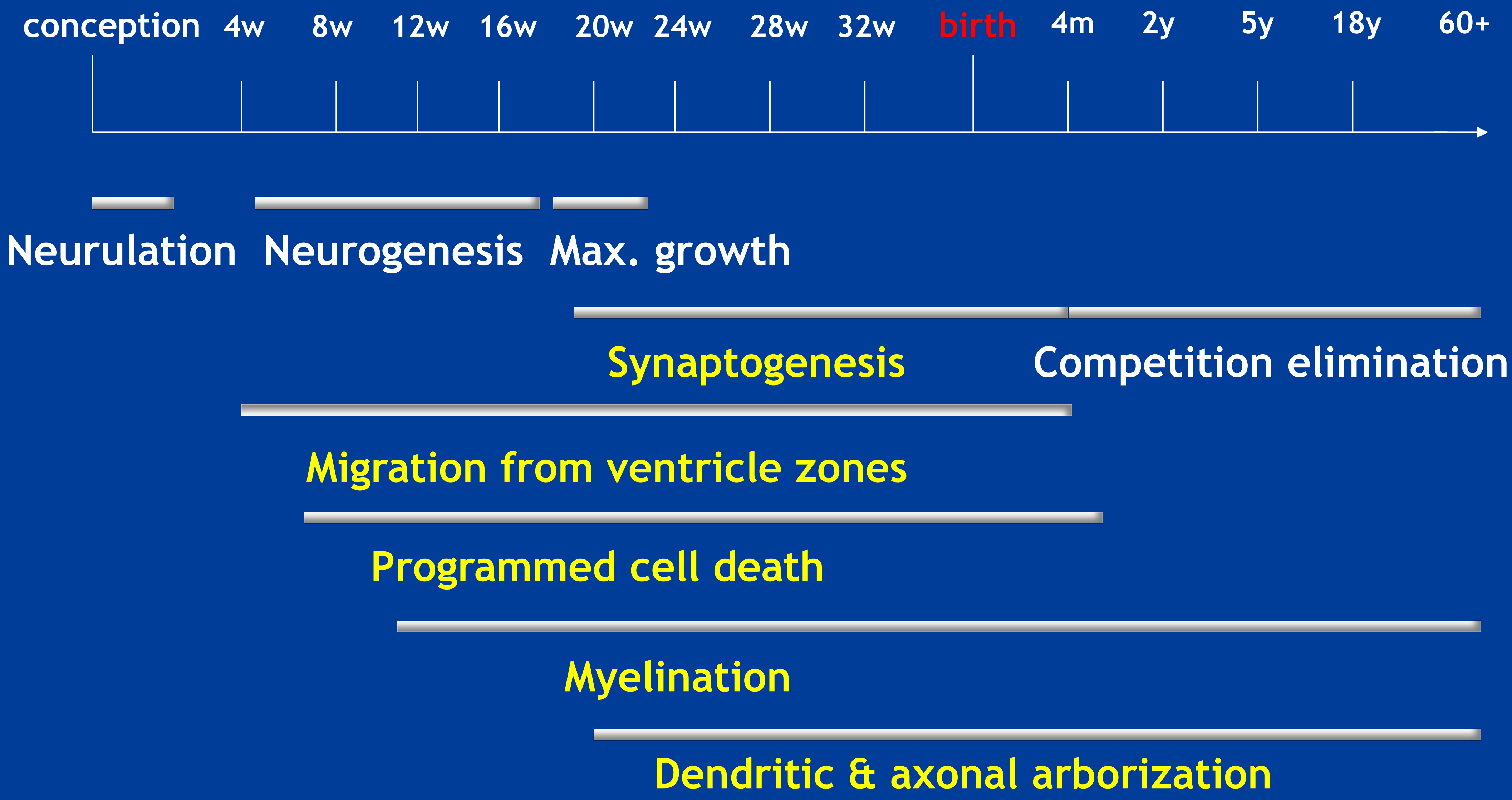
Evidences of Neuroplasticity in Neonates

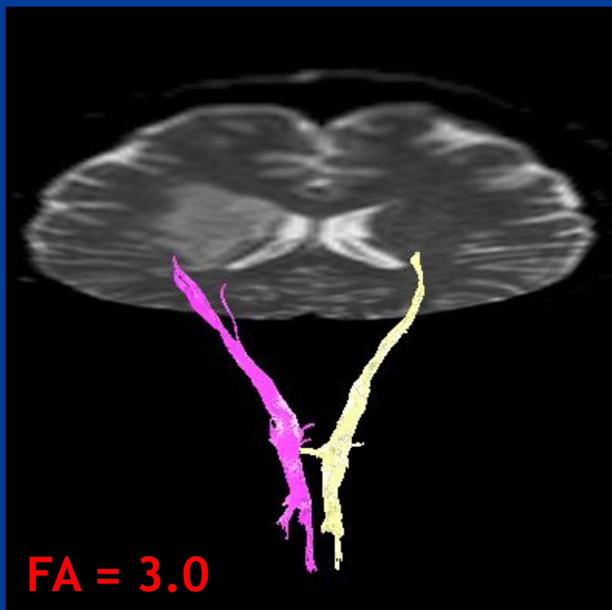
Yeungnam University
Dept. of Physical medicine & Rehabilitation
Su Min Son

Neuroplasticity?

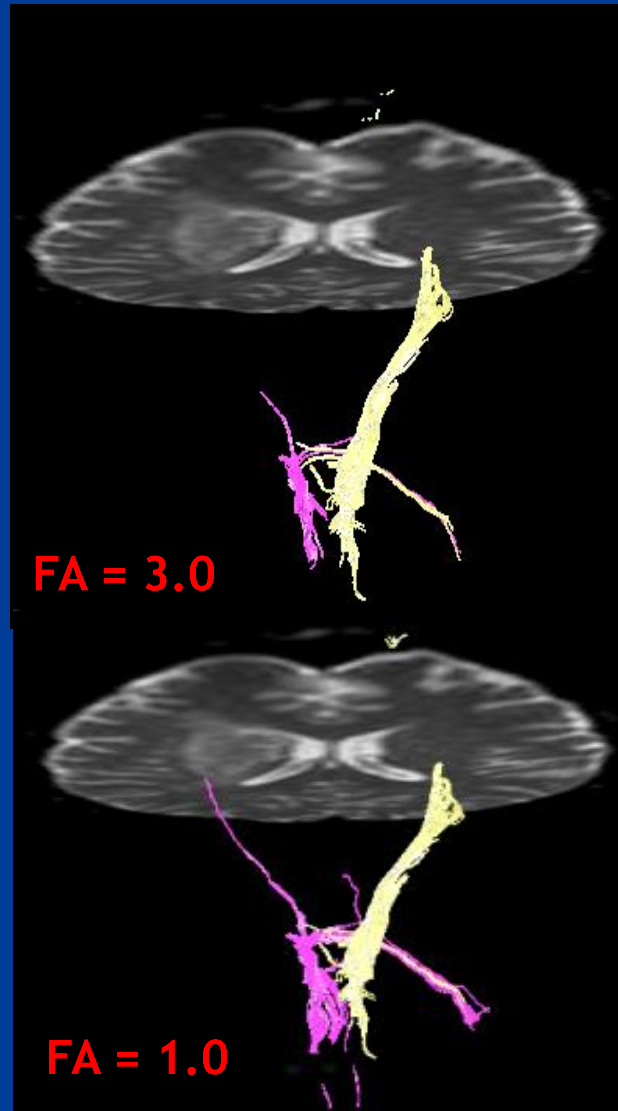
Time line of critical events of human brain morphometry



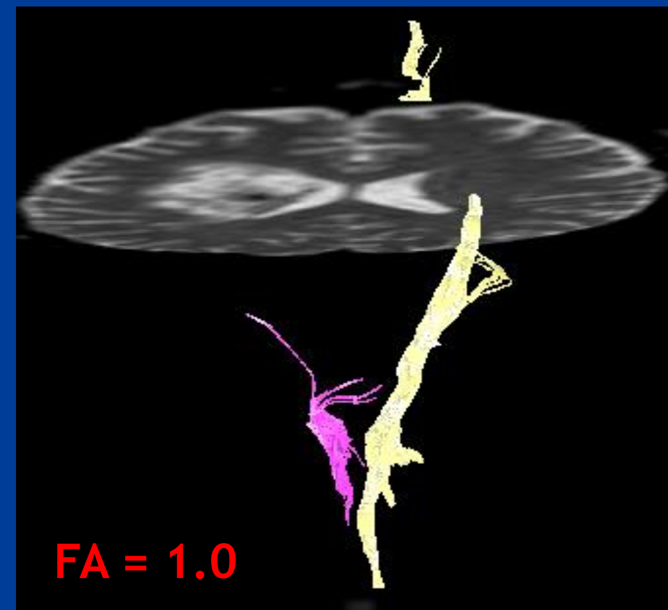
Natural course of CST after stroke



Stroke onset 2 days



9 days

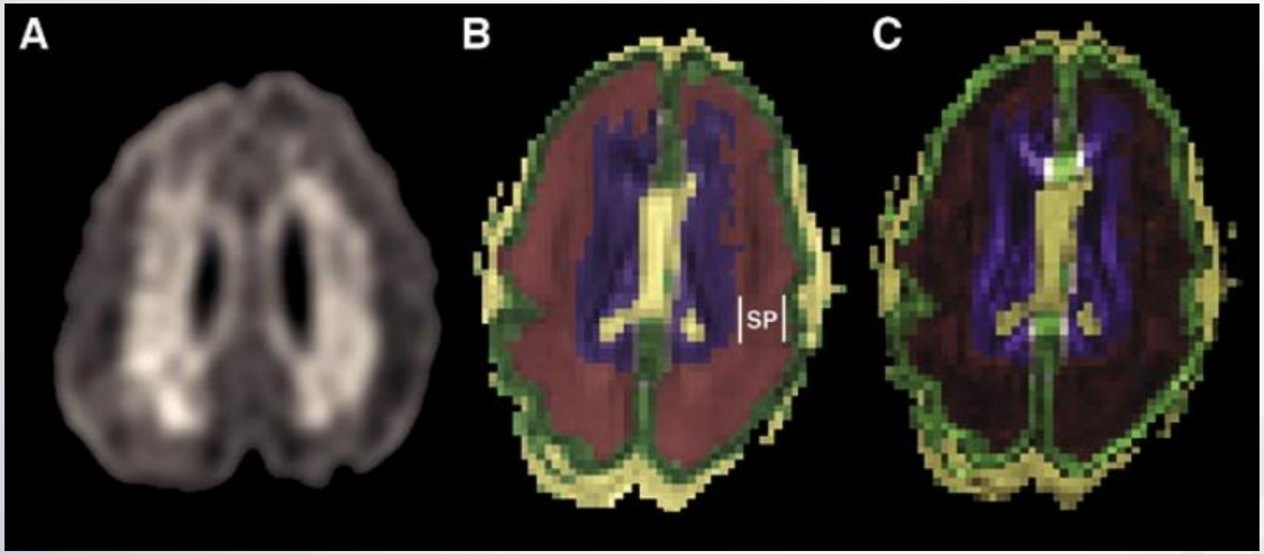


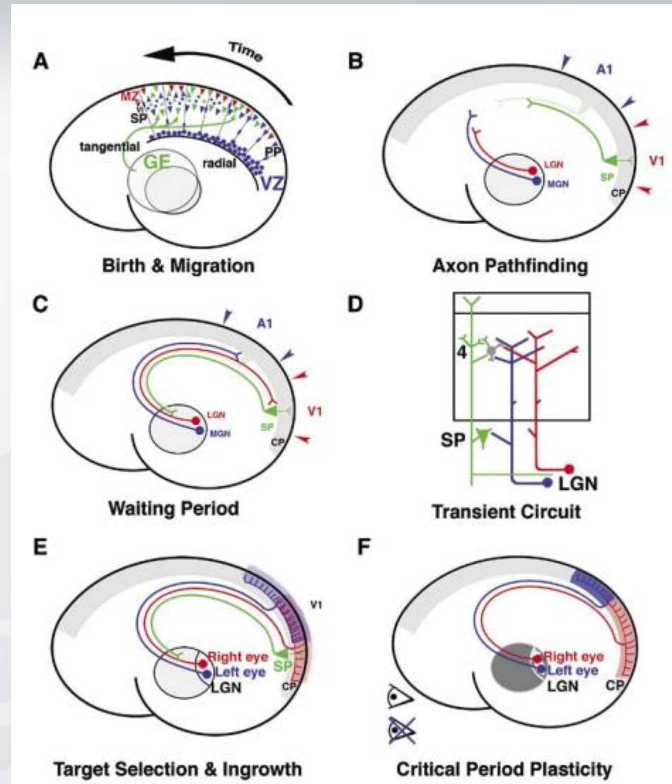
16 days

Basic mechanism of neuroplasticity

- Neurogenesis
- Programmed cell death
- Activity dependent synaptic plasticity
- Reduction of plastic changes related to vulnerability

