



# Congenital Zika Virus Exposure Impacts Rhesus Macaque Neonatal Neurobehavior

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## Introduction

Prenatal Zika virus (ZIKV) exposure results in severe neurodevelopmental deficits for 10% of children (termed congenital Zika syndrome [CZS])<sup>1-3</sup>

30% of children with prenatal ZIKV exposure without CZS at birth will develop neurodevelopmental deficits by 2 years<sup>4</sup>

- The full spectrum of developmental deficits is unknown
- There are no early predictors to indicate which children are at risk for developing late onset deficits

## Purpose

1. Identify distinct developmental trajectories in rhesus macaque infants prenatally exposed to ZIKV
2. Identify birth characteristics (5- minute Apgar scores, birthweight,) that may predict differences in developmental trajectories

## Research Design & Methods

### Non – Human Primate model

- Rhesus macaques develop 3 – 4x faster than humans<sup>5</sup>
- Highly controlled, longitudinal design for comprehensive developmental assessment

N = 17, n (ZIKV exposed) = 13, n (control) = 4

### Apgar Score

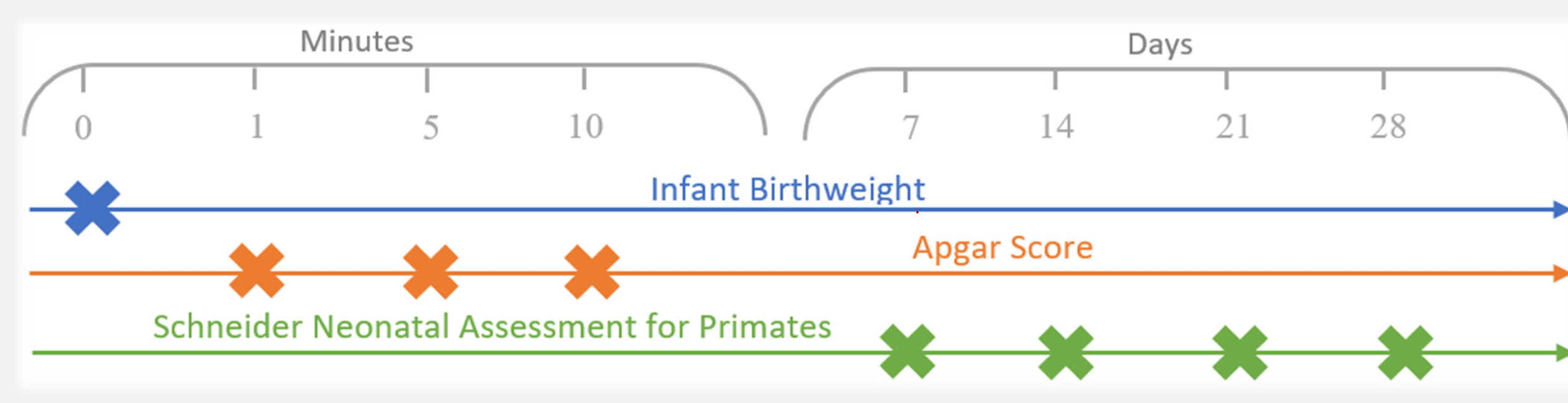
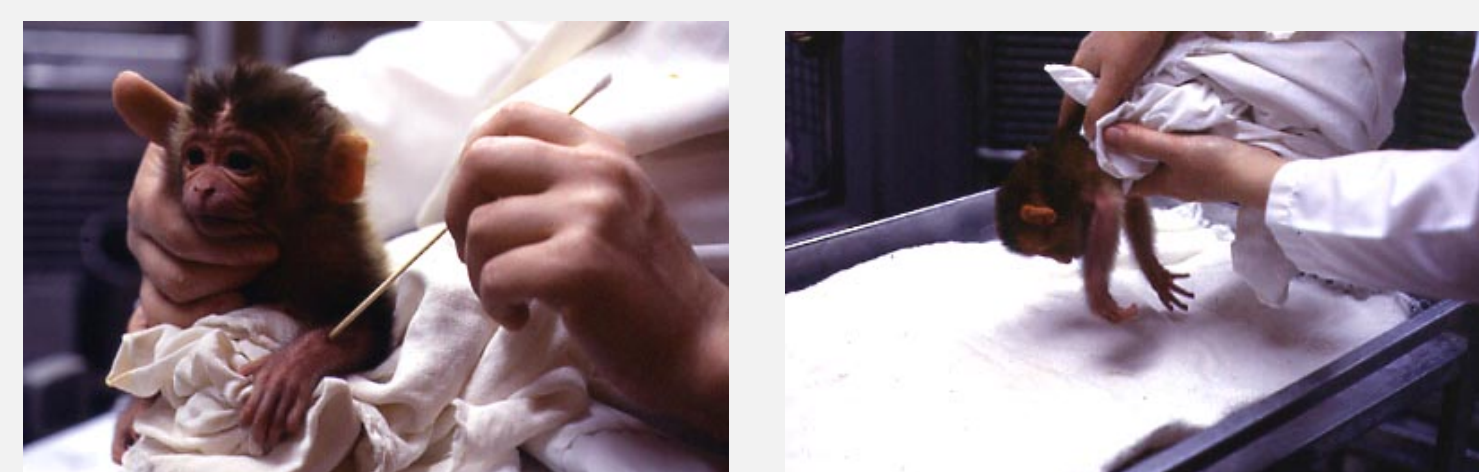
- Respiration, heart rate, muscle tone, behavioral status, skin coloration
- Rated 0, 1, 2 by anesthesia technician

