

Psychology Working Group

Kevin Krull, PhD

CCSS

Childhood Cancer
Survivor Study



St. Jude Children's
Research Hospital

An NCI-funded Resource

- Broad scope of Psychology Working Group is outcomes and interventions focused on neurocognitive and psychosocial function.
- Specific outcomes:
 - Neurocognitive, emotional distress (*anxiety, depression, suicidal ideation, PTSD, psychoactive medication*), quality of life (*pain, sleep, vitality, socialization, functional limitations*), growth and resilience, social attainment (*education, marriage, employment, income, independence*).
- Intervention approaches targeting outcomes above
 - Cognitive behavioral therapy, psychoeducation, mindfulness, self-monitoring/regulation....

Working Group Membership

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| Name | Discipline | Institution |
|--------------------|------------------------------|---------------------------------------|
| Kevin Krull | Neuroscience/Neuropsychology | St. Jude Children's Research Hospital |
| Tara Brinkman | Psychology | St. Jude Children's Research Hospital |
| Pim Brouwers | Neuroscience | National Institute of Mental Health |
| Austin Brown | Epidemiology | Baylor College of Medicine |
| Lauren Daniel | Psychology | Rutgers University |
| Kim Edelstein | Neuropsychology | Princess Margaret Cancer Center |
| Bob Hayashi | Pediatric Oncology | Washington University – St. Louis |
| Meg Lubas | Social Work/Public Health | Radford University |
| Jordan Marchek | Psychology | Emory University |
| Kathy Ruble | Nursing | Johns Hopkins University |
| Ellen van der Plas | Neuropsychology | University of Iowa |
| Emily Walling | Pediatric Oncology | University of Michigan |
| AnnaLynn Williams | Epidemiology | St. Jude Children's Research Hospital |

- 15 Published/In Press Manuscripts (since June 2019)
- 6 Currently Submitted Manuscripts
- 15 Analyses/Manuscripts in Process
- 10 Concepts in development
- 10 New AOIs (total, since June 2019)

2021 Career Development Awardees

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Faculty: Kelly Rentscher, PhD; University of California Los Angeles

“Psychological distress, social functioning, and phenotypic aging in adult survivors of childhood cancer”

Mentor: Kiri Ness, PhD

Trainee: Christina Sharkey, PhD; Children’s National Medical Center

“The impact of physical activity and psychological distress on neurocognitive functioning over time”

Mentor: Kristina Hardy, PhD

Highlights of Recently Completed Research

Barlow-Krelina et al., Consistent physical activity and future neurocognitive problems. *JCO*. 2020.

| Analysis | Task Efficiency | | Emotion Regulation | | Organization | | Memory | |
|------------------------------------|-----------------|-----------------|--------------------|-----------------|--------------|-----------------|--------------|-----------------|
| | β (SE) | <i>P</i> | β (SE) | <i>P</i> | β (SE) | <i>P</i> | β (SE) | <i>P</i> |
| Changes in NCQ scores ^c | | | | | | | | |
| CNS | | | | | | | | |
| Consistent activity | -5.9 (2.99) | <.001 | -3.6 (2.17) | .01 | -6.0 (2.11) | <.001 | -4.2 (2.90) | .01 |
| Inconsistent activity | -4.0 (2.21) | .007 | -2.5 (1.57) | .04 | -3.7 (1.64) | .004 | -3.0 (1.70) | .02 |
| Non-CNS | | | | | | | | |
| Consistent activity | -3.2 (0.32) | <.001 | -2.6 (0.30) | <.001 | -2.5 (0.27) | <.001 | -2.5 (0.34) | <.001 |
| Inconsistent activity | -1.7 (0.23) | <.001 | -1.7 (0.18) | <.001 | -1.4 (0.18) | <.001 | -1.4 (0.24) | .004 |
| Siblings | | | | | | | | |
| Consistent activity | 0.2 (4.70) | .94 | 0.2 (3.87) | .94 | 2.3 (3.03) | .18 | 2.1 (4.07) | .30 |
| Inconsistent activity | -1.1 (3.92) | .58 | 0.1 (2.94) | .96 | 1.0 (2.04) | .47 | 0.1 (3.48) | .95 |