Perinatal subplate neuron injury

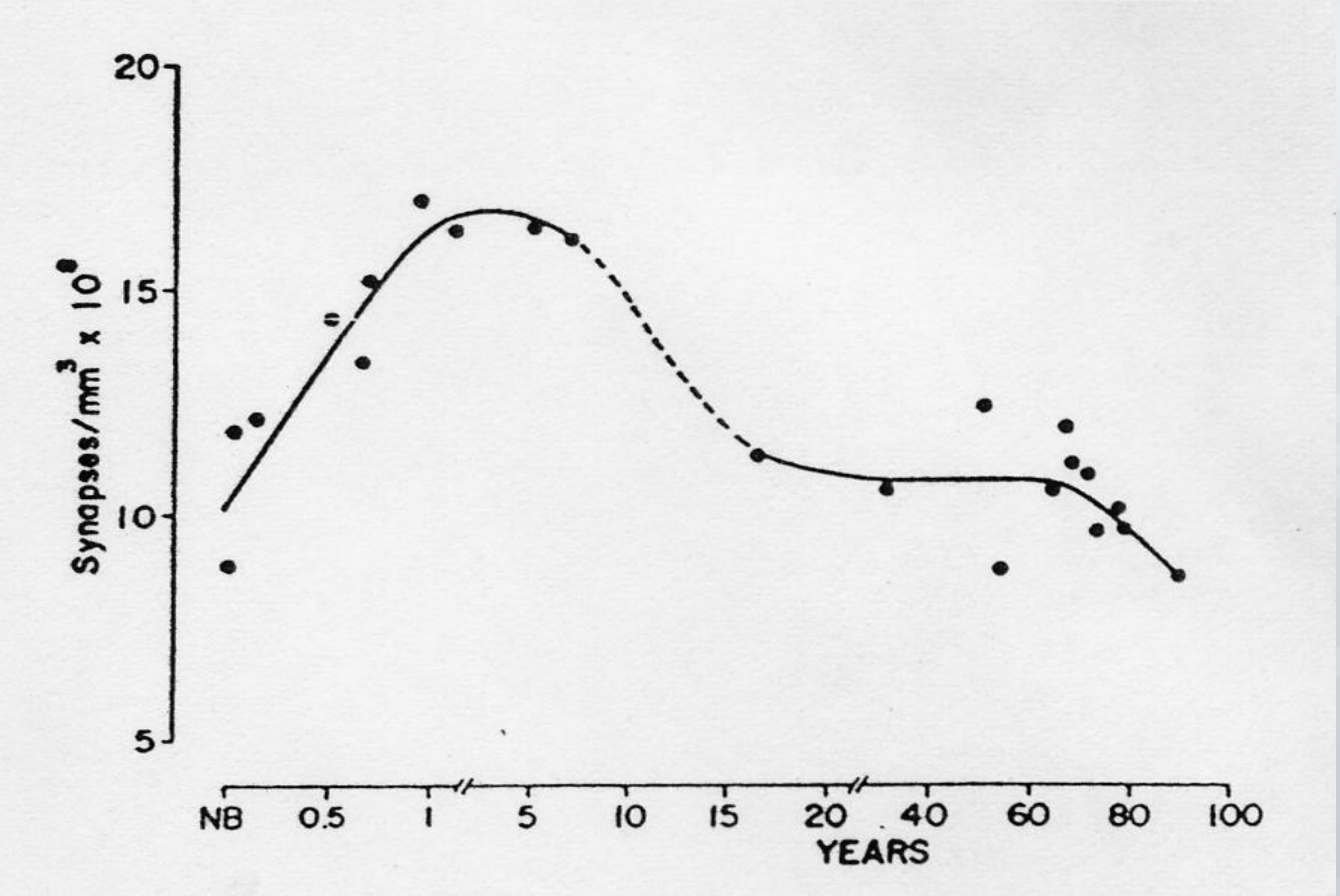




Species	Subplate Birthdate	Waiting Period	Subplate Death	Ocular Dominance Critical Period
Mouse	E11-13 (138)	E14-P0 (35)	E18-P20 (116, 138, 141)	†P19-32 (physiologic plasticity) (59)
Rat	E12-15 (11)	E16-17 (40) (None? [17])	E20-P30 (2, 45)	†P21-P35 (physiologic plasticity) (42)
Cat	E24-30 (107)	E36-50 (55)	P0-28 (22)	P28 - 56 (81, 146)
Primate	E38-48 (94)	E60-80 (95)	*E104(vis.)/E120(sens.) – PND7 (96)	PNW1-12 (79, 104)
Human	GW5-6 (12, 96)	GW20-26 (71, 92)	GW34–41 (142) (see also [96])	NR (see [58])

McQillen et al. brain pathol. 2005

Densities of Synapse



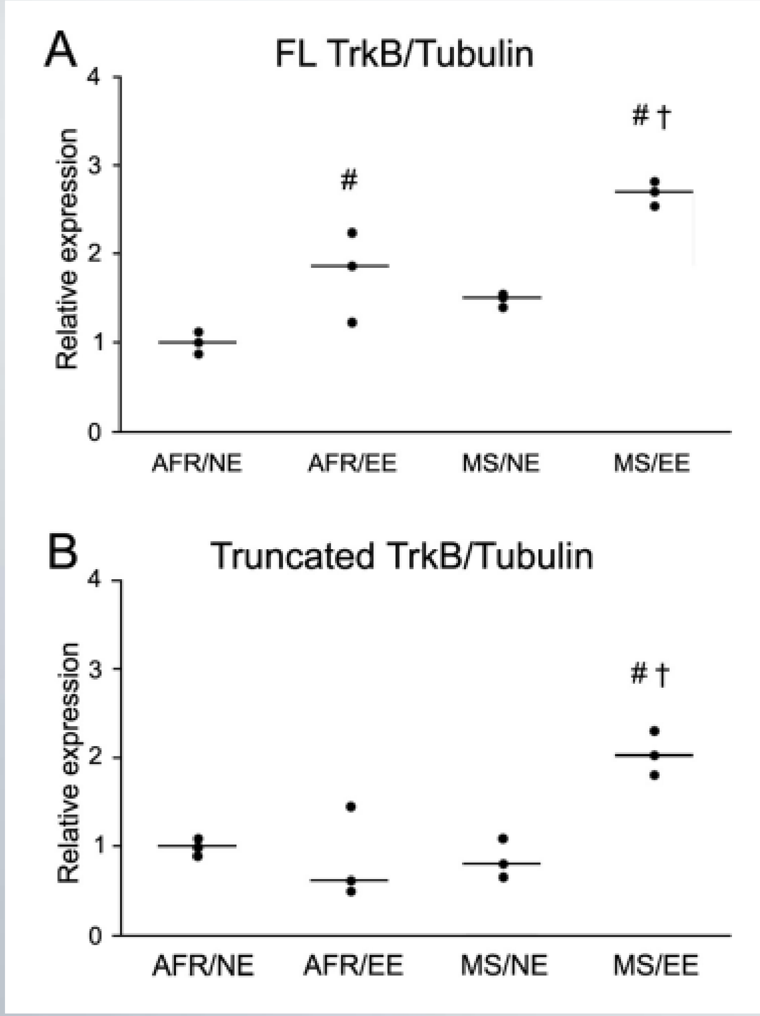
Huttenlocher P. Brain research. 1975

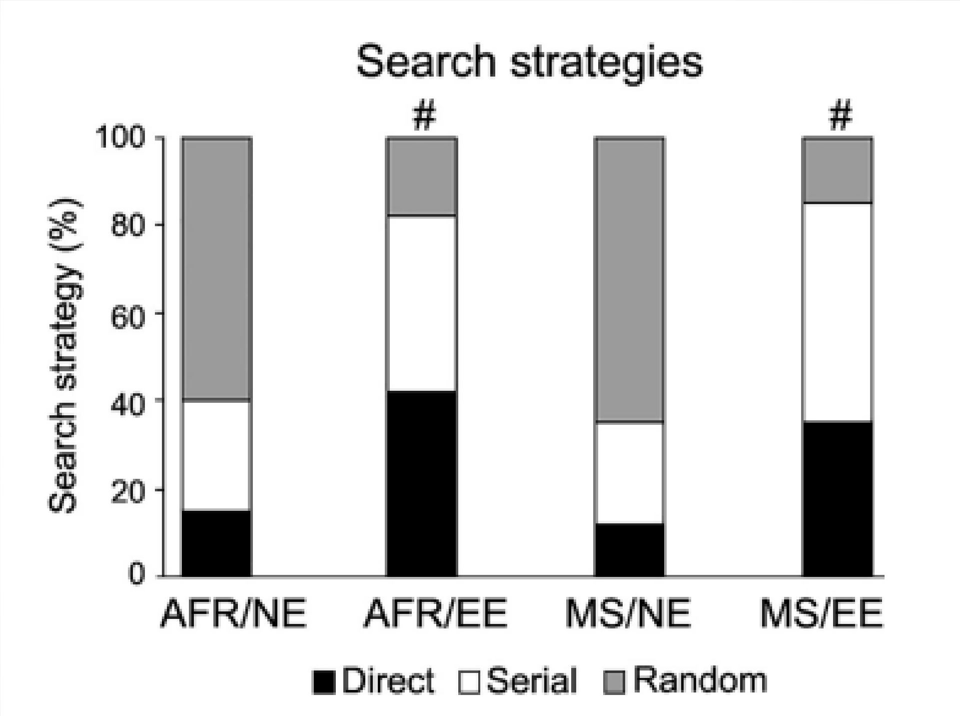
Early intervention in prematurity

References	Population	Time of assessment	Sample size (N)	Stress measure	Outcome
Brain development					
Brummelte et al. (120)	Infants (born 24–32 weeks)	32 and 40 weeks	86	Number of invasive procedures: early (birth-scan 1) and late (scan 1-scan 2).	Greater invasive procedures: ↓ white matter FA, ↓ subcortical gray matter NAA/choline. Effects dependent on timing stress.
Chau et al. (125)	Children (born <32 weeks)	8 years of age	57	Number of invasive procedures during the stay in the NICU	Greater invasive procedures: ↓amygdala volume, ↓ thalamus volume. Stress × COMT ↓ hippocampal subregional volume
Doesburg et al. (128)	Children [born extremely preterm [24–28 weeks], very preterm [28–32 weeks], and full-term]	8 years of age	54	Number of invasive procedures during the stay in the NICU	Greater invasive procedures: atypical spontaneous neuromagnetic activity *(only in extremely preterm born children)*
Duerden et al. (123)	Infants [born very preterm [<33 weeks]]	32 and 40 weeks	138	Number of invasive procedures during the stay in the NICU: categorized into two groups	Greater invasive procedures: no association with hippocampal growth
Duerden et al. (121)	Infants [born extremely preterm [24–28 weeks] or very preterm [29–32 weeks]]	32 and 40 weeks	155	Number of invasive procedures: early (birth-scan 1) and late (scan 1-scan 2)	Greater invasive procedures: ↓ lateral thalamus volume, ↓ metabolic growth (NAA/Cho), ↓ FA corpus callosum, posterior white matter, cingulum, and fornix. *(only in extremely preterm born children in combination with early stress)*
Kozhemiako et al. (129)	Children [born extremely preterm [24–28 weeks], very preterm [29–32 weeks], and full-term]	8 years of age	100	Number of invasive procedures during the stay in the NICU	Greater invasive procedures: atypical spontaneous neuromagnetic activity *(only in extremely preterm born children)*
Ranger et al. (127)	Children [born very preterm [27–32 weeks]]	8 years of age.	42	Number of invasive procedures during the stay in the NICU	Greater invasive procedures: ↓ cortex thickness (e.g., frontal, parietal, and temporal regions)
Ranger et al. (126)	Children [born very preterm [27–32 weeks]]	8 years of age	42	Number of invasive procedures during the stay in the NICU	Greater invasive procedures: ↓ cerebellar volumes
Schneider et al. (49)	Infants [born very preterm [<30 weeks]]	29, 31, and 40 weeks	51	Number of invasive procedures during the stay in the NICU	Greater invasive procedures: ↓ growth thalamus, basal ganglia, total brain volumes
Smith et al. (119)	Infants [born very preterm [<30 weeks]]	Term equivalent age	44	Neonatal Infant Stressor Scale: during stay in the NICU or until term equivalent age	Greater number of stressors: ↓ frontal and parietal diameter, and ↓ interhemispheric connectivity temporal lobes
Tortora et al. (122)	Infants [born very preterm [<33 weeks]]	Term equivalent age	46	Number of invasive procedures: categorized into four groups	Greater invasive procedures: ↓ connectivity thalami—bilateral somatosensory cortex, ↓ connectivity insular cortex—ipsilateral amygdala/hippocampus

Lammertink et al.
Front in Psychiatry. 2021

The impact of enriched environment

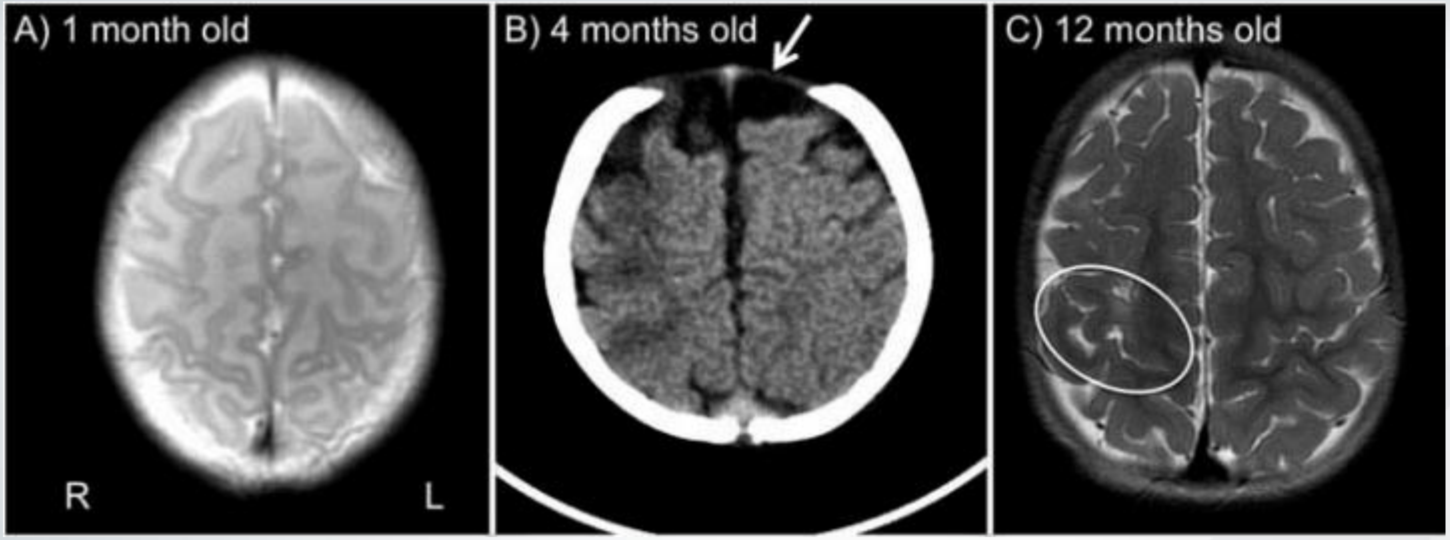


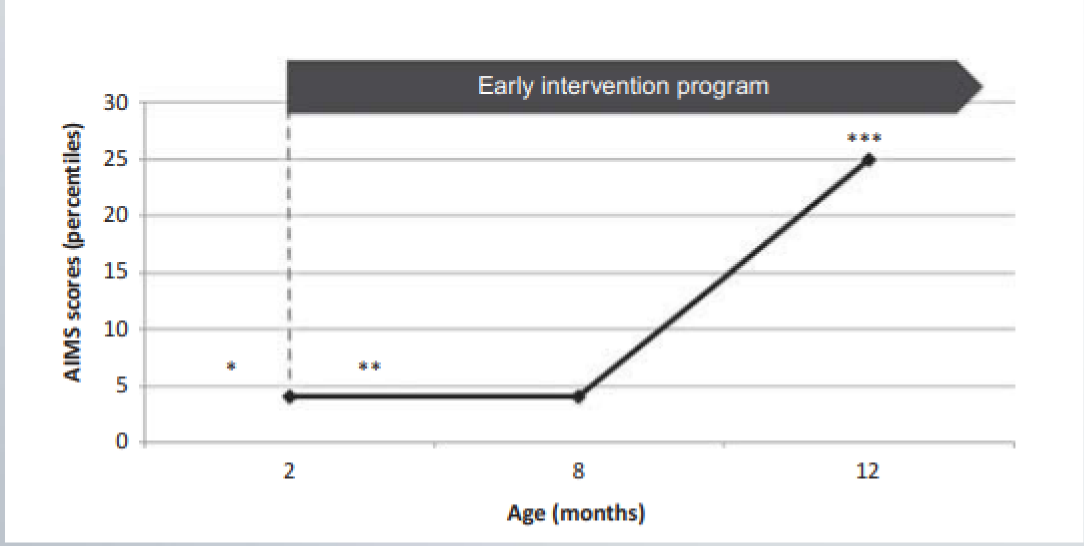


AFR: animal facility rearing
MS: neonatal maternal separation
EE: enriched environment
NE: non- enriched environment

