cus, correlate with a higher risk of developing cognitive deficits and temporal lobe epilepsy as adults, suggesting that they may permanently change the developmental trajectory of neuronal circuits. The mechanisms underlying these effects are not clear. Cation-chloride cotransporter KCC2 decreases intracellular Cl^- levels and renders GABA responses hyperpolarizing. Recent data suggest that KCC2 also modulates excitatory synapse development. Here, we demonstrated that KCC2 expression is altered by early-life febrile status epilepticus and investigated the functional impact of this alteration on subsequent synapse formation.

We analyzed KCC2 expression and spine density in the hippocampus of a well-established rodent model of atypical febrile seizures, combining a cortical freeze lesion at post-natal day 1 (P1) and hyperthermia-induced seizure at P10 (LHS rats). At P20, we found a precocious increase in KCC2 protein levels, accompanied by a negative shift of E_{GABA} following high-frequency stimulation. In parallel, we observed a striking reduction in dendritic spine density and of mEPSC amplitude and frequency in CA1 pyramidal neurons. To investigate whether KCC2 precocious overexpression plays a role in spine alterations, we mimicked it in hippocampal organotypic cultures by biolistic transfection and *in-vivo* by *in-utero* electroporation. We found that both manipulations decreased spine density. Finally, to causally link KCC2 increased expression to spine loss in the LHS model, we blocked KCC2 *in vivo* by *in utero* electroporation of shRNA, and induced the dual pathologies as explained above. Our preliminary results suggest that reducing KCC2 expression levels in LHS rats rescued spine density loss. Therefore, increased KCC2 levels induced by early-life seizure affect spine formation and may be a contributing factor to the occurrence of hippocampal atrophy and associated cognitive deficits.

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Effects of PQQ on cognitive function induced by MK801 and its molecular imaging evaluation

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Introduction: Pyrroloquinoline quinone (PQQ), an essential nutrient, antioxidant and nerve growth factor has received attention for its ability to protect the brain against oxidative damage. An accumulating evidence has indicated that the neuroprotective function of PQQ is extraordinary and worthy of further exploration. PQQ administration significantly attenuated MK-801-induced increases in stereotypical behavior and ataxia were found in our previously study. To elucidate the underlying mechanisms of PQQ, future studies are necessary. In this study, we evaluated the effects of different doses of PQQ on uptake value of cortex/cerebellar in MK-801-induced mice using ^{18}F-FDG imaging.

Methods: Mice were divided into four groups: (1) control group: saline was injected after injection saline 30 min; (2) model group: MK-801 (0.6 mg/kg) was injected after injection saline 30 min; (3) risperidone group: MK-801 (0.6 mg/kg) was injected after injection risperidone (0.5 mg/kg) 30 min; (4) PQQ group: Twenty minutes after the first injection of 20% mannitol, PQQ was injected (0.001, 0.01, 0.1, 1, 10, 20, 50 mg/kg), 30 min after, MK-801 (0.6 mg/kg) was injected. ^{18}F-FDG was injected (6 MBq, 0.2 mL). Mice were scanned by microPET and cortex/cerebellum was quantitative analysis.

Results:

	Dose (mg/kg)	Cortex/cerebellar
Control group		1.395
Model group		0.979
Risperidone group		1.092
PQQ group	0.001	1.013
	0.01	1.031
	0.1	1.052
	1	1.064
	10	1.107
	20	1.161
	50	1.003

Discussion: PET imaging showed that the radioactivity uptake of the cortex/cerebellar decreased in the MK-801-induced mice than in normal. After intervention by risperidone, the cortex/cerebellar radioactivity uptake was increased. The value was also increased with increase of PQQ dose. The results indicate that PQQ may prevent the development of MK-801-induced cognitive deficits if used in appropriate doses, which suggests new treatment approaches for schizophrenia in humans.

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Age-related changes in the topological organization of white matter structural networks across the human lifespan

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Introduction: Lifespan is a dynamic process with remarkable changes in brain structure and function. Previous neuroimaging studies have indicated age-related changes in regional gray matter morphology and specific white matter (WM) tracts across lifespan. Recently, researchers have suggested the brain can be modeled as a network by characterizing the interactions between regions. However, the age-related alterations in the topological architecture of WM structural networks across the human lifespan remain largely unknown and are crucial to understanding the dynamic functional changes with age.

Methods: We employed diffusion MRI and deterministic tractography approaches to reconstruct whole-brain WM structural connectivity networks in a group of 113 healthy individuals ranging from 9 to 85 years old from a public NKI/Rockland Sample (http://fcon_1000.projects.nitrc.org/indi/pro/nki.html), followed by a graph theoretical analysis.

