Functional neurological disorders: pathophysiology and new treatments

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Psychiatre - Chef de clinique - Université de Montpellier

33 ème Congrès de l'ANLLF

25 Septembre 2020

30 %

30 %

Neurology out-patients with unexplained symptoms

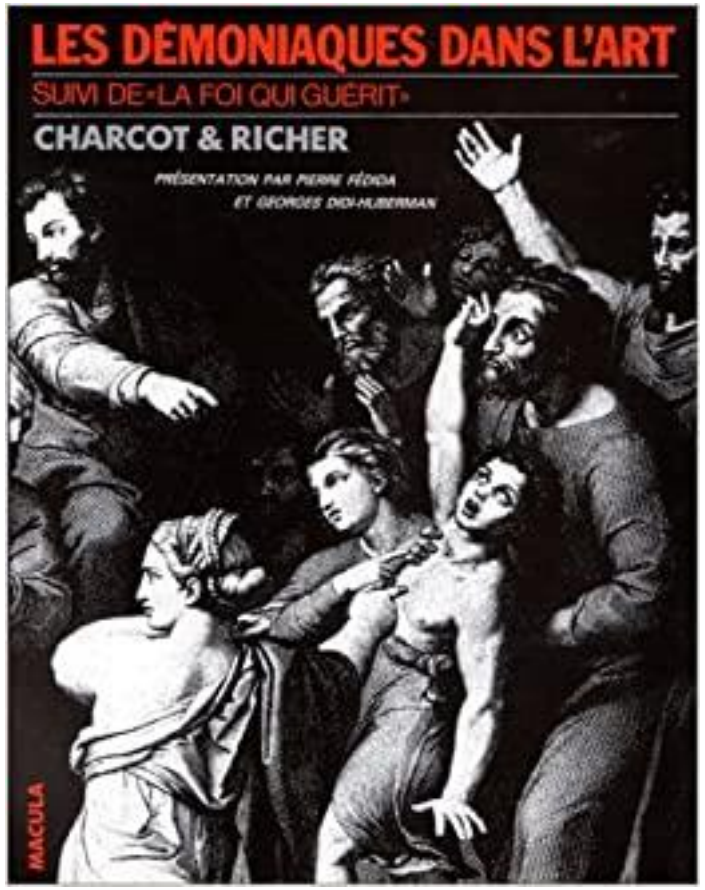
(3781 consecutive patients)

Stone et al., 2010

Neurology or Psychiatry ?

André Brouillet, *Une leçon clinique à la Salpêtrière*, 1887

Functional neurological disorders and art



Les démoniaques dans l'art, Charcot 1887

Definition

Functional neurological disorders (DSM-5)

Dissociative disorders (CIM-10)

Definition:

- ✓ **Motor or sensory symptoms**
- ✓ **Not compatible with known organic neurological disorder**
- ✓ **High functional impairment**

Functional neurological disorders in history

Shell shock syndrome, 1st world war

Clinical features

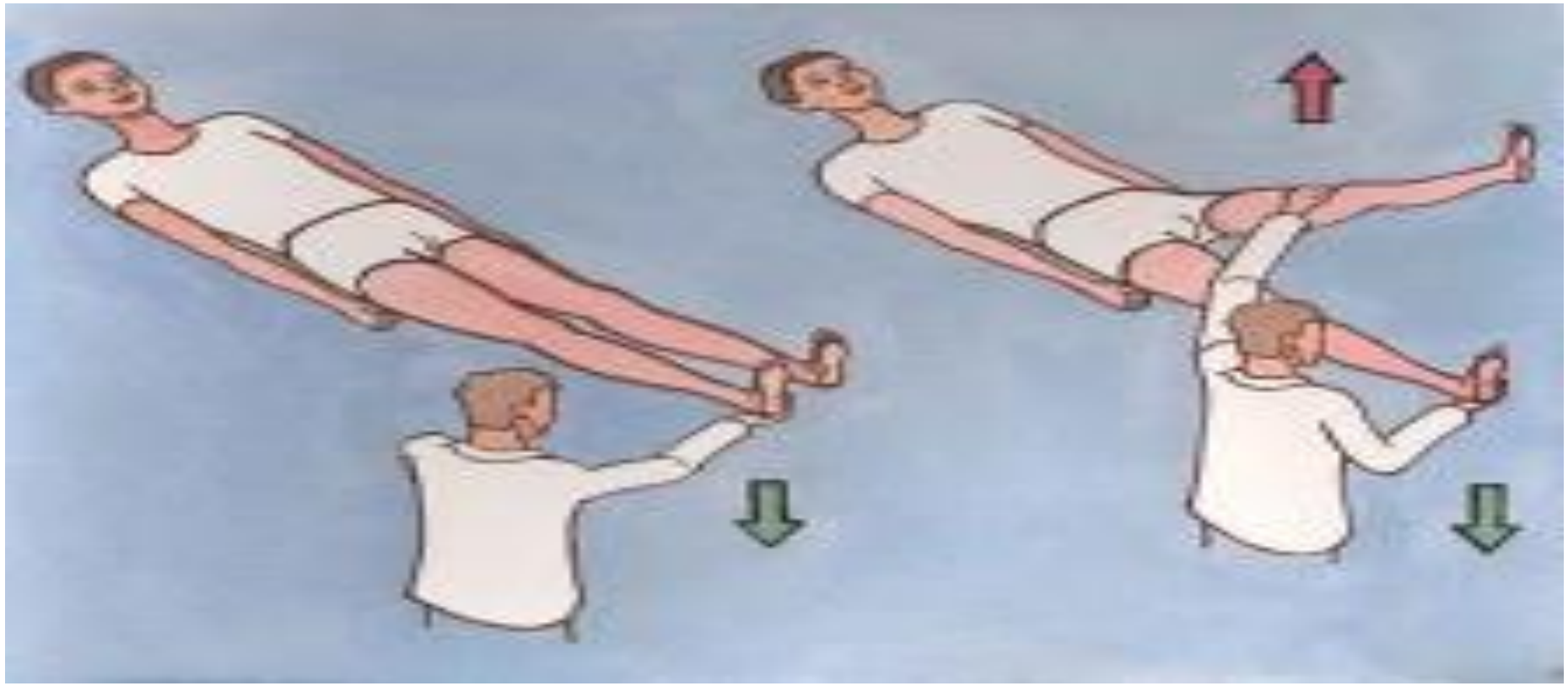
Acute (< 6 months) or persisting symptoms

Different types:

- **Motor / sensitive impairment**
- **Sensory symptoms**
- **Movement disorder**
- **Gait disorders**
- **Swallowing or phonation disorder,**
- **PNES**

Not constant/ not consistant (variability, distraction)

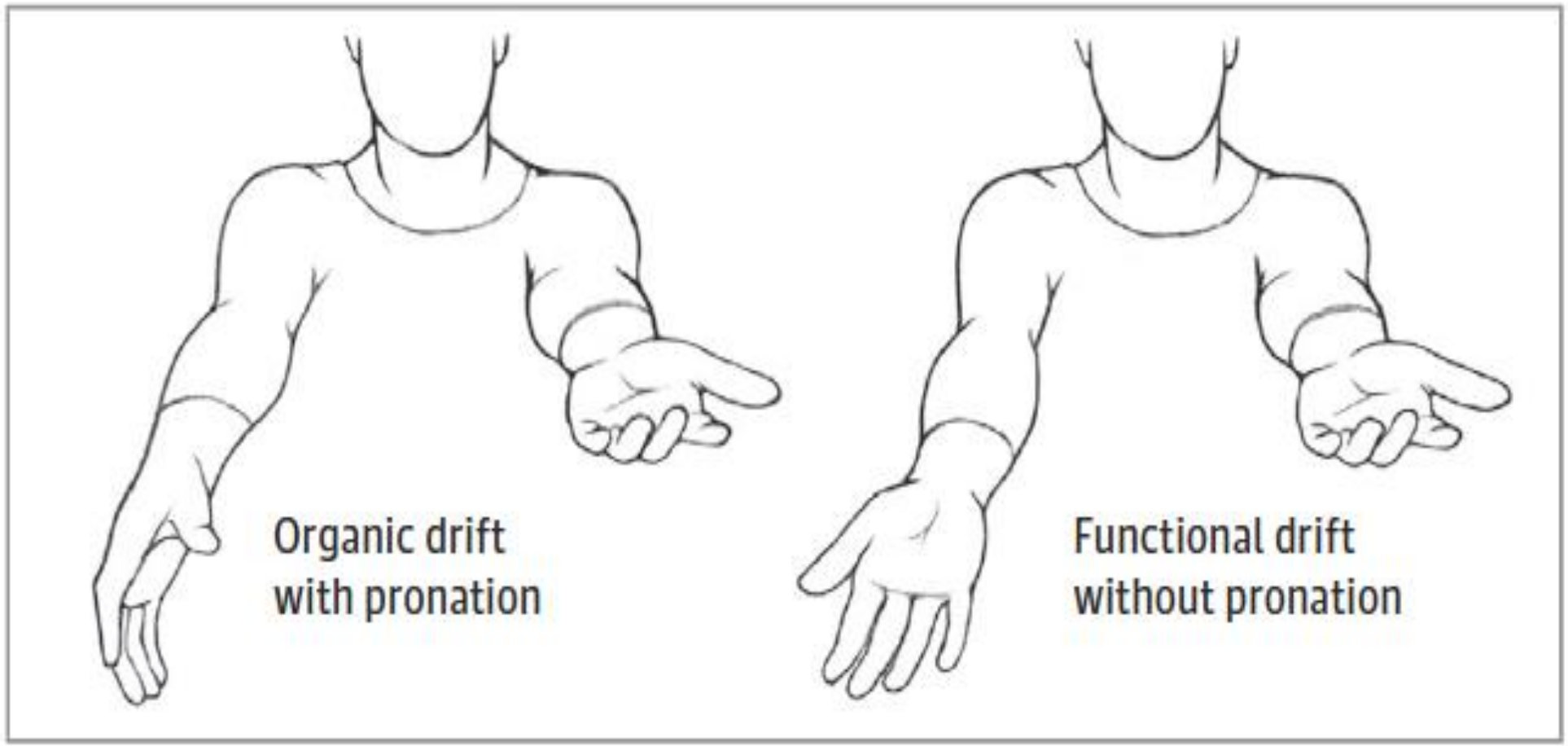
Clinical features



Hoover sign (1908)