Cordier et al. Neurosci. 2021

The impact of early intervention





Gallagher et al. Devel Neurorehab. 2017

Evidences of Plasticity in Immature brain

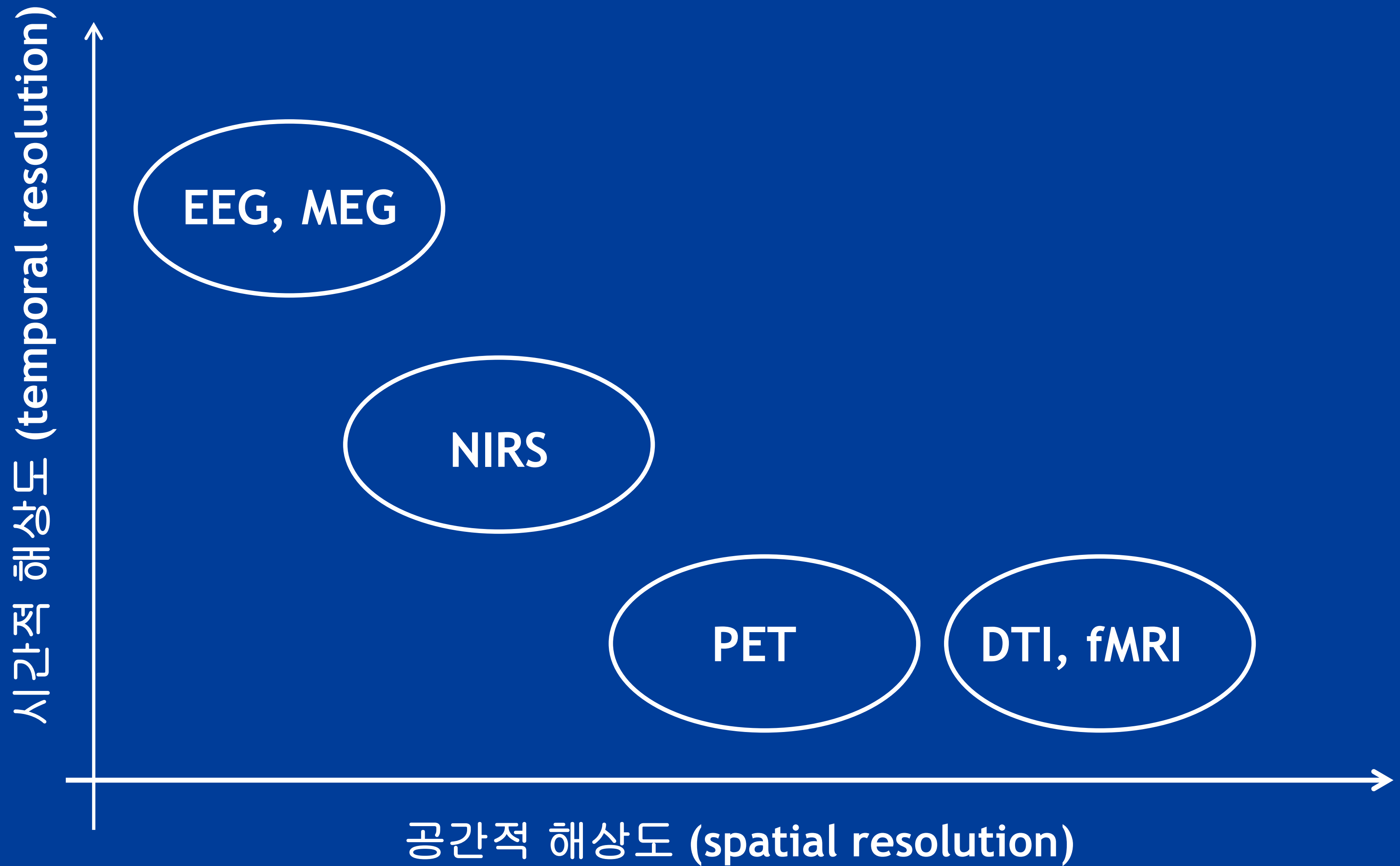
Evaluation & treatment modality

Evaluation

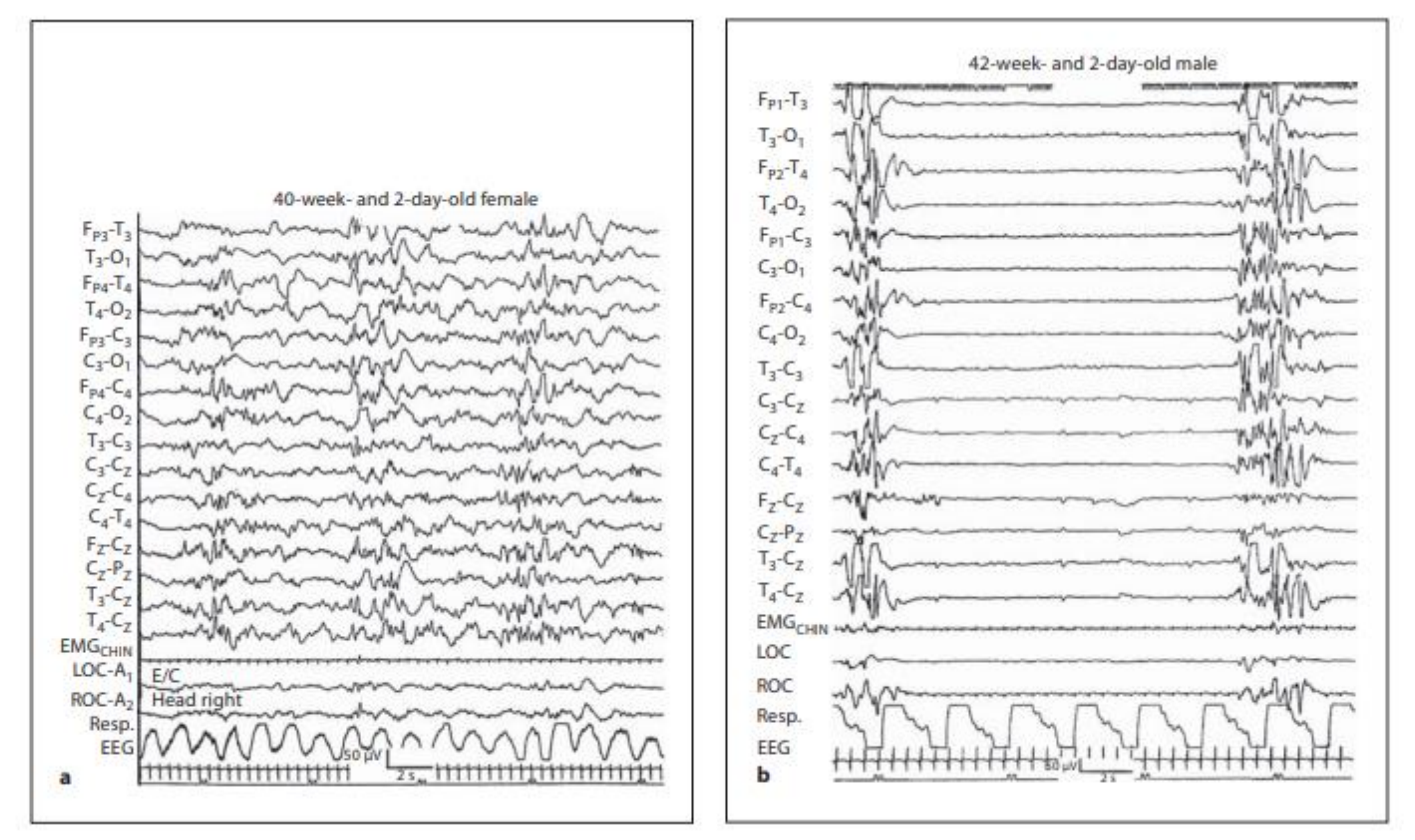
- Structural imaging: MRI, diffusion MRI,DTT
- Functional imaging: fMRI
- metabolic imaging: MRS (magnetic resonance spectroscopy)
- TMS (transcranial magnetic stimulation)
- EEG (electroencephalography)
- MEG (magnetoencephalography)

Treatment

- Manual tx (PT/OT..)
- rTMS (repetitive transcranial magnetic stimulation)
- tDCS (transcranial direct current stimulation)
- Education & counselling of the family

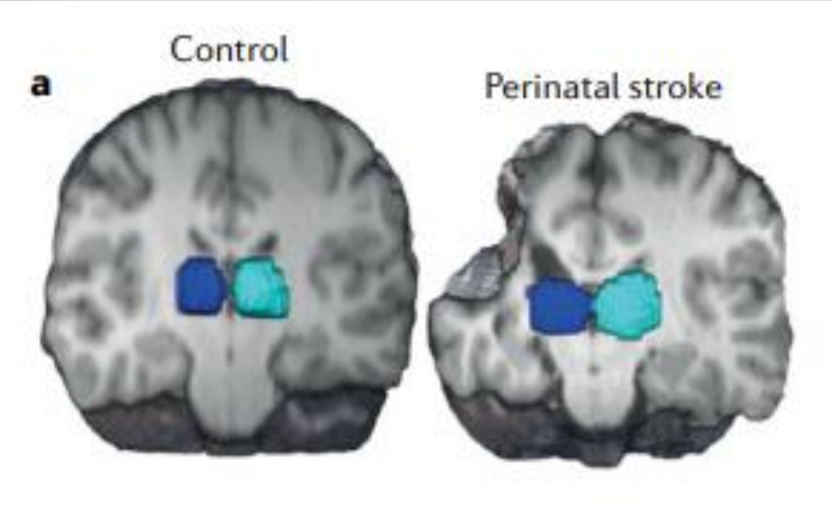

시간적 해상도 (temporal resolution)
EEG, MEG
NIRS
PET
DTI, fMRI
공간적 해상도 (spatial resolution)