Highlights of Recently Completed Research

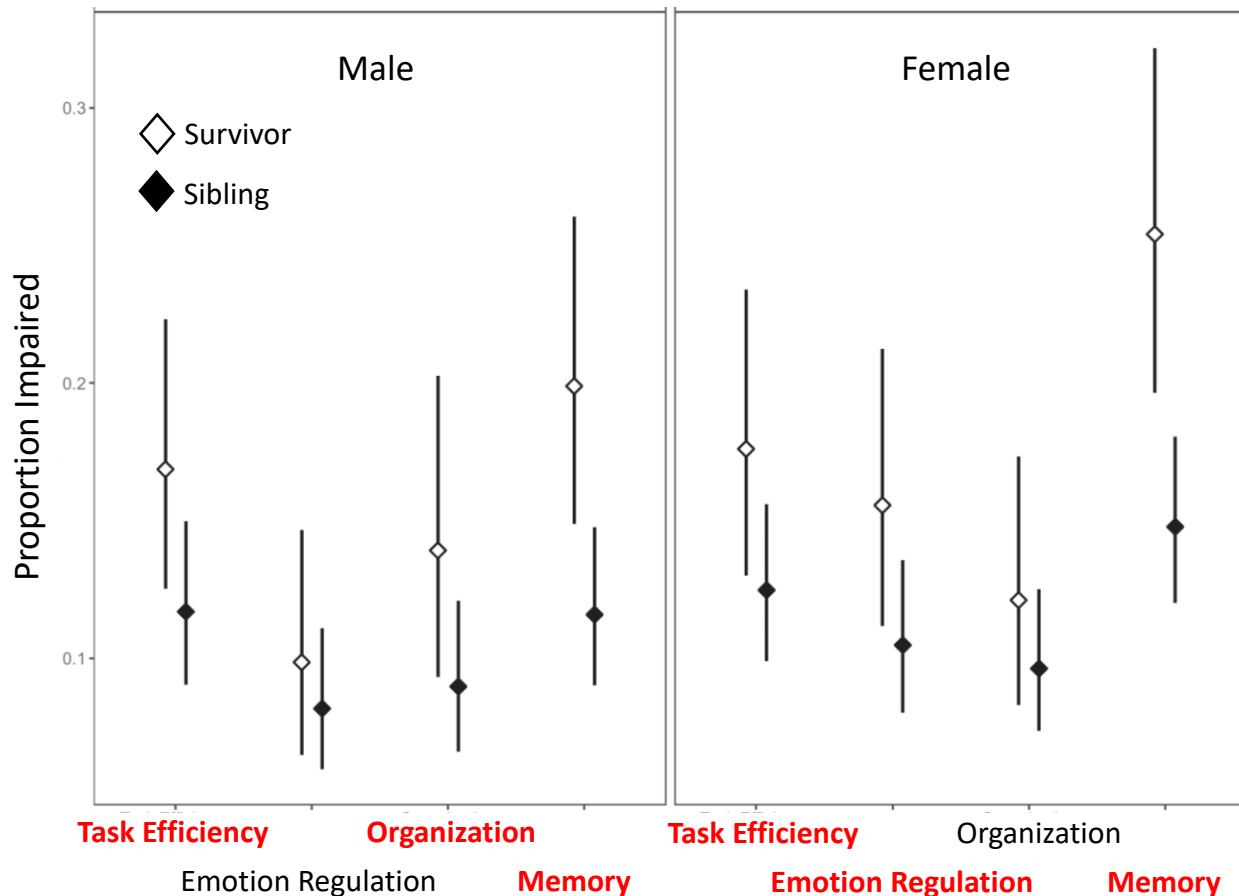
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Stefanski et al., Long-term neurocognitive/psychosocial outcomes in AML. *JNCI*. 2021.

| Outcome and group | % Impaired | RR (95% CI) | p ^a |
|-----------------------------------|------------|---------------------|----------------|
| CCSS Neurocognitive Questionnaire | | | |
| Memory | | | |
| IC | 25.5 | Referent | |
| BMT | 23.7 | 0.92 (0.63 to 1.34) | .66 |
| Organization | | | |
| IC | 21.4 | Referent | |
| BMT | 21.6 | 1.01 (0.67 to 1.50) | .98 |
| Emotional regulation | | | |
| IC | 19.5 | Referent | |
| BMT | 15.3 | 0.81 (0.50 to 1.30) | .38 |
| Task completion | | | |
| IC | 25.5 | Referent | |
| BMT | 25.9 | 1.03 (0.72 to 1.47) | .88 |

Highlights of Recently Completed Research

van der Plas et al., Sex-specific outcomes in ALL treated with chemotherapy. *JNCI*. 2021.



