BRAIN MRI FINDINGS IN FETAL ALCOHOL SPECTRUM DISORDER: A COMBINATION OF NEUROANATOMICAL MARKERS TO SUPPORT DIAGNOSIS

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A COMBINATION OF NEUROANATOMICAL FEATURES TO SUPPORT FETAL ALCOHOL SPECTRUM DISORDERS DIAGNOSIS

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INTRODUCTION

- brain is a major target of ethanol developmental toxicity
- prenatal alcohol exposure (PAE): underdiagnosed cause of cognitive & behavioral disabilities
- **Fetal Alcohol Spectrum Disorder (FASD)**
  - ✓ **Fetal Alcohol Syndrome (FAS)**
  - ✓ **Non-Syndromic Fetal Alcohol Spectrum Disorder (NS-FASD)**

INTRODUCTION

- **FAS** ⇨ facial features, body, and brain growth deficiency

- apart from **microcephaly, neuroanatomical features** involved in diagnosis are unspecified & contribute little to specificity

- in the absence of the characteristic facial features, the diagnosis of **NS-FASD** remains difficult and probabilistic

OBJECTIVE

- to assess the presence of objective MRI neuroanatomical abnormalities in patients with FASD and see how they can contribute to the diagnosis

MATERIAL & METHODS

- retrospective study
- 89 FASD subjects, aged 6 to 20 years
- 94 typically developing controls aged 6 to 20 years, with no report of PAE nor family history of neurological or psychiatric condition (in 1st degree relatives)
- **FASD subjects**
- 4-digit diagnostic code (4-DDC) ⇒ 2 groups FASD
  - ✓ 52 (58.4%) syndromic or FAS (including partial FAS)
  - ✓ 37 (41.6%) non-syndromic or NS-FASD

no significant group effect for age & sex

- D/d included systematic brain MRI and genetic testing

MRI PROTOCOL

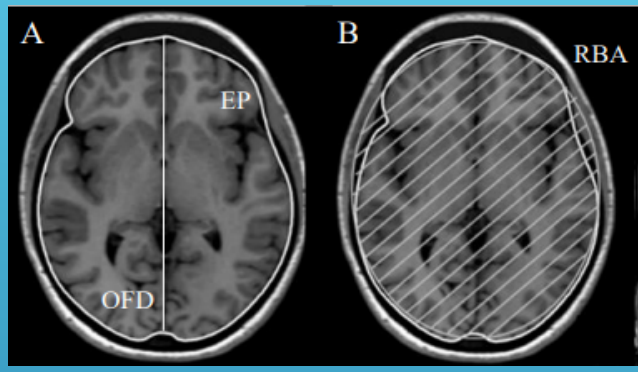
- 1.5T
- isotropic 3D T1-weighted FFE-TFE sequence for FASD subjects and 41 sequence-matched controls
- 3T
- isotropic 3D T1-weighted MPRAGE sequence for other controls (53)

  - **neuroanatomical quantitative measurements**
  - **semi-quantitative assessment of upper vermis foliation**

NEUROANATOMICAL QUANTITATIVE MEASUREMENTS

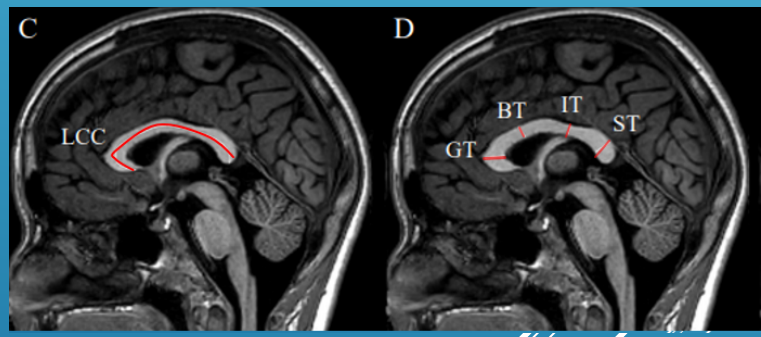
PACS measurement tools

- one operator (JF) blind to diagnosis



- brain size: axial reference brain area (RBA)