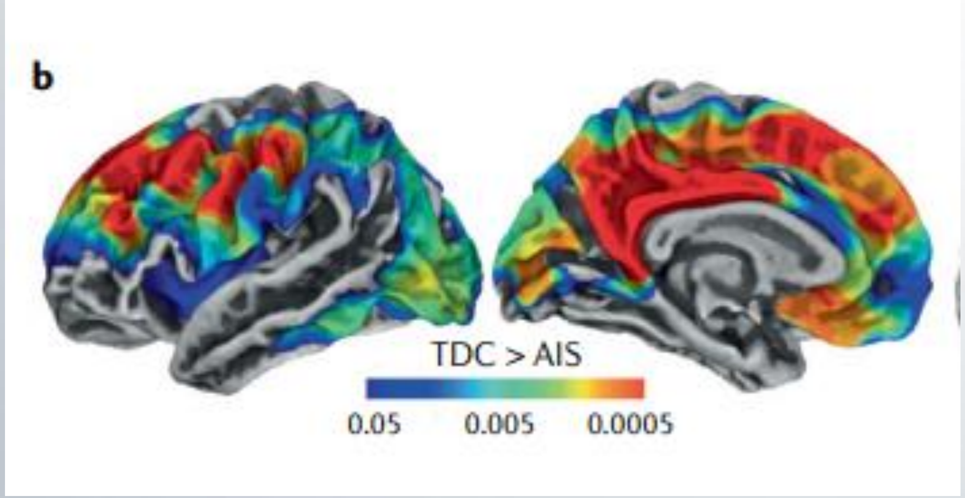
EEG

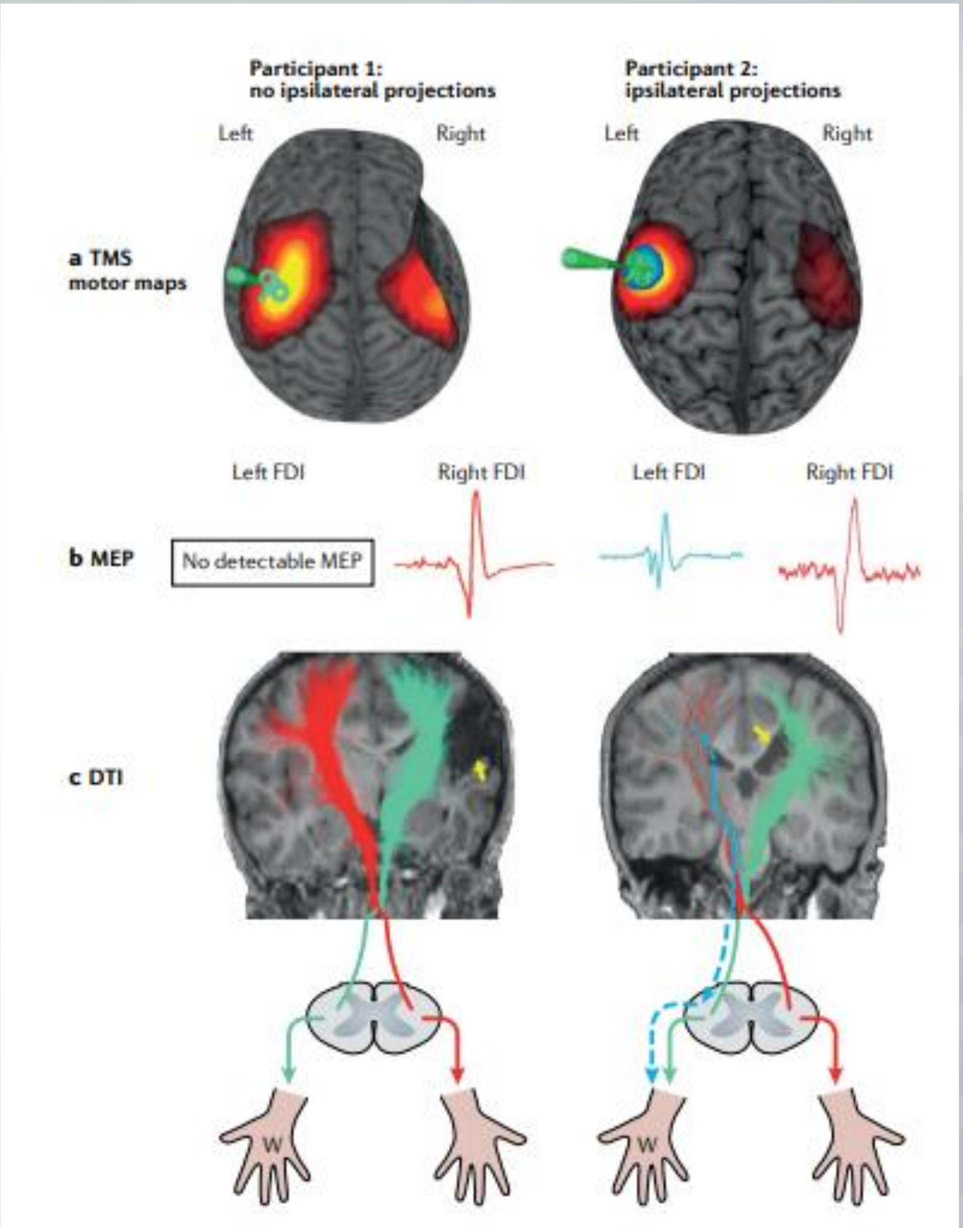


Scher et al. Dev Neurosci. 2009

Structural imaging

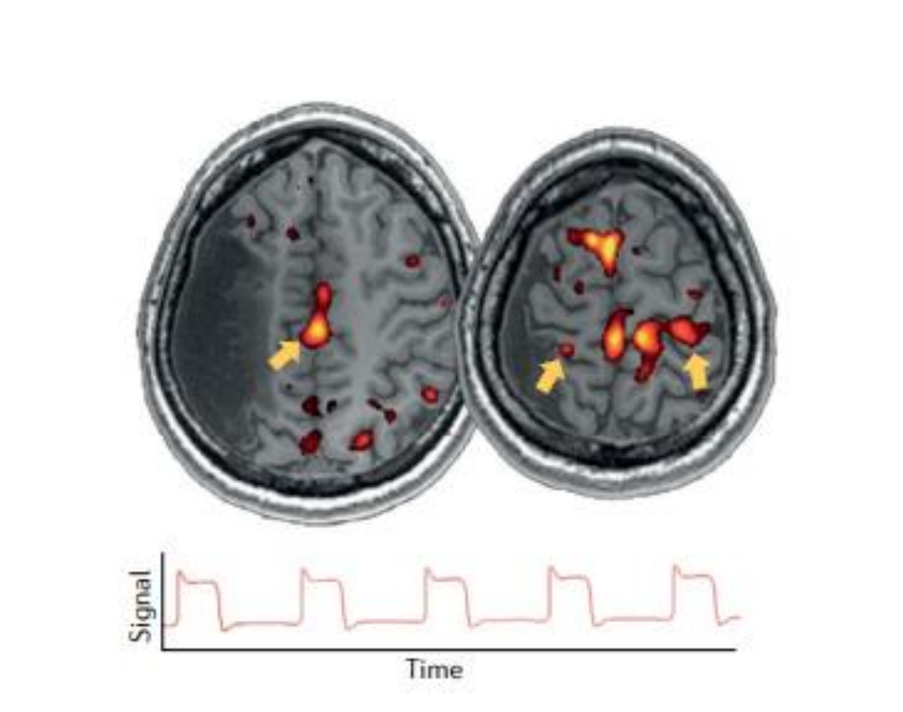




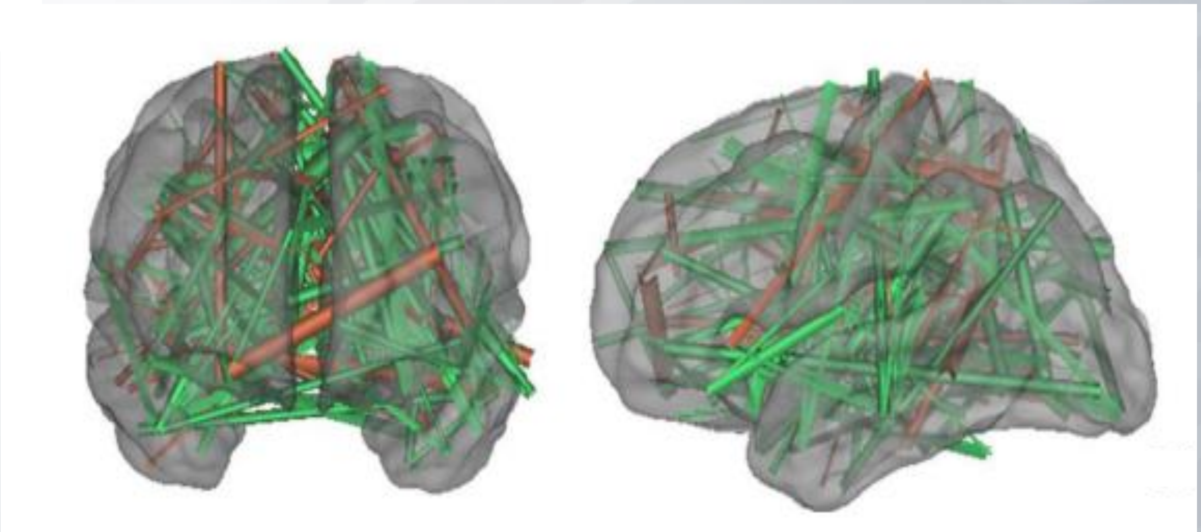


Kirton et al. nature review neurol. 2021

Functional MRI

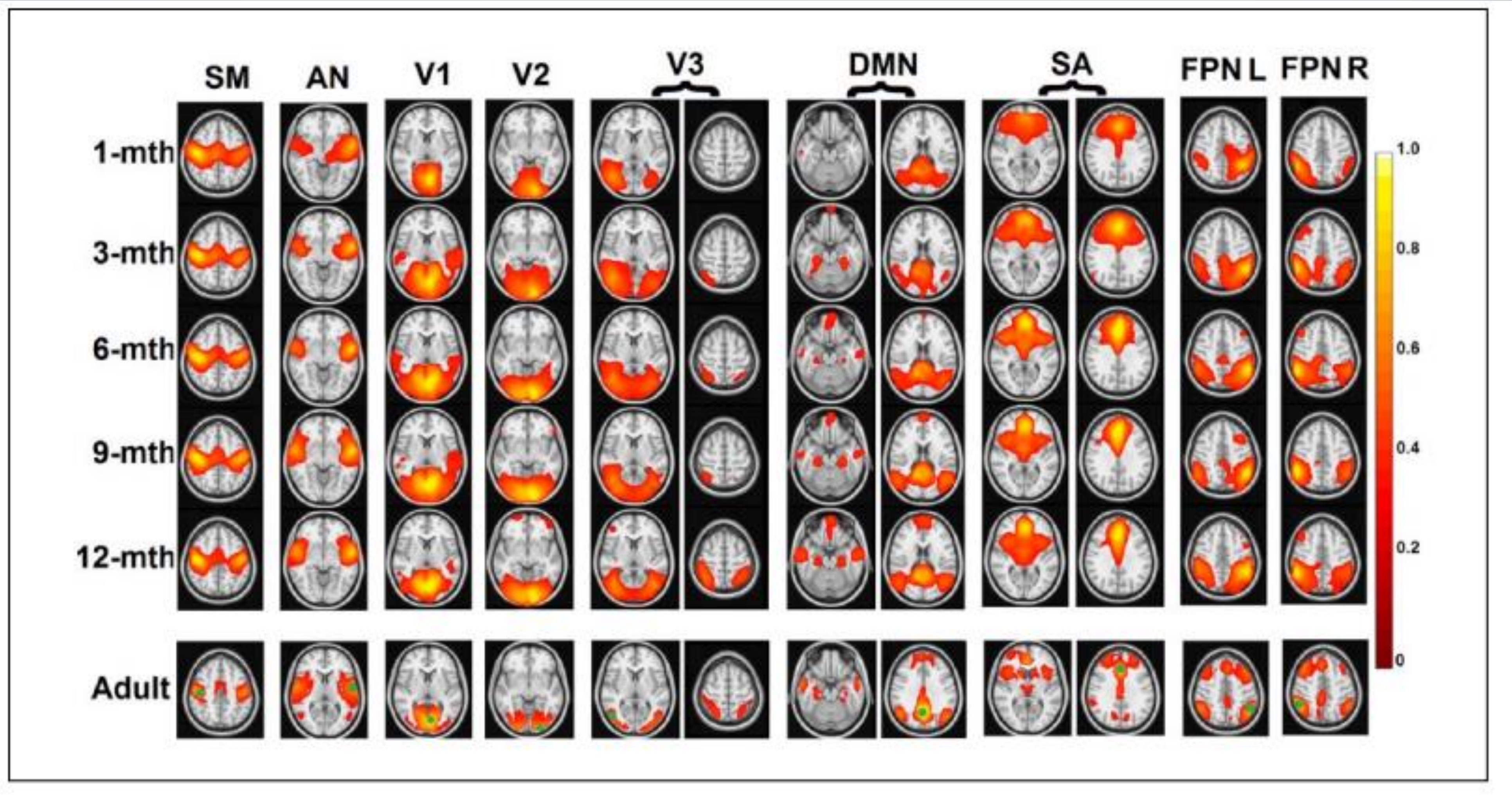


Kirton et al. nature review neurol. 2021



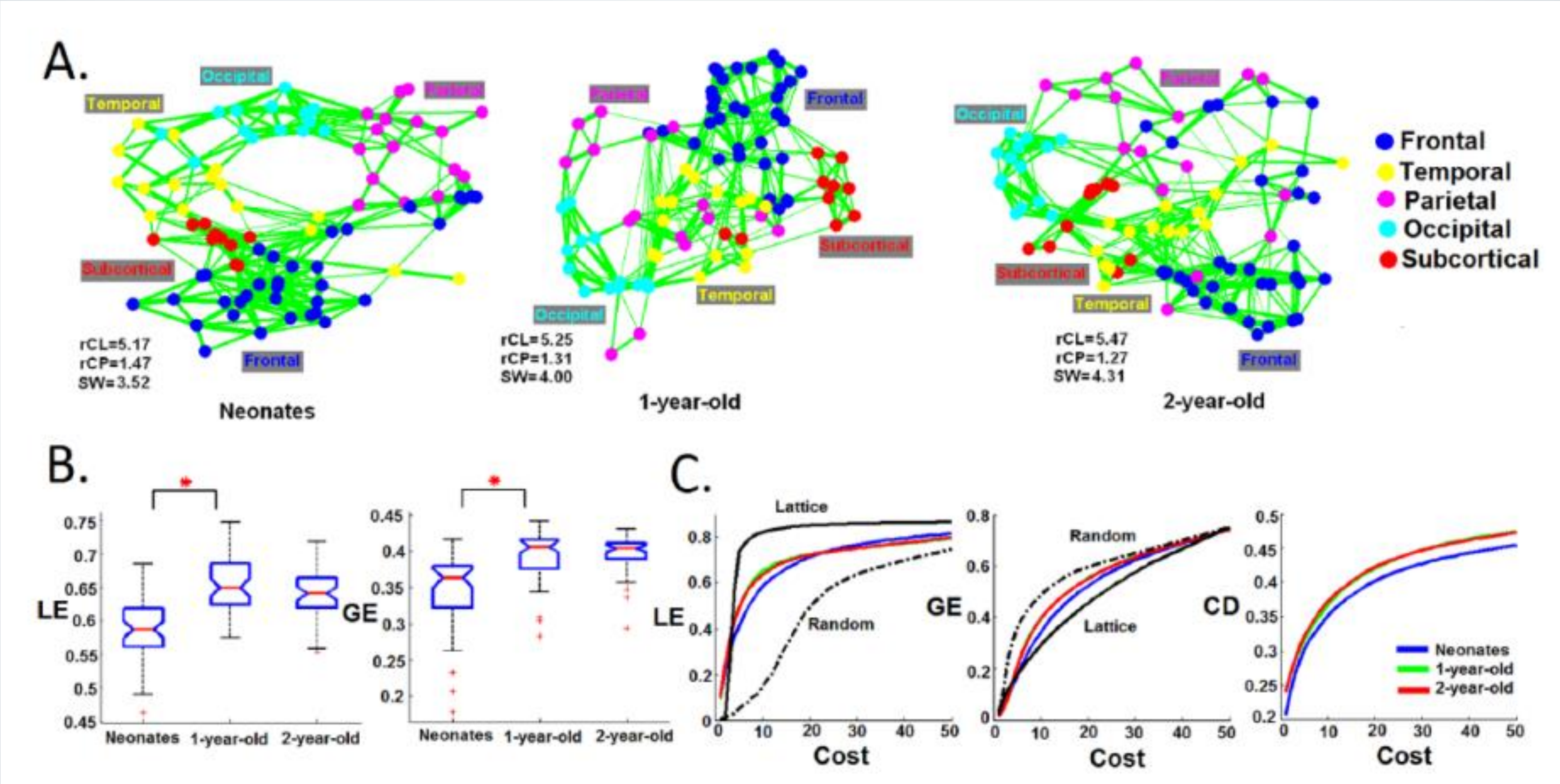
Smyser et al. semi neonatol. 2015

Functional connectivity network during 1st year



