UKE Paper of the Month August 2019

Spatiotemporal ontogeny of brain wiring

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ABSTRACT:
The wiring of vertebrate and invertebrate brains provides the anatomical skeleton for cognition and behavior. Connections among brain regions are characterized by heterogeneous strength that is parsimoniously described by the wiring cost and homophily principles. Moreover, brains exhibit a characteristic global network topology, including modules and hubs. However, the mechanisms resulting in the observed interregional wiring principles and network topology of brains are unknown. Here, with the aid of computational modeling, we demonstrate that a mechanism based on heterochronous and spatially ordered neurodevelopmental gradients, without the involvement of activity-dependent plasticity or axonal guidance cues, can reconstruct a large part of the wiring principles (on average, 83%) and global network topology (on average, 80%) of diverse adult brain connectomes, including fly and human connectomes. In sum, space and time are key components of a parsimonious, plausible neurodevelopmental mechanism of brain wiring with a potential universal scope, encompassing vertebrate and invertebrate brains.

STATEMENT:
The developmental mechanisms that sculpt the wiring of the brain are unknown, but such knowledge is crucial for linking pathological miswiring to developmental abnormalities. With the aid of computational modeling, we demonstrate a parsimonious mechanism of connectivity formation that is rooted in the spatiotemporal development of the brain. Our results highlight that pathological miswiring might be the result of not only disturbances in the expression of axonal guidance cues, but also of disturbances of the normative spatiotemporal unfolding of brain development. Moreover, we demonstrate the universal and fundamental nature of these developmental mechanisms, by demonstrating their applicability to humans as well as a wide and diverse range of animal models, including flies and mice, thus bridging results from non-human to human research.

BACKGROUND:
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