Neurocognitive development in paediatric epilepsy

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Mental retardation is highly prevalent in epileptic children

- Age group 1 month-16 years: 26,4%
  (Berg 2008)

- In preschool children, prevalence of mental retardation even higher (Rantanen 2011)
  - Cohort 3-6 years
  - 50% have IQ < 70

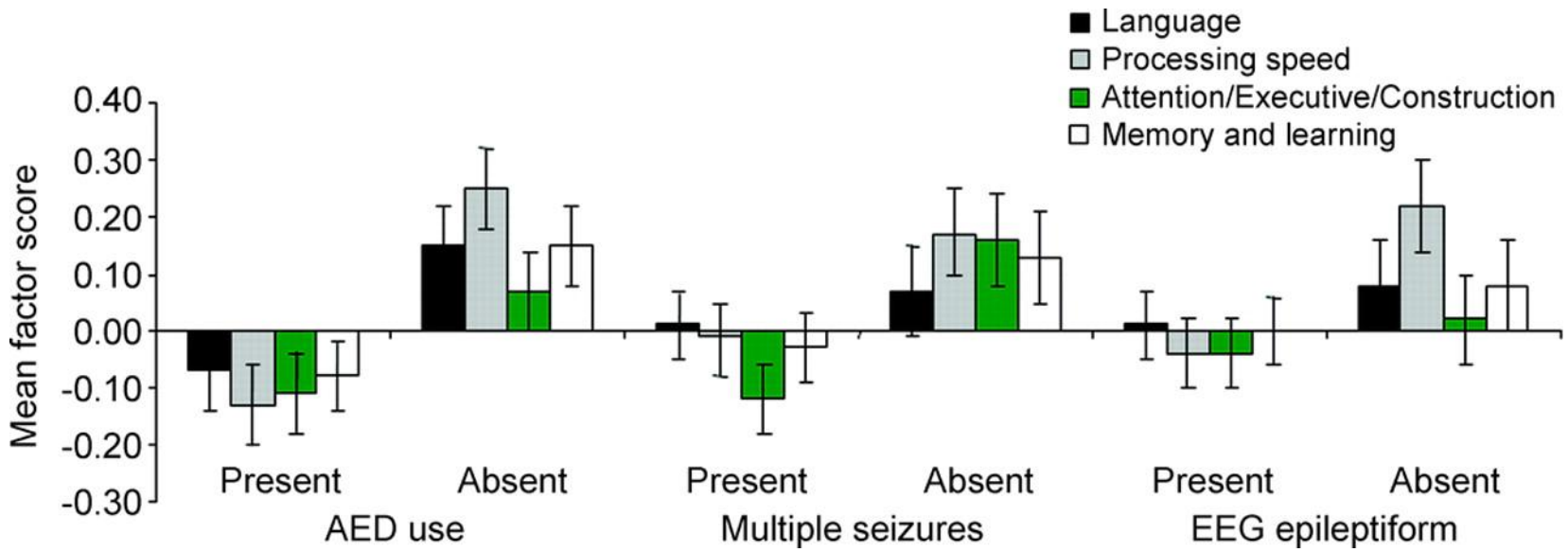
We know the risk factors

- Young age at epilepsy onset
- Taking anti-epileptic drugs
- Having abnormal MRI
- Having persistent seizures on treatment
- Having an epileptic encephalopathy*

**condition in which the epileptic activity itself may contribute to severe cognitive decline, i.e. West syndrome, Dravet syndrome, epilepsy with continuous spike-waves during sleep (CSWS),…*

Some deficits are present from the onset

- Children 6-14 years evaluated within the first 3 months after a first seizure



Fastenau P S et al. Neurology 2009;73:526-534

Cognitive deficits progress over time

- Longitudinal study of a cohort with epilepsy onset < 3 years

TABLE 1. Mean Vineland Scores at Initial Study Entry and Over Time for the Full Study Sample (n = 172)

Domain	Baseline, Mean (SE)	1 Year, Mean (SE)	2 Years, Mean (SE)	3 Years, Mean (SE)	P Value for Trend
Composite	92.0 (1.5)	86.6 (2.0)	82.9 (2.4)	81.5 (2.7)	<.0001
Communication	93.4 (1.5)	90.4 (2.0)	87.2 (2.0)	85.2 (2.3)	.0003
Daily Living	89.6 (1.4)	79.0 (1.6)	76.5 (2.0)	74.6 (2.4)	<.0001
Motor	94.4 (1.7)	90.0 (2.2)	83.1 (2.5)	80.5 (3.3)	<.0001
Social	96.1 (1.7)	92.7 (2.0)	90.0 (2.2)	88.8 (2.4)	.0015

