

European Course on Pediatric Neuroradiology in Latin America (ECPNR-LATAM)

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3rd Cycle - Module 1
de 1º a 4 de outubro

Local: Sede da APM
Associação Paulista de Medicina
São Paulo - Brasil

Outcome of some of the more frequent fetal-MRI findings. *(the big five and others...)*



Andrea Righini M.D.

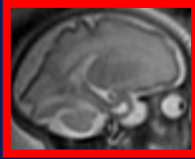
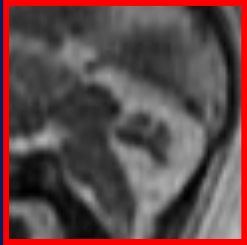
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«no conflicts of interest to declare»

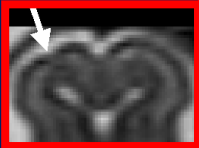
the big five
and more...

huge gap between imaging and long term prognosis...

verm.
rotation

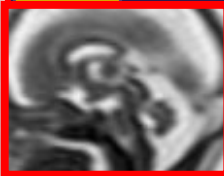
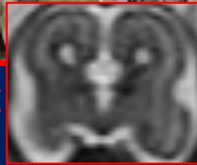


CMV
minor
lesions.



focal
cort.
malf.

Isolated ACC



short CC

???

lack of large
Fetal cohorts with
«clean»-truly
isolated findings



school-age
outcome?

Accuracy of in-utero MRI to detect fetal brain abnormalities and prognosticate developmental outcome: postnatal follow-up of the MERIDIAN cohort

Anthony R Hart et Al.

Follow-up at **only 3 years**

“.....antenatal counselling should **avoid overconfidence** when discussing the developmental significance of brain abnormalities. This is true for significant structural abnormalities and of more subtle changes, such as isolated mild ventriculomegaly, that are usually associated with good outcome.

....more participants had good prognosis with iuMRI compared with ultrasonography, suggesting iuMRI is better at excluding abnormal developmental outcome than ultrasonography, either through better visualisation of the abnormalities or identification of false positives on ultrasonography.

Morphology and function: from fetal brain image to childhood outcomes.

Commentary to Hart AR et Al. *Lancet Child Adolesc Health* 2019
Andrea Righini M.D. *Lancet Child Adolesc Health* 2020

In the past two decades, intrauterine MRI has been widely applied in clinical and research settings

....a gap in prenatal medicine between the ability to collect novel neuroimaging findings and to provide reliable mid-term to long-term neurological prognosis.

.....a warning against overconfidence in the sole use of iuMRI-based prognostication. Considering that Hart AR et Al work was limited to 3 years of follow-up, **our knowledge of outcomes in school-age children is currently unexplored territory.**

FETAL MRI OUTCOME PREDICTION: confidence level



not reliable

reliable

1a

confidence level



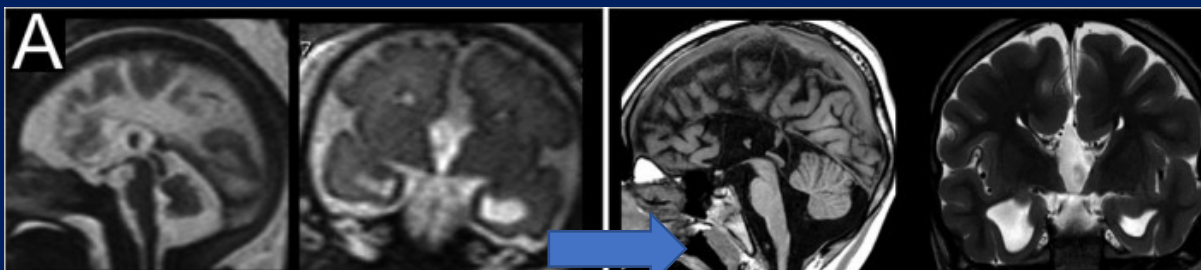
Isolated complete Agenesis of Corpus Callosum

Ann Clin Transl Neurol 2021

Long-term follow-up in a cohort of children with isolated corpus callosum agenesis at fetal MRI

Romina Romaniello et Al.

38 children at school-age (>6 years):

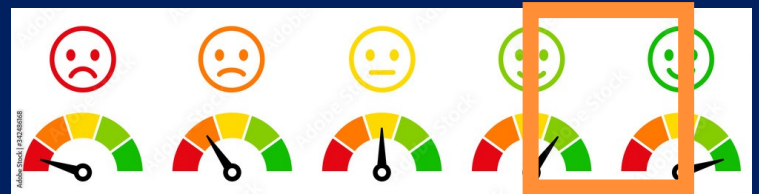


Caveat!

Additional findings (21%) at postnatal MRI. Significant association between additional findings and abnormal neurodevelopment.

1b

confidence level



Isolated complete Agenesis of Corpus Callosum

Ann Clin Transl Neurol 2021

Long-term follow-up in a cohort of children with isolated corpus callosum agenesis at fetal MRI

Romina Romaniello et Al.

38 children at school-age (>6 years):

1- normal intellectual functions (50%), intellectual disability (21%), borderline intelligence (29%).

2- Motor Deficits (58%), executive functions (37%), language (61%), memory abilities (58%), and academic performances (53%). 21% behavioral difficulties.

Almost half of the participants underwent rehabilitation.

2

confidence level



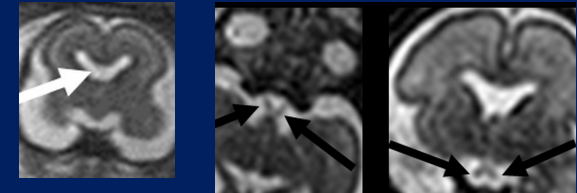
Isolated Agenesis of Septum Pellucidum

Neuropediatrics 2022.

School-Age Outcome of Fetuses with Isolated Complete Septum Pellucidum Agenesis at Prenatal Magnetic Resonance Imaging

Andrea Righini et AL.

12 children at school-age (>6 years):



optic nerve and chiasm OK

NONE among the 12 cases of the resulting final cohort presented visual or stature deficits.

1 required special teaching assistance in school. All other 11 children resulted without any notable academic issue.