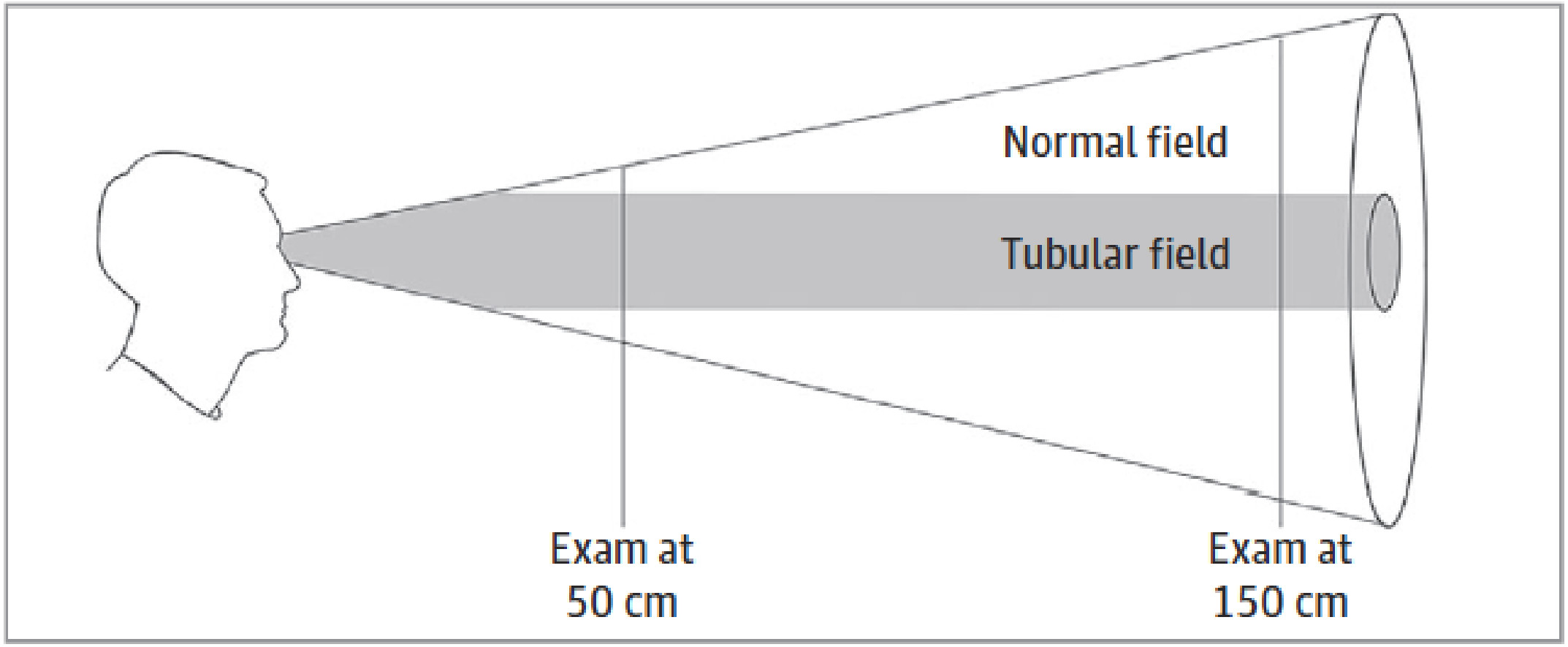
Clinical features

Espay et al., 2018 (JAMA Neurology)



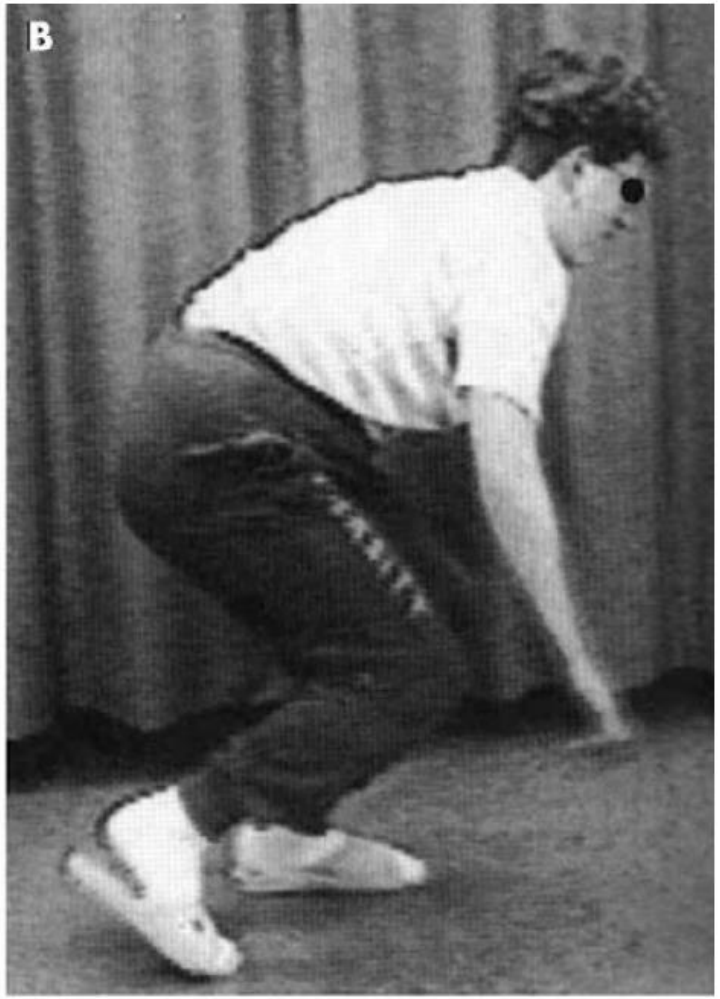
Clinical features

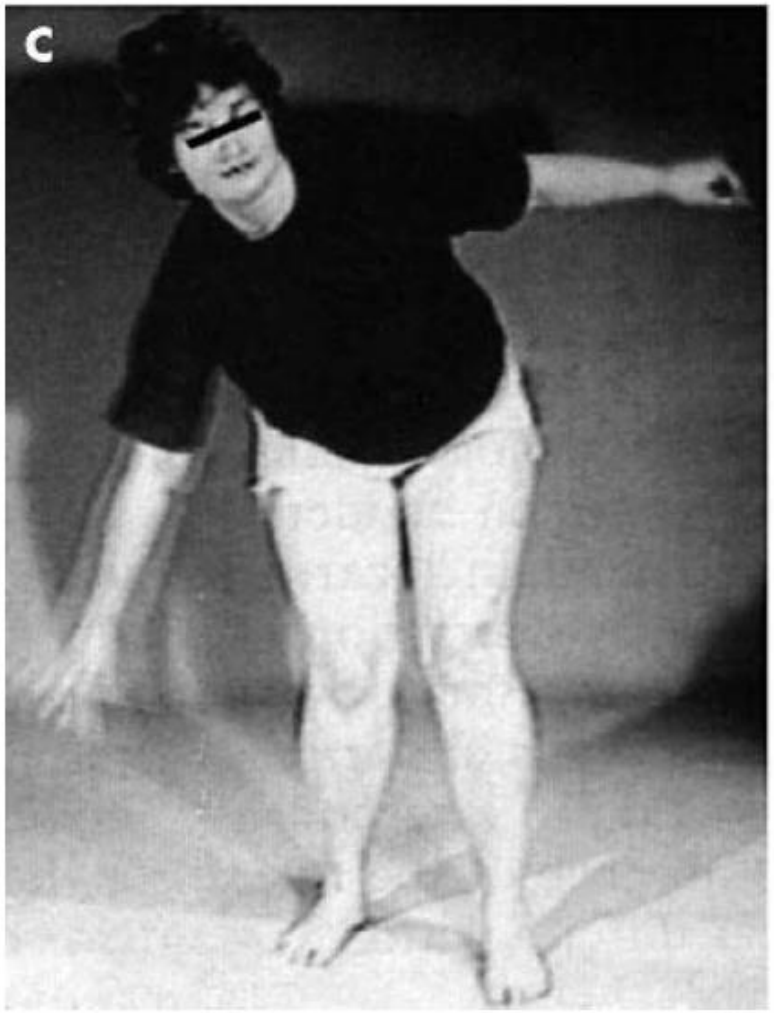
Espay et al., 2018 (JAMA Neurology)



