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Original Article

High-Resolution Diffusion Tensor Imaging and Tractography in Joubert Syndrome: Beyond Molar Tooth Sign

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ABSTRACT

BACKGROUND: We undertook diffusion tensor imaging analysis of brainstem fiber tracts in two Joubert syndrome patients. **METHODS:** Two Joubert syndrome patients underwent magnetic resonance imaging brain examination with diffusion tensor imaging. Imaging findings were compared with five age- and sex-matched control subjects with approval from the institutional ethic committee. The medical history and clinical examination findings in both patients were documented. **RESULTS:** Diffusion tensor imaging analysis of the first patient demonstrated absence of the dorsal pontocerebellar tract and thinning of the middle cerebral peduncle. Diffusion tensor imaging analysis of the second child revealed thinning of the both the dorsal pontocerebellar and ventral pontocerebellar tract. Both patients exhibited thickened and horizontally oriented superior cerebellar peduncles. The superior cerebellar peduncles also failed to decussate in the mesencephalon. **CONCLUSION:** Pontocerebellar tract abnormalities in Joubert syndrome patients have not been previously recognized. The difference in the pontocerebellar tract between the two Joubert syndrome patients suggests a spectrum of severity of pontine axonal migration abnormality.

Keywords: joubert syndrome, magnetic resonance imaging, diffusion tensor imaging

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Introduction

Joubert syndrome is a rare disorder