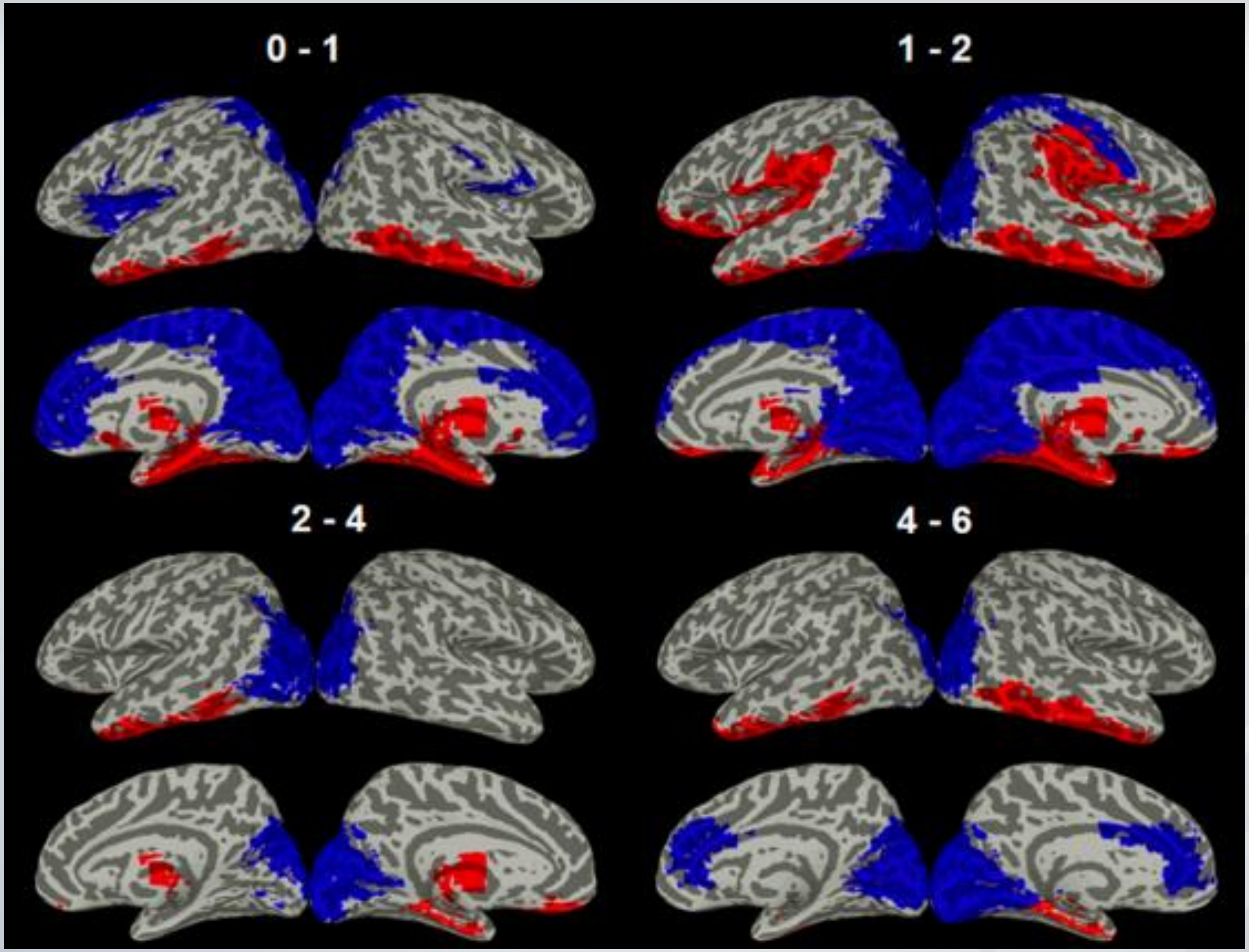
Gao et al. cerebral cortex. 2015

Development of functional connectivity



Gao et al. Neuroscientist. 2017

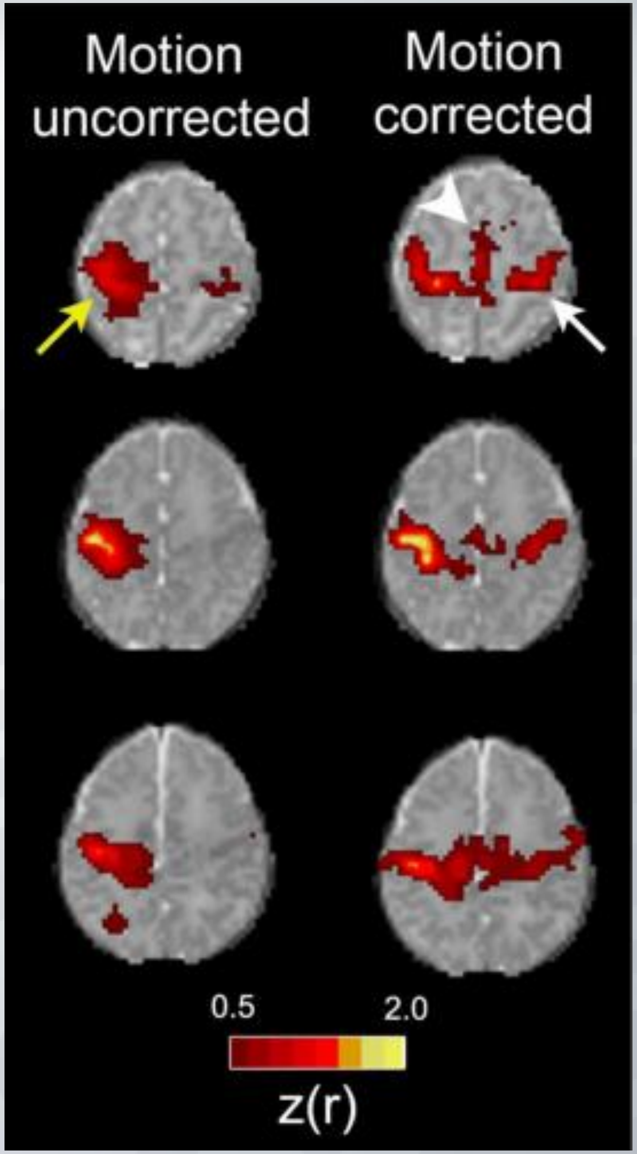
Development of functional connectivity



Chen et al. Develop Cog Neurosci. 2021

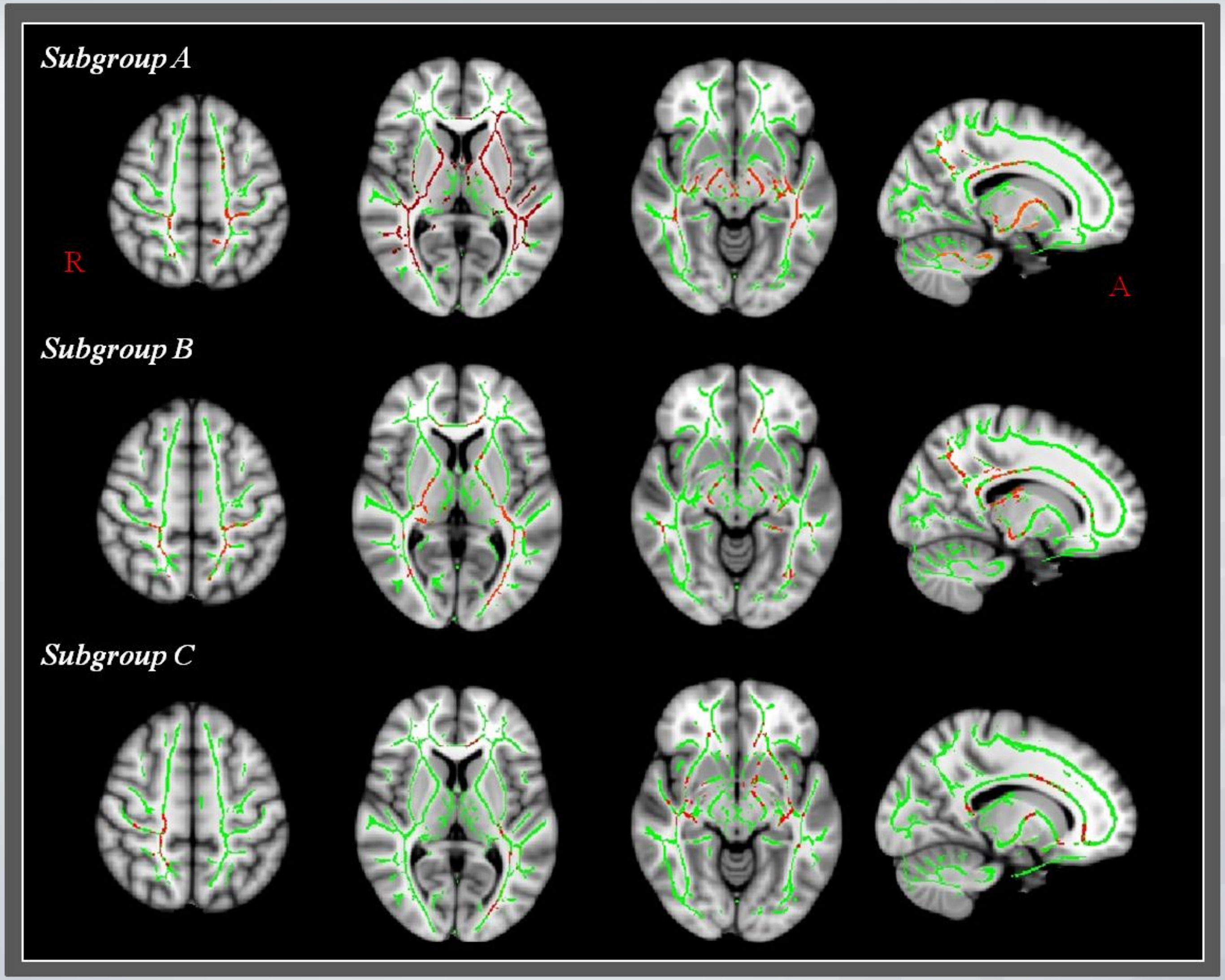
Technical issues of fcMRI

- Sedation vs natural sleep
- Sleep stage
- Motion issue



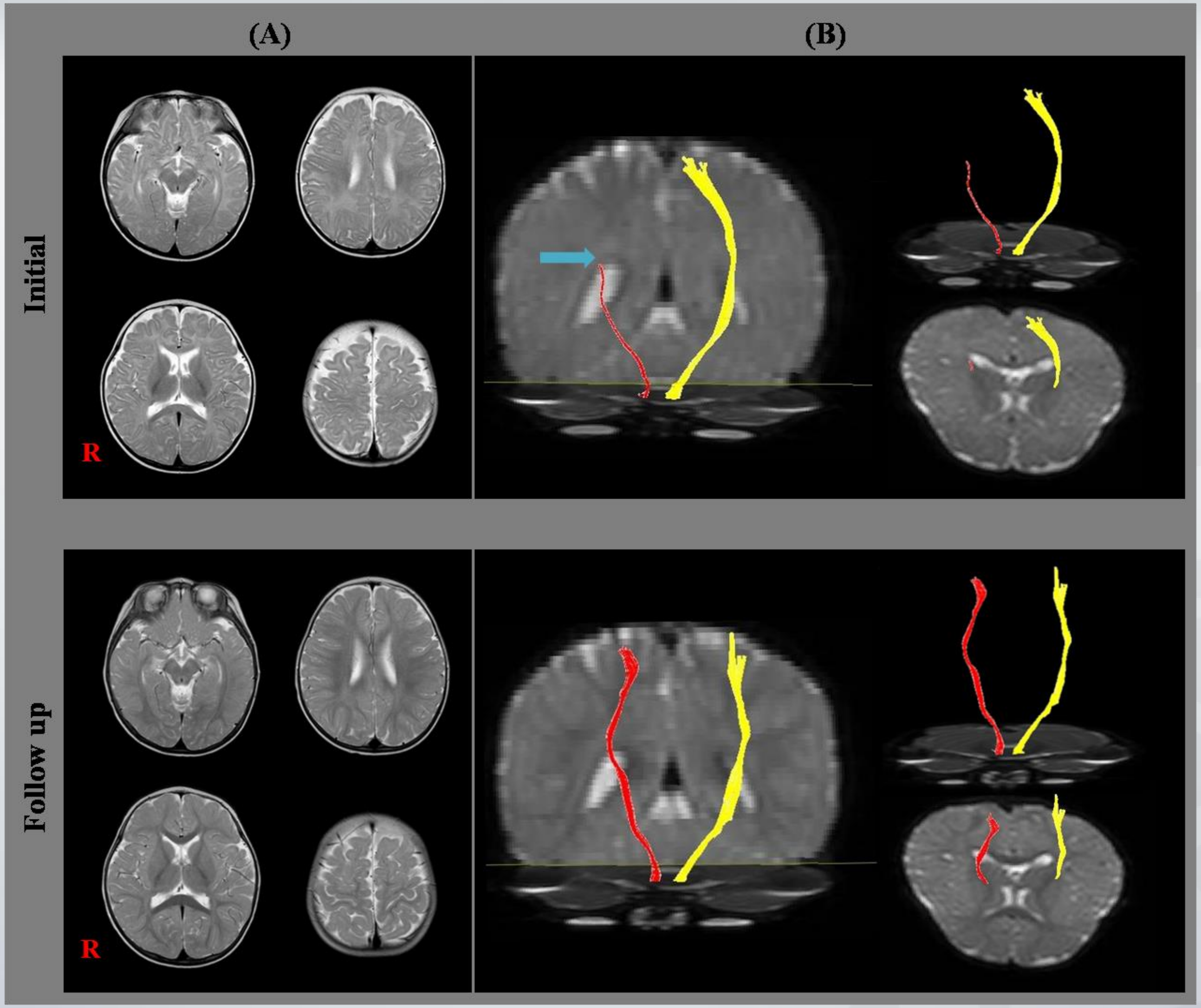
Neil et al. Semi Peinatol. 2015

TBSS (Tract based spatial statistics)



