer, John Deluca, Maureen Lacy, Joel Morgan, Neil Pliskin, Tony Stringer, Desiree White, John Woodard

Organizational Representatives: Jacobus Donders (APPC), Beth Slomine (AITCN), Katy Mateer (ADECN), John Strang (ANST), Deborah Weber (Division 40 Early Career Psychologists Committee)

Recent activities of the EAC include the following:

1. Dr. Doug Ris, who served as Chair of the EAC since 2004, has ended his term of office. We thank Dr. Ris for his time and efforts and for ably serving the committee during this time. Dr. Cindy Cimino will serve as new Chair of the EAC for 2008-2011.

2. The structure of the EAC committee has been reorganized to include Continuing Members and Organizational Representatives. Continuing Members will serve as the core of the committee to ensure continuity and to maintain momentum for the activities of the committee. Organizational Representatives, who may vary from year to year, will serve to assure close communication with relevant training organizations in neuropsychology and to facilitate joint efforts to improve educational initiatives and activities at all levels of training.

3. Dr. Cimino represented the EAC and Division 40

at the APA Consolidated Meeting in October 2008 in Washington, DC. Several issues of significant interest to education in neuropsychology were discussed. The most immediate issue concerns licensure at the doctoral level and how this will be implemented by state licensing boards. More information on this and other issues will follow from the Education Advisory Committee as it becomes available.

4. The Division 40 website listing of training programs has continued to grow and includes 30 Doctoral programs, 38 Internship programs and 74 Postdoctoral programs as of this date.

5. The EAC in conjunction with ANST plans to implement a Frequently Asked Questions (FAQ) section to the EAC portion of the Division 40 website to aid students who seek information about various levels of training. Please submit your thoughts and suggestions to cimino@mail.usf.edu.

Newsletter

Newsletter 40 is the official publication of Division 40.
The Editor is Michael McCrea, PhD, ABPP-CN.
Dr. McCrea's address is:
721 American Avenue, Suite 501,
Waukesha, WI 53188.
Email: Michael.mccrea@phci.org
Division 40's website is: www.div40.org
Webmasters are William Barr, PhD, ABPP-CN and
Michael Cole, PhD

Newsletter