### Schneider Neonatal Assessment for Primates

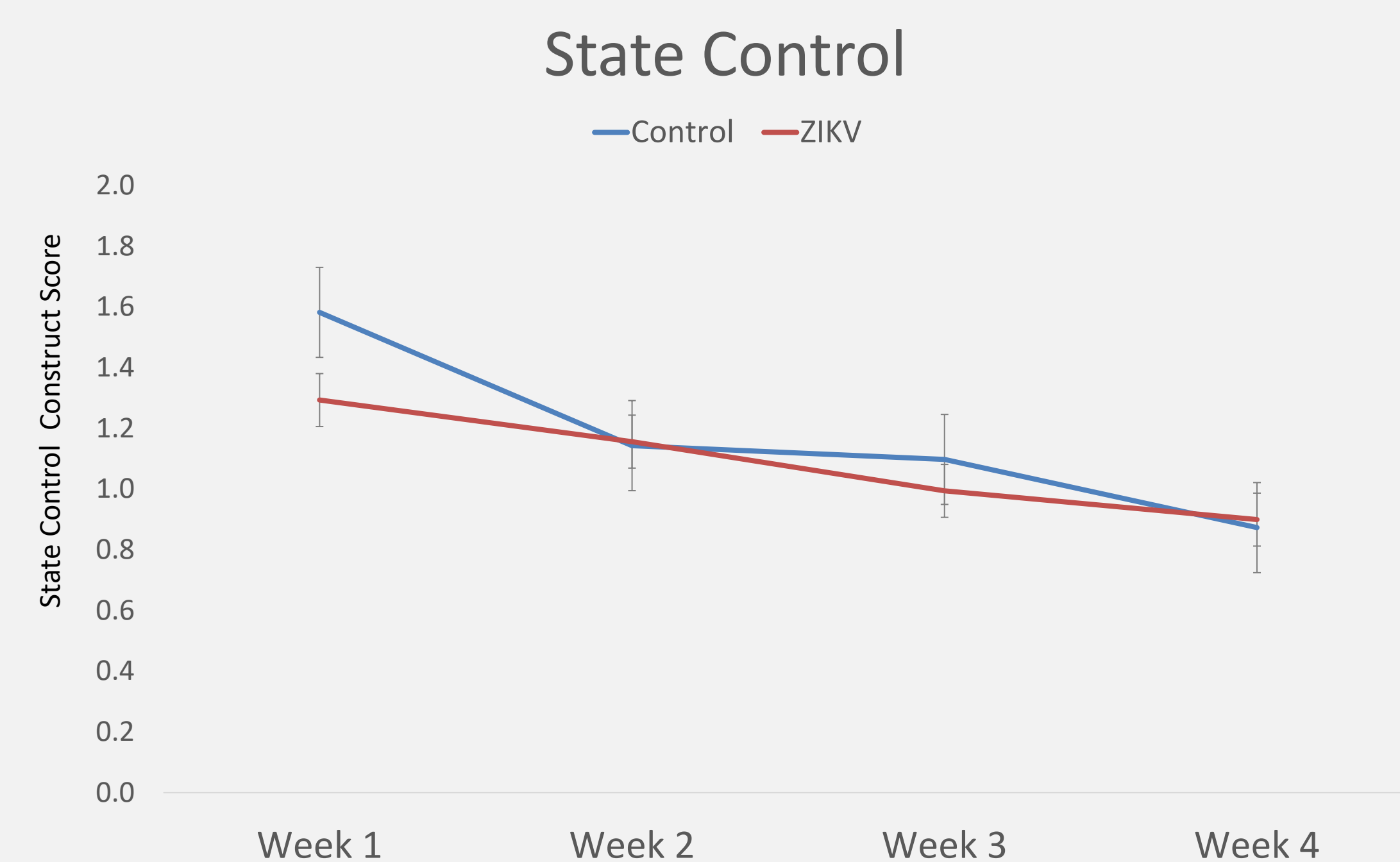
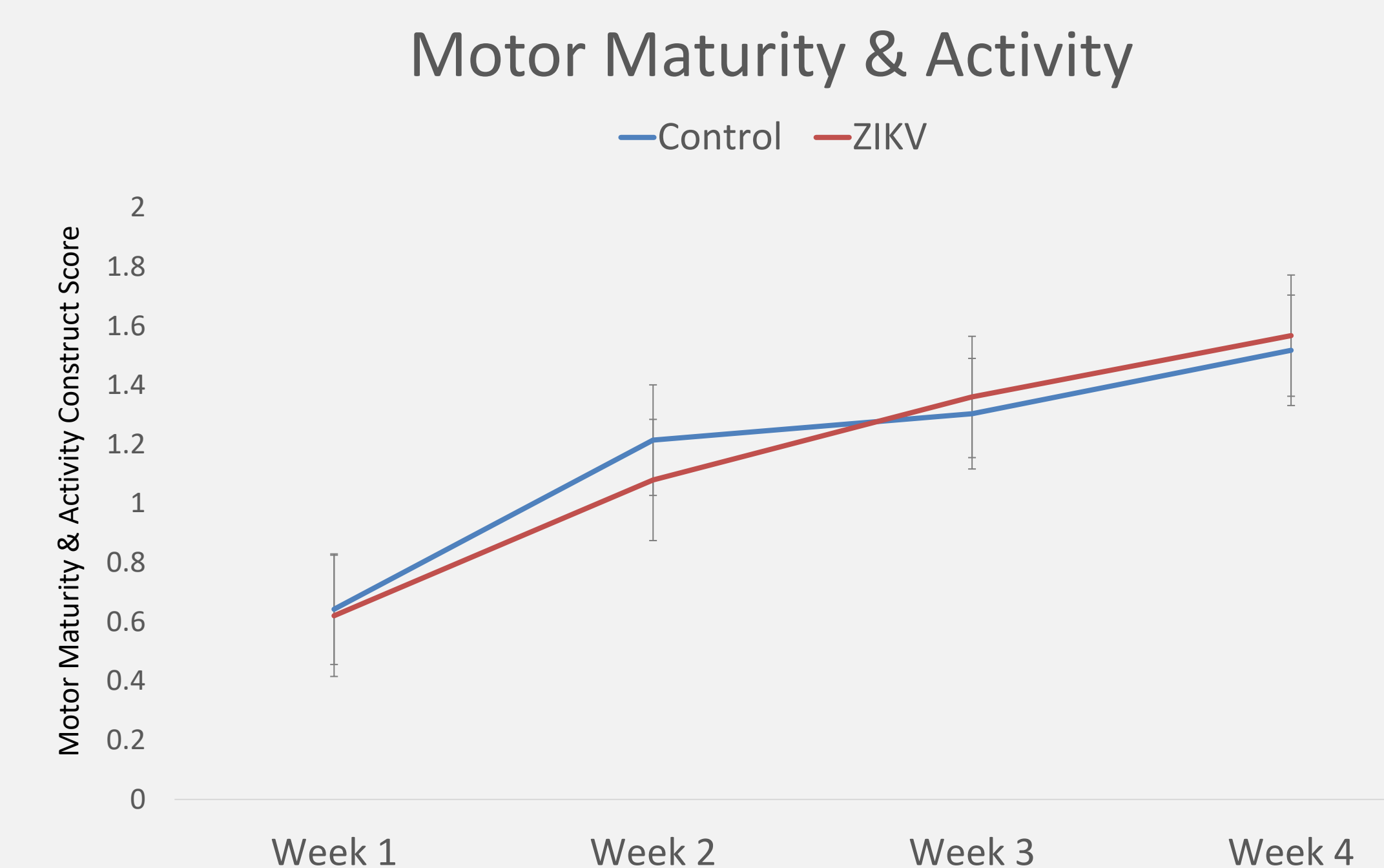