3a

confidence level



Minor apparently isolated white matter signal alterations in CMV fetuses

Congenital cytomegalovirus infection with minor lesions at fetal MRI: a 12 years experience to improve counselling skills

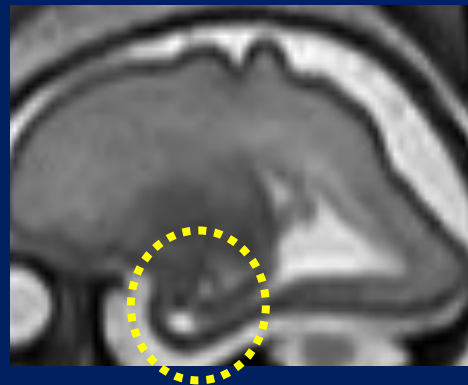
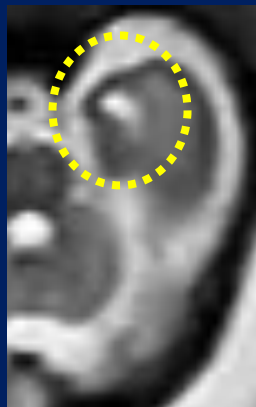
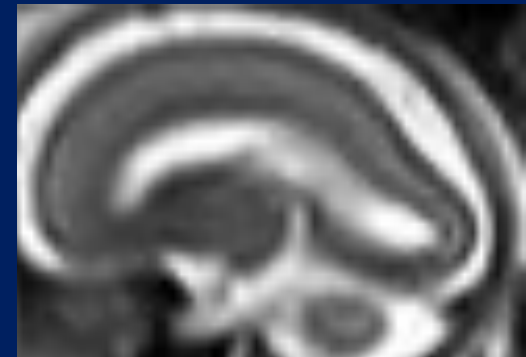
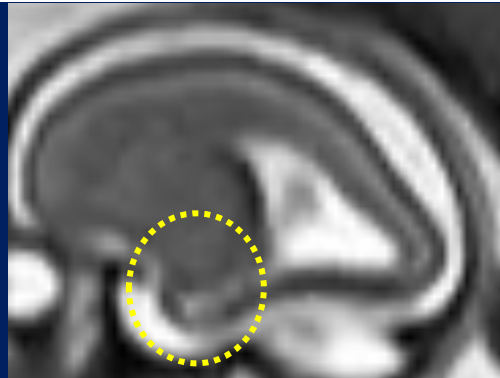
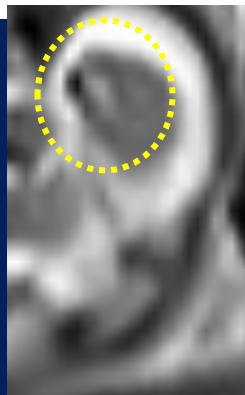
Chiara Doneda et Al.

Under submission

22w



29w



3b

confidence level



**Minor apparently isolated white matter
Signal alterations in CMV fetuses**

35 children at average age of 64.5 months (range 25-138)

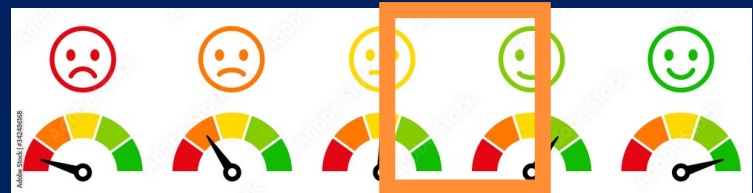
**15/35 cases (43%) resulted free from
CMV-related symptoms**

**20/35 (57%) cases presented
mild/moderate long-term disabilities***

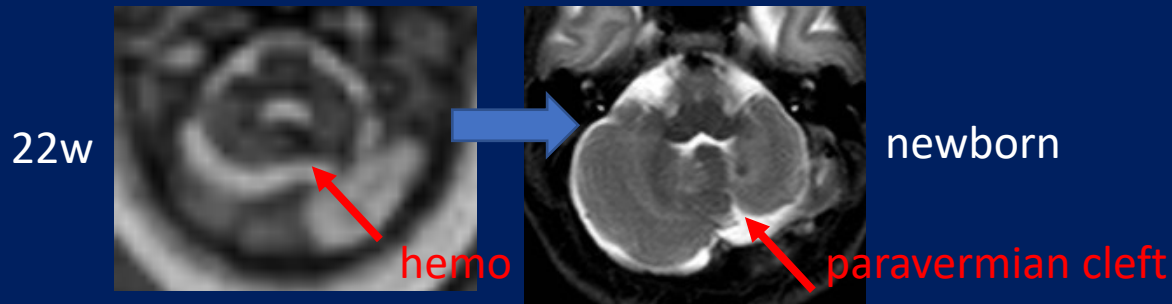
**(the possible effect of neurogenic deafness has to be considered)*

4

confidence level



Isolated cerebellar haemorrhage



- Dev Med Child Neurol 2010 **Outcome of severe unilateral cerebellar hypoplasia**

Andrea Poretti et Al.

- Eur Radiol 2016. **Prenatal MR imaging features of isolated cerebellar haemorrhagic lesions.** Francesca Martino et Al.

- Cerebellum 2021.. **Prenatal Diagnosis and Neurodevelopmental Outcome in Isolated Cerebellar Hypoplasia of Suspected Hemorrhagic Etiology: a Retrospective Cohort Study**

Barbara Scelsa et Al.

10 children > 4 yrs

6 normal neurodevelopment and cognition,

3 mild-moderate neurological signs, i.e., mild dyspraxia and visuoperceptual impairment.

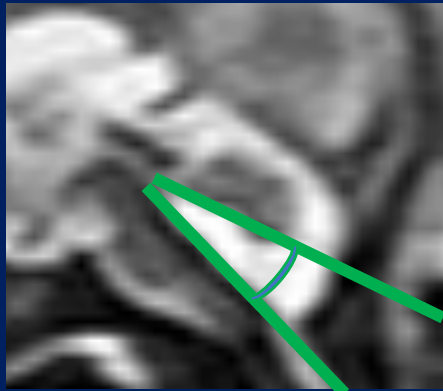
1 severe outcome, i.e., autism spectrum disorder.

5a

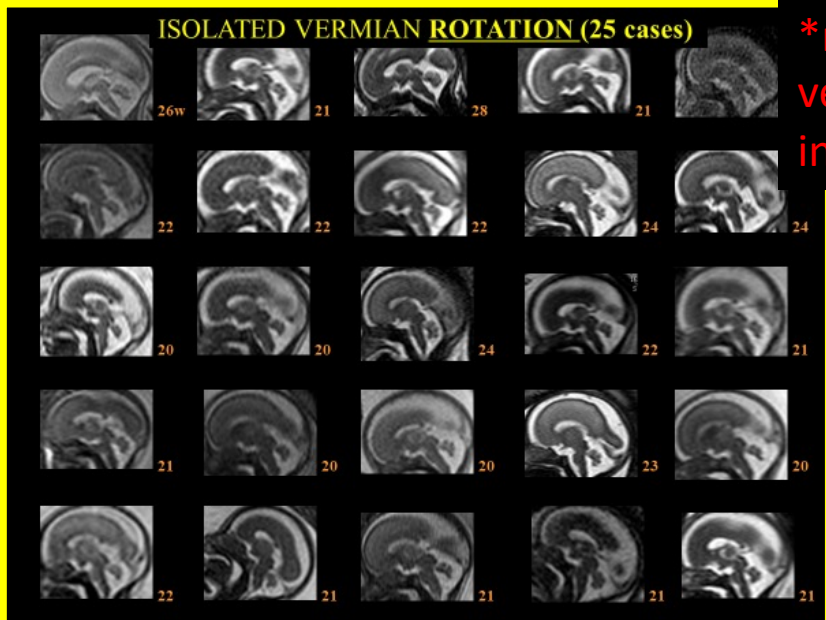
confidence level



Apparently isolated* «upwards vermian rotation»



<23° rotation
tends to normalize
with gestation



*mild
ventriculomegaly
included

Eur Radiol 2020. Prenatal magnetic resonance imaging within the 26th week of gestation may predict the fate of isolated upward rotation of the cerebellar vermis: insights from a multicentre study
Giorgio Conte et AL.