Berg et al, 2004

Early intervention might prevent cognitive deterioration

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Example 1: candidates for epilepsy surgery

- Consecutive cohort of 50 infants
  - operated between 3 and 7 years
  - 66% seizure-free after surgery
- Influence of duration of epilepsy before surgery on IQ gain after surgery

Freitag et al, 2005

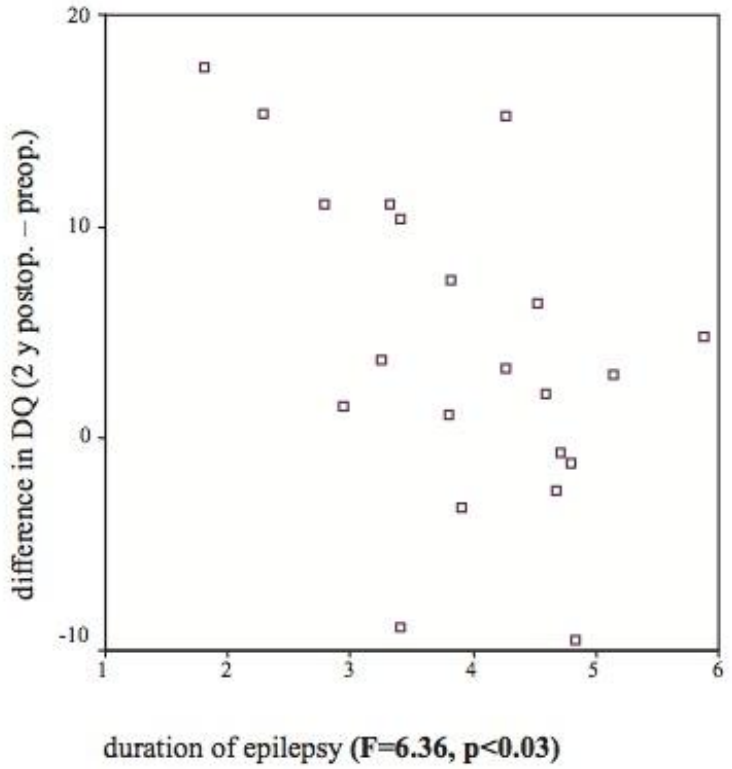
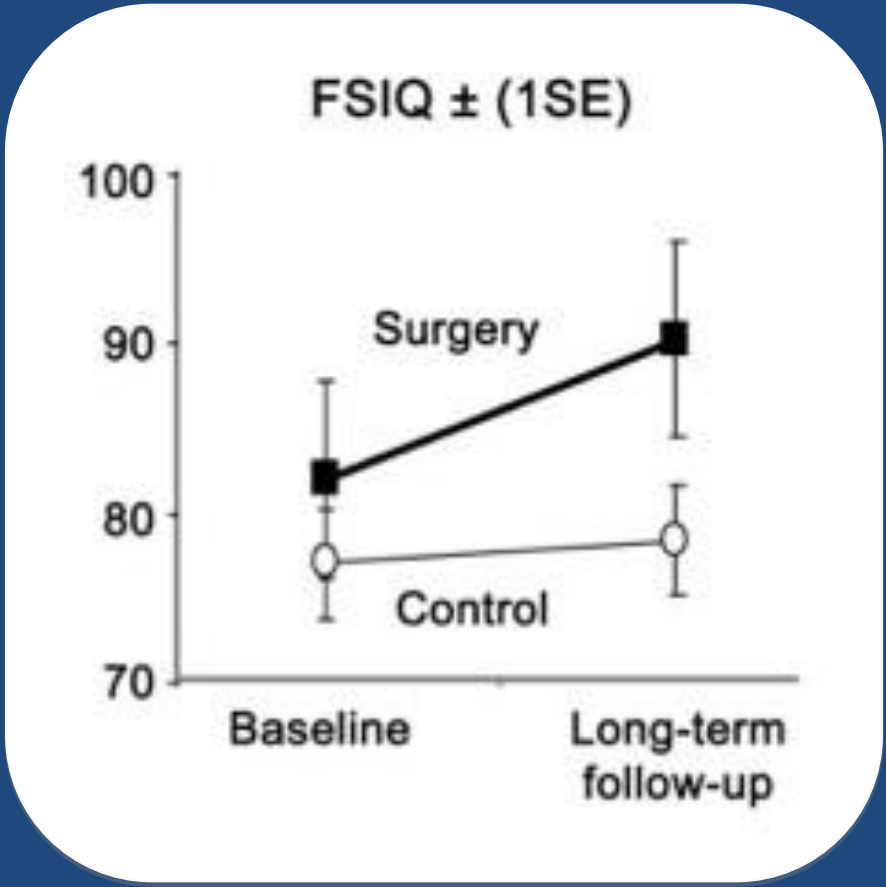


FIG. 2. Relation between gains/losses in DQ and duration of epilepsy.

