

MPDZ pathogenic variants cause obstructive ventriculomegaly related to diencephalosynapsis and third ventricle atresia

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Objective

- To define the **anatomical mechanism of ventriculomegaly associated with biallelic *MPDZ* variants** using prenatal imaging, postnatal MRI and fetopathological correlation

Methods

- Retrospective multicenter study : 3 families, 6 affected individuals (**4 fetuses, 2 children**)
- Exome or genome sequencing confirmation of *MPDZ* variants

Results

Key Prenatal Imaging Findings

- ✓ Lateral **ventriculomegaly** with an obstructive pattern
- ✓ Partially **fused thalami** (diencephalosynapsis)
- ✓ Atretic third ventricle
- ✓ Frequently non-visible aqueduct

Fetopathology data

- ✓ Thirid ventricle atresia
- ✓ Fused thalami
- ✓ Aqueductal involvement

Postnatal outcome

- ✓ Marked **intra-familial variability**
- ✓ Outcomes ranged from **normal neurodevelopment** with spontaneous stabilization of ventriculomegaly to **mild neurodevelopmental delay** and severe ventriculomegaly requiring neurosurgical care
- ✓ Reported **ophthalmological** involvement : macular dystrophy, retinal dysplasia, chorioretinal coloboma

Conclusion

- *MPDZ*-related is responsible for an obstructive ventriculomegaly.
- Symmetrical bilateral ventriculomegaly with a non-dilated third ventricle should prompt clinicians to look for fused thalami and subsequently to identify *MPDZ* variants on exome sequencing.