Fetal Diagn Ther 2021. Isolated Upward Rotation of the Fetal Cerebellar Vermis (Blake's Pouch Cyst) Is a Normal Variant: An Analysis of 111 Cases
Ginevra Salsi et AL.

Main drawback: unknown-unclear specificity.
Case segregation limit.

5b

confidence level

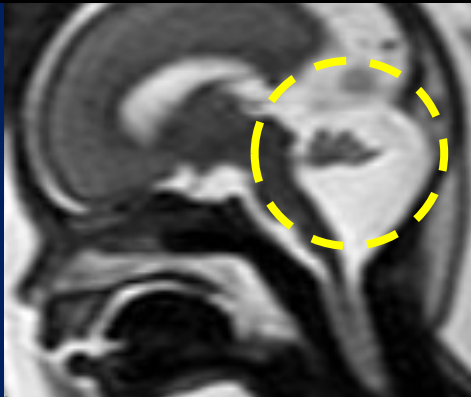


Apparently isolated «upwards vermian rotation»

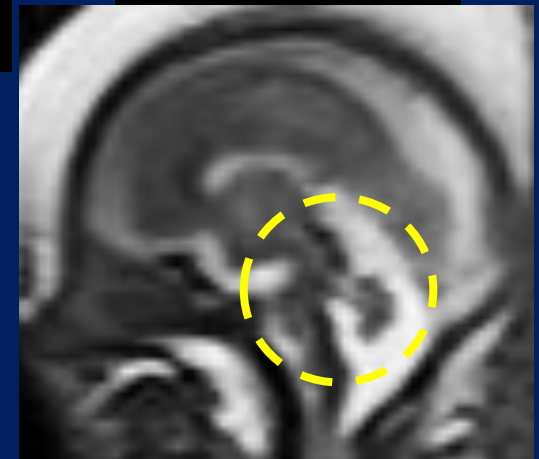
NOT WELL DEFINED CONDITION!; HETEROGENEOUS ENTITY!
therefore big confusion to prognosticate!

«caudal vermis hypoplasia»?

DW malformation or «variant» ?



Persistent Blake's Pouch cyst ?



5c

specificity needed!!

Apparently isolated «upwards vermian rotation»

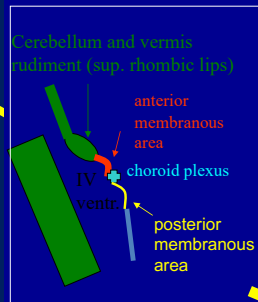
NOT WELL DEFINED CONDITION!; HETEROGENEOUS ENTITY

anterior membranaceous area pathophysiology «*hate using DW definition!*»

posterior membranaceous area pathophys. –BLAKE CYST

Post. fossa membranes pathophysiology

after A. Rossi and P. Tortori Donati (1996), A. J. Robinson (2014)

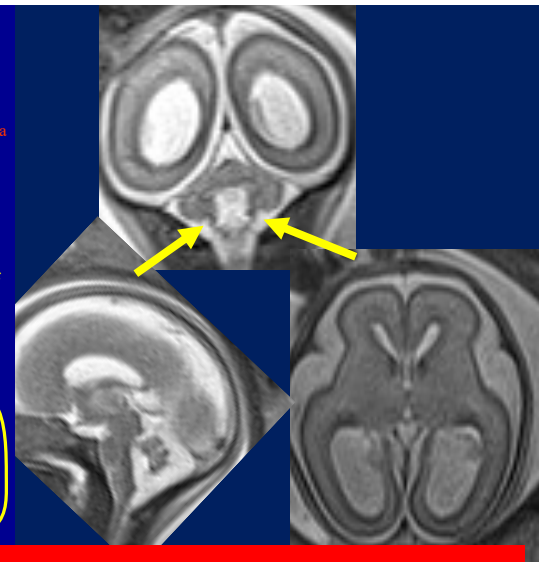


DANDY WALKER
PERSISTING anterior membranous area

DELAYED PERFORATION OF POSTERIOR MEMBRANOUS AREA (Blake's metapore)

foramen of Magendie

- 1) MEGA CISTERNA MAGNA
- 2) PERSISTENT BLAKE'S POUCH (unperforated IV ventr. outlet foramina)



choroid tela lateral and caudal position

choroid tela mesial and cranial position

5d

confidence level

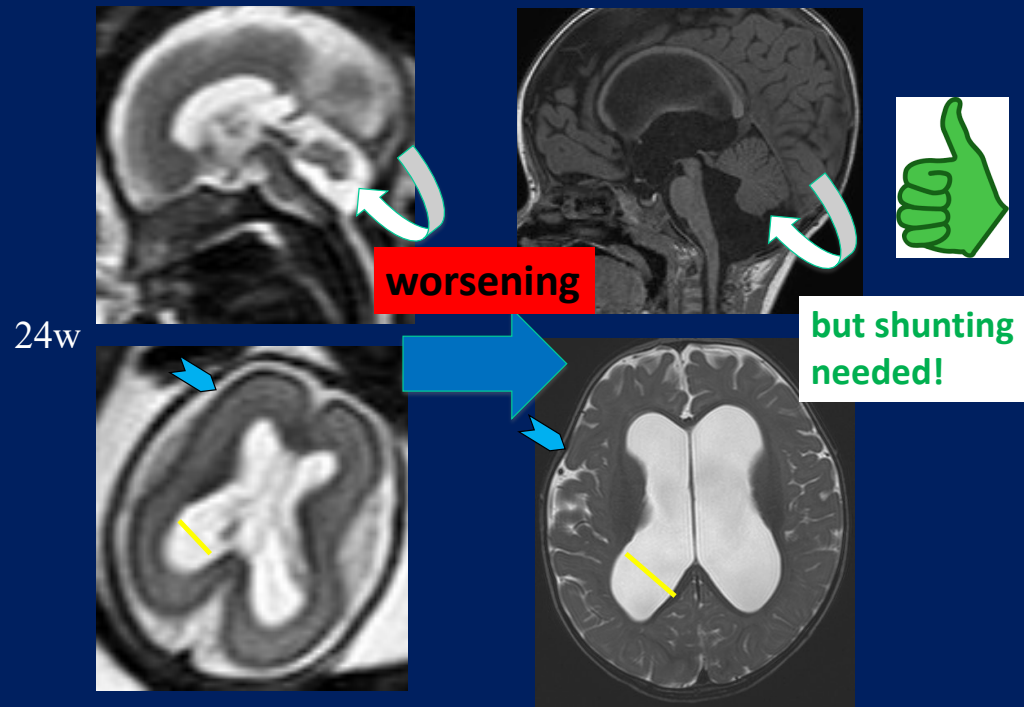
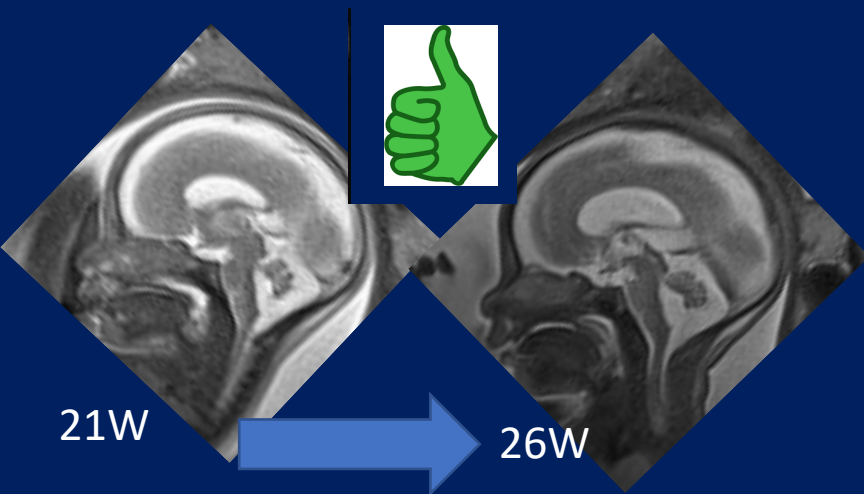