Clinical features

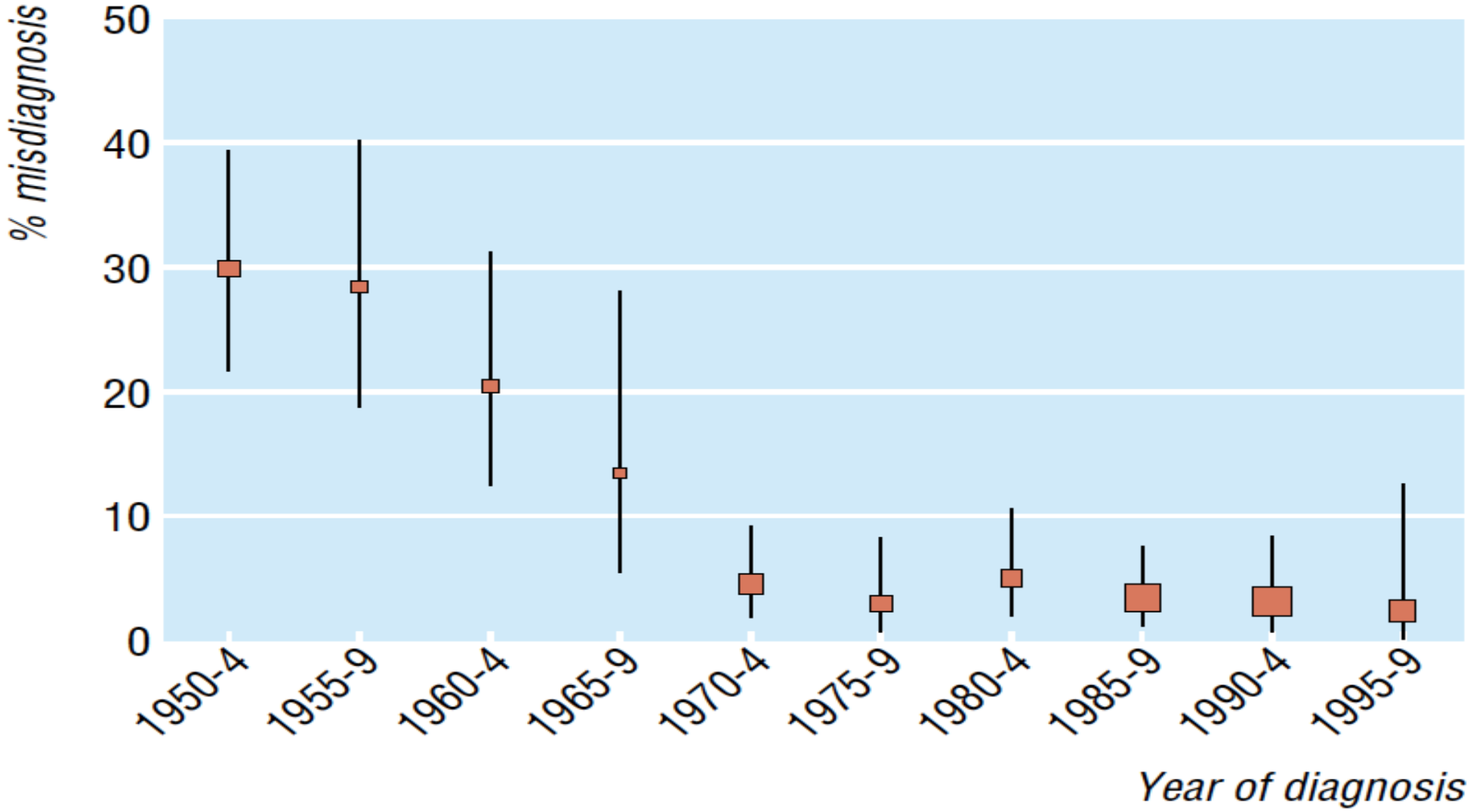
Stone et al., 2005 (Jnnp)





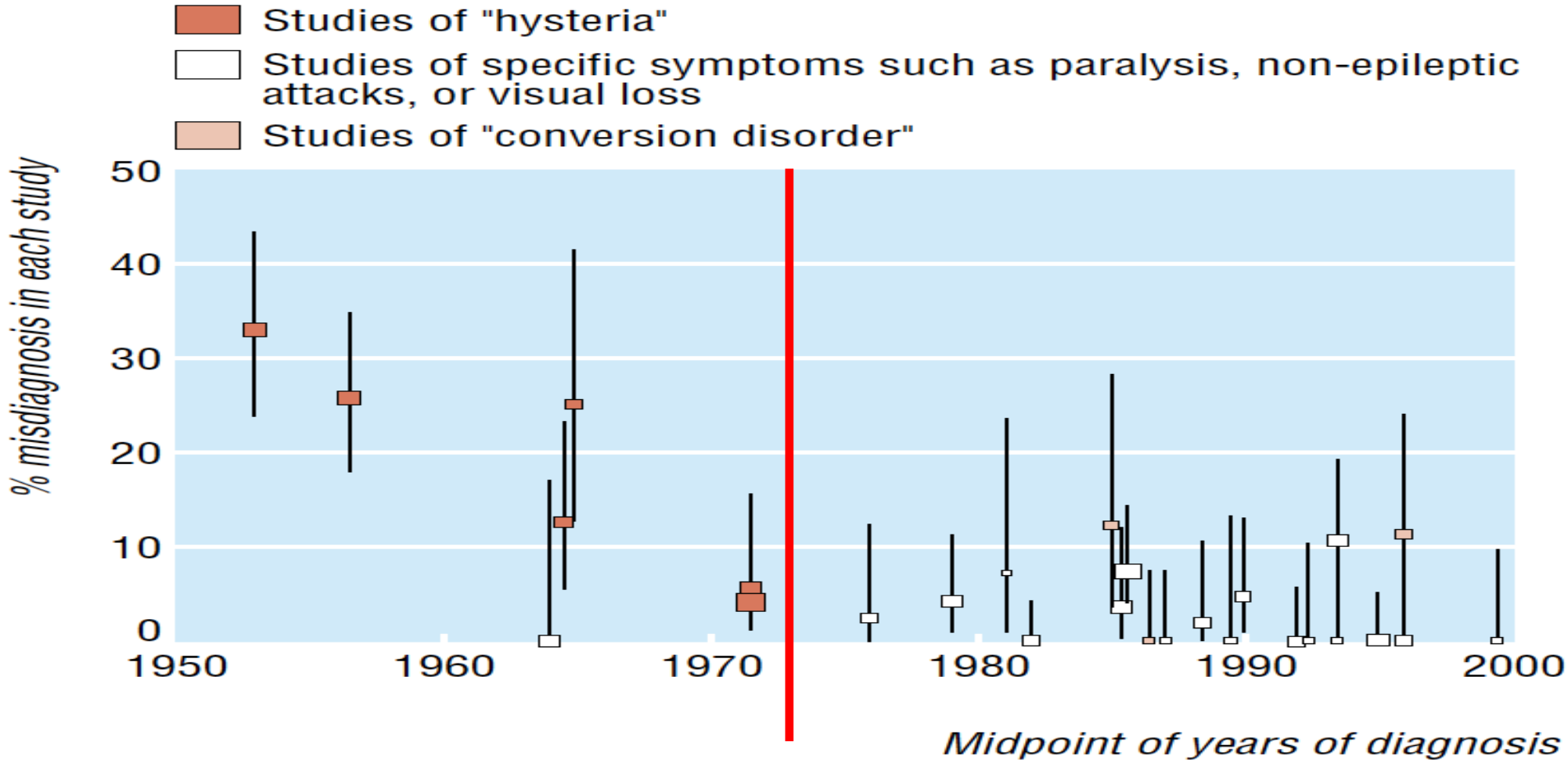
Diagnosis validity

Stone et al., 2005



Diagnosis validity

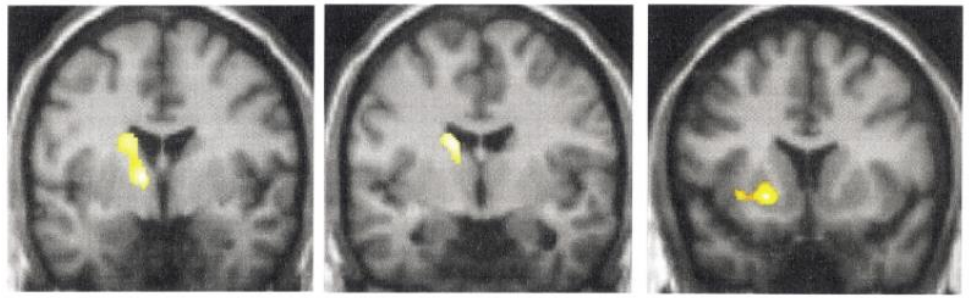
Stone et al., 2005

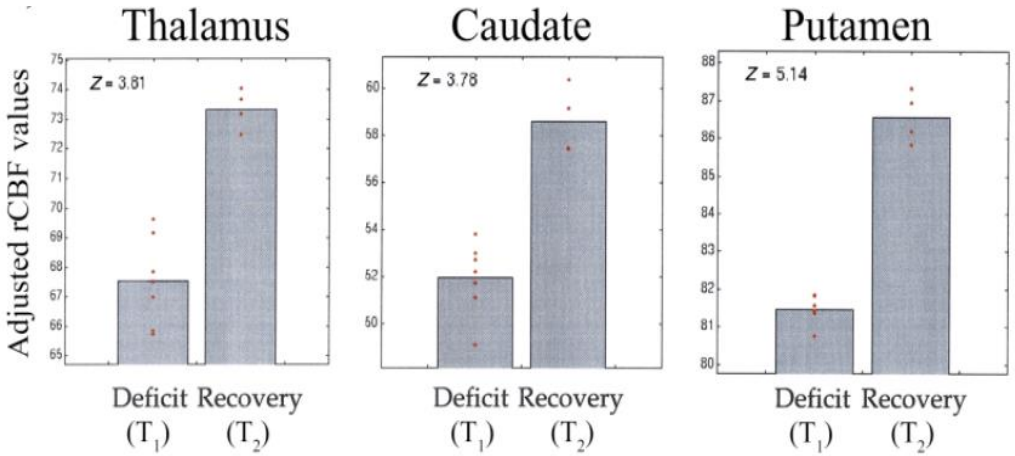


Godfrey Newbold Hounsfield
Prix Nobel médecine

Systematic review of the literature

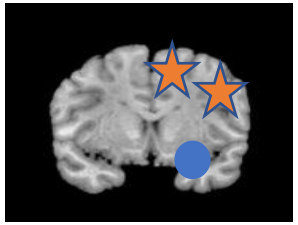
Vuilleumier et al., *Brain* (2001)



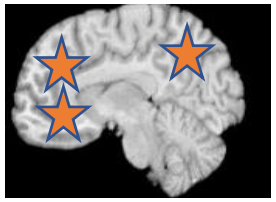


Low activation of controlateral caudate associated with poor recovery

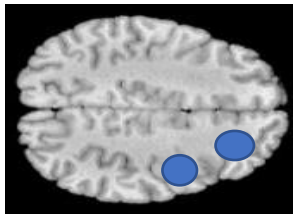
Conejero et al., (2017)



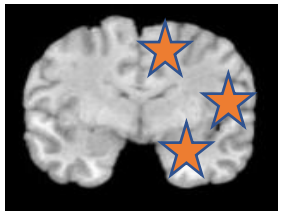
Memory suppression



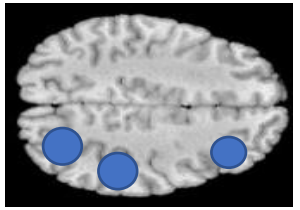
Action monitoring



Selection of motor patterns



Salience network



Self-agency

: Hyperactivated regions

: Underactivated regions

HYCORE study (Hysterical conversion recovery)

❖ **Hypothesis:**

Initial cerebral activation at rest is associated with persistent motor disability at 3 and 6 months follow-up

❖ **Main objective:**

Evaluating alterations of brain metabolism by SPECT imaging at rest during a first episode of motor FND, and their association with persistent physical disability at 3 and 6 months follow-up.