| | Task Efficiency OR (95% CI) | Emotion Regulation OR (95% CI) | Organization OR (95% CI) | Memory OR (95% CI) |
|---------------------|--------------------------------|-----------------------------------|-----------------------------|--------------------------|
| Males | | | | |
| IT MTX (/100mg) | 1.04 (0.98-1.12) | 1.00 (0.93-1.08) | 1.05 (1.00-1.09) | 1.68 (1.16-2.46) |
| Dex (Yes v No) | 1.40 (0.69-2.84) | 1.48 (0.61-3.63) | 1.06 (0.48-2.35) | 2.44 (1.19-5.01) |
| Neurologic CC (2-4) | 6.32 (2.25-17.72) | 2.29 (0.84-6.21) | NA | 4.33 (1.76-10.68) |
| Endocrine CC (2-4) | 1.54 (0.78-3.05) | 1.11 (0.50-2.49) | 1.69 (0.81-3.53) | 1.18 (0.61-2.31) |
| Females | | | | |
| IT MTX (/100mg) | 1.23 (0.87-1.76) | 1.02 (0.72-1.44) | 1.15 (0.76-1.74) | 0.85 (0.60-1.20) |
| Dex (Yes v No) | 1.64 (0.85-3.14) | 0.95 (0.50-1.82) | 0.82 (0.35-1.94) | 1.33 (0.74-2.37) |
| Neurologic CC (2-4) | 1.45 (0.54-3.89) | 1.74 (0.67-4.50) | NA | 1.49 (0.58-3.83) |
| Endocrine CC (2-4) | 2.19 (1.20-3.97) | 1.25 (0.67-2.34) | 2.12 (1.04-4.34) | 2.26 (1.31-3.92) |

Highlights of Recently Completed Research

- Phillips et al., Late onset and progressive neurocognitive impairment. *In preparation.*

Frequency of neurocognitive impairment

| Domain | Siblings | | CNS Tumor | |
|-----------------|----------|---------------|-----------|---------------|
| | Imp FU2 | Newly Imp FU5 | Imp FU2 | Newly Imp FU5 |
| Memory | 15 (7%) | 17 (8%) | 125 (25%) | 134 (35%) |
| Task Efficiency | 32 (14%) | 14 (7%) | 221 (43%) | 66 (23%) |
| Organization | 25 (11%) | 6 (3%) | 91 (18%) | 61 (15%) |
| Emo Regulation | 13 (6%) | 11 (5%) | 73 (14%) | 68 (16%) |

N = 512 CNS tumor survivors, 52% female, mean[SD] 30.6 [7.1] years at FU2

Risk of new onset memory impairment after ~11.6 years

| Parameter | RR (95%CI) |
|-------------------------------------|---------------------------|
| CNS Tumor vs Sibling | 4.2 (2.6 - 6.9) |
| CDC exercise guidelines (no vs yes) | 1.43 (1.09 - 1.89) |
| Ara-C (yes vs no) | 1.70 (1.02 - 2.83) |
| Cranial Radiation Dose >50 Gy | 1.82 (1.31 - 2.54) |
| Cardiopulmonary Grade 3-4 (FU2) | 1.48 (1.02 - 2.15) |
| Neurologic Grade 3-4 (FU2) | 1.06 (0.74 - 1.51) |
| Neurologic Grade 3-4 (FU5) | 2.27 (1.66 - 3.10) |

Approved Concept Proposals

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1. Neurocognitive outcomes in rhabdomyosarcoma (Bob Hayashi, Wash U)
2. Psychological distress and neurologic morbidity (Chiara Papini, St. Jude Children's Research Hospital)
3. Special education outcomes (Lisa Bashore, Texas Christian University)
4. Loneliness (Ameer Fayad, SUNY Buffalo)
5. Longitudinal change in HRQOL (Fiona Schulte, University of Calgary)
6. Mental health in ALL (Caleb Nannes, Duke)
7. Longitudinal change in functional independence (Katharine Lange, Children's Hospital Minnesota)
8. Temporal change in neurocognitive outcomes in CNS (Tara Brinkman, St. Jude Children's Research Hospital)

Approved Concept Proposals...