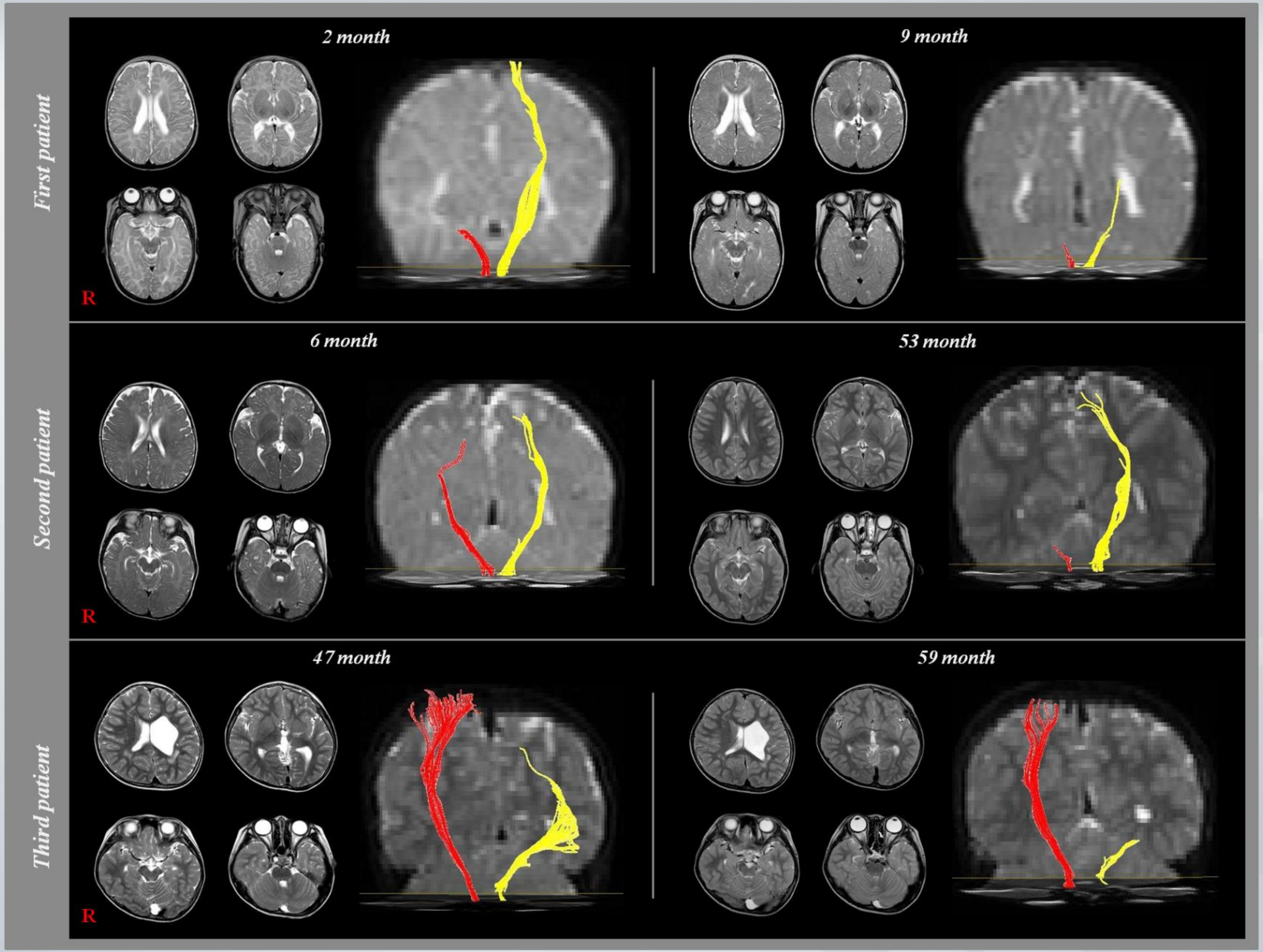
Lee et al. Pediatr Radiol. 2013

Regeneration of CST After rehab tx



Baek et al. Neurosci Lett. 2013

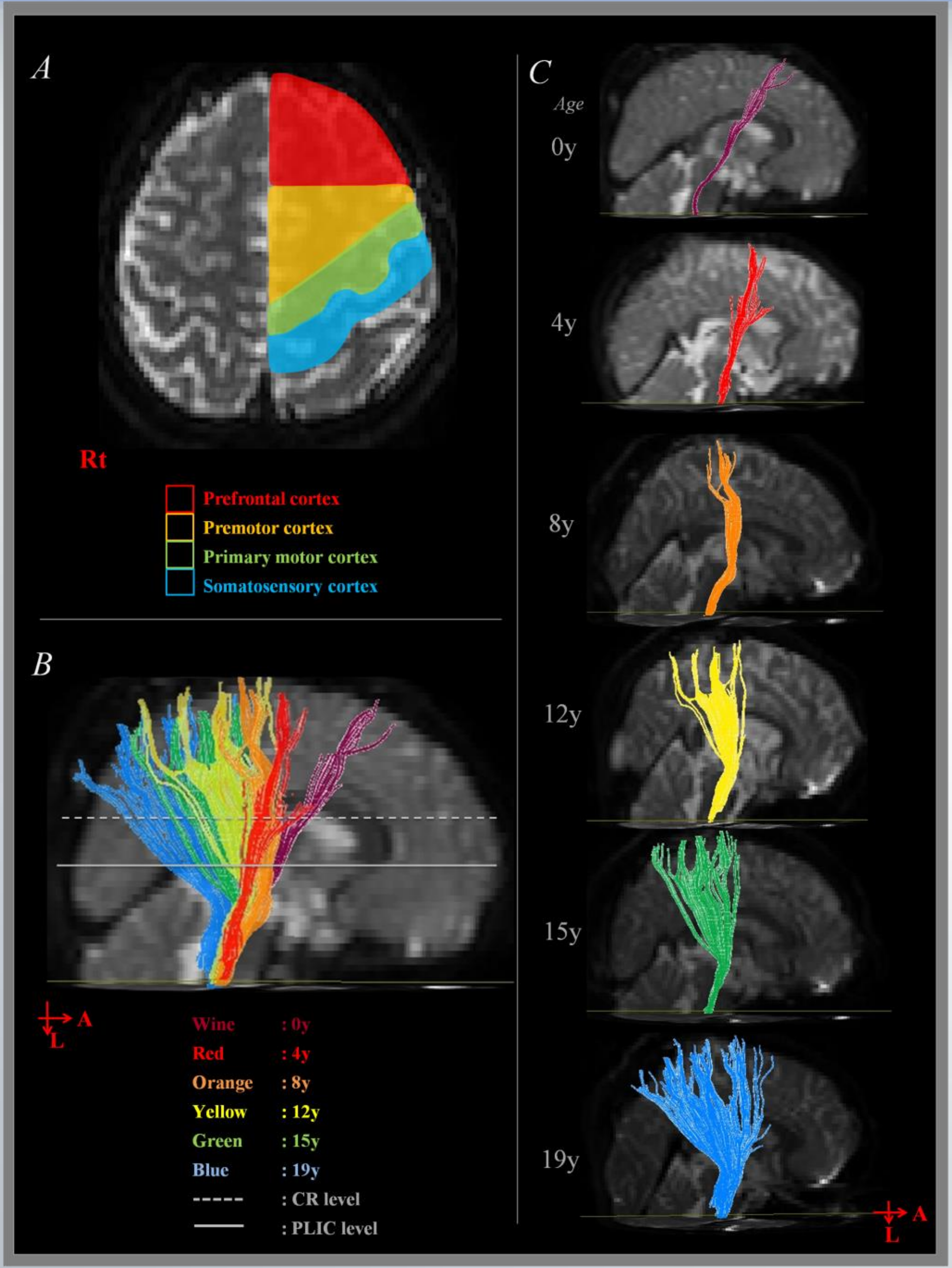
Degeneration of CST after refusal of rehab tx