square rooted for the sake of dimensional homogeneity

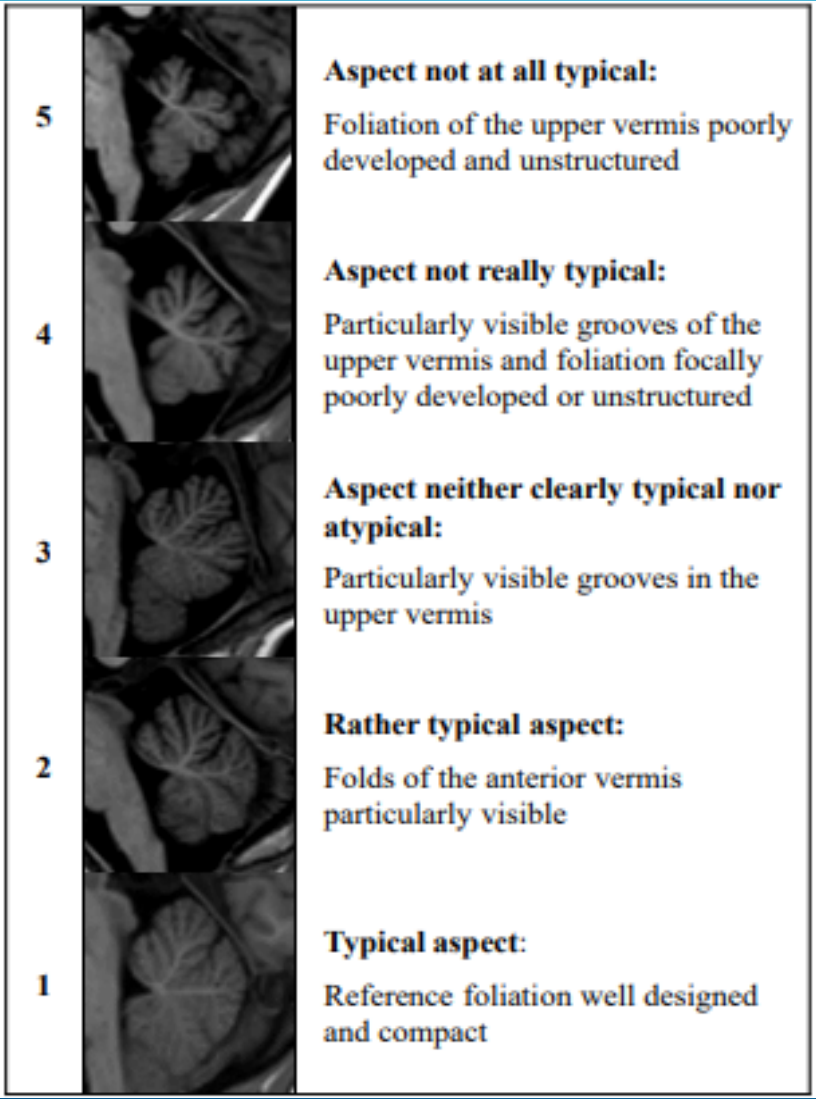


- length of the corpus callosum (LCC)
- genu (GT), body (BT), isthmus (IT) & splenium (ST) thickness

- height of the vermis (HV)

SEMI-QUANTITATIVE ASSESSMENT OF UPPER VERMIS FOLIATION

- a five-point Likert scale was proposed to evaluate the upper vermis foliation



- 3 operators performed blind and independent ranking of FASD subjects & matched controls
- the rank finally assigned was the nearest-rounded average of the 3 operators

- observer agreement: Cohen's Kappa coefficient (κ)
- considering the 5 ranks separately and then grouping ranks 1 to 3

