NEURotransmitter Communicating our message.

Cognitive Late Effects in Children Treated with Radiation for Brain Tumors: Can Physical Activity Improve Your Child's Functioning?

Feature Article:

By Pam Wolters & Amanda Rhodes, Pediatric Oncology Branch, National Cancer Institute, (NCI)

Children treated with cranial radiation therapy (CRT) for brain tumors are at risk for developing difficulties with cognitive functions such as attention, mental processing speed, and memory.^{1,2} In turn, these difficulties can affect learning and school performance. These changes are called "cognitive late effects" because they can emerge months or years after treatment ends. Research indicates that cognitive late effects can be due to a significant loss of a fatty substance in the brain that speeds up the signals between brain cells (white matter)³ and a loss of neuron cells in a brain structure involved in memory (hippocampus)⁴ after CRT. Scientists are starting to under-



stand the pattern and cause of these cognitive effects, but there is limited research on interventions to reduce or prevent the cognitive difficulties associated with CRT.

Interventions to remediate cognitive late effects are emerging but need more research. Studies have investigated the use of medication for attention difficulties,⁵ individualized educational training programs to teach strategies to enhance learning,⁶ and computerized cognitive training to improve working memory problems.⁷ Some positive results were found from these studies, but other outcomes remained unchanged. A potential new intervention for cognitive late effects involves physical activity. Research indicates that physical activity affects the same brain mechanisms and cognitive functions that are damaged by CRT and chemotherapy. For example, physical activity increases white matter⁸ and the development of new neurons in the hippocampus.⁹ Further, physical activity has improved the attention and behavior of children with ADHD and the cognitive and academic outcomes of children, including those with physical impairments and learning problems.¹⁰ In children and adults with cancer, physical activity interventions have been beneficial for improving health and well -being.^{11, 12}

NCI's Physical Activity for Cognitive Effects (PACE) Study

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Please support the Foundation and our mission!



The re-scheduled **19th** International Symposium on Pediatric Neuro-Oncology (ISPNO) took place in beautiful Karuizawa, Nagano, Japan as a hybrid meeting from December 13 through December 16, 2022. In 1986, the first ISPNO meeting was held in Tokyo, Japan and has expanded greatly over the years becoming a

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CBTF RAISES FUNDS FOR RESEARCH

Funds raised benefit pediatric brain tumor research and other CBTF programs

The Childhood Brain Tumor Foundation

Our mission is to support and fund basic science or clinical research for childhood brain tumors. We are dedicated to heightening public awareness of this devastating disease. and improving the quality of life for those that it affects by funding vital research initiatives.



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Roster, Featured Article

Featured Article (continued from page 1)

Based on this previous research, could physical activity help remediate the cognitive late effects of CRT? To answer this question, scientists at the NCI have created an at-home physical activity program specifically for children treated with CRT for brain tumors! The study involves pre- and post-study evaluations (fasting blood draw, fitness testing, and brief cognitive assessment) at the NCI, and a 12-week home physical activity program (with an activity monitor and website). Eligible children (8-18 years) are randomly assigned to 1) a group doing the physical activity program or 2) a group doing their usual activities. After 12 weeks, the group doing their usual activities then do the physical activity program while the other group will continue the program for 12 weeks. Children receive a small monetary compensation and keep their activity monitors at the end of the study. If participants live more than 50 miles from the NIH, travel and lodging will be covered. We hope that this program, which is tailored to each child's favorite physical activities, will help improve cognitive function and physical health, and be fun to do.

We plan to resume enrolling participants this spring/summer after pausing the study due to the COVID-19 pandemic. If you would like more information, please email or call Drs. Pam Wolters (woltersp@mail.nih.gov) or Amanda Rhodes (amanda.rhodes@nih.gov) at 240-760-6040.

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CBTF Superheroes 5K 2021— Sunday, June 27, Sligo Creek Parkway or virtual depending if COVID restrictions are in place. **CBTF Party December 4, 2021** Glenview Mansion in Rockville, MD

If you are interested in learning more about the Childhood Brain Tumor Foundation, Inc.,

Please contact: E-MAIL: cbtf@childhoodbraintumor.org or jeanneyoung@childhoodbraintumor.org (<u>E-mail preferred</u> due to high volume of robo-calls) TELEPHONE: 877-217-4166 or 301-515-2900

Volunteers welcome!