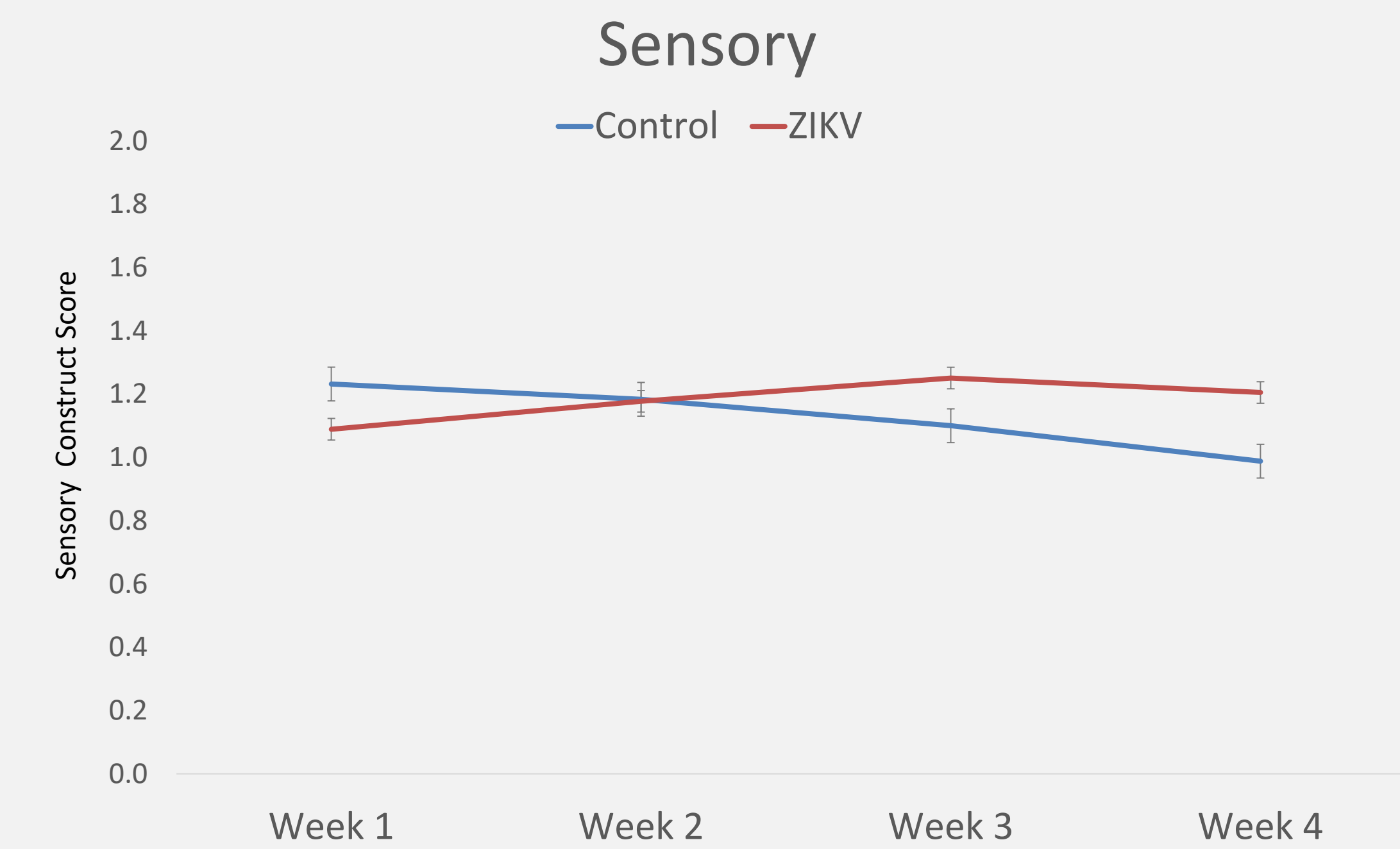
