REWARD PROCESSING AND DECISION MAKING IN CHILDHOOD CANCER SURVIVORS: A PILOT STUDY

Mei-Heng Lin[1], Sally Cole[1,2], Peter Cole[3], Miriam Rosenberg-Lee[4], Nicole Lalta[1], Travis Baker[1]

[1]Center for Molecular and Behavioral Neuroscience, Rutgers University-Newark, [2]Florida State University,
[3]Cancer Institute of New Jersey, [4]Psychology Department, Rutgers University-Newark

Introduction

Dopaminergic Functioning in Childhood Cancer Survivors

- While most children with cancer can be cured with chemotherapy, survivors are at risk of persistent organ dysfunction and cognitive deficits.[1-2]
- Studies find that dopamine transmission is compromised following cancer therapy, suggesting that the dopamine system is a plausible mechanism contributing to long-term cognitive impairment in cancer survivors.[3-4]
- Dopamine neurons produce the reward prediction errors (RPEs), which are utilized by its neural targets, the anterior midcingulate cortex (aMCC) and the striatum, play a critical role in reward processing, decision-making, and learning.[5]
- However, little is understood about how chemotherapy-induced neurotoxicity altered the neurocognitive functioning of the dopamine system.

Purpose

- To evaluate the effect of chemotherapy on the functions of two dopaminergic neural targets, the anterior midcingulate cortex (aMCC) and the striatum, via electrophysiological and behavioral indices of reward processing and decision-making in childhood cancer survivors.

Methods

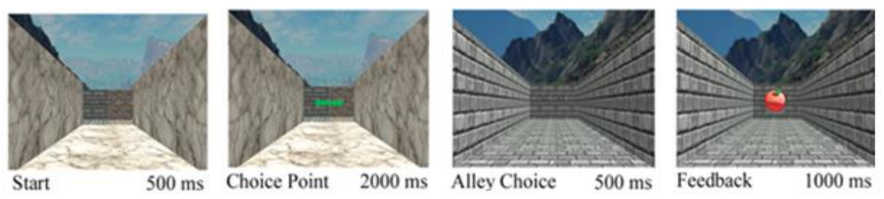
Participants

- Eight childhood cancer survivors (acute lymphoblastic leukemia: n = 7, non-central nervous system solid tumor: n = 1) aged 6-17-year-old (M_{age} = 12.75 yrs ± 1.31; 4 males; $M_{age\ at\ diagnosis}$ = 4 yrs ± 0.53) were recruited from the Cancer Institute of New Jersey. Survivors had completed all planned chemotherapy treatment at least one year prior to recruitment for this study ($M_{years\ since\ last\ chemo}$ = 3.05 yrs ± 1.15). Eight age-and-sex-matched controls were also recruited.

The T-maze task[6]

- Participants navigated through mazes by pressing buttons (left or right) and received feedback (reward and no-reward).

Figure 1. The computer-based T-maze task.



Probabilistic Selection Task[7]

- Participants learn through trial and error to approach one stimulus with a higher probability of being correct and avoid the other one.

Phase	Phase1: Training (trial and error)	Phase 2: Testing
Feedback	Provided	Not provided
Design	3 blocks of 60 trials	60 trials
Stimuli	AB pair: ま み — 80% ✓ 20% ✗ / 20% ✓ 80% ✗ CD pair: そ の — 70% ✓ 30% ✗ / 30% ✓ 70% ✗	• New combinations: AC, AD, BC, BD pairs • Learning from positive feedback: A C / A D • Learning from negative feedback: B C / B D