EVENTS UPDATE

ISPNO (continued from page 1)



prominent comprehensive scientific symposium. The 2020 meeting was led by co-chairs, Koichi Ichimura, M.D., Ph.D. and Ryo Nishikawa, M.D., Ph.D. and included Education Day, the symposium sessions, keynote presentations, and panel discussion. Over 1,432 participants, a record-breaking attendance number, were in attendance, and there were 865 abstracts, the highest number of abstracts submitted to date.

The Childhood Brain Tumor Foundation provided a Silver Sponsorship and some additional funding. We were pleased to provide some general support, the special awards, and several opening day keynote speeches. After a welcoming opening performance, the awards and keynote speeches began.

Dr. Ichimura (Japan) gave a heartwarming welcome to attendees. He shared details of the ISPNO history. He addressed the COVID pandemic and showed appreciation for the healthcare professionals who have worked diligently to take care of their patients during this difficult time. With great enthusiasm, he announced that this will be the first year the ISPNO will give high recognition to several groups of people in three categories. He introduced Eric Bouffet (Toronto, Canada) to provide an update and to introduce Dr. Roger Packer, the recipient of the first prestigious award. The award was given in recognition of Dr. Packer's significant research and unparalleled contributions to the pediatric brain tumor community.

Dr. Bouffet provided an overview of the progress against medulloblastoma and shared a timeline that covered decades. He presented the challenges of the past and future directions, highlighting Dr. Packer's dedication to the care of children with brain tumors.

Opening Day

Award Ceremony 1: *Lifetime Achievement Award* to Roger J. Packer, M.D. Dr. Bouffet described Dr. Packer's accomplishments and dedication throughout his distinguished career, describing Dr. Packer as an internationally acclaimed neurologist with a rich knowledge



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Thank you so much!	Grants
Special thanks from CBTF to our supporters and the research and medical community for their dedication!	CBTF plans to re-open our grants application process for 2022 in the fall of 2021. A limited number of applications will be funded.
Upcoming Events 2021	
 CHECK our Website for more information regarding 5K registration a events. Childhood Brain Tumor Conference: Education and Updates: (TBD—date change due to COVID-19 or may change to a video conference) our website will have updates and other information. CBTF Superheroes 5K 2021— Sunday, June 27, Sligo Creek Parvirtual depending if COVID restrictions are in place. Check our wupdates. Thanks. CBTF Party 2021—The CBTF GALA is scheduled to take place or December 4, 2021 at the Glenview Mansion in Rockville, MD If you would like to donate something for the auction, let us known of the second s	and otherCBTF Sponsorships:erence.We will provide sponsorship for the 20th International Symposi- um on Pediatric Neuro- Oncology (ISPNO) for the 2022

ISPNO, In Honor of

(continued from page3)

base and firm compassion for patients and families. Dr. Bouffet also praised Dr. Packer for his dedication as a family man. Dr. Ichimura presented the award virtually and expressed his sincere appreciation for Dr. Packer's outstanding achievements. Dr. Packer accepted the award while praising the advancements and dedication of others, including those in multi-disciplinary areas that interact with neuro-oncology.



Keynote: Roger J. Packer, M.D., Senior Vice-President, Center for Neuroscience and Behavioral Medicine, Director of the Brain Tumor Institute, and the Gilbert Family Neurofibromatosis Institute, Children's National Hospital, DC, *Pediatric Neuro-Oncology: Perspectives of the New Decade*

An overview of new areas of research spanned 2010 to 2020 and included topics such as the acceptance of molecular classification, better understanding of biological underpinnings, molecular-targeted therapies, proliferation of proton beam units, expansion of immunology approaches,

and the recognition of familial syndromes and genetic predispositions. Dr. Packer noted that while greater acceptance of molecular classification is critical in research, it is important to understand the clinical ramifications of handling various tumor types. For example, medulloblastoma is not only four (4) groups, but multiple subgroups. In addition, supratentorial PNETs have been shown to be multiple tumor types with more than 30 subgroups which raises concerns about how best to approach treatment for those patients. Concerns were also noted about developing countries regarding how they will be able to do the molecular classifications. Drugs developed through other cancer research have resulted in some remarkable improvements in molecular targeted therapies. Dr. Packer provided details on the WHO Classification of Tumors in the CNS for neuronal and glioneuronal tumors.