❖ **Secondary objective:**

Research of state and trait markers by the use of second SPECT imaging at rest at 3 months follow up.

Materials and methods

Inclusion criteria:

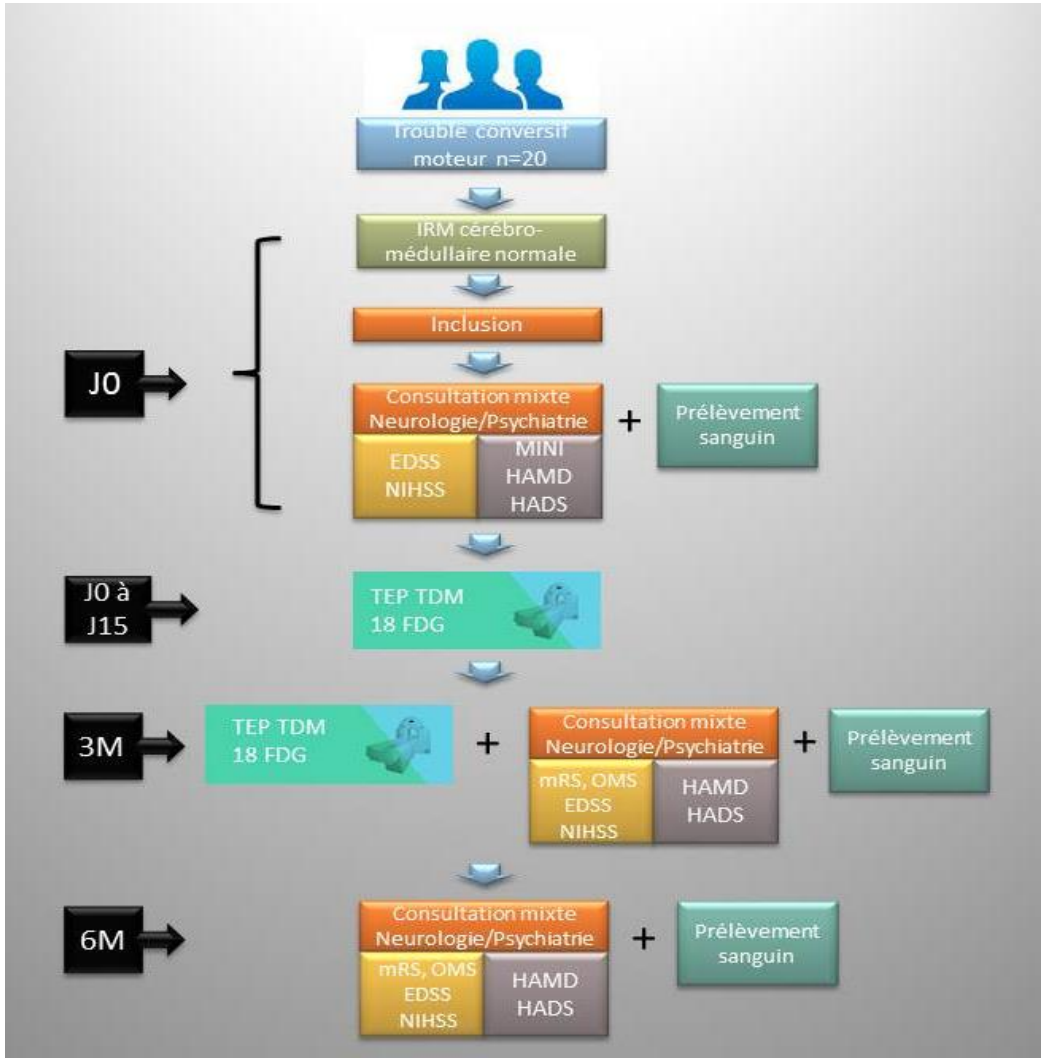
- ✓ **19 patients included**
- ✓ **First episode of motor FND**
- ✓ **Symptom onset < 1 month**

Exclusion criteria:

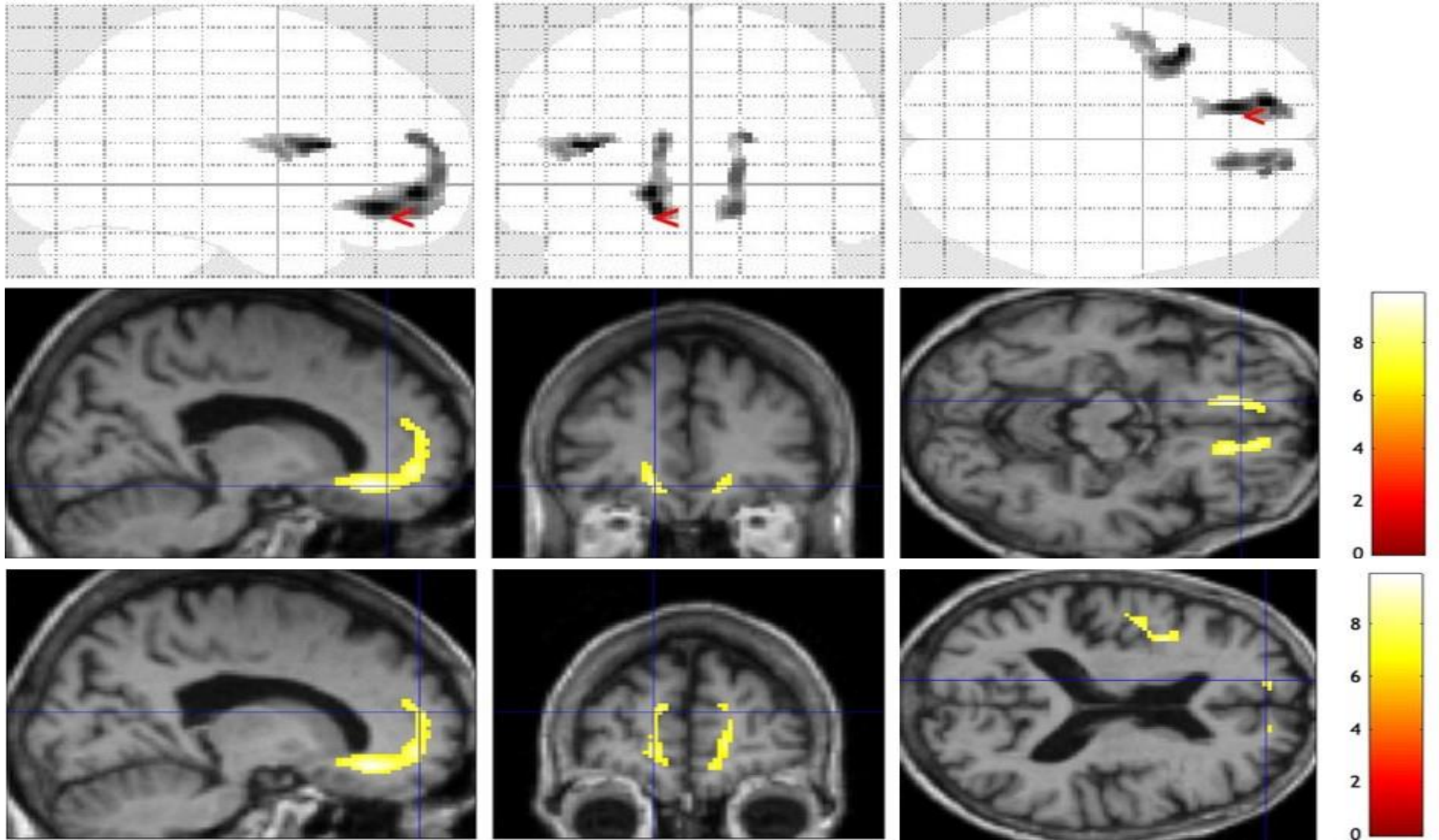
- ✓ **Severe depressive disorder**
- ✓ **Abnormal MRI (DWI, FLAIR)**
- ✓ **Organic neurological disease**

Neuroimaging at M0 and M3:

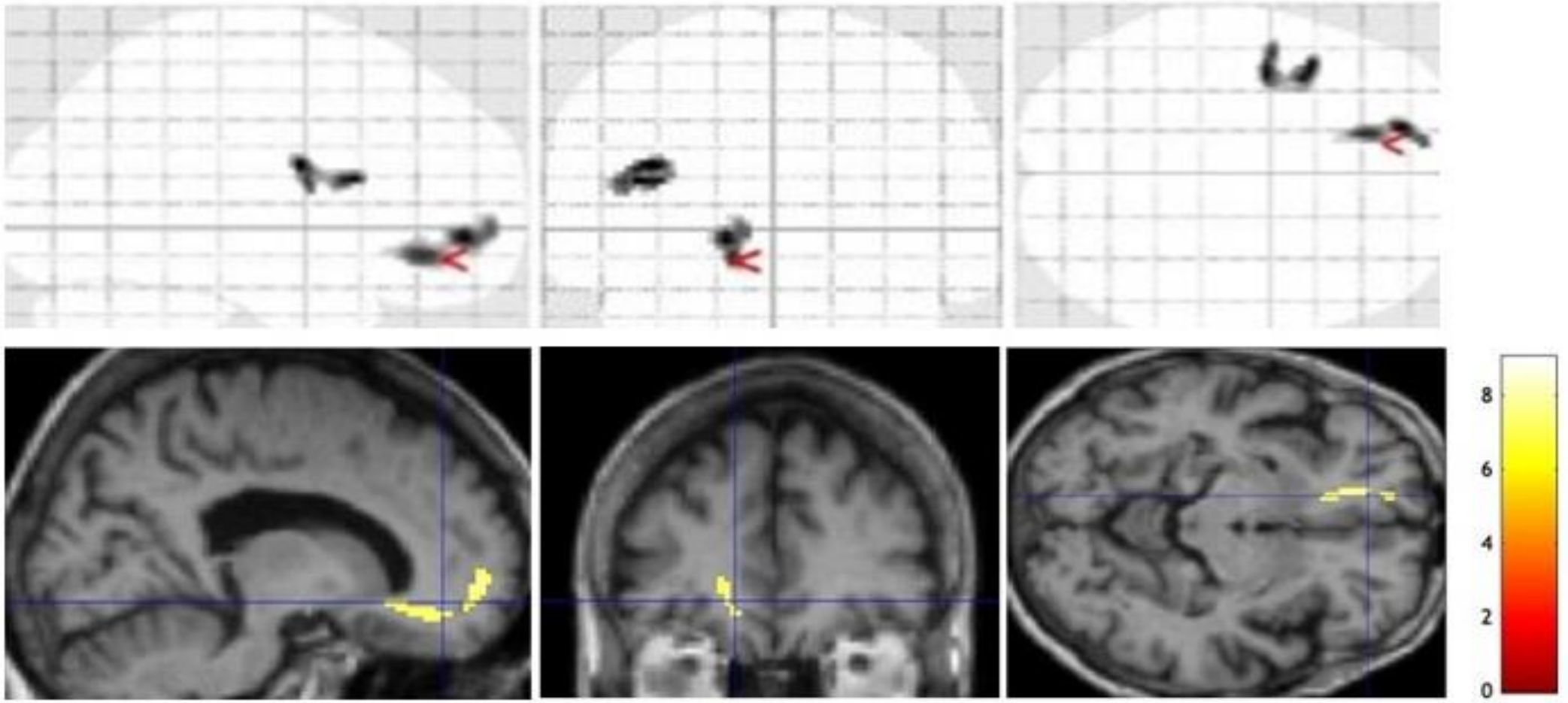
- ✓ **Brain H0 ^{18}FDG-PET-scan**
- ✓ **Whole brain and ROI (Caudate, Putamen, Thalamus, PFDLC, ACC, OFC, Primary motor cortex , and SMA)**