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9. Neurocognitive/psychosocial outcomes in Asian/Pacific islanders (Satomi Sato, St. Luke's International University, JAPAN)
10. Genetic determinant of PTSD (Donghao Lu, Dana Farber Cancer Institute)
11. Cognitive aging (Nick Phillips, St. Jude Children's Research Hospital)
12. Neurocognitive/psychosocial outcomes in early AYA survivors (Amy Wang, University of Chicago)
13. Psychosomatic profiles in survivors (Rachel Tillery, St. Jude Children's Research Hospital)
14. Sex mediation of neurocognitive/psychosocial outcomes (Rachel Peterson, Johns Hopkins University)
15. Accelerated aging as an accumulation of deficits (AnnaLynn Williams, St. Jude Children's Research Hospital)

Ancillary Studies: Symptoms

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MPI's: I-Chan Huang and Kevin Krull (St. Jude Children's Research Hospital)

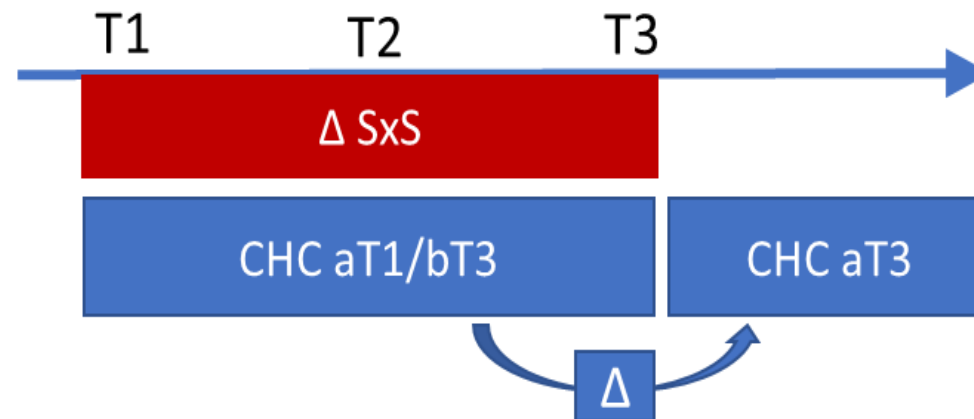
Title: Symptom Progress and Adverse Health Outcomes in Adult Survivors of Childhood Cancer

Funding Source: National Cancer Institute (R21); \$489,133

Aims:

1. To investigate symptom categories and clusters across multiple time points
2. To examine their prediction of future chronic conditions.

Status: Funding complete, analyses finalized, initial manuscript in development.



Ancillary Studies: Insomnia

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MPI's: Tara Brinkman and Kevin Krull (St. Jude Children's Research Hospital)

Title: Impact of eHealth intervention for insomnia on late effects of childhood cancer

Funding Source: National Cancer Institute (R01); \$4,271,243

Aims:

1. To assess impact of eHealth insomnia treatment.
2. To assess impact of improved sleep on neurocognitive impairment, emotional distress, and cardiovascular health.

Status:

- Timeline extended and study procedures adapted due to COVID-19:
 - No longer using EMSI to collect of NIH Toolbox, HR/BP, and serum
 - Instead, using CNS-VS, WHOOP, and blood spot cards
- Recruitment ongoing

Ancillary Studies: Pain

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PI: Nicole Alberts (Concordia University)

Title: Treating Chronic Pain After Childhood Cancer: A Digital Health Intervention

Proposed Funding Source: Canadian Institutes of Health Research

Aims: 1. To examine efficacy of mHealth respiratory feedback and CBT on pain control.

Status: Submitted October 2020, Unscored
Resubmission planned for October 2021.

Ancillary Studies: Pain

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MPI's: Sophia Smith and Eric Elbogen (Duke University)

Title: Integrating Technological Approaches for Pain Management in Adult Survivors of Childhood Cancer

Proposed Funding Source: National Institutes of Health (R01)

Aims:

1. To determine efficacy of neurofeedback on reduction of pain symptoms
2. To evaluate additive effect of neurofeedback and CBT
3. To identify moderators (depression/anxiety) and mediators (self-efficacy) of intervention effects

Status: Submitted October 2020, unscored

Resubmission planned after additional pilot data obtained

Top Priorities: Five Year Plan

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1. Interventions to improve neurocognitive and psychosocial outcomes
 - Remotely delivered therapies targeting pain, distress, sleep/fatigue and cognition
2. Direct assessment of neurocognitive function
 - Implementation of CNS-VS
3. Neurocognitive and psychosocial progression with age
 - CNS-VS completed by survivors/siblings twice over next 5 years
 - NCQ in FU7 provides 3rd timepoint in original cohort and 2nd in expansion

- Threats or Challenges:

- Participant burden associated with assessing change vs innovative content
- Self-reported in survivors with cognitive impairment and limited insight

- Major Opportunities:

- “Significant others” survey to enhance accuracy of reported functional limitations in an aging cohort at risk for dementia
- Assessment of social isolation and networks
- Identification of factors associated with growth and resiliency

Thank you for your attention.