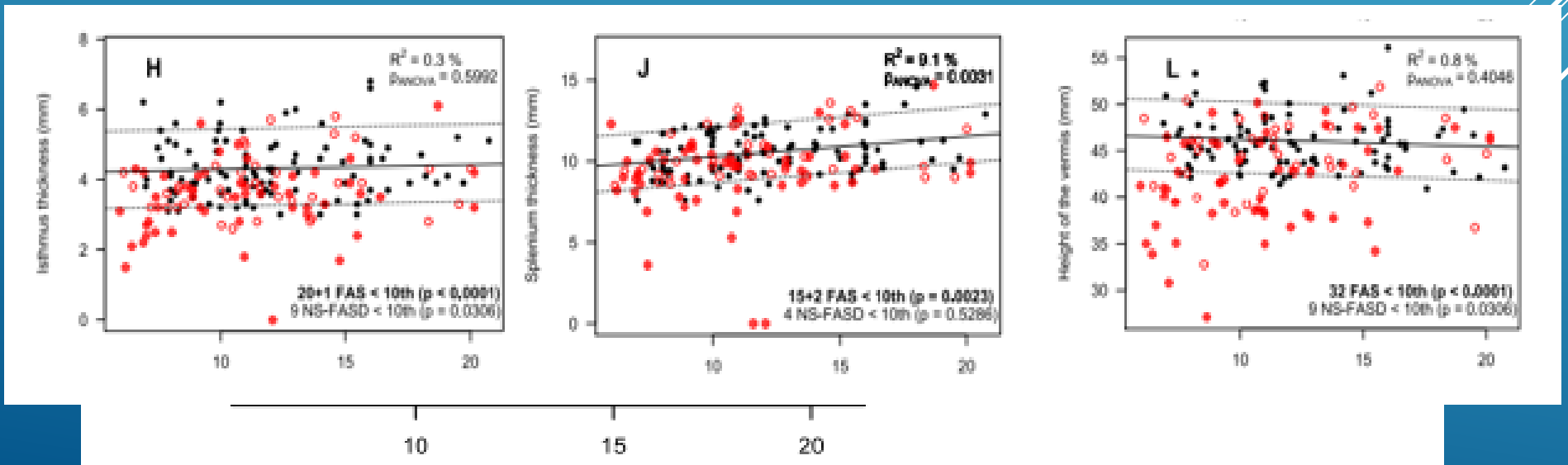
RESULTS: GROWTH DEFICIENCY

- ***measurements as a function of age (growth curves – effect of age)***

  94 controls: callosal and vermian measurements did not significantly change with age

  89 FASD:

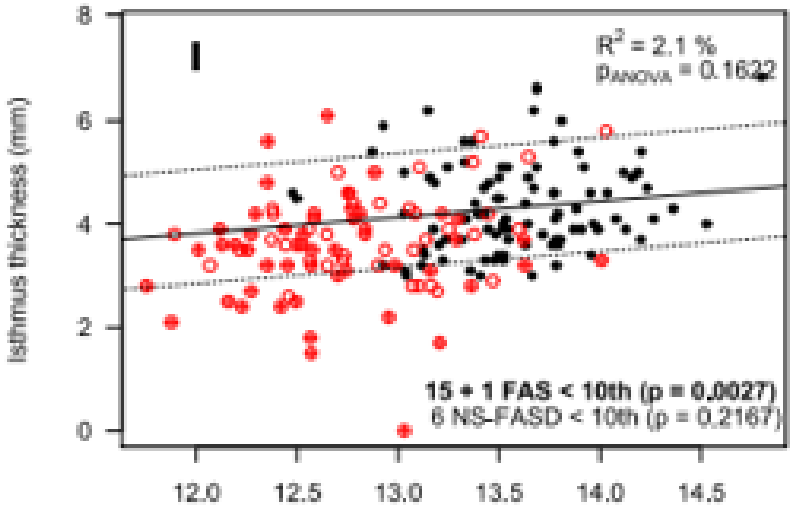
  - RBA <10th p. of controls for 74.2% (48 FAS and 27 NS-FASD)
  - excess of FAS: abnormally small LCC, IT, ST, and HV measurements for age ($p<0.0001$ and $p=0.0023$ for ST)

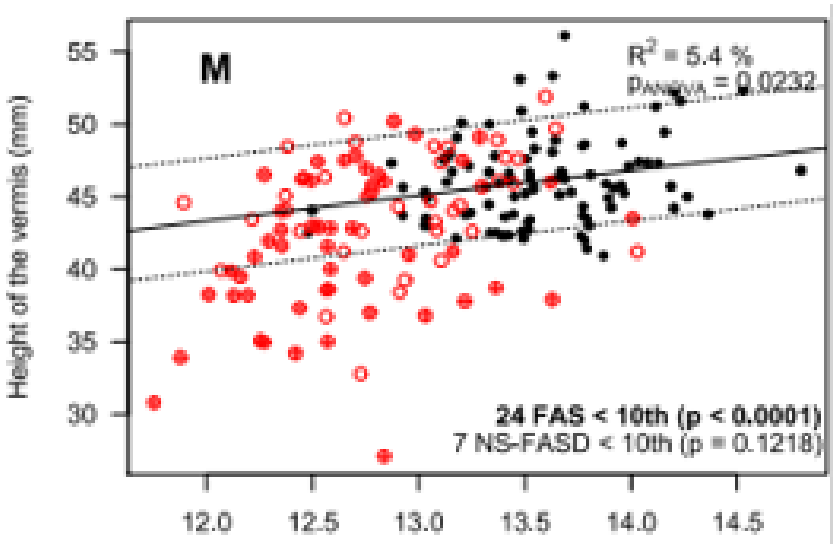


RESULTS: GROWTH DEFICIENCY

- ***individual measurements as a function of brain size***
- scaling curves for controls ➡ anomalies independent of the overall brain size deficit
  - LCC: significantly correlated with brain size ($p<0.0001$)
  - FASD: <10th p. for IT, $p=0.0027$ (16 FAS and 6 NS-FASD)