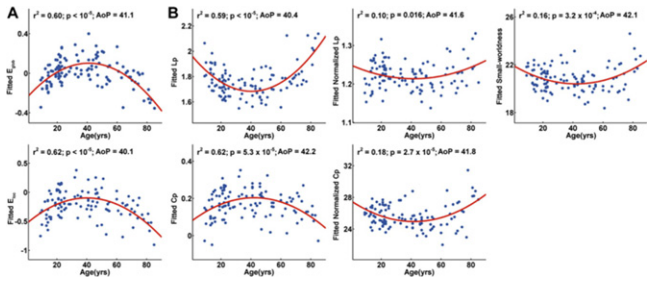

Fig. 1. The lifespan trajectories of the global network metrics of Wm networks. (A) Tje lifespan trajectories of global and local efficiency. (B) The lifespan trajectories of small-world parameters (Lp, Cp, normalized Lp, normalized Cp and small-worldness). The blue dots represent the adjusted values of each subject after controlling for age, gender, and brain size. The curve-fitted lines are shown in red. Significant age-related trajectories were found for all global metrics of the WM networks.

Results: Most of the global network properties, including network strength, topological efficiency, and robustness, followed an inverted U-shaped trajectory with an age peak at the fourth decade (Fig. 1). The brain areas with the most prominent quadratic changes with age were primarily located in the prefrontal and temporal cortices and exhibited heterogeneous trajectories: several default-mode regions displayed prolonged maturation and aging compared to the prefrontal cortex (Fig. 2). Rich-club organization was evident across lifespan, whereas hub integration decreased linearly with age, especially accompanied by the loss of frontal hubs and their connections. Finally, we identified age-related quadratic changes in WM connectivity strength predominantly within and between prefrontal and temporal modules.

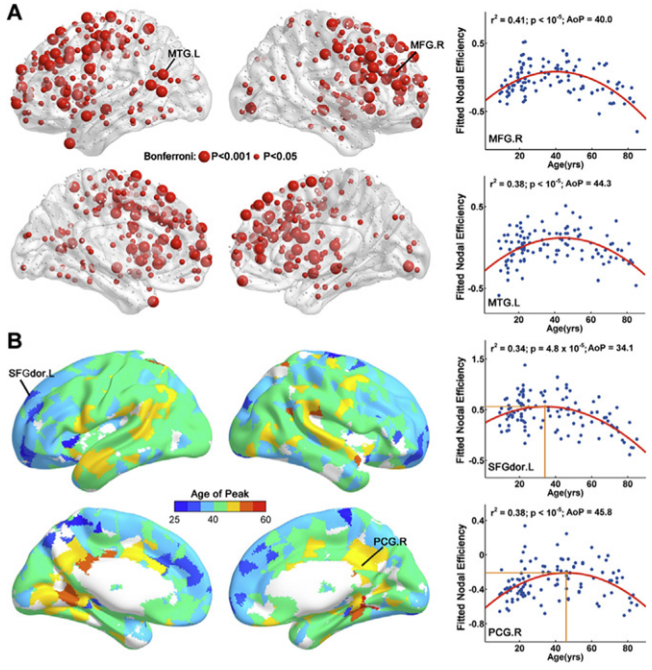

Fig. 2. The distribution of regions with significant age related alterations and the AoPs across regions. (A) A 3D representation of brain regions illustrating age-related alterations of nodal efficiency. Two representative nodes were selected to depict the age-related trajectory curves of nodal efficiency, one is the right MFG (upper right panel) and the other is the left MTG (lower right panel). (B) 3D representation of the AoPs across the regions with quadratic trajectories ($p < 0.05$, uncorrected). To present the early and the late AoPs, left SFGdor and right PCG were selected to depict the trajectory curves, and the AoPs were marked with orange lines.

Conclusion: These data indicated lifespan changes in the topological organization of human whole-brain WM networks, thus providing possible structural substrates underlying behavioral and cognitive changes with age.

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Reversal of immobilization stress-induced anorexia and endogenous leptin levels by *Rauwolfia serpentina* in rats: Relationship with adaptation to stress

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Clinical observations supported the hypothesis that stress is the major precipitating factor in the onset of depression, anorexia nervosa, diabetes and obesity. The objective of present work is to investigate the effects of post stress administration of *Rauwolfia serpentina extract* on adaptation to immobilization stress in rats. The plant extract (10 mg/kg) was orally administered after the termination of immobilization stress, daily for 5 days, to monitor drug-induced behavioral change and tolerance in immobilization stress-induced anorexia. We also tested effects of *R. serpentina* extract on endogenous leptin and glucose level in unstressed and stressed animals to explore the possible role of HPA axis in the modulation of stressed induced behavioral deficits and adaptation to stress. We find that that *R. serpentina extract* can blunt stress-induced anorexigenic as well as anxiogenic-like effects. Moreover, *R. serpentina extract* reversed adverse effects of stress and facilitate adaptation to an uncontrollable stressor by reducing stress perception. The present study shows that immobilization stress induced decreases in food intake, body weight as well as behavioral deficits were reversed by *R. serpentina extract* suggesting anxiolytic like profile of drug. This effect of *R. serpentina extract* can be explained in terms of additive effects of stress on serotonin (5-hydroxytryptamine; 5-HT) neurotransmission particularly via postsynaptic $5HT_{2C}$ as well as $5HT_{1A}$ receptors. It is therefore suggested that post stress administration of *R. serpentina extract* provides an innovative approach for the treatment of stress related disorders.

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