A critical time window for early-life antibiotic exposure on autistic-like behavior and gut microbiota dysbiosis in mice

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Background
Autism spectrum disorder (ASD) is a neurodevelopmental disorder with early-onset and increase prevalence. Both genetic and environmental risk factors contribute to the etiology of ASD (Modabbernia et al., 2017). Clinical studies indicated that preterm infants have high risk developing ASD (Chen et al., 2019). Due to the immature immune system, the administration of antibiotic in preterm infants is a common practice to combat infections. However, the causal role for antibiotic exposure in the occurrence of ASD is not well characterized.

Aims & Objectives
Therefore, the hypothesis of this study is that early-life antibiotic exposure during infancy is a major risk factor for adverse neurobehavioral outcomes.

Methods
To characterize the neurobehavioral outcomes in mice exposed to antibiotic in early-life, the first-line antibiotics widely used in infants were given to the mice in three defined critical time window during development, namely pre-, peri-, and post-weaning stage. The offspring were tested for their behaviors, gut motility, colonic inflammatory response, and gut microbiome at adult stage.

Results
Treatment of antibiotic in mice at pre- and peri-weaning stage decreased the sociability and increased anxiety-like behavior, while antibiotic treatment at post-weaning stage had no effect. In addition, only peri-weaning antibiotic-treated offspring displayed increase of depression-like behavior. Interestingly, the increased gut motility was observed in mice treated antibiotic at pre-, and peri-weaning stages, but not at post-weaning stage. Moreover, the acute pro-inflammatory cytokines were only increased in pre-weaning antibiotic-treated offspring. To further understand whether the early-life antibiotic exposure shifts the gut microbiome, we profiled the fecal 16S rRNA and revealed a long-lasting dysbiosis of gut microbiome caused by early-life antibiotic exposure.

Discussion & Conclusion
Altogether, this study demonstrates that the early-life antibiotic exposure at a defined time window impacts the neurobehavioral outcomes, gut motility, colonic immune system, and the symbiosis of gut microbiome.