    <10th p. for HV, $p<0.0001$ (24 FAS & 7 NS-FASD)



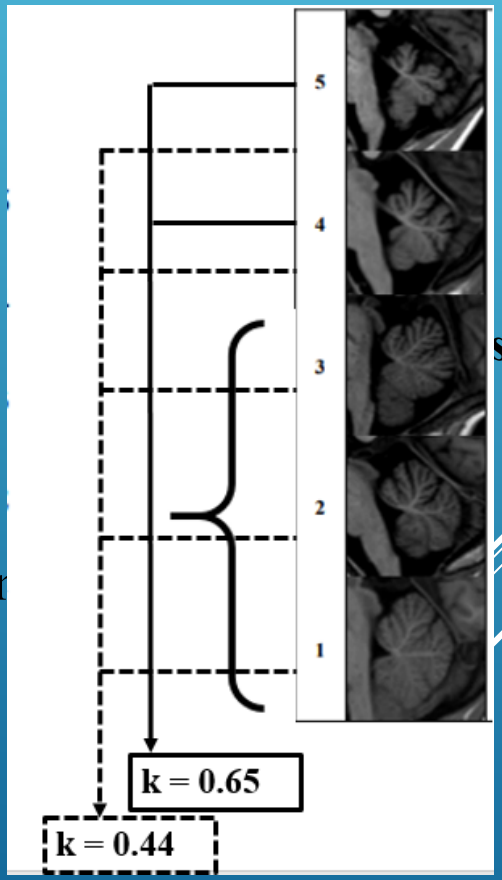


RESULTS: UPPER VERMIS FOLIATION

- ***5-rank scale***
  - moderate interobserver agreement (κ=0.44) considering the 5 ranks separately
  - increased to strong (κ=0.65) grouping ranks 1-3 "not very typical" & ranks 4-5 "not at all typical" foliation

- **controls were ranked 1-3**
- **11 subjects ranked 4: 8 FAS & 3 NS-FASD**
- **5 subjects ranked 5: 3 FAS & 2 NS-FASD**

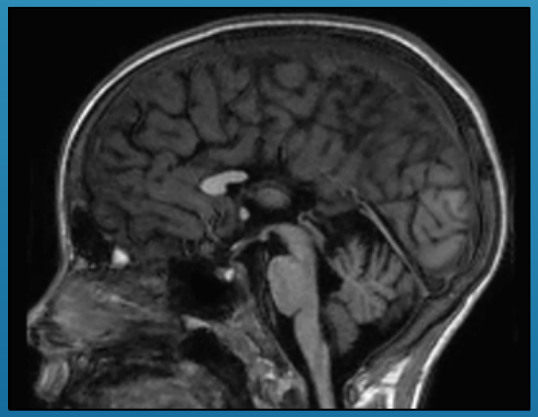
- !!! 4subjects ranked 4 or 5 did not show a small ver

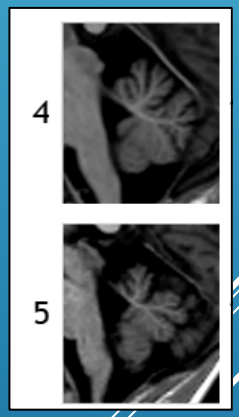


RESULTS: IN TOTAL

- **3 recurrent neuroanatomical abnormalities in FASD**
  - not trivially associated each other
  - not plain consequences of brain size deficit

1. **brain size deficit for age**: clinically (HC) or radiologically (RBA)
2. **CC abnormalities**: partial ACC or narrowed callosal isthmus for brain size
3. **vermis abnormalities**: disrupted upper vermis foliation and/or insufficient HV