Results

Survivors showed attenuated RewP amplitude

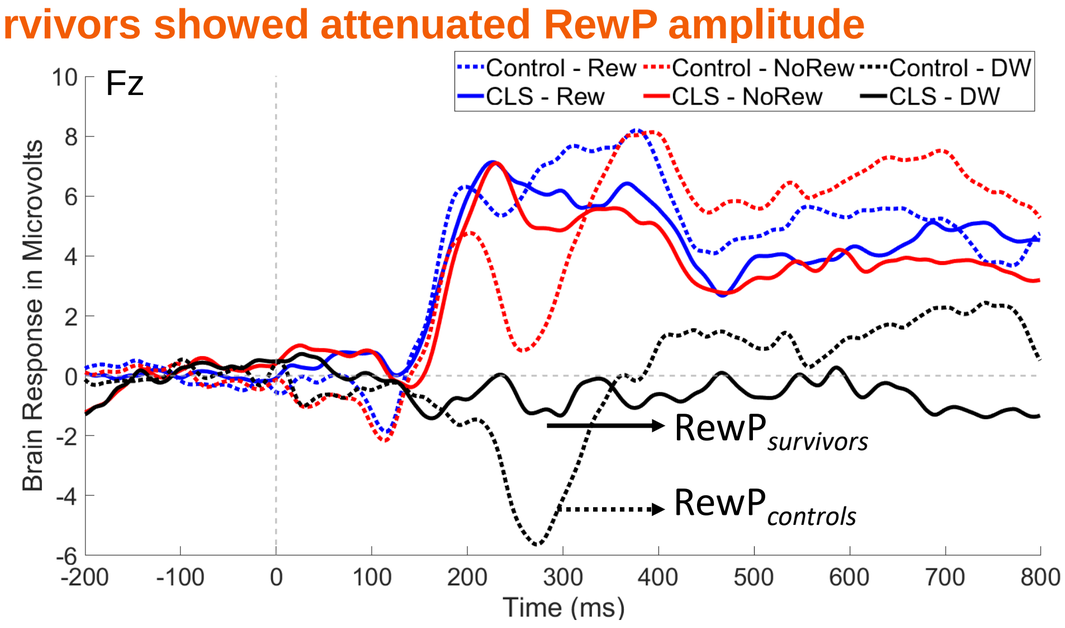


Figure 2. Event-related potentials elicited by reward (Rew) and no reward (NoRew) feedback, and difference wave (the reward positivity; RewP) on the T-maze task