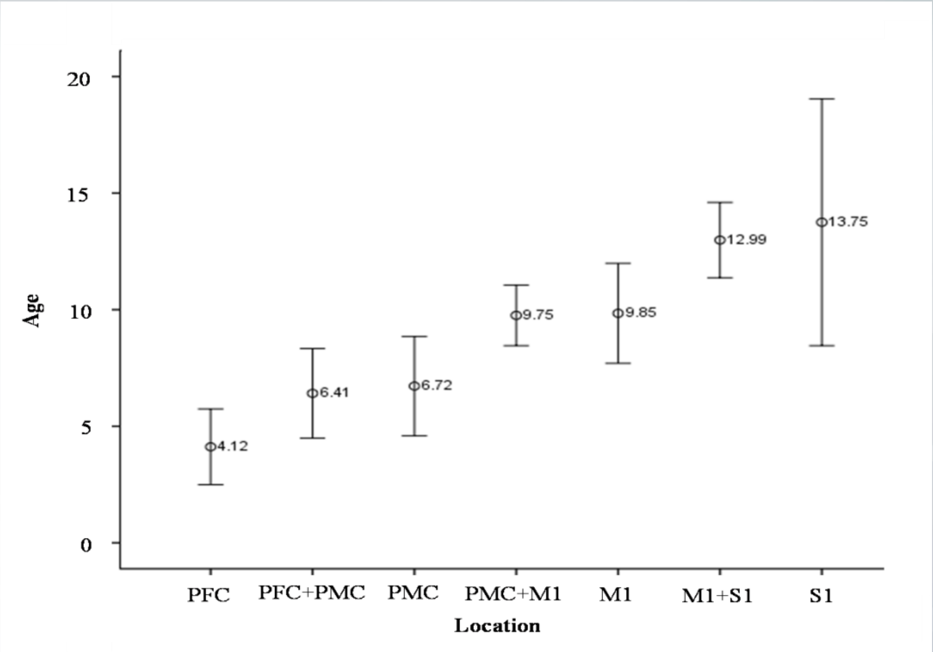


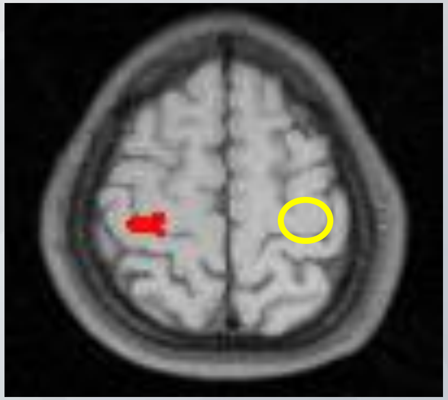
Chang et al. Devel neurorehabil. 2013

Immaturity vs lesion

Normal maturation of CST

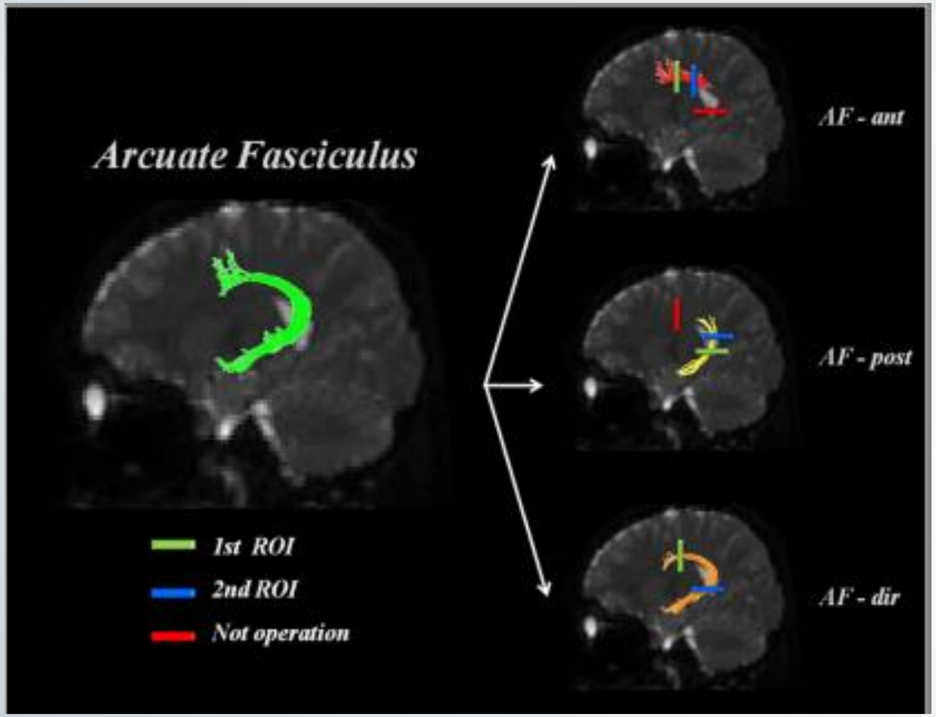


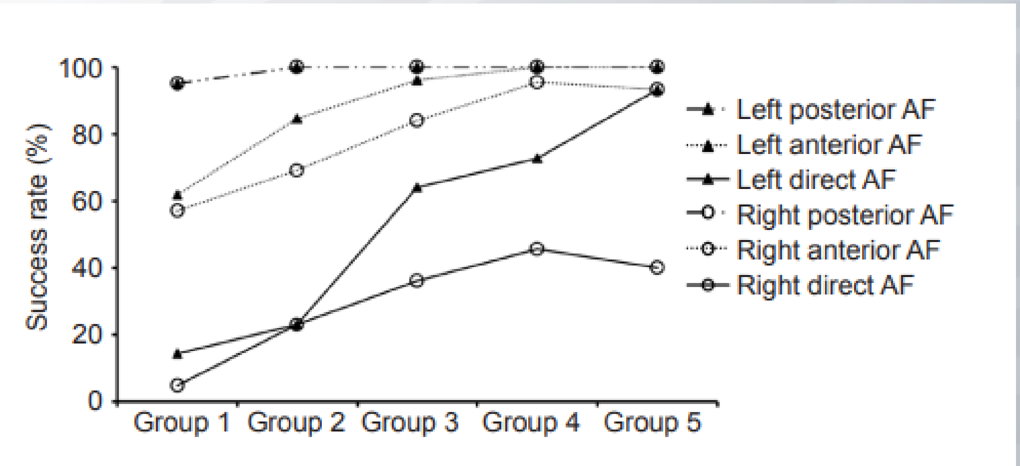




Kwon et al. Front Hum Neurosci. 2016

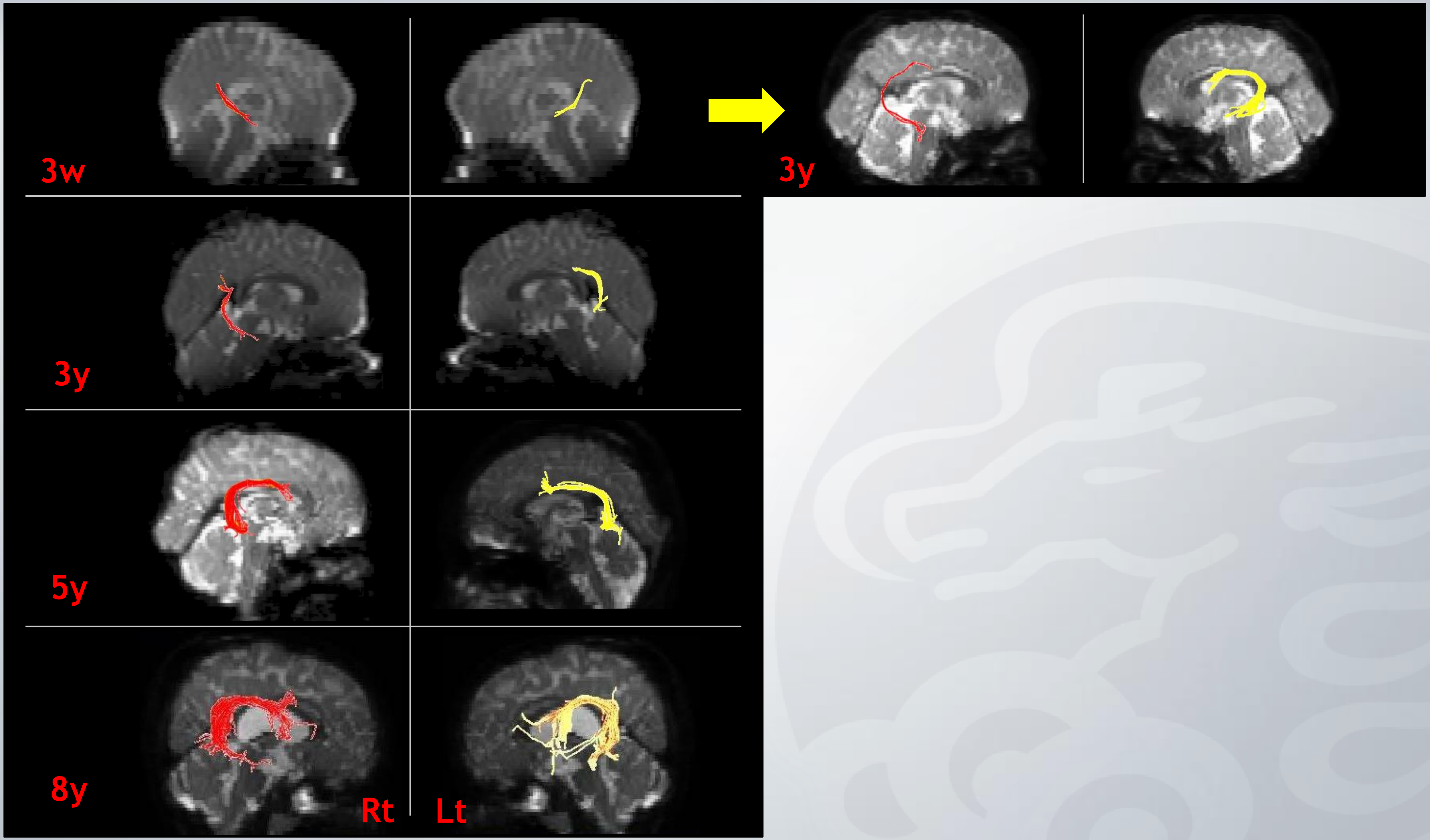
Normal maturation of AF



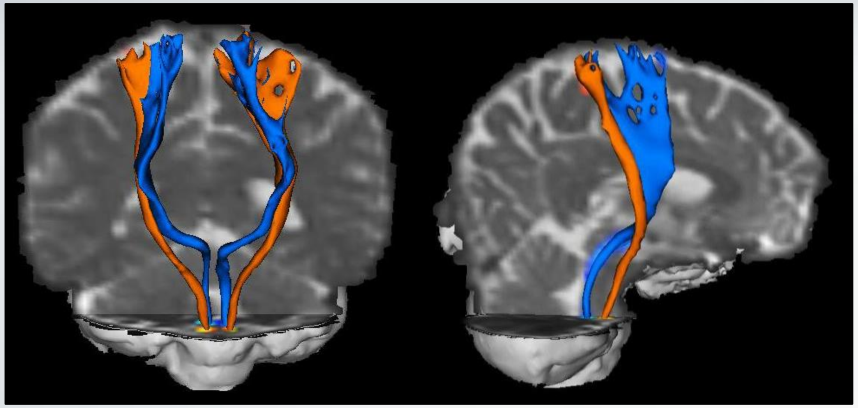


Tak et al. Neural Regene Res. 2016

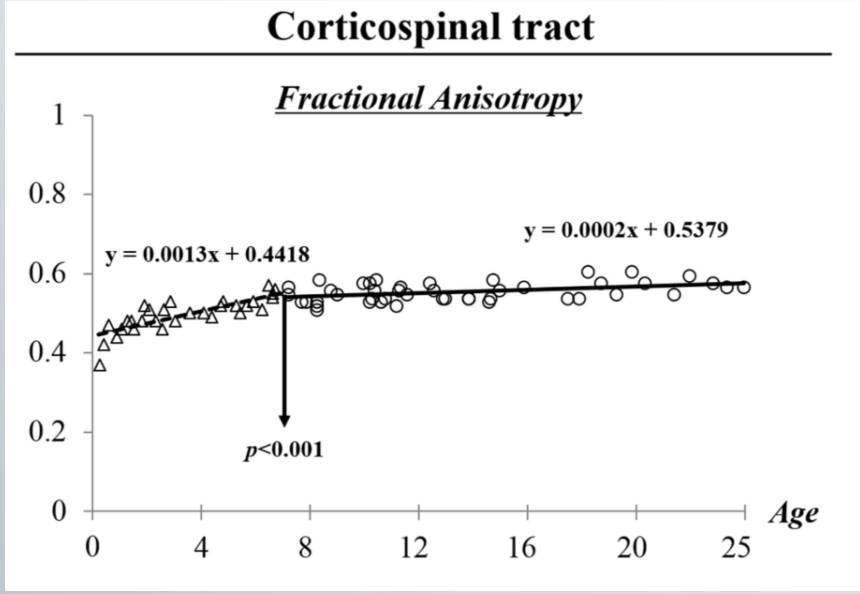
Normal maturation of AF

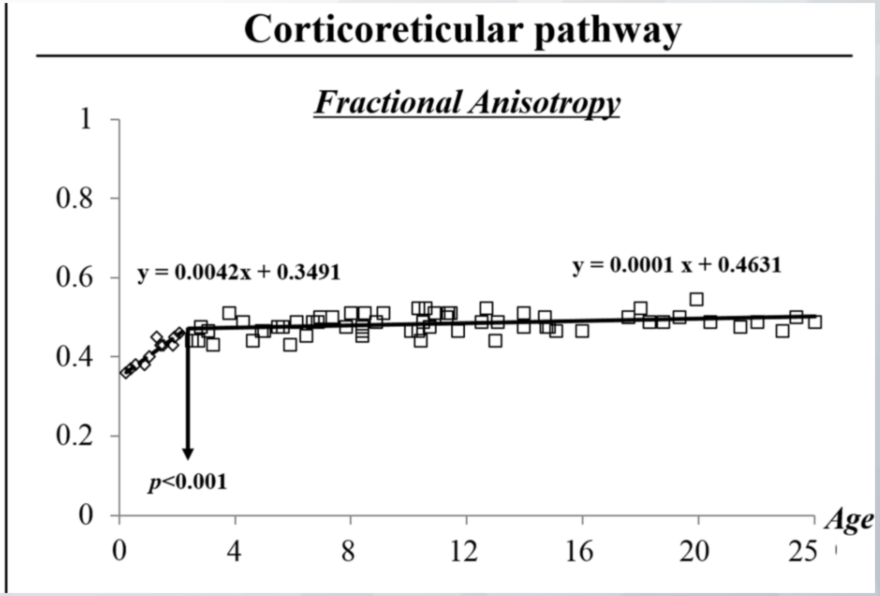


Normal maturation of CST vs CRT



Orange : CST/ Blue : CRT



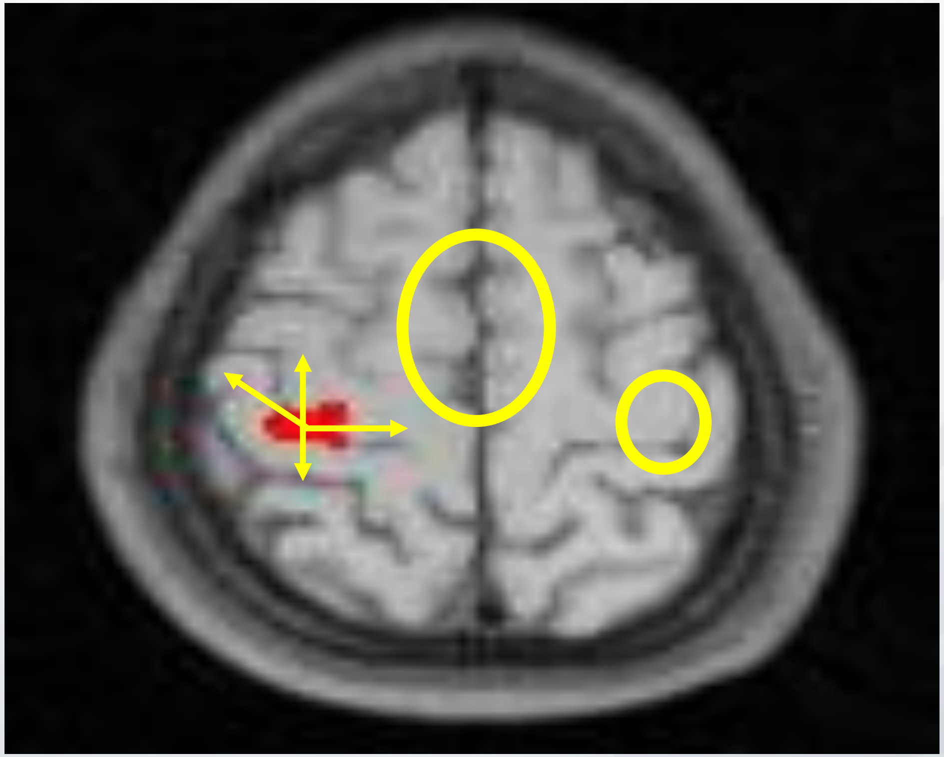


Yeo et al. Front Hum Neurosci. 2014

Maladaptive plasticity

Recovery mechanism after perinatal injury

Possible motor recovery mechanism in mature brain



Possible motor recovery mechanism in immature brain

- Motor: ipsilateral ?
- Sensory: thalamocortical projection ?
- Language: opposite hemisphere ?

Review > Semin Perinatol. 2010 Feb;34(1):87-92. doi: 10.1053/j.semperi.2009.10.009.