Apparently isolated «upwards vermian rotation»

IF BLAKE'S CYST CONFIRMED: PROGNOSIS GOOD (unless part of syndrome)

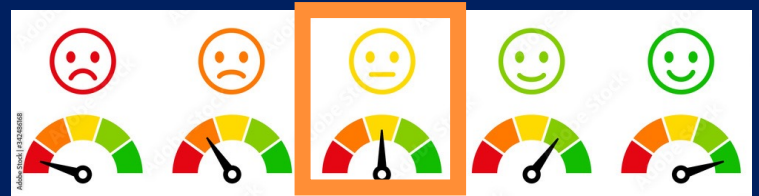


posterior membranaceous area pathophysiology –BLAKE CYST



5e

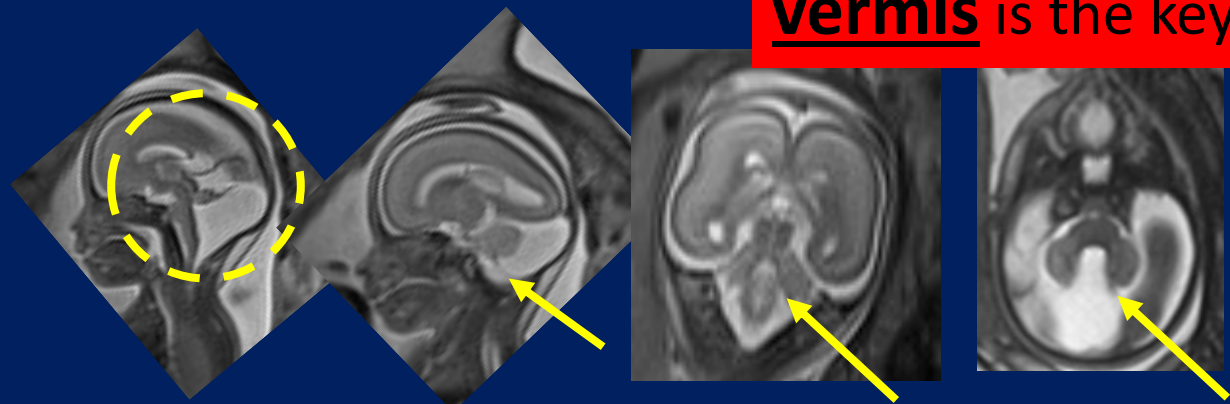
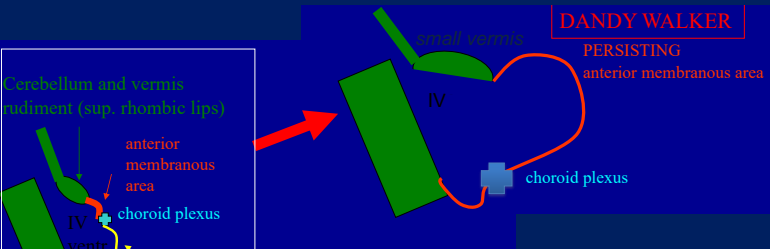
confidence level



Apparently isolated «upwards vermian rotation»

anterior membranaceous
area pathophysiology «*hate using DW definition!*»

School age outcome unclear from literature.
 Probably the amount and size of vermis is the key factor.