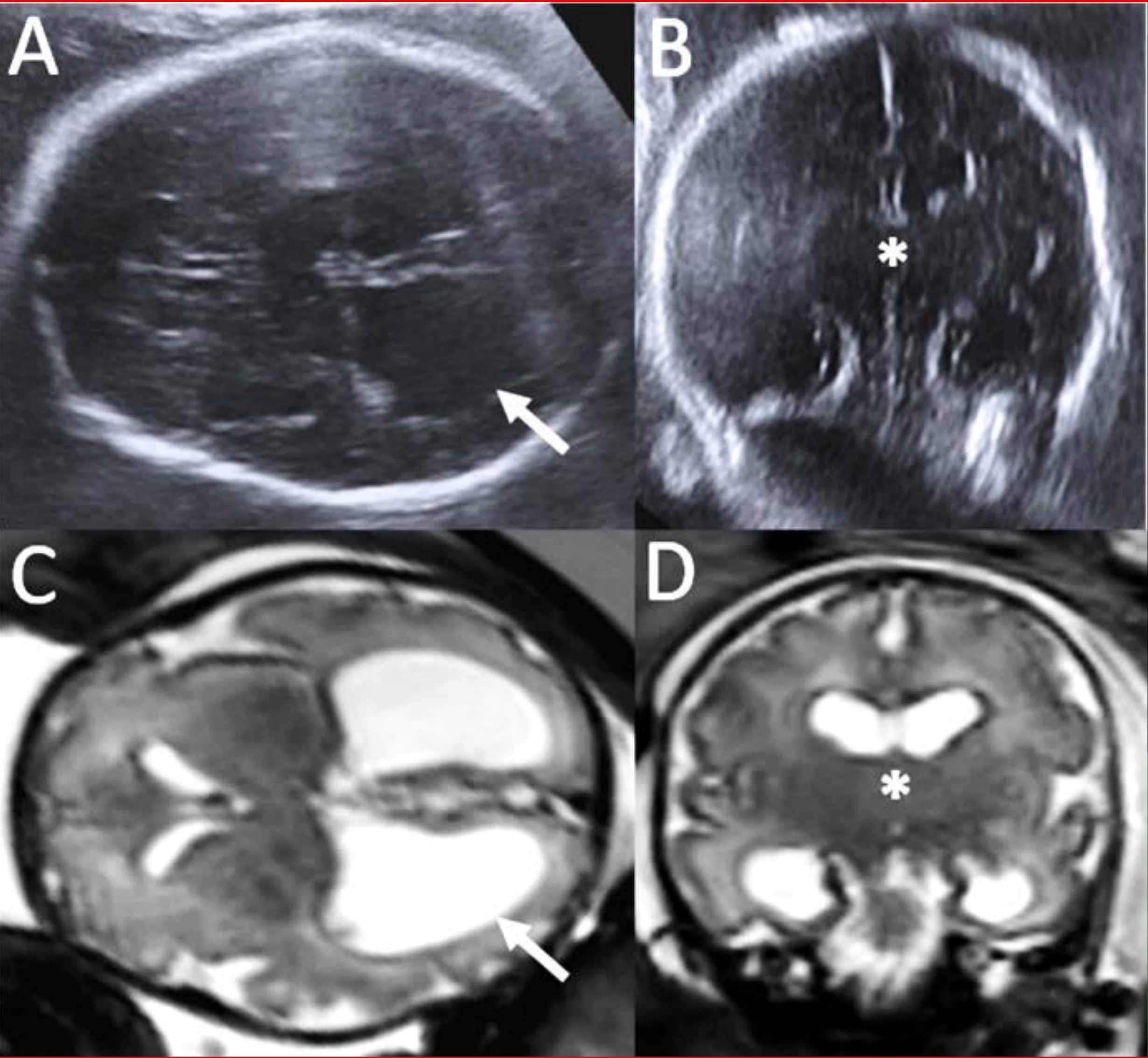


Figure 1. Fetal brain US (A,B) and MR (C) axial,(D) coronal T2 weighted images images at 33 WG showed dilation of the lateral ventricles (arrows) without dilated third and fourth ventricles, with an aspect of fused thalami on the midline (*)

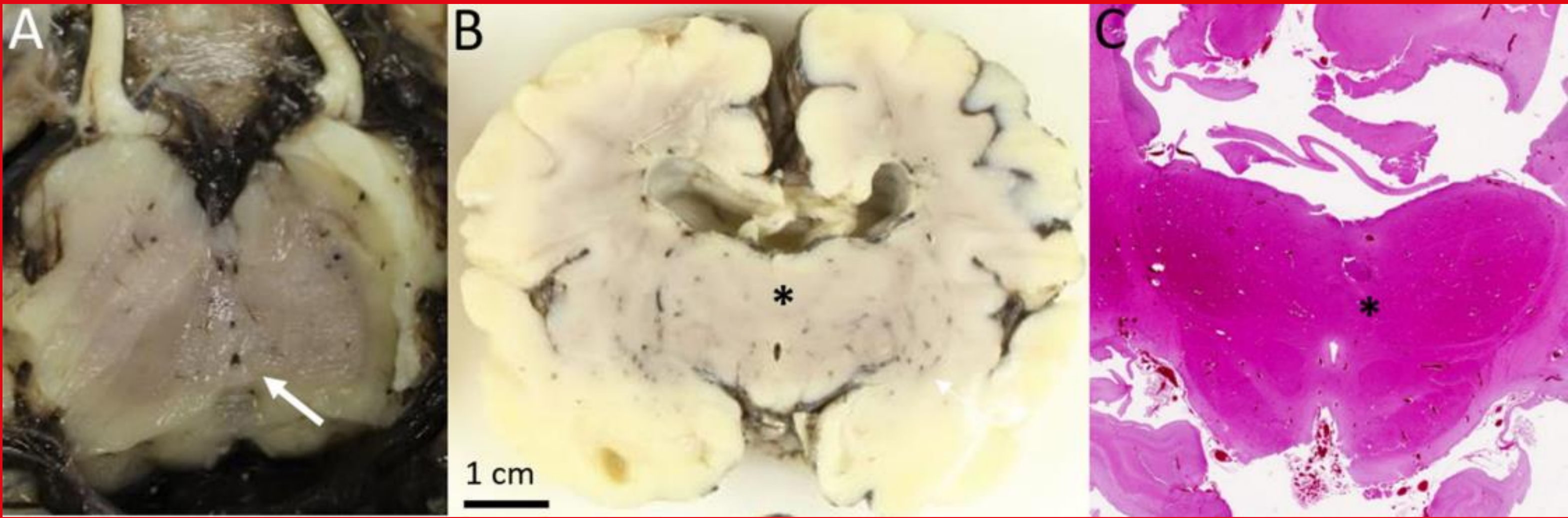


Figure 2. Fetopathology examination at the macroscopic (A,B) and microscopic (C) scales at 34 WG : atresia of the third ventricle with fusion of the thalami (*) and superior atresia of the aqueduct of Sylvius (arrow)

Want to learn more ?
See Cabet S et al. MPDZ Pathogenic Variants Cause Obstructive Ventriculomegaly Related to Diencephalosynapsis and Third Ventricle Atresia. Genes (Basel). 2025;16(6):707. doi: 10.3390/genes16060707. PMID: 40565599; PMCID: PMC12192413.