

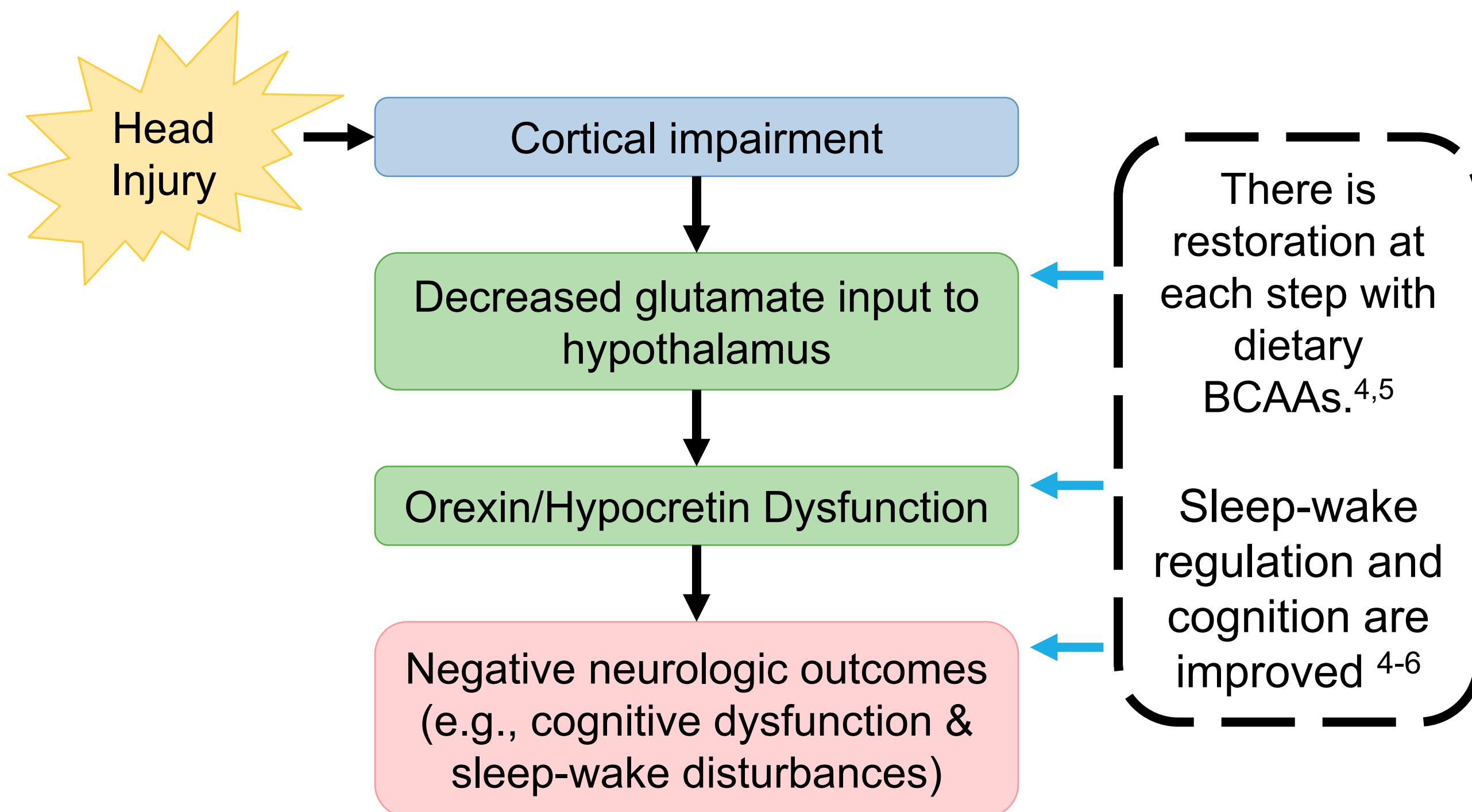
Improved Sleep in Veterans with Traumatic Brain Injury Following Dietary Amino Acid Supplementation: A Randomized Clinical Trial

Hannah A. Cunningham MS^{1,2}, Savanah J. Sicard¹, Cosette Olivo¹, Jessica S. Brewer¹, Katherine L. Powers¹, Laura Dovek¹, Rachel Champaigne¹, Andrea Hildebrand MS,³ Akiva S. Cohen PhD,⁴ Jonathan E. Elliott PhD^{1,3,5}, Miranda M. Lim MD, PhD^{2,3,5,6}

¹ VA Portland Health Care System, Research Service, Portland, OR, USA; ² Oregon Health & Science University (OHSU), Department of Behavioral Neuroscience, Portland, OR, USA; ³ OHSU, Dept. of Neurology, Portland, OR, USA; ⁴ Perelman School of Medicine, Anesthesiology and Critical Care Medicine, University of Pennsylvania, & Anesthesiology, Children's Hospital of Philadelphia, Joseph Stokes Research Institute, Philadelphia, PA, USA; ⁵ VA Portland Health Care System, Mental Illness Research Education and Clinical Center; Neurology; National Center for Rehabilitative Auditory Research, Portland, OR, USA; ⁶ OHSU, Dept. of Pulmonary and Critical Care Medicine; Oregon Institute of Occupational Health Sciences, Portland, OR, USA