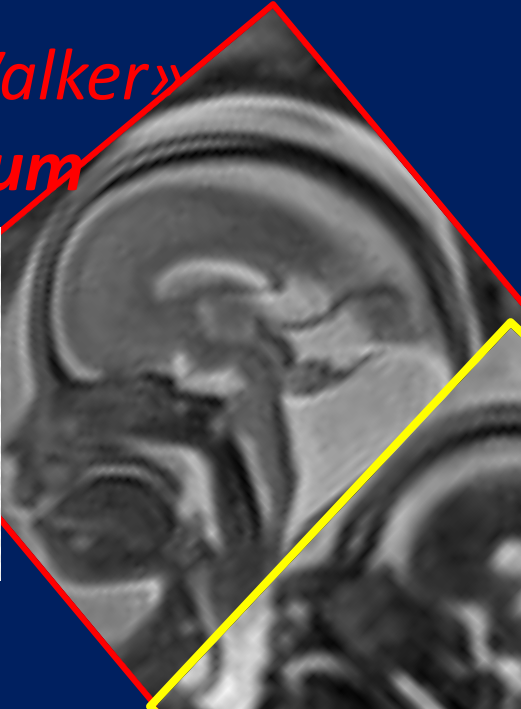


tela choroid. displaced inf. lateral

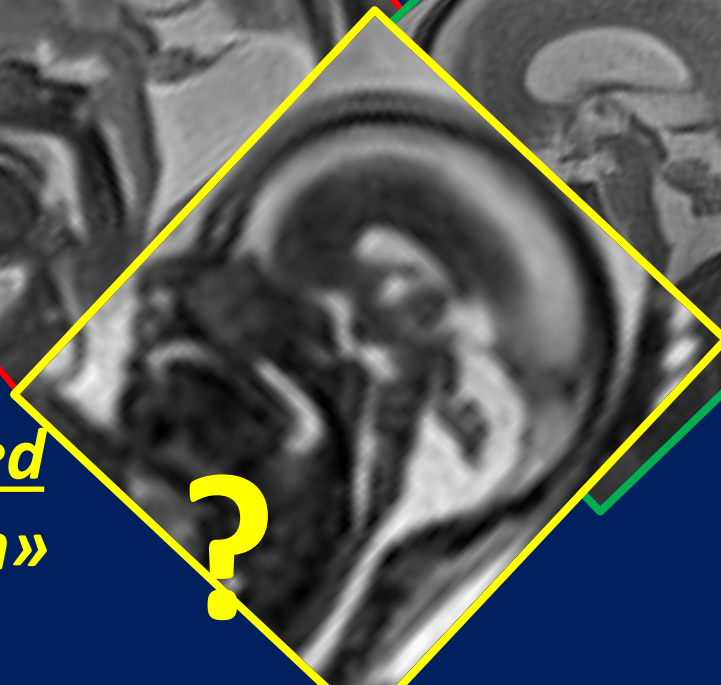
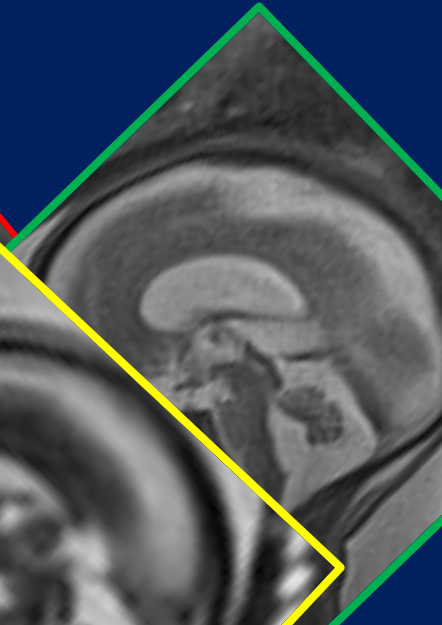
90% of our daily post. fossa «business»
deals with these three entities

5f

«Dandy-Walker»
full spectrum



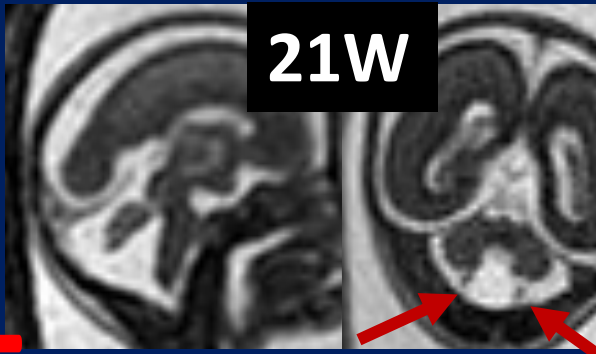
unperforated
late-perforated
Blake's pouch



apparently isolated
«vermian rotation»

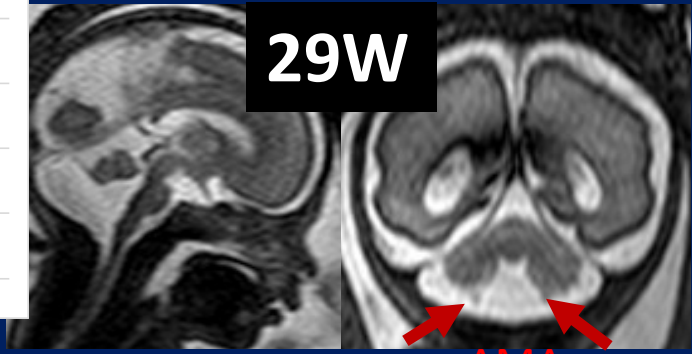
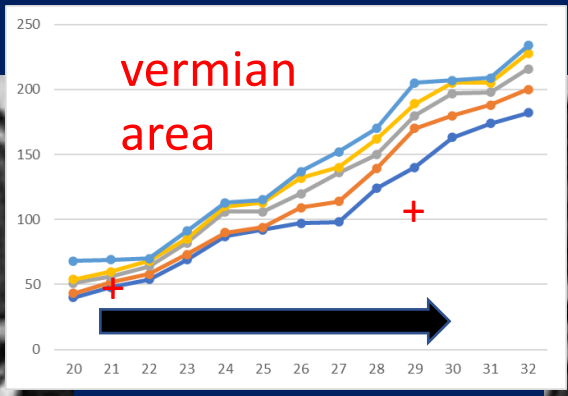
AT MRI they may overlap especially <22W

5g



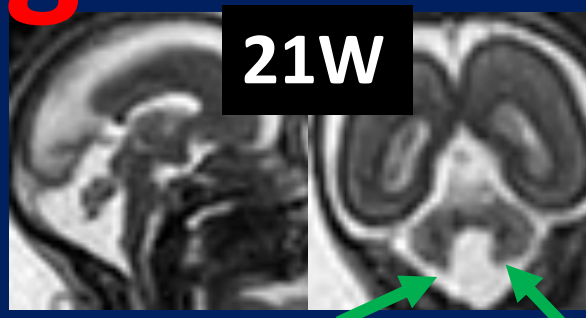
21W

AMA



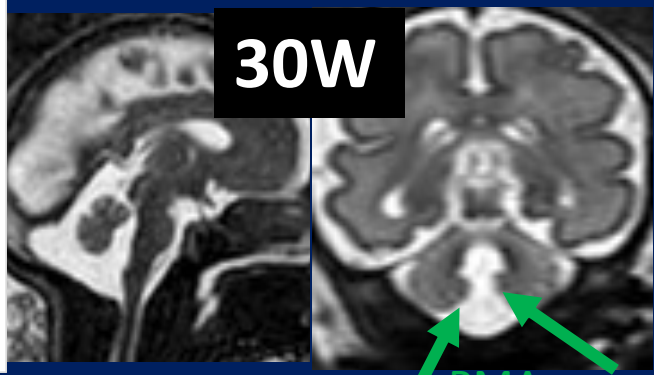
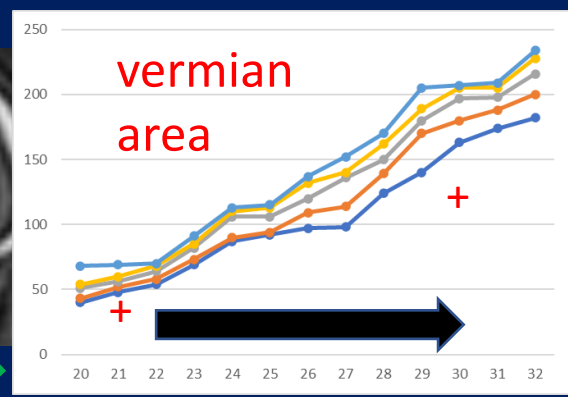
29W