Dr. Packer commented on proton beam radiation proliferation noting that this therapy is now available to patients with medulloblastoma although toxicities need to be evaluated. He also expressed concerns about children in developing countries with no access to this vital therapy. Dr. Packer continued by noting that it is important to consider all subgroups going forward, by assessing the subgroups and determining the best treatment approach for each subgroup. Researchers will look at the impact of micro-environment and study biologics to understand single cell technology and therapeutics in the hope of refining preclinical models.

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Support CBTF: Due to the pandemic a few of our scheduled fundraising events in 2020 were canceled and impacted our ability to fund research programs and sponsorships significantly. We hope the 2021 events can open so we can see our supporters. Your monetary support is always meaningful to CBTF and we hope we can count on your continued support.

Please support the Childhood Brain Tumor Foundation Visit our GIVE ONLINE donation button: https://www.givedirect.org/donate/?cid=1605 Be part of the solution in helping fund vital research initiatives cure childhood brain tumors!

In Honor of

The dedicated medical professionals who have tirelessly dedicated their time to care for the patients and families during the COVID-19 pandemic.

Special congratulations to all of the award winners at the ISPNO. Their passionate dedication to children with brain tumor is outstanding.

ISPNO

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Dr. Packer discussed DIPGs/DMGs and how much has been learned about these tumors through biopsies and autopsies. Researchers are also studying the role of immunotherapy and the microenvironment. He commented on minimally invasive/non-invasive neurosurgery techniques that have expanded applications. These techniques include Optune, which uses low-intensity, wave-like electric fields; hyperthermia; high-intensity focused ultrasound; thermal laser ablation Visualase®; MRI-guided laser ablation; low-intensity focused ultrasound, and targeted uncaging of nanodroplets for drug delivery. Dr. Packer also pointed out the use of MEK in low-grade gliomas may be premature with preliminary data suggesting recurrence. The patient, however, can go back on the treatment if the patient has had a good response in the first place, provided the patient has not progressed before going off treatment.

To sum up, Dr. Packer pointed out there has been great scientific progress with some notable advances. There have been some frustrations, but more advances since the previous decade. The 2020s promise great challenges but also great opportunities

Question to Dr. Packer from the audience: Is Visualase® for low-grade gliomas being used for optic pathway gliomas? Response: Some institutions will ablate a small tumor, but it is not commonly used. High-intensity focused ultrasound (HIFU) is non-invasive and can be monitored in real time.

Dr. Packer looks forward to the future advancements that will be made in the years ahead.



Award Ceremony 2: Lifetime Contribution to Asian Neuro-Oncology Community Award, presented by Annie Huang. Awardee: Tai-Tong Wong (Taiwan)

Dr. Annie Huang was pleased to introduce Dr. Tai-Tong Wong, Director of the Pediatric Brain Tumor Program at Taipei Medical University Hospital/TMU and founder of the Taiwan Foundation. Dr. Wong has trained a large generation of doctors in Taiwan. He has worked tirelessly by devoting his life to neuro-oncology in Asia.

Dr. Wong expressed his deep appreciation for being honored with the award stating it was the greatest moment of his life.



Award Ceremony 3: *Pediatric Neuro-Oncology Community Service Award*, Angela & Neil Dickinson, presented by Barry Pizer, M.D. (United Kingdom)

Angela and Neil Dickinson are dedicated supporters of brain tumor research. The Dickinsons have funded research through their foundation the Brain Tumour Research Charity since 1996 in memory of their daughter Samantha. Dr. Pfizer described their passionate dedication to the cause. The Dickinsons shared the story of their daughter and her life's journey as she fought her brain tumor until 1996 when she lost the battle at 16 years old. Due to the lack of support for brain tumor research they were determined to create awareness.

CBTF congratulates all the awardees for their amazing passion and dedication to make a difference in the lives of children and their families in striving to improve treatments and find cures. We know more advances and updates will continue to develop in the years ahead.