BACKGROUND

- Supplementation with Amino Acid Rehabilitative Therapy in TBI (SmART-TBI) is a randomized, double-blinded, placebo-controlled clinical intervention trial to improve sleep in Veterans with mild traumatic brain injury (TBI).
- Long-lasting sleep and cognitive disturbances affect 50-90% of those with TBI.^{1,2} Current treatments focus on managing symptoms rather than targeting the underlying biological mechanism.
- Branched-Chain Amino Acids (BCAAs) are the major de novo substrates for glutamate/GABA synthesis, which play a key role in cortical excitation/inhibition.³

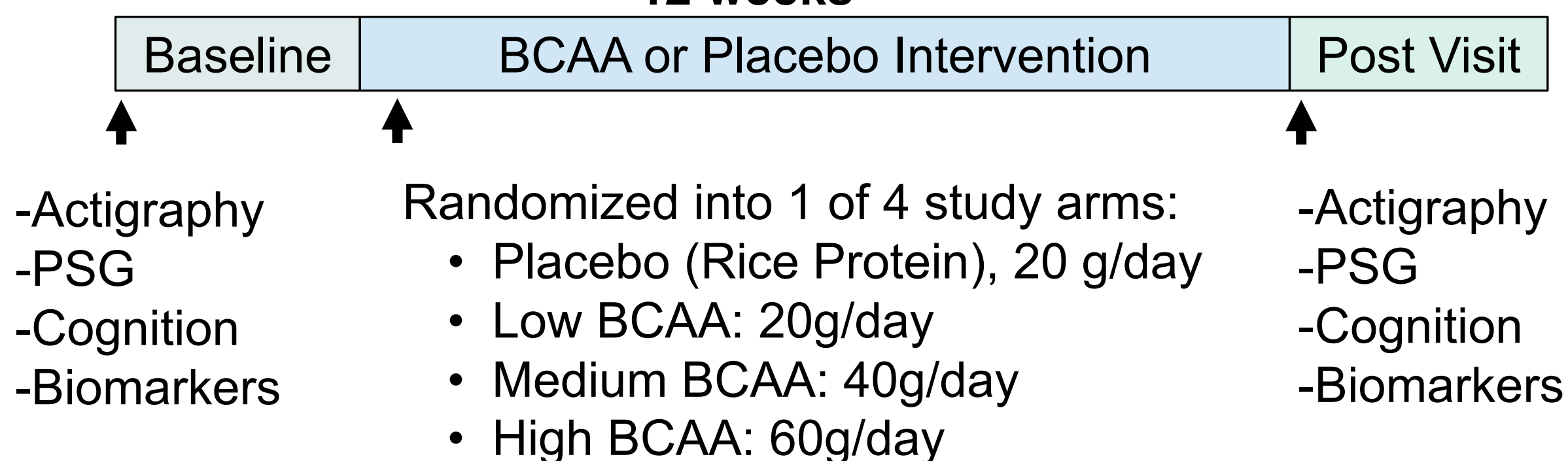


PURPOSE: To determine the effect of 12-weeks of BCAA supplementation on actigraphy-measured sleep

METHODS

- Veterans aged 18-65 with TBI and sleep disturbances
- 20-oz drink is consumed, split into 2 drinks/day for 12 weeks
- Double-blinded and placebo-controlled

12 weeks



- Actigraphy data were visually inspected by a single, blinded person and corroborated with the daily sleep diary when available.
- Linear mixed-effects models with an autoregressive correlation structure were used to analyze changes in sleep outcomes over 84-days.**

RESULTS & CONCLUSIONS

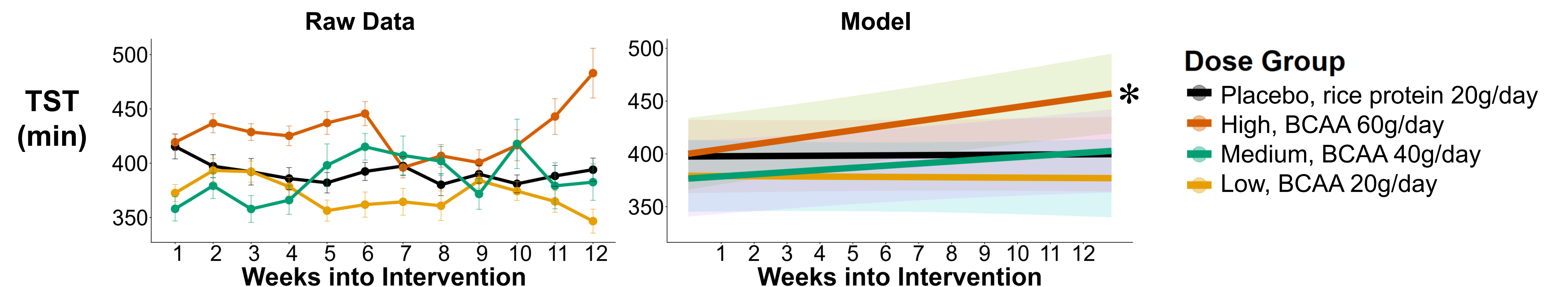


Figure 1. Participants in the high-dose group demonstrated an increase in total sleep time (TST) of 4.3 minutes/week (~51 minutes over 12 weeks, $p<0.003$) compared to placebo. *Left:* Average TST data by intervention group. *Right:* Linear mixed-effects model adjusted for sex, age, PTSD, depression, TBI recency, and pain.