AMA



21W

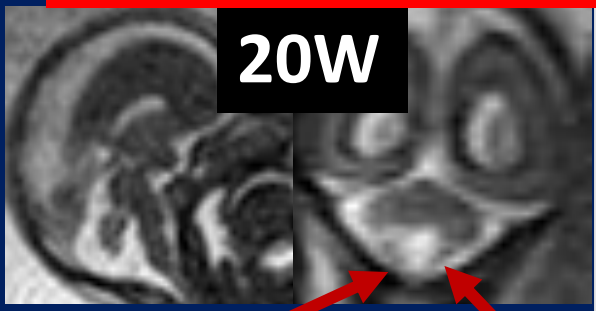
PMA



30W

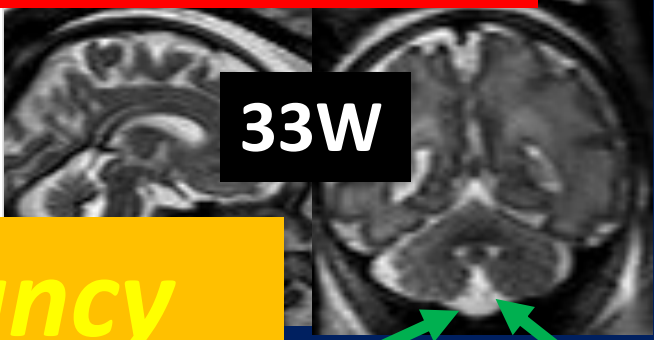
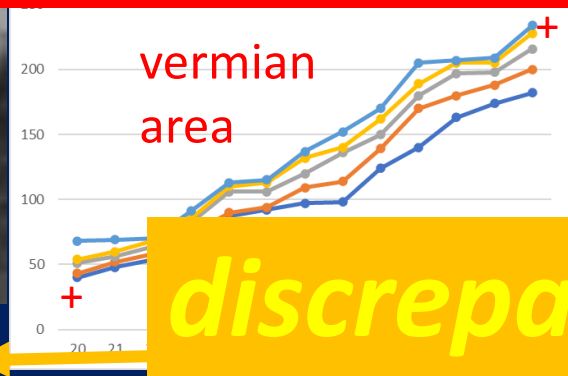
PMA

33% disagreement between 3 raters!!



20W

AMA



33W

PMA

CRITERIA

IV-ventricle choroid plexus and tela choroidea displacement

Ultrasound achievement

Paladini D et Al. **Differentiating features** of posterior fossa at 12–13 weeks' gestation in fetuses with Dandy–Walker malformation and Blake's pouch cyst. *Ultrasound Obstet Gynecol* 2019

Volpe P et. Al. **Position of the choroid plexus** of the fourth ventricle in first- and second-trimester fetuses: a novel approach to early diagnosis of cystic posterior fossa anomalies. *Ultrasound Obstet Gynecol* 2021

Paladini D. **The hidden story of the fourth ventricular choroid plexus: the flower basket of an old anatomist...**
Ultrasound Obstet Gynecol 2021

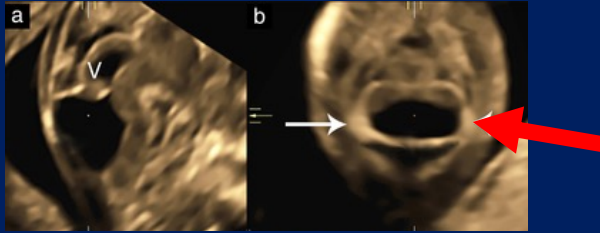


AMA

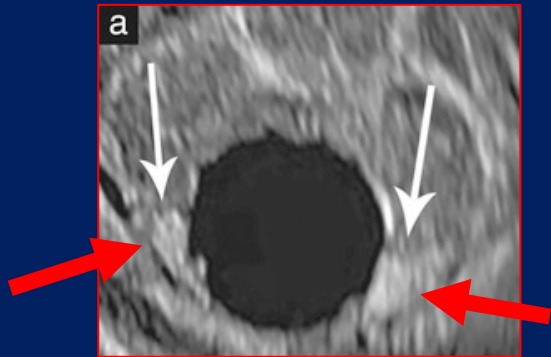
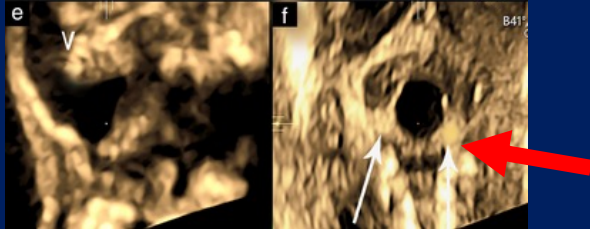
Ultrasound and choroid. plexus-tela

DWM

12w



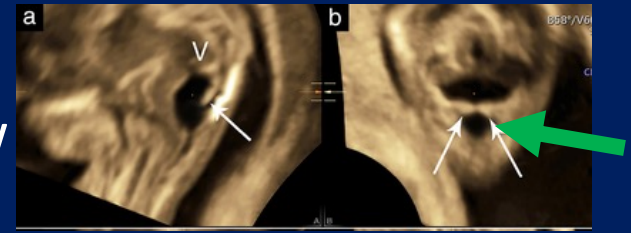
20w



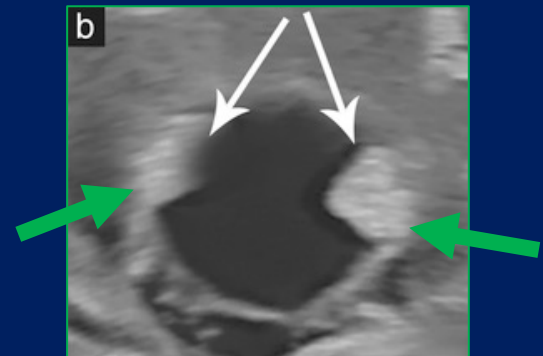
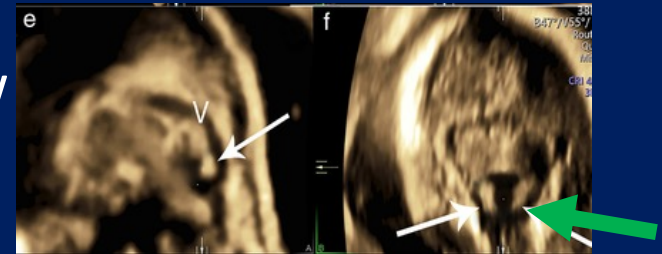
PMA

Blake's cyst

12w



20w



Upward rotated and isolated vermis at MR imaging: spectrum of entities* and long term prognosis?

5h

MRI weakness



- No other MRI anomalies
- Body OK at US
- Karyotype OK
- TORCH OK

*Neuro-ultrasonographers are better in accurately defining this entity (*anterior or posterior membraneous area anomaly?*)

OPEN ISSUE

Entity accurate definition
by MR imaging?