Early intervention might prevent cognitive deterioration

Example 1: candidates for epilepsy surgery

- Cohort with long follow-up (> 5 years)
  - 10-16 years at surgery
  - temporal lobectomy
  - 86% seizure-free
- Increase of IQ after surgery associated with stop of anti-epileptic drugs (57%)



Skirrow et al, 2011

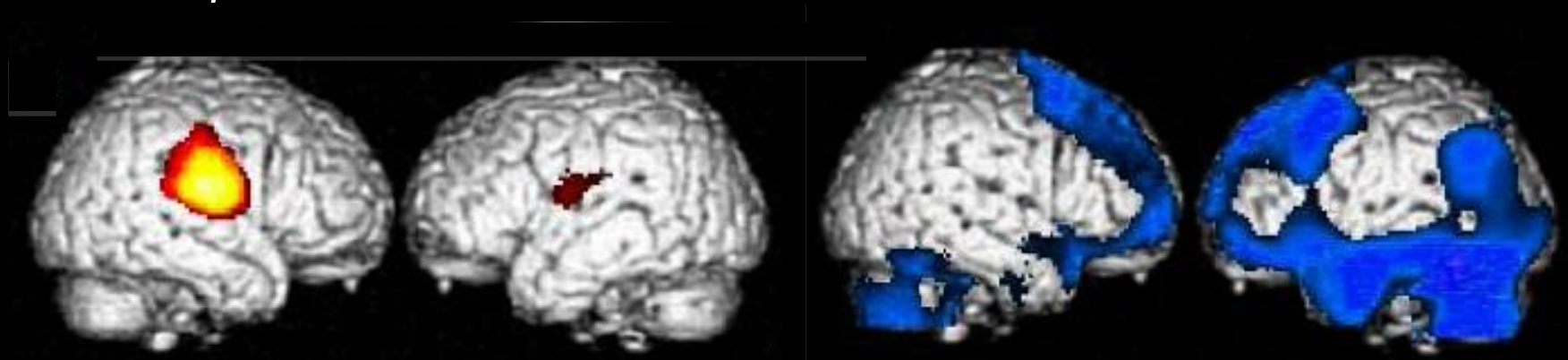
Early intervention might prevent cognitive deterioration

Example 2: epileptic encephalopathy with CSWS

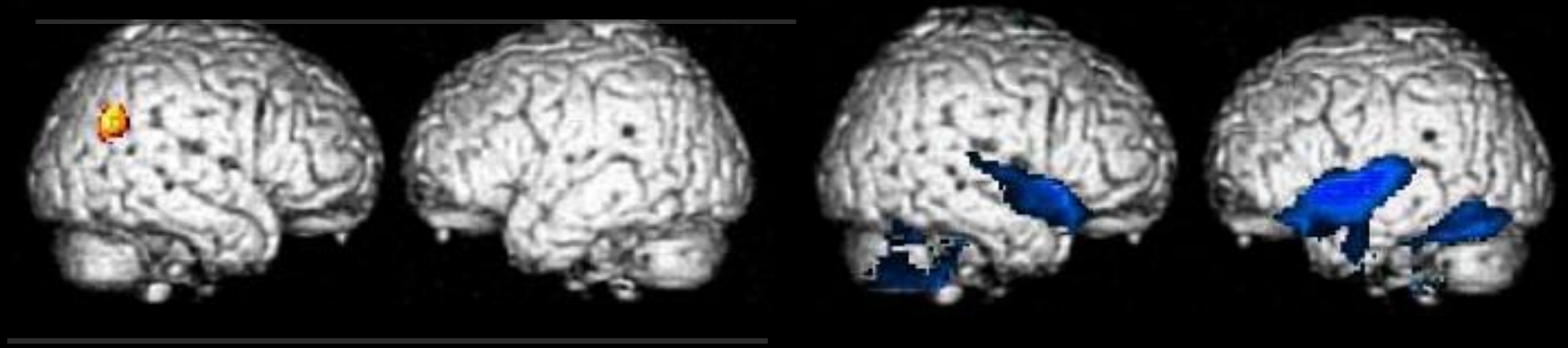
- Cognitive regression associated with particular sleep EEG pattern, with or without clinical seizures
- Long duration of CSWS associated with bad cognitive outcome (Kramer et al 2009, Seegmuller et al 2012)