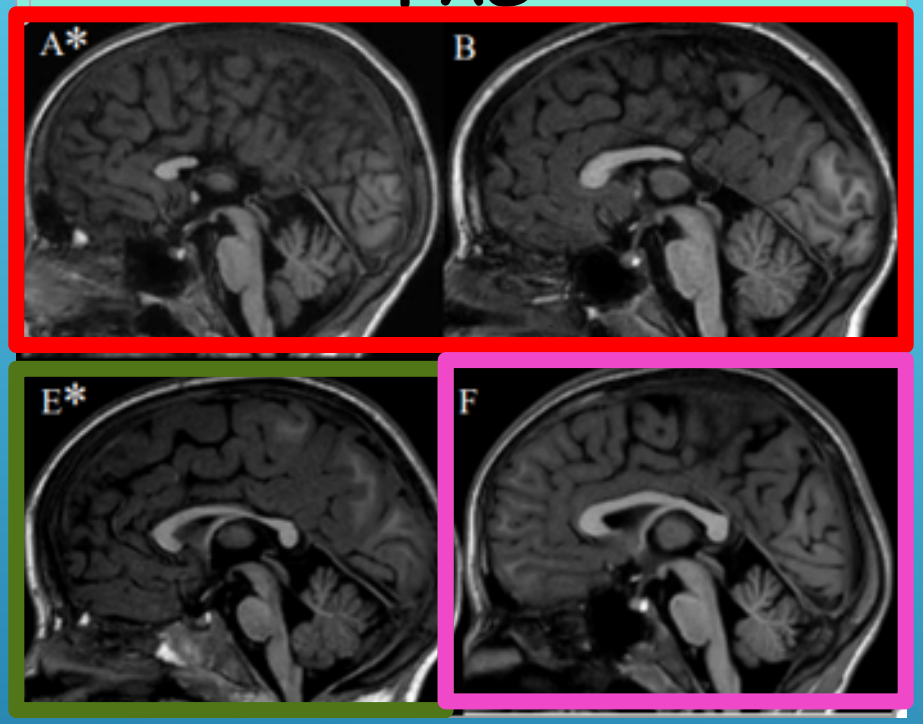


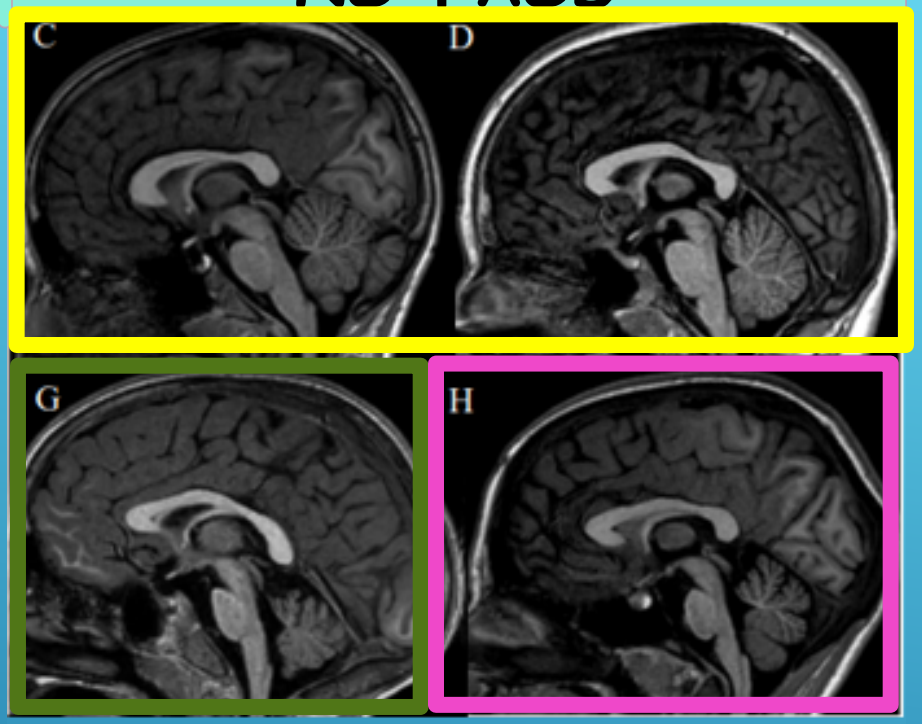


- **2 out of 3 abnormalities: 38% FAS, 27% NS-FASD and only 2% controls**
- **3 abnormalities: 19% FAS**

FAS

NS-FASD





- A, B: Partial agenesis of CC
- C, D: Narrowed callosal isthmus for brain size
- E, G: Upper vermis ranked 5
- F, H: ranked 4.

CONCLUSION

- **FAS but also NS-FASD** patients present **corpus callosum and cerebellar vermis abnormalities** that in combination **with microcephaly** could help suggest a FASD **in a context of neurodevelopmental disorders**, and contribute to the specificity of the diagnosis especially in non-syndromic patients