Long term (school-age)
prognosis?

Current literature drawbacks

Unclear inclusion criteria, overlapping entities , «not clean» cohorts, not isolated entities

Prognosis assessment too short : unclear behavioural and intellectual skills

- Childs Nerv Syst 2003 O Klein

Few cases.

10yrs old

- Prenat Diagn 2000 J L Ecker.

Few cases. and heterogeneous

- Ultrasound Obstet Gynecol 2021 P Volpe.

Large cohort

No prognostic data

- Arch Dis Child Fetal Neonatal 2014 T Tarui.

Isolated.

6 yrs age

School-age prognosis?

«unsolved issue»

Fetal MRI predictors?

«unsolved issue»

Large fetal cohort of Isolated vermian-rotation at prenatal-MRI and school-age prognosis.

H. Buzzi and Mondino Institute collaborative study

«The ultimate study....?»

Preliminary data

Results: research adherence

- The phone interview was conducted with **44** mothers
- **12** patients participated to onsite visit
- **5** patients performed an online neuropsychological evaluation
- **23** patients underwent postnatal brain MRI
- **6** patients underwent brain US at 1-3 months of life

5

Results

Age at time of interview	Mean	Minimum	Maximum	SD
44 cases at mean age 9.5yrs				
	9.6 y	2 y	22 y	4.08

N of patients	Clinical phenotype
3	ID/ syndromic conditions (<i>Charge syndrome; deletion syndrome</i>)
3	Motor coordination problems
6	Minor neuropsychological and learning difficulties
32 (72%)	Normal (no clinical / neuropsychological issues)

Results:

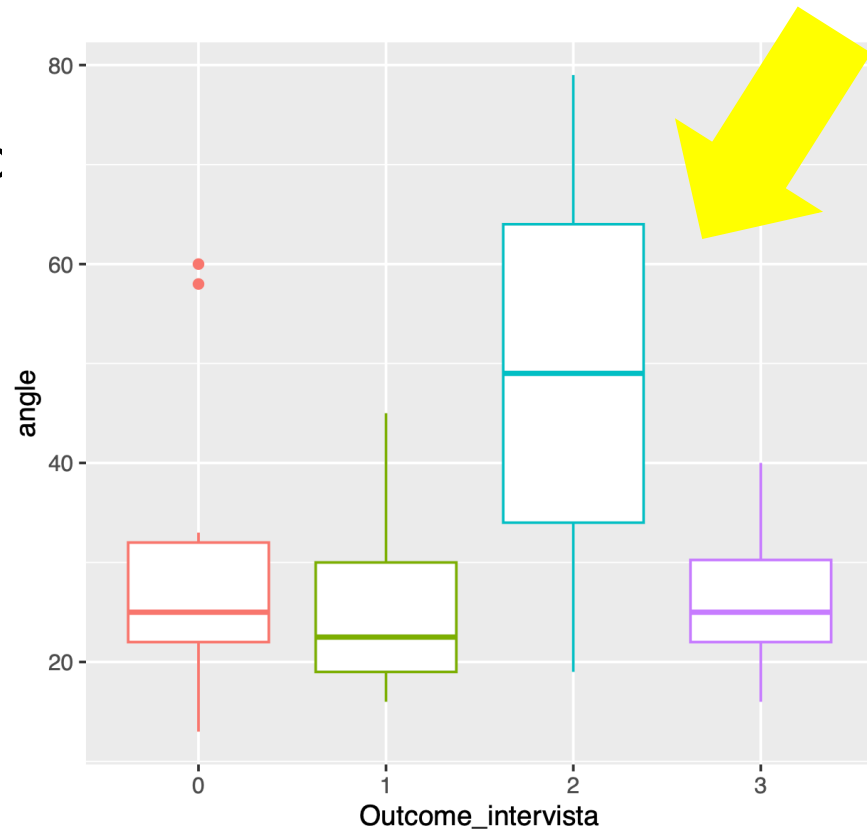
Child neuropsychiatry take-over	28%
Ongoing or previously performed rehabilitation	20%
Normal motor development	88%
Normal language development	74%
School problems	20%
Behavioral problems	28%
Previous abortion	37%

Any predictor?

Vermian area (percentile)?

Vermian AP diameter?

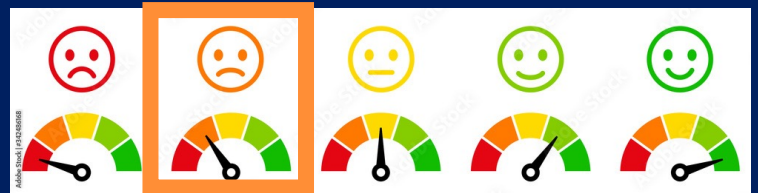
Angle rotation



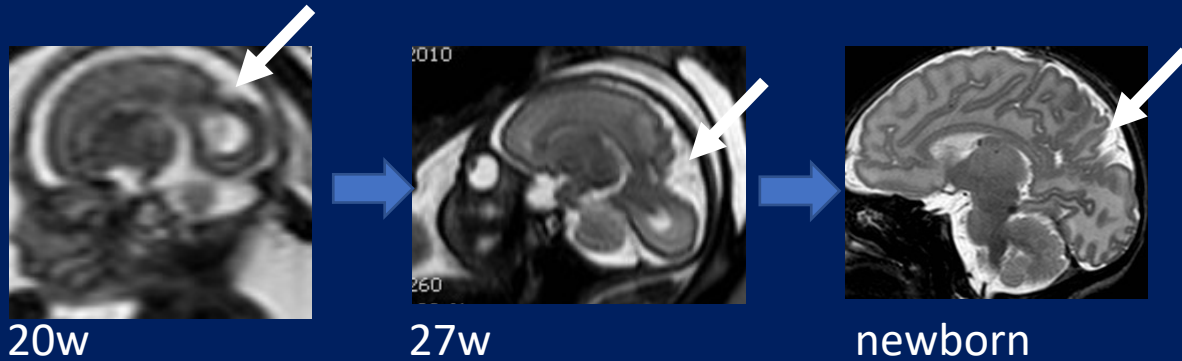
A greater vermian angle rotation was more likely associated with a negative outcome

6a

confidence level



Apparently «isolated» focal cortical malformations

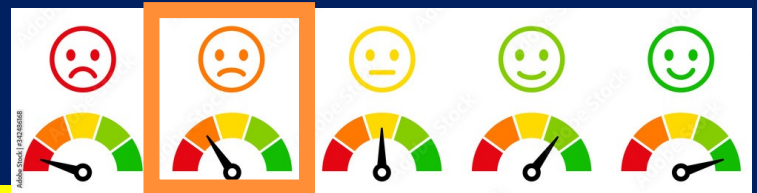


????????????????????????????????????

good common sense « look..in the worst scenary the baby will be affected by intractable seizures..but no motor deficit or severe intellectual disability ...»