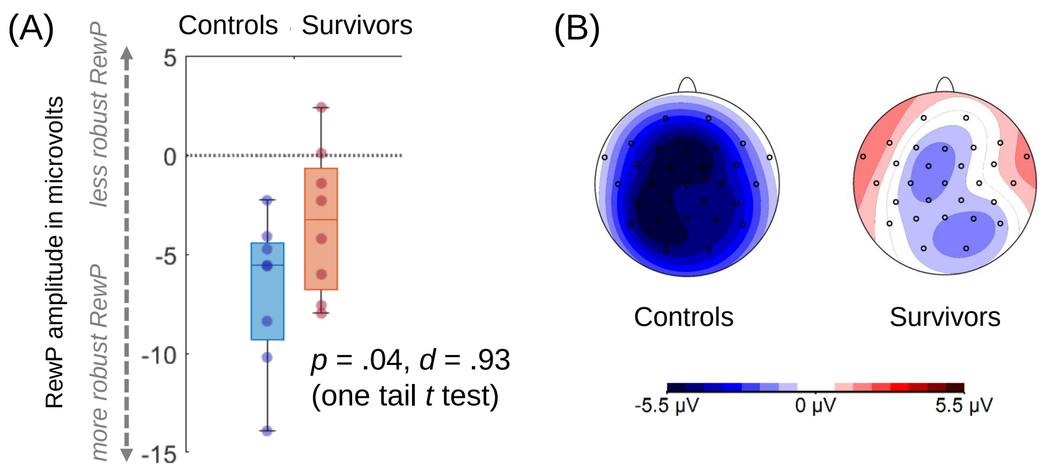


Figure 3. (A) Peak RewP amplitude and (B) topographical map for RewP

Survivors showed lowered accuracy to avoid negative feedback

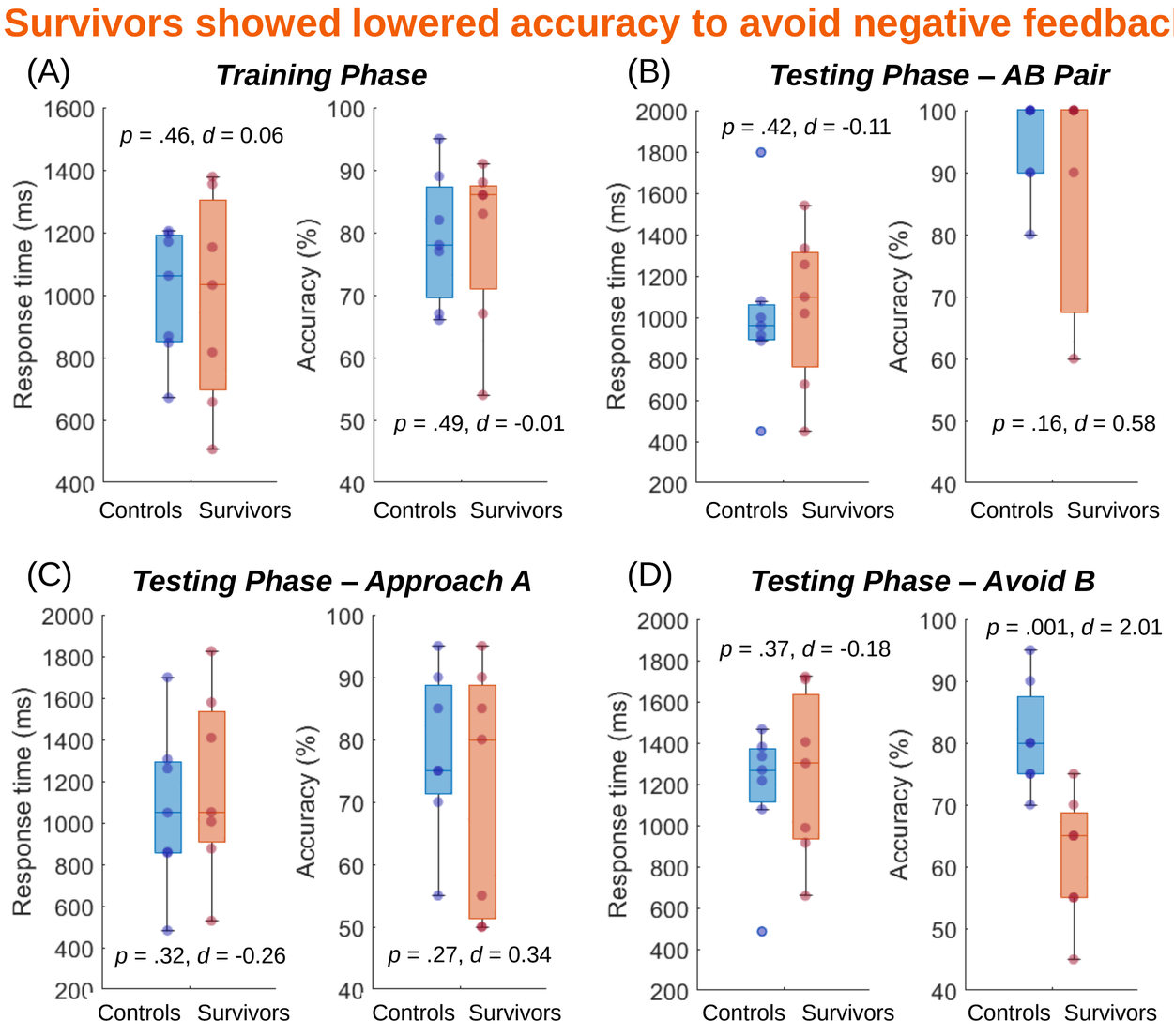


Figure 4. Behavioral performance on the Probabilistic Selection Task (PST). Note: Results from one-tail t-tests are reported. One subject (control, 6 y/o) did not complete the PST task, thus only data from 7 subjects (per group) are reported.

Discussion

- The preliminary results showed that RewP, an electrophysiological signal reflecting the sensitivity of the aMCC to rewards versus the absent of rewards, is reduced in the survivor group compared to the controls, suggesting that the neural processes associated with the aMCC may potentially be affected in childhood cancer survivors (Figures 2-3).
- While both groups showed comparable performance to learning from positive feedback (Figure 4C), the survivor group demonstrated lower accuracies to learning from negative feedback (Figure 4D), suggesting that survivors may be less effective in acquiring task-related information based on negative feedback.
- Taken together, this study shows differential neural and behavioral patterns between survivors and controls, pointing to the potential impacts of chemotherapy-related neurotoxicity on the cognitive functioning of the dopamine system in pediatric cancer survivors.
- Given the limited sample size, increasing subjects of the survivor group is needed to establish the robustness of findings.

Acknowledgments

- This project is funded by the New Jersey Commission of Cancer Research (DCHS20PPC001), Rutgers Brain and Health Institute, and the National Cancer Institute. (5R21CA262491-02)
- We thank the families participating in the study.
- We thank Dr. Beth Savage and research assistants from the Baker's lab for their assistance with subject recruitment and data collection.

References

1. Krull, K. R., Hardy, K. K., Kahalley, L. S., Schuitema, I., & Kesler, S. R. (2018).
2. Moleski, M. (2000).
3. Gibson, E. M., Monje M. (2020).
4. Wilson, C. J., Finch, C. E., & Cohen, H. J. (2002).
5. Schultz (2017).
6. Baker, T. E., & Holroyd, C. B. (2009).
7. Cavanagh, J. F., Frank, M. J., Klein, T. J., & Allen, J. J. B. (2010)