Hypometabolism in frontal regions at inclusion (19 patients vs controls)



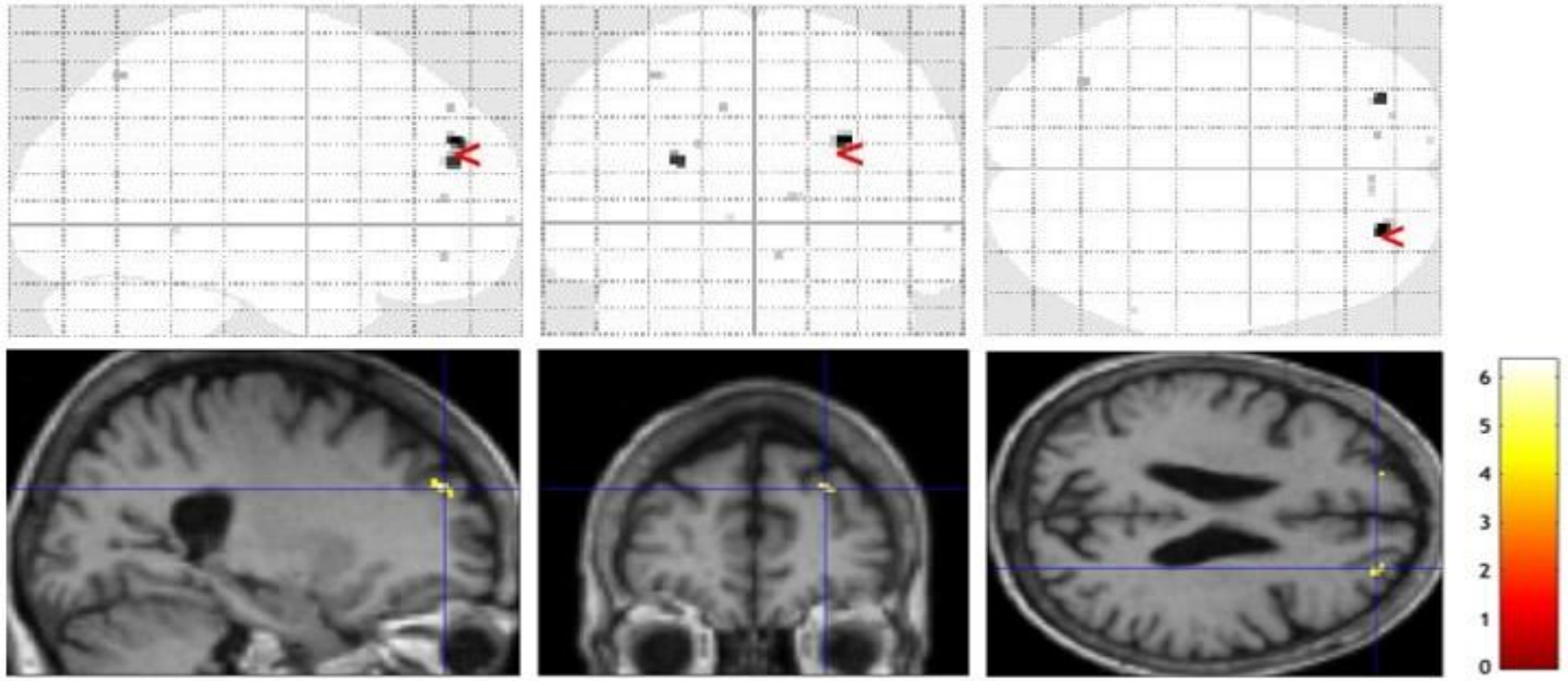
Hypometabolism in frontal regions at inclusion (Sensitivity analysis)



14 patients followed at 3 months vs controls

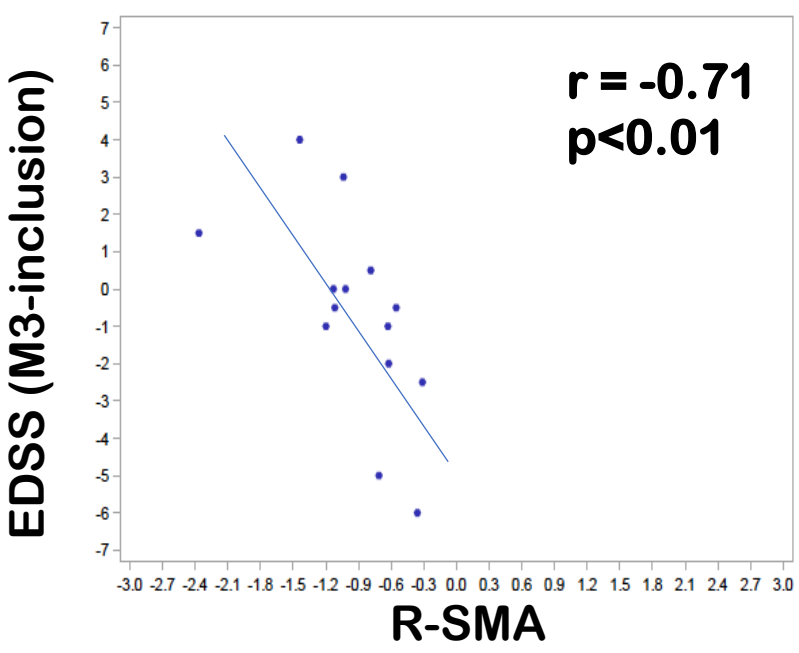
Remission marker at 3 months follow-up

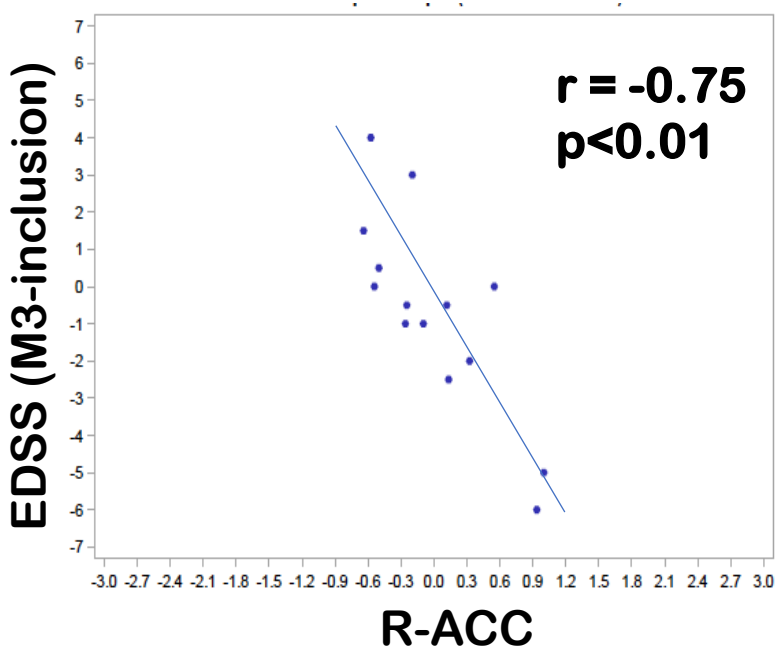
- ✓ At 3 months follow-up, no difference between patients (N=14) and controls
- ✓ At 3 months, remitted patients (with decreased EDSS) show higher PFDLC metabolism than non-remitted