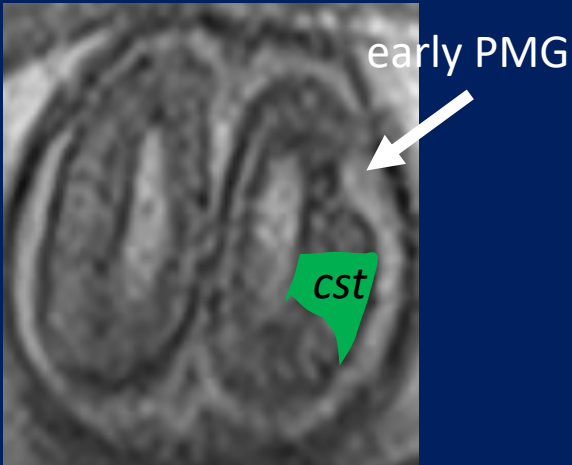
6b

confidence level

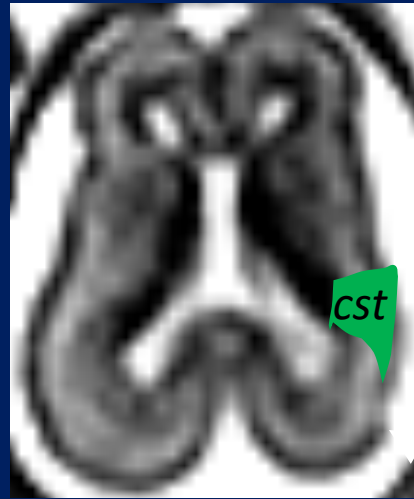


Apparently «isolated» focal cortical malformations

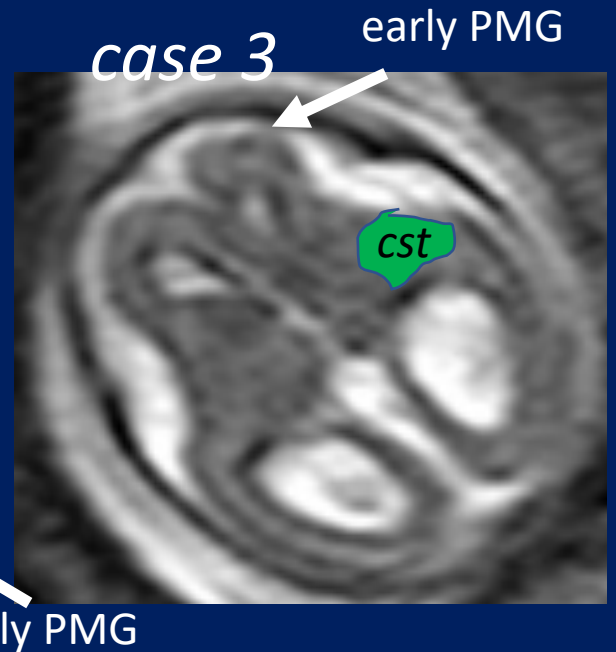
case 1



case 2



case 3

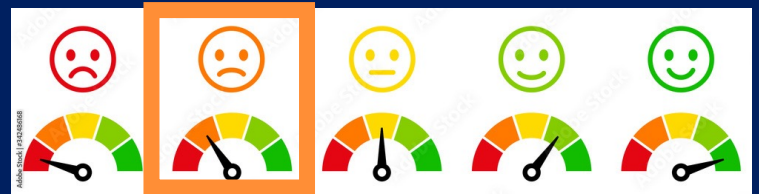


cortical-spinal tract likely to be spared

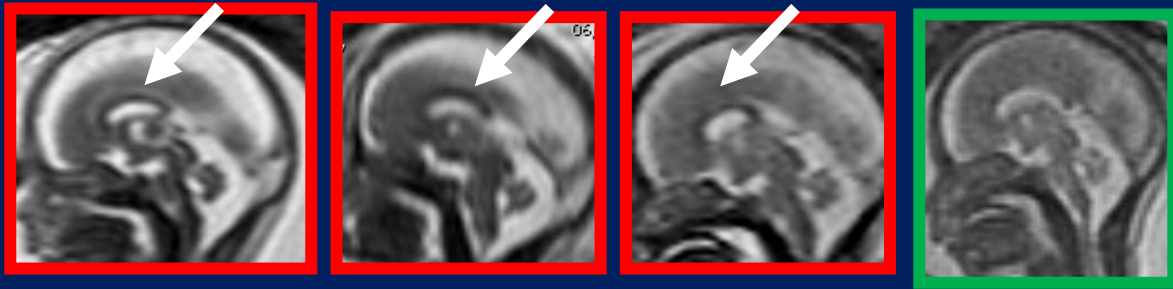
*No statistics but good common sense:
emiparesis unlikely*

7

confidence level

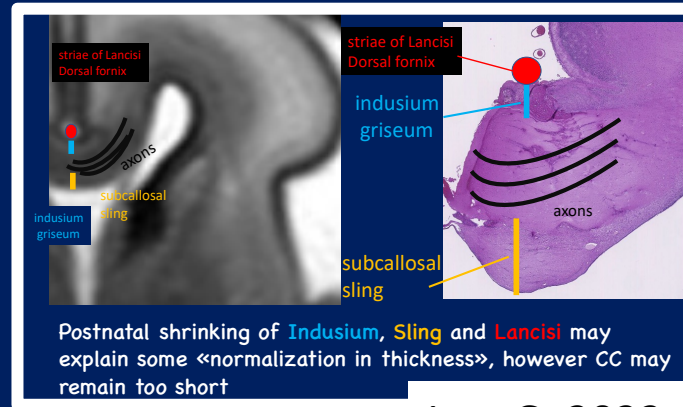


Apparently «isolated» short-thick corp. callos.



Three different exemplificative cases

normal control



Postnatal shrinking of Indusium, Sling and Lancisi may explain some «normalization in thickness», however CC may remain too short

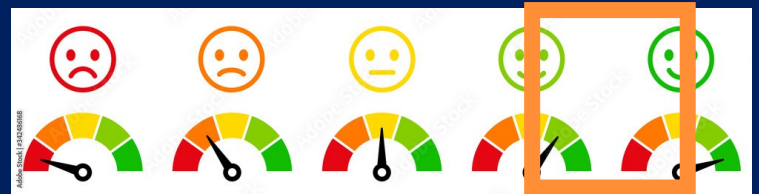
Izzo G. 2022

??

good common sense « look..in the worst scenary the baby will be affected by some degree of intellectual disability but not by major motor deficit».

8

confidence level



ISOLATED BORDERLINE ventriculomegaly

(10-12mm atrial width)

**If truly isolated and with normal karyotyping
normal neurological outcome normal in 90% or more
of cases.**

Thanks!