Brain plasticity following early life brain injury: insights from neuroimaging

Martin Staudt [1]

Affiliations + expand

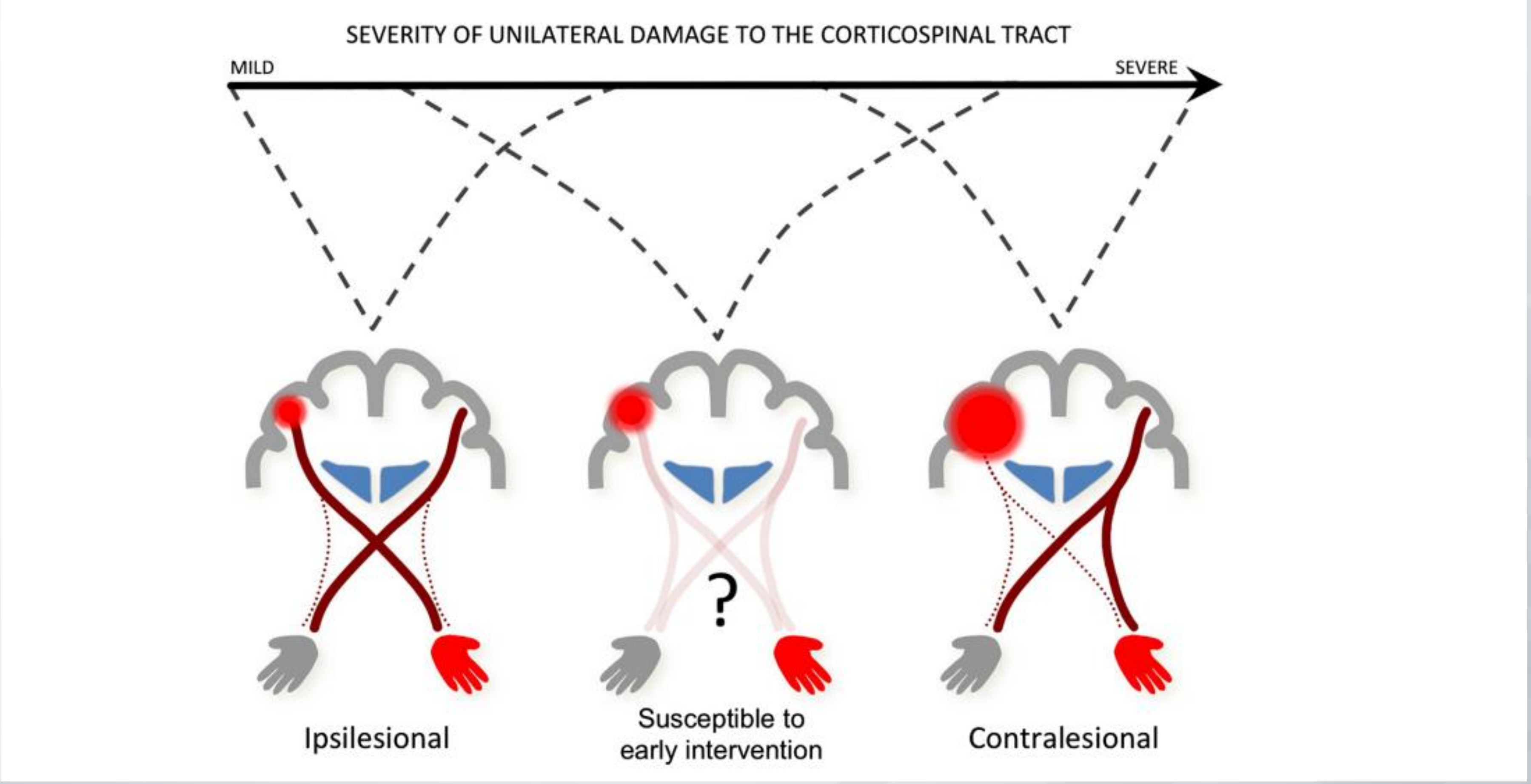
PMID: 20109976 DOI: 10.1053/j.semperi.2009.10.009

Abstract

The developing human brain possesses a superior capacity to reorganize after focal lesions. This review describes mechanisms of reorganization following pre- and perinatally-acquired, unilateral brain lesions for motor, somatosensory, and language functions. In the motor system, unilateral damage to the corticospinal tract can lead to the maintenance of normally-transient ipsilateral corticospinal projections from the contralesional hemisphere. In some patients, this type of corticospinal (re)organization can achieve an active grasp function of the paretic hand, while in others no useful hand function develops although such projections exist. In the somatosensory system, periventricular lesions can be compensated by outgrowing thalamocortical projections forming "bypasses" around the defective white matter to reach the postcentral gyrus. By contrast, lesions in the postcentral gyrus often lead to marked somatosensory deficits. Finally, language functions can be taken over by the right hemisphere in cases of left hemispheric damage, often with excellent functional outcome. Knowledge of these mechanisms is necessary for establishing a "prognostic corridor" of development derived from neuroimaging in newborns with brain lesions.

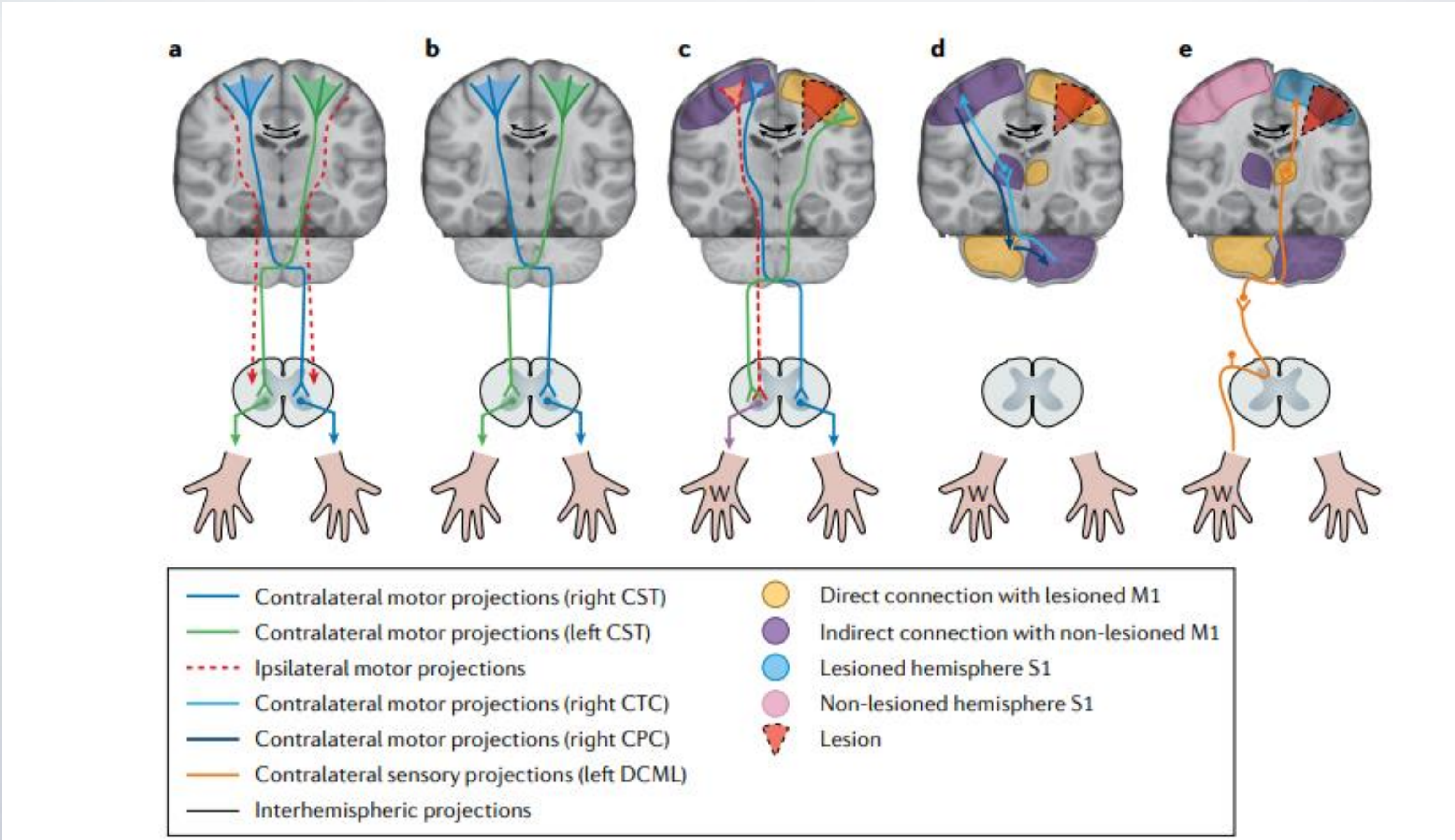
Marin Staudt. Semin Perinatol. 2010

Possible motor recovery mechanism in immature brain



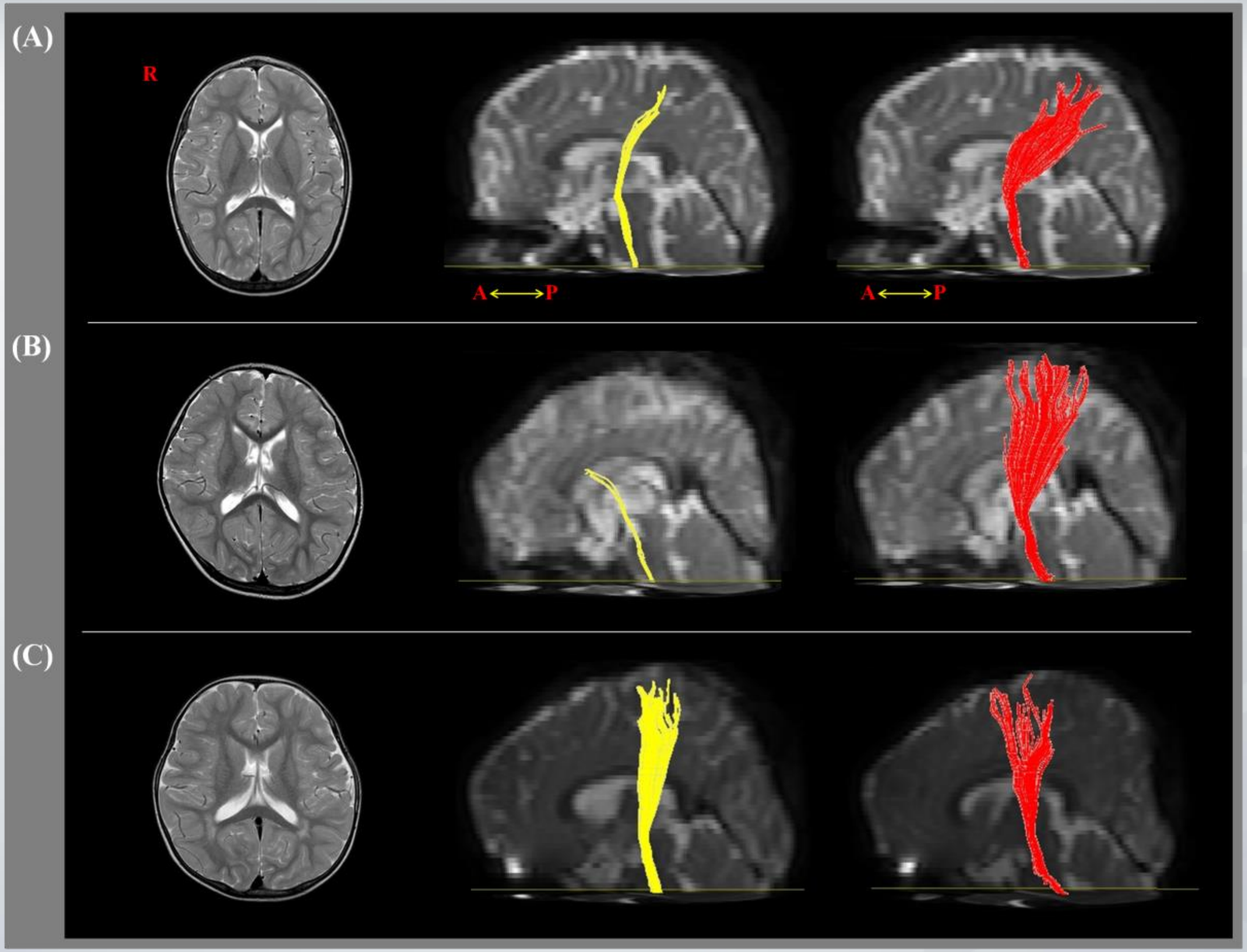
Fiori et al. Semin Perinatol. 2015

Possible motor recovery mechanism in immature brain



Kirton et al. nature review neurol. 2021

Less aff activation & poor motor outcome



Kim et al. Neural Regen Res. 2015

Neuromodulation

Neuromodulation in pediatric patients

- Intensive motor learning
- Education & counselling of the family
- rTMS
- tDCS

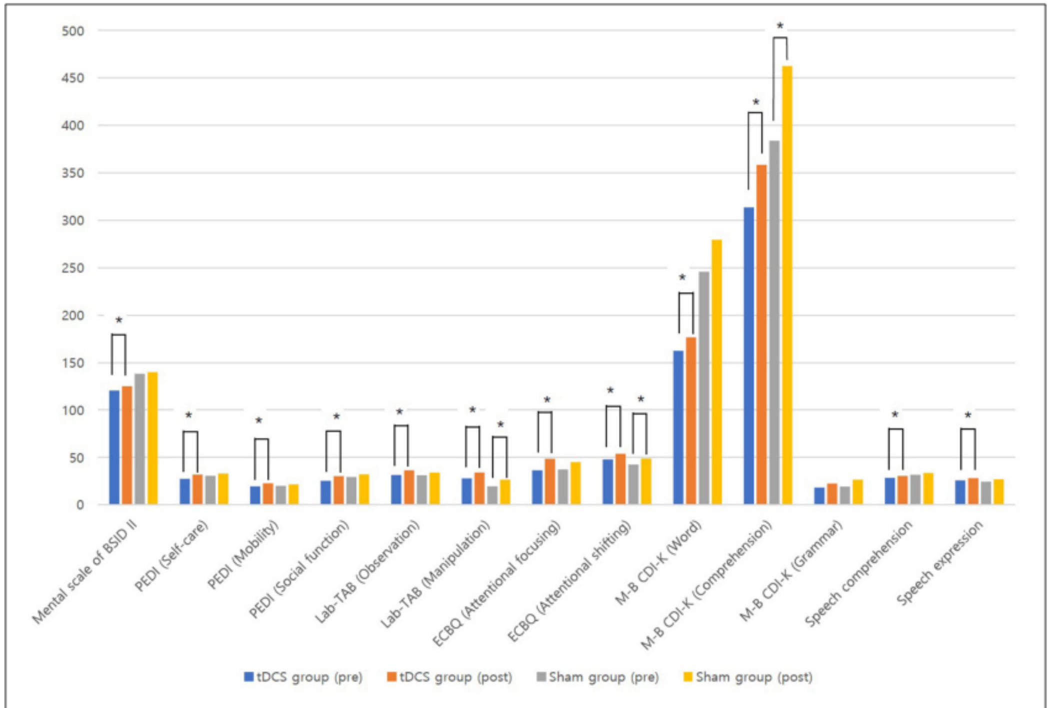


FIGURE 2 | Comparisons of outcomes before and after treatment in tDCS and sham groups. *$p < 0.05$ by Wilcoxon signed-rank tes.

Ko et al. Front in Ped. 2021

경청해 주셔서 감사합니다