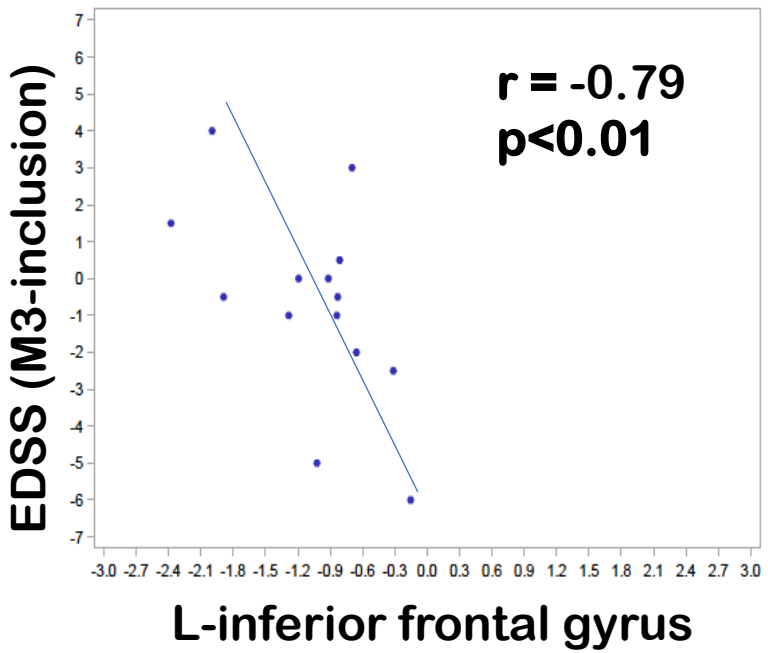


Remitted patients vs non-remitted at 3 months

Correlation between baseline metabolism and motor disability (EDSS) at 3 months

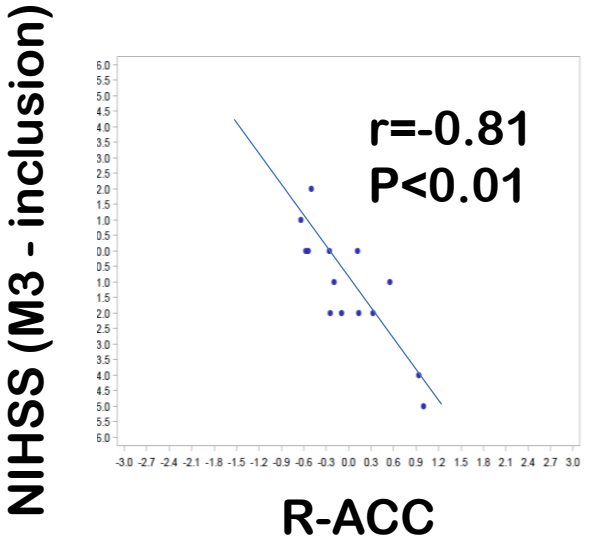


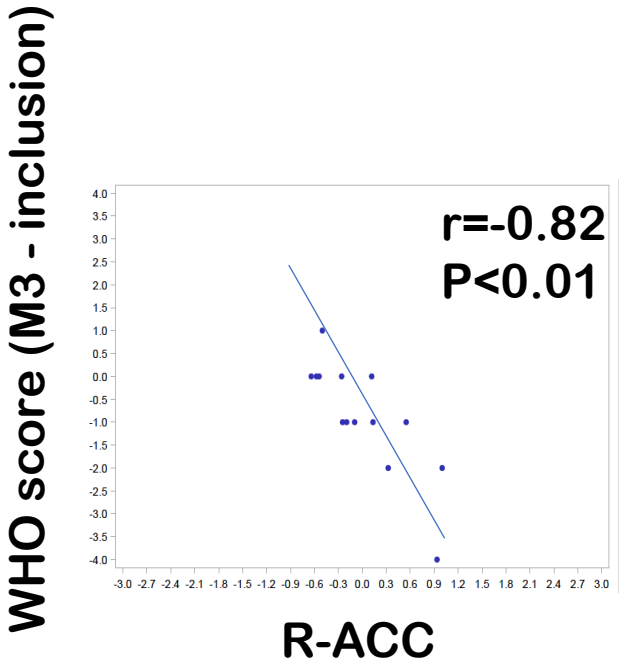


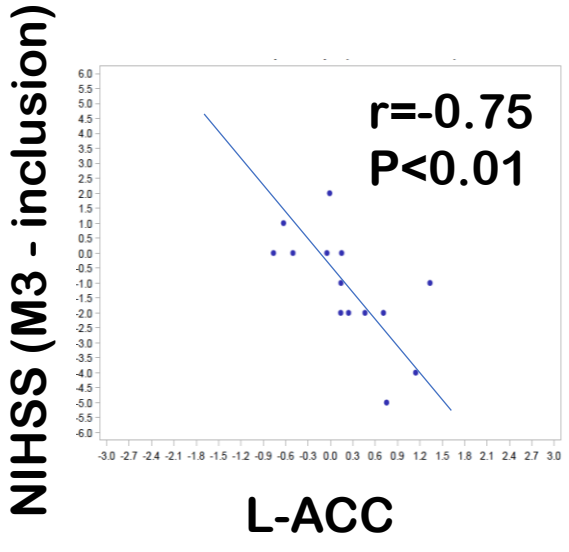


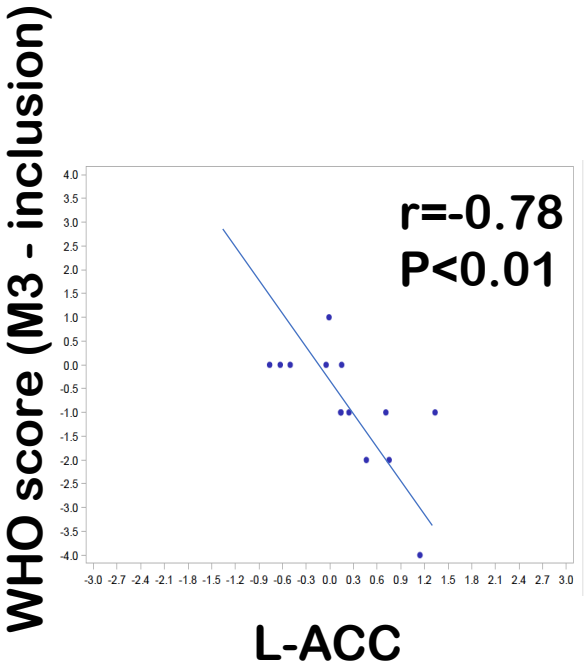
Association between EDSS decrease at M3 and ROI activation at baseline

Correlation between baseline metabolism and motor disability (NIHSS and WHO status) at 3 months









Association between NIHSS and WHO status decrease at M3 and ROI activation at baseline

To conclude

- ✓ State marker (frontal hypometabolism) of motor FND
- ✓ PFDLC activation is a marker of recovery
- ✓ Activation of SMA, ACC and Inferior frontal gyrus at symptom onset associated with recovery at 3 months
- ✓ Limitation: clinical heterogeneity of our sample

CONVERSTIM study

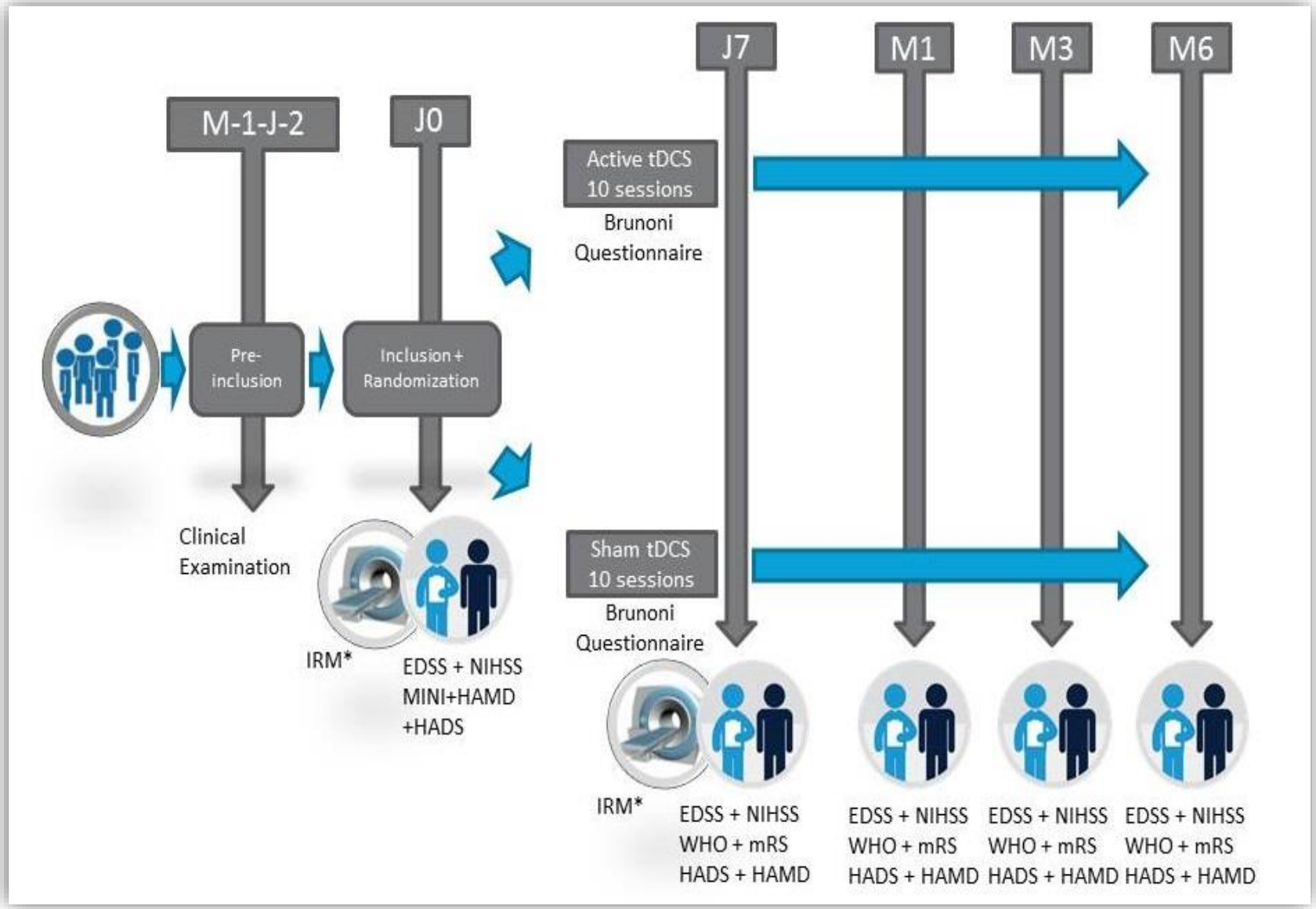
- ✓ PHRC National (2018), principal investigator: I. Conejero
- ✓ Aim: To evaluate the efficacy of transcranial direct current stimulation (tDCS) of PFDLC patients with motor FND at 3 months post-stimulation
- ✓ Randomized multicentre double blind assay
- ✓ NSN: 96 patients
- ✓ Inclusion criteria: Conversion disorder (DSM-5), motor type, EDSS ≥2, For more than 1 month
- ✓ Initial assessment: EDSS, NIHSS, mRS, WHO, MINI, HADS, HAMD, Brunoni questionnaire, GDI