Education Day:

Cynthia Hawkins, M.D., Ph.D. FRCPC. Division of Pathology, Labatt Brain Tumor Research Centre, The Hospital for Sick Children, Toronto, Canada: *WHO Classification/cIMPACT-NOW Update*

Principles of tumor Classification include: 1) Denomination -assigning a name to a group; 2) Qualification—relevant descriptive features; 3) Prediction --expected course and outcome, likely response; 4) Classification—important in allowing the medical community and research to communicate effectively and provides concept,

GRACIOUS GIVING

ISPNO (continued from page 5)

determining possible tumor type. She explained the difference between lumpers versus splitters. Lumpers follow broad classifications and splitters favor sub-classification seeing more complex cases. Dr. Hawkins explained that they are moving away from assigning tumor grade based on entity name to looking within the entity to grade. The World Health Organization (WHO) is restructuring diffuse gliomas noting pediatric versus adult brain tumors and identifying molecularly defined entities. There are no current rules regarding the distinction in classifications. Dr. Hawkins included some additional details on different tumor types.

Special Lecture 6: Moderator Yukihiko Sonoda (Japan); Speaker, Murali Chinagumpala, Texas Children's Hospital (USA), *Neurofibromatosis 1*

Affecting one in 3,000 worldwide, NF1 is a common disorder of low-grade glioma and high-grade brainstem glioma. Twenty percent of patients carry the diagnosis low-grade glioma of the optic pathway, primarily juvenile pilocytic astrocytoma. 15-20% of children with NF1 are diagnosed before the age of six, and the natural history is highly unpredictable. One-half to two-thirds are indolent and have minimal progression. Forty percent of patients will develop visual symptoms. These tumors are usually not biopsied and may be hard to separate from the NF related white manner abnormalities. The non-optic pathway gliomas are typically brainstem gliomas with a mean age of 7.2 at diagnosis with a range of 0.6 to 23 years of age.

Forum 4: Immunotherapy

Moderator: Naoya Hashimoto (Japan); Speaker, Eugene Hwang, M.D. (Children's National Medical Center, USA) Today's immunotherapy for pediatric CNS tumors: briefly during the Gordian Knot

Dr. Hwang explained the Gordian Knot, a legend from the time of Alexander the Great, which is a metaphor for a problem that is considered unsolvable but in reality, is a solvable problem. Challenges: Immunotherapy and the complexities include obstacles such as the blood brain barrier (BBB) which is a strong antagonist for delivering therapeutics. He discussed the BBB role, how to overcome resistance, tumor microenvironments and immunosuppression, targets, molecular phenotypes, and tumor heterogeneity. Molecular alterations affect immune response and mutations can alter immunophenotypes. Despite challenges, immunotherapy is bringing opportunities that are revolutionizing cancer therapeutics. However, a clear understanding of the BBB remains a challenge regarding the tumor microenvironment.

The conference closed with Dr. Ichimura's expressing his sincere appreciation for the support given by so many. The next location for the ISPNO conference will be in Germany. The Childhood Brain Tumor Foundation was among the sponsors and enjoyed viewing many excellent sessions virtually. This article provides some highlights of the meeting that had outstanding speakers throughout.



Remembrances, CFC, UW, Maryland Charities

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Many companies offer a matching gifts program to support charitable organizations.

Your human resources department can tell you if such a program exists at your company. Ask them about the form that can be sent to the Childhood Brain Tumor Foundation reporting a contribution (donation or event contribution). The form states that they will match your contribution.

We return the form to the employer with the proper acknowledgment and information required.

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friends who donated through work-

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Our website: https://www.childhoodbraintumor.org



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Thank you donors!

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The Childhood Brain Tumor Foundation participates in the **Combined Federal Campaign (CFC) and Maryland Charities.**

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cbtf@childhoodbraintumor.org

Our treasurer will provide you with the necessary details to proceed with your donation.

Thank you.





Address change requested

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ANUUAL Superheroes 5 K and Kids' Run 2021, Sligo Creek Pkwy Tantsiyo dotol Syndon Iyno 27

Tentative date: Sunday June 27 Registration will open on the Potomac River Running website. Donations are also welcome for supporting teams or individuals. Check: www.childhoodbraintumor. org more details will be posted and confirmed. will be posted.

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