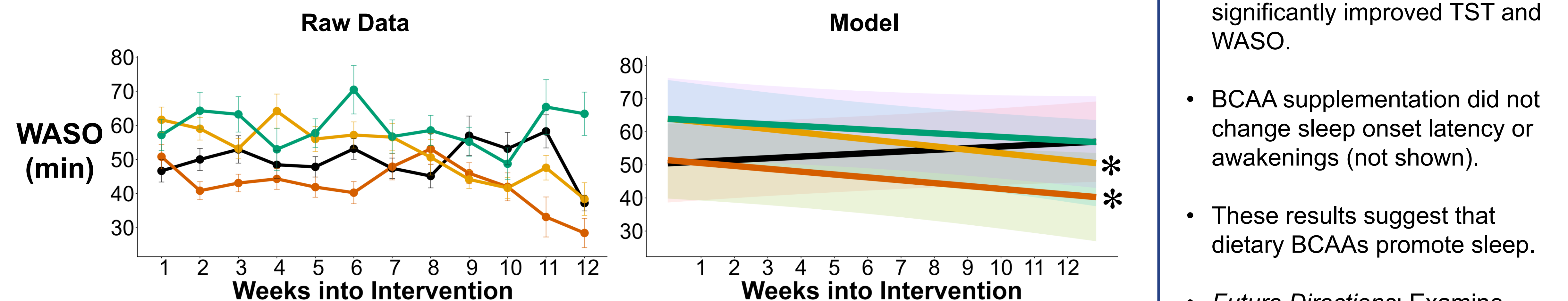


Figure 2. Participants in the high-dose group had decreased wake after sleep onset (WASO) of 1.4 minutes/week (~16 minutes over 12 weeks, $p=0.015$) compared to placebo. Similarly, the low-dose group decreased by 1.54 minutes/week (~19 minutes over 12 weeks, $p=0.004$) compared to placebo. *Left:* Average WASO data by intervention group. *Right:* Linear mixed-effects model adjusted for sex, age, PTSD, depression, TBI recency, and pain.

Conclusions:

- BCAA supplementation significantly improved TST and WASO.
- BCAA supplementation did not change sleep onset latency or awakenings (not shown).
- These results suggest that dietary BCAAs promote sleep.
- Future Directions:* Examine BCAA effects on EEG spectral power and cognition.

Table 1. Participant Characteristics				
	Placebo (n=28)	Low (n=32)	Medium (n=26)	High (n=28)
Age, years	50 ± 10	47 ± 10	49 ± 11	50 ± 9
Sex, % Male	20 (71%)	23 (72%)	20 (77%)	20 (71%)
Age at injury, years	26 ± 11	27 ± 14	28 ± 15	31 ± 12
TBI recency, years	23 ± 14	19 ± 13	20 ± 14	19 ± 13
Number of TBIs				
1	7 (25%)	7 (22%)	4 (15%)	4 (14%)
2-3	9 (32%)	14 (44%)	15 (58%)	13 (46%)
4-5	7 (25%)	7 (22%)	3 (12%)	5 (18%)
>5	5 (18%)	4 (12%)	4 (15%)	6 (21%)
Type				
Blast	3 (10 %)	1 (3%)	2 (7%)	4 (14%)
Fall	6 (20 %)	8 (25%)	4 (13%)	6 (21%)
Sport	4 (13%)	4 (13%)	3 (10%)	5 (17%)
Motor Vehicle Collision	6 (20%)	5 (16%)	11 (37%)	11 (38%)
Other	11 (37%)	14 (43%)	10 (33%)	3 (10%)

ACKNOWLEDGEMENTS

We would like to express our sincere appreciation and gratitude for the participation of our research participants.

Funding

VA CSR Merit Award I01 CX002022
VA RRD IK2RX002947

No Financial or Non-financial Disclosures

The interpretations and conclusions expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs, the National Institute of Health, or the United States government.

References

- Mathias, J. & Alvaro, P. *Sleep Med.*, 2012.
- McInnes, K., et al., *PLOS ONE*, 2017.
- Fernstrom, JD., *J. Nutr.*, 2005.
- Lim, MM., et al., *Sci. Transl. Med.*, 2013.
- Elliott, JE., et al., *SLEEP*, 2018
- Elliott, JE., et al., *Front. Syst. Neurosci.*, 2022