CONVERSTIM study

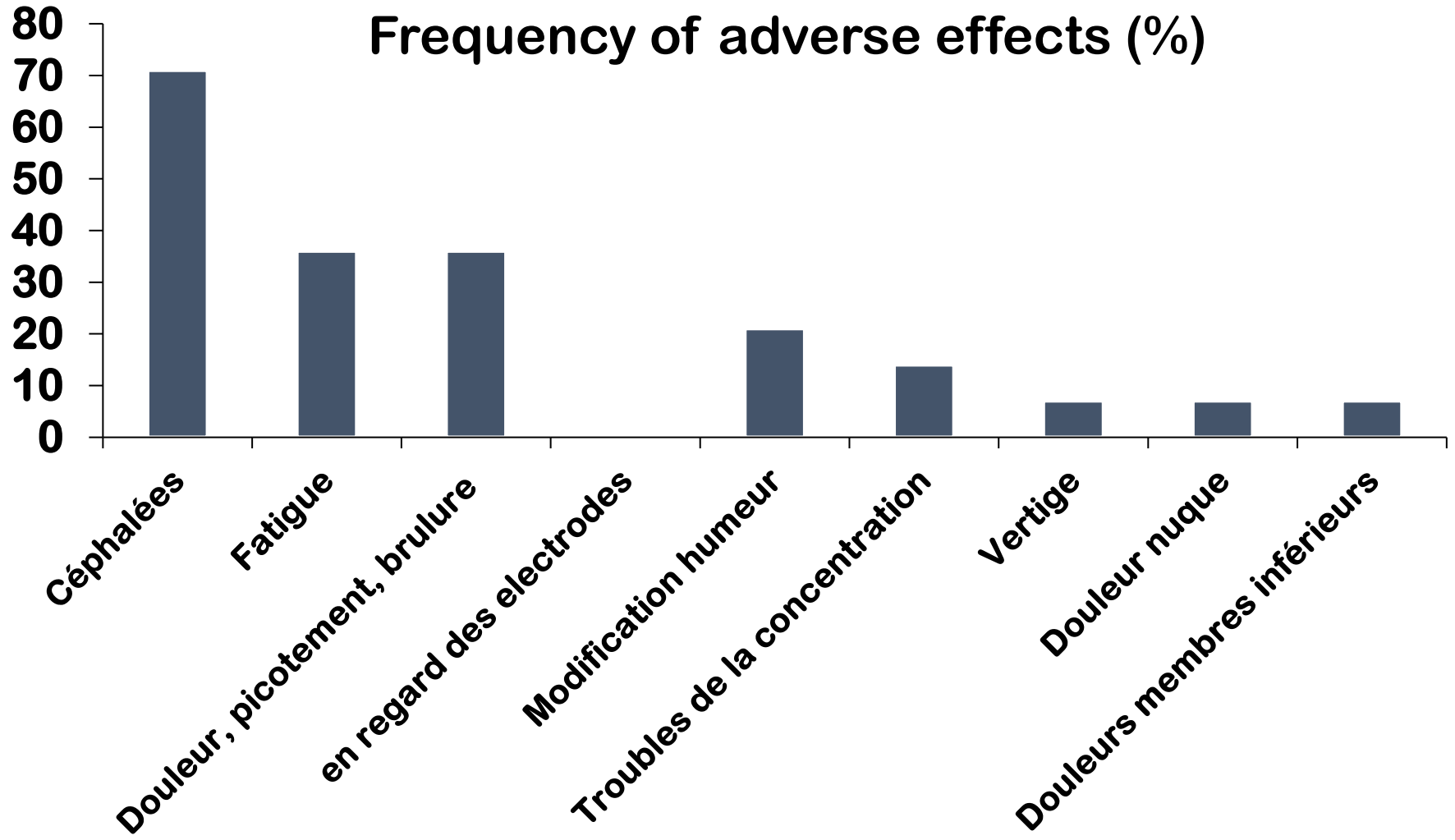
tDCS device

MRI at J0 and J7:

- ✓ **Structural**
- ✓ **Resting state and activation**

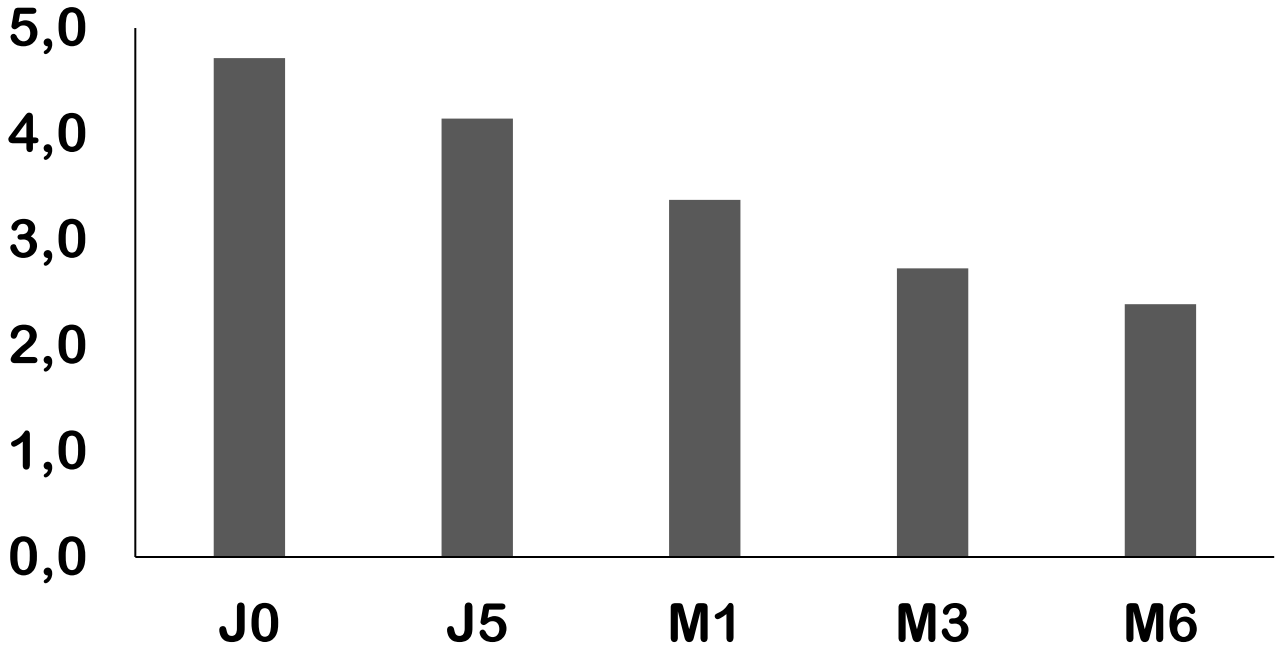


Retrospective study of tDCS stimulation in 14 patients with FND

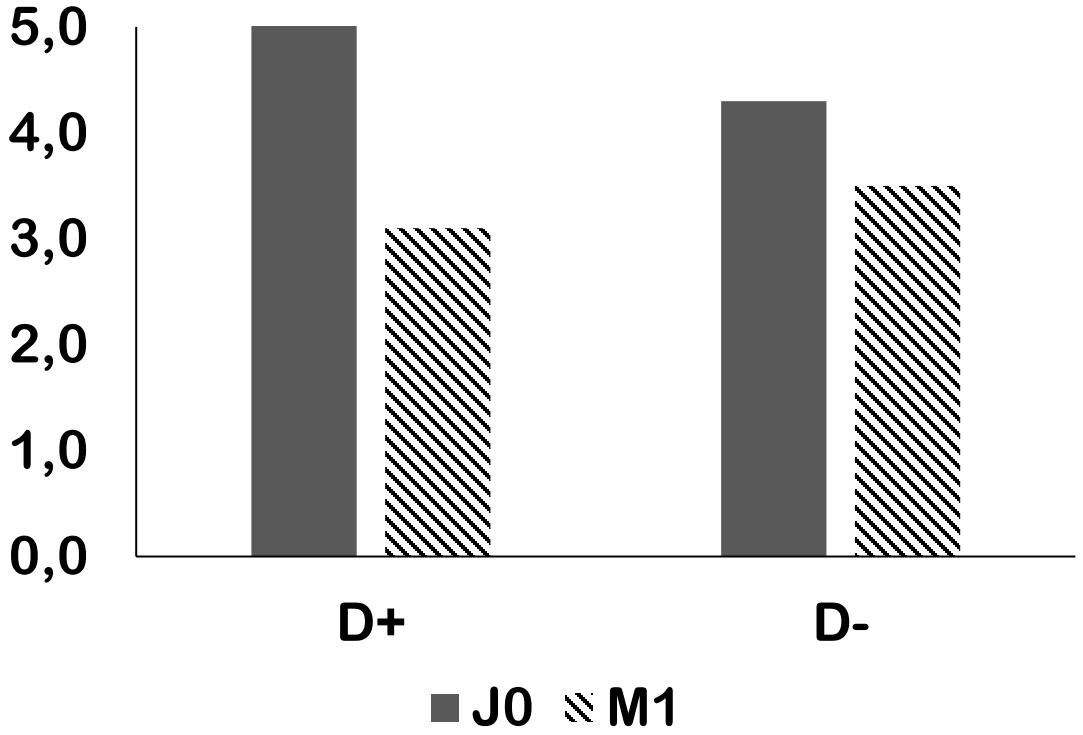


Retrospective study of tDCS stimulation in 14 patients with FND

Mean EDSS score at J0 and at follow-up



EDSS at J0 and 1 month (dissociated vs non dissociated patients)