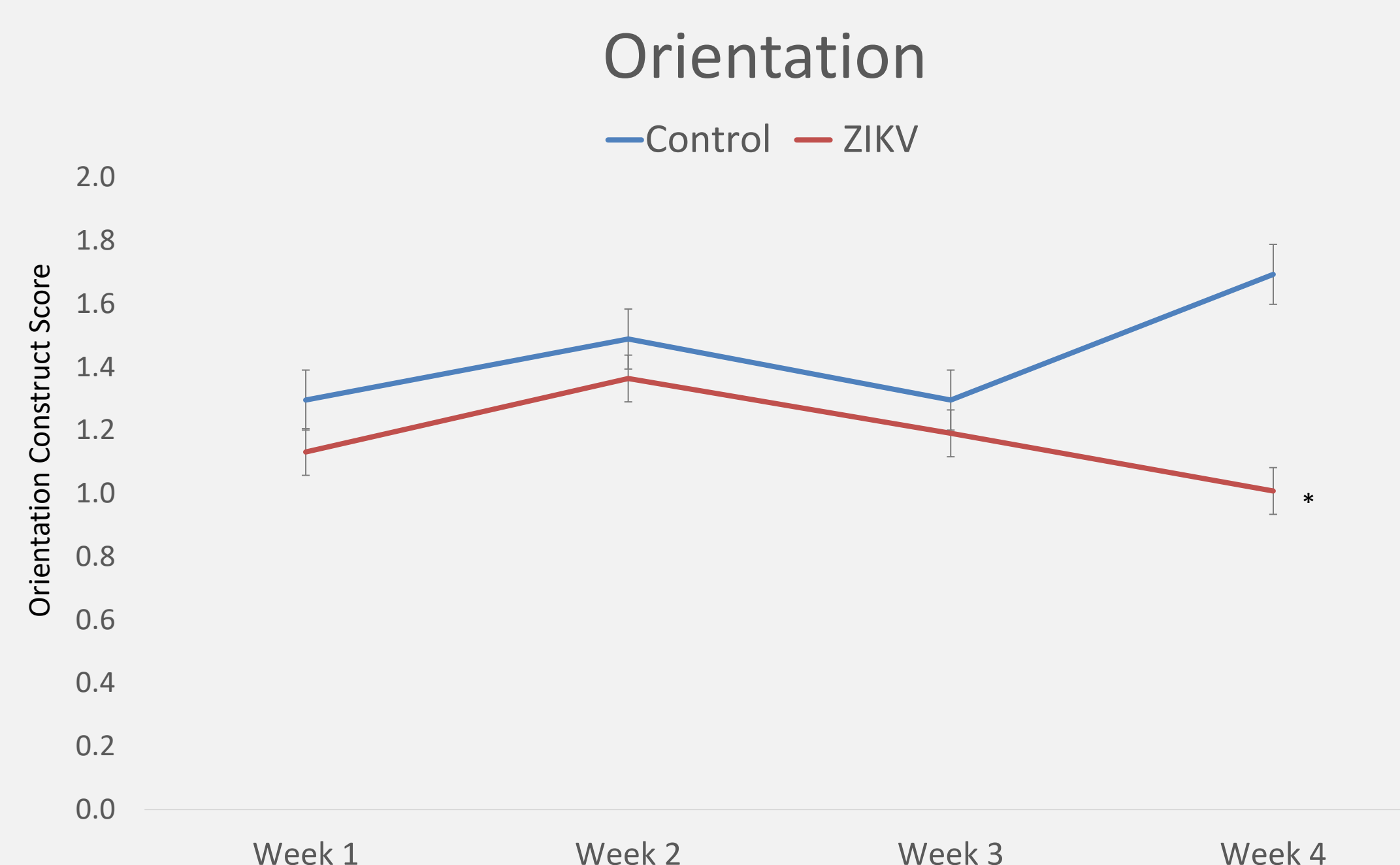
- 0 – 2, 5- Point Likert Scale