Regional glucose metabolism studied at rest (awake) by PET

At acute phase of CSWS

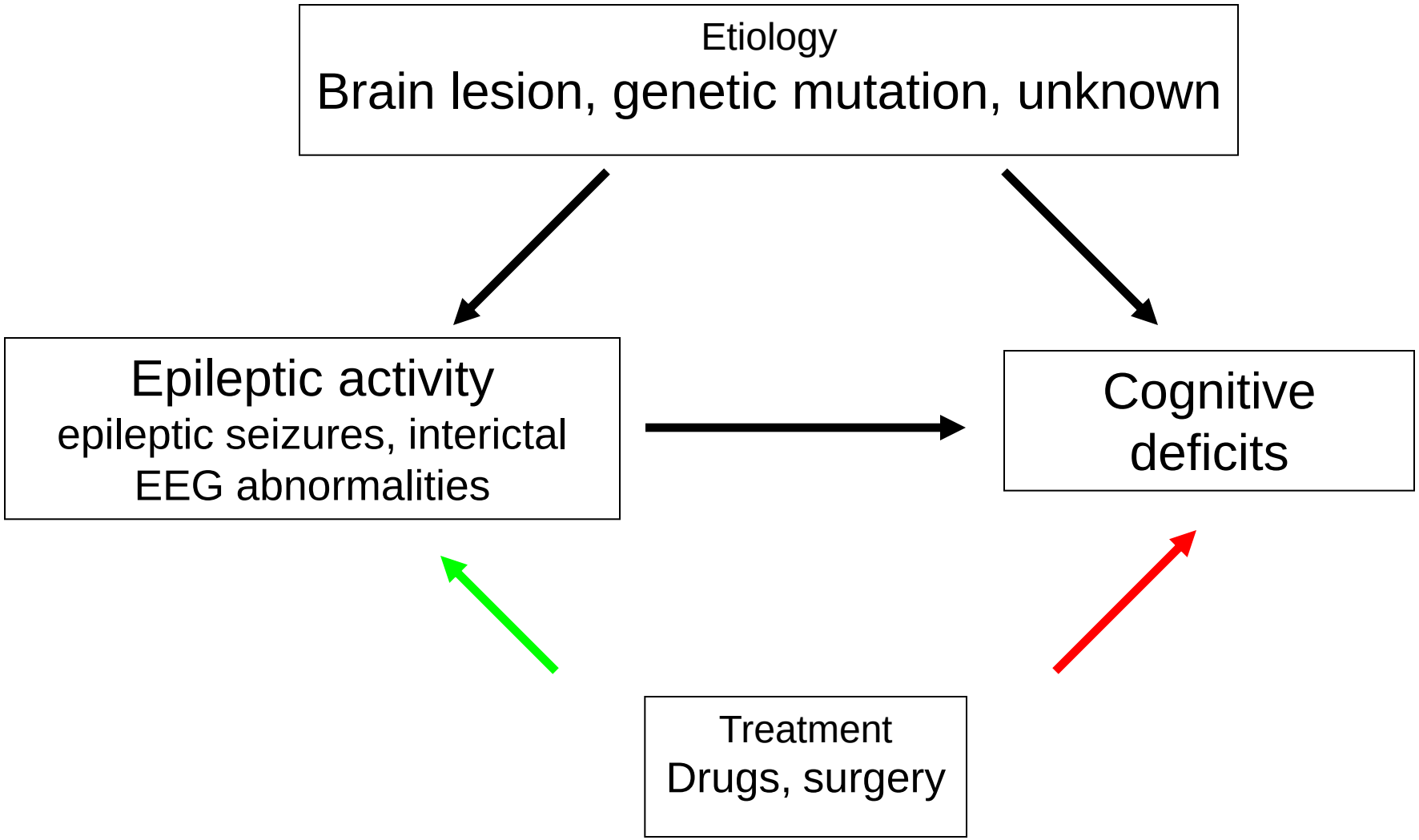


At recovery after steroids treatment



De Tiège et al, 2008

How to pose the problem?



Challenges for the future

- Develop more sensitive tools to assess brain dysfunction (particularly in the very young)
  - i.e. study of resting state networks
- Better understand mechanisms underlying changing epilepsy-related brain dysfunction across development
- Improve imaging techniques to detect earlier surgical candidates
- Develop new drugs more active on epilepsy (including infraclinical activity) with less side effects on cognition