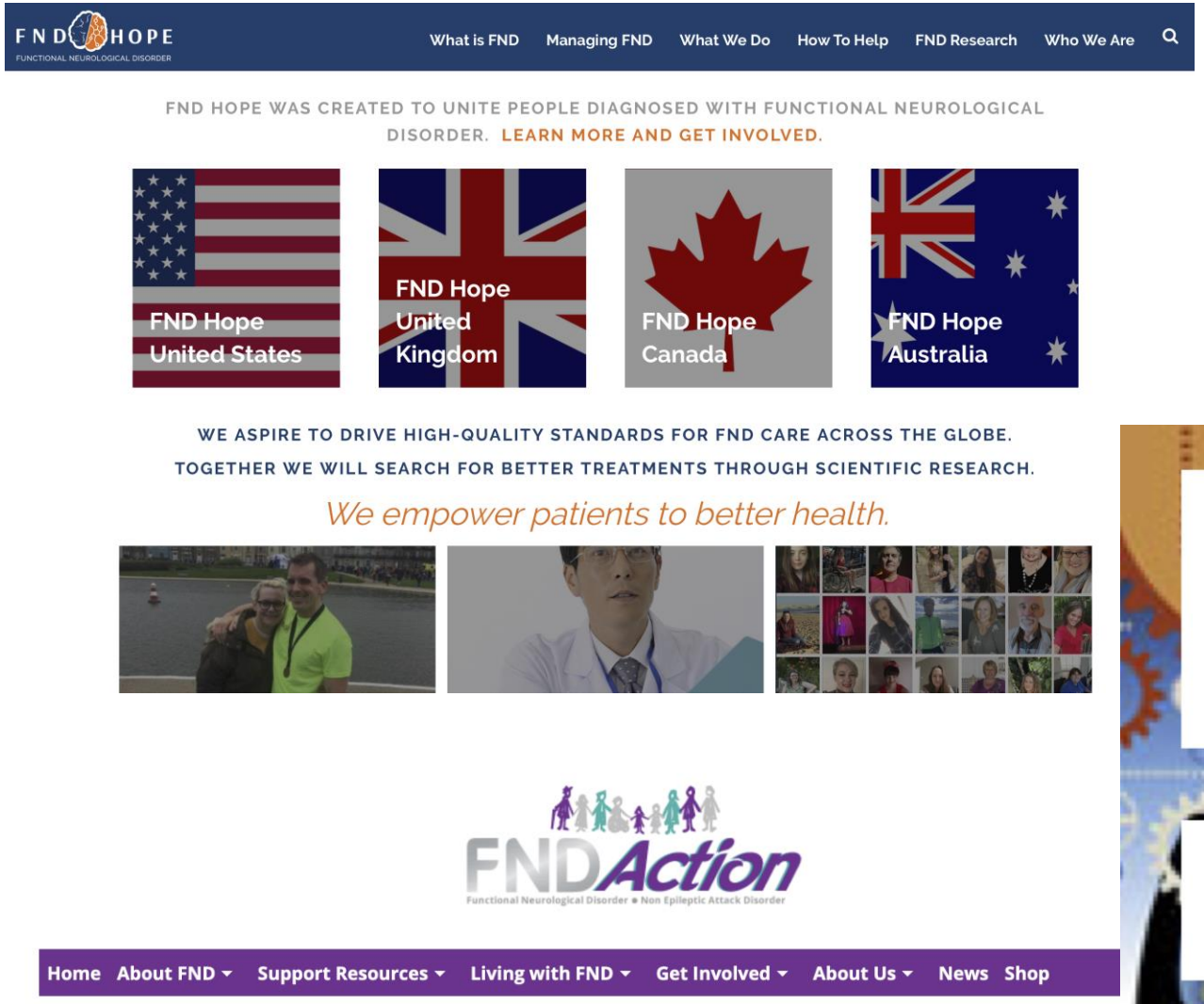


D+ : DES scale > 25; D- : DES < 25

To conclude

- ✓ tDCS stimulation seems well tolerated in this population
- ✓ Sustained response to tDCS at 6 months post-stimulation
- ✓ Patients with psychic dissociation may better respond to tDCS than non dissociated patients

Des réseaux !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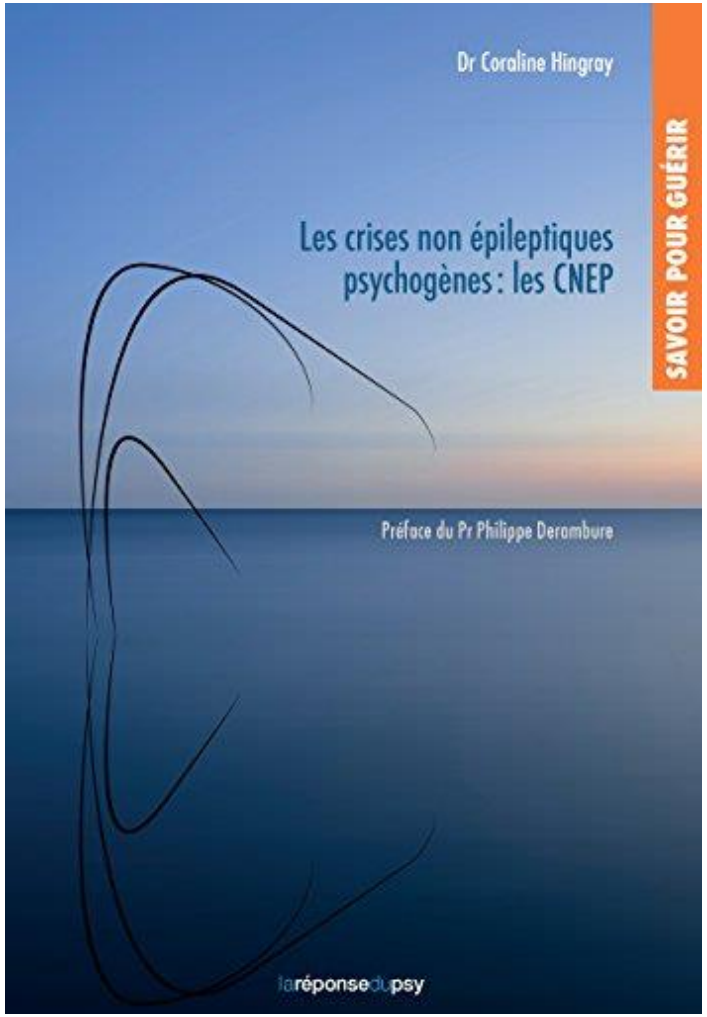
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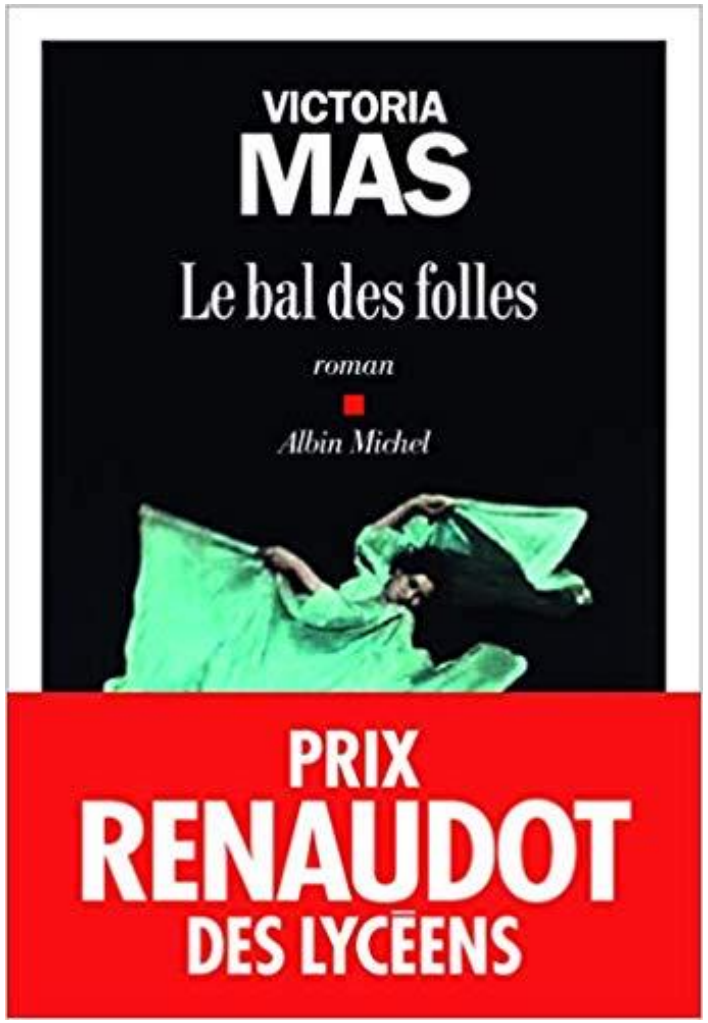
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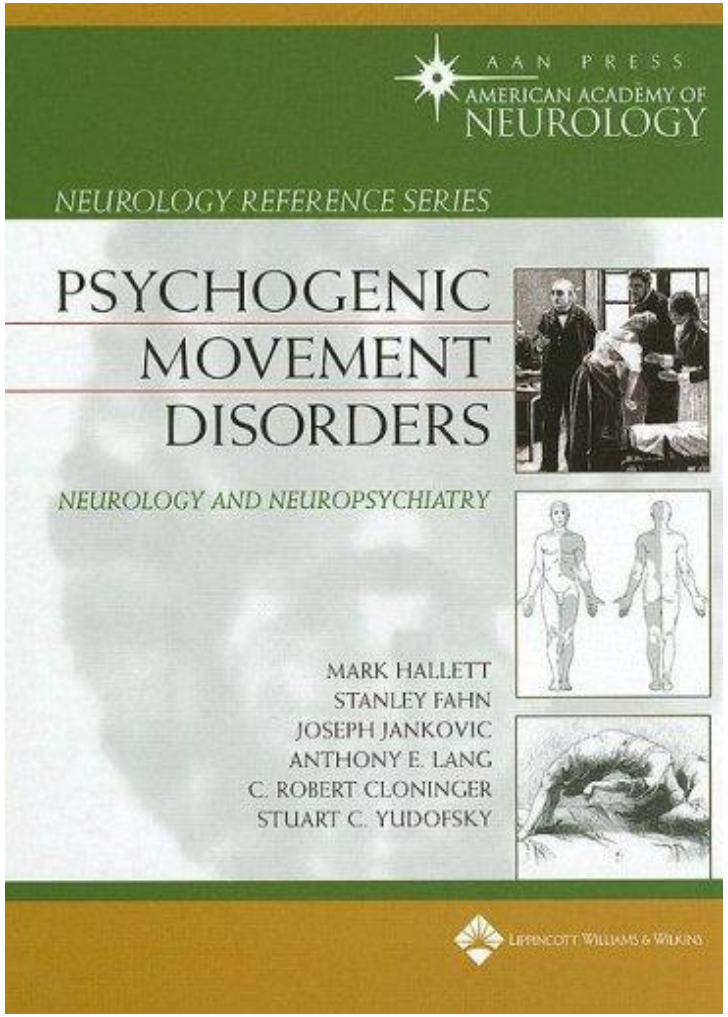
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