### Constructs

- Orientation
- Motor Maturity & Activity
- State Control
- Sensory



## Results



## Conclusions

- ZIKV-exposed infants demonstrate decreased orientation skills by 4 weeks
- No differences in developmental assessment scores in the motor maturity and activity, sensory, or state control variables at any timepoint
- No differences in 5 – minute Apgar scores and birthweight in the ZIKV-exposed and control groups
- 5- minute Apgar scores and birthweight did not predict developmental assessment score at 4 weeks

## Implications for Practice

- Developmental trajectories of children with prenatal ZIKV exposure may be subtly different from typically developing children in the context of visual and auditory orientation skills.
- These children are potentially at risk for accumulated developmental deficit that may impact long-term developmental outcomes if these early, subtle deficits go unnoticed
- Important to provide frequent, sensitive testing for children with potential prenatal ZIKV exposure

## References

1. Pierson TC, Diamond MS. The emergence of Zika virus and its new clinical syndromes. *Nature*. 2018;560:573-581. doi:10.1038/s41586-018-0446-y.
2. Reynolds MR, Jones AM, Petersen EE, et al. Vital Signs: Update on Zika Virus–Associated Birth Defects and Evaluation of All U.S. Infants with Congenital Zika Virus Exposure — U.S. Zika Pregnancy Registry, 2016. *MMWR Morb Mortal Wkly Rep*. 2017;66(13):366-373. doi:10.15585/mmwr.mm6613e1.
3. Pessoa A, van der Linden V, Yeargin-Allsopp M, et al. Motor Abnormalities and Epilepsy in Infants and Children With Evidence of Congenital Zika Virus Infection. *Pediatrics*. 2018;141(Supplement 2):S167-S179. doi:10.1542/peds.2017-2038F.
4. Nielsen-Saines K, Brasil P, Kerin T, et al. Delayed childhood neurodevelopment and neuro-sensory alterations in the second year of life in a prospective cohort of ZIKV-exposed children. *Nat Med*. 2019;25(8):1213-1217. doi:10.1038/s41591-019-0496-1.
5. Malkova L, Heuer E, Saunders RC. Longitudinal magnetic resonance imaging study of the rhesus monkey brain development. *Eur J Neurosci*. 2006;24(11):3204-3212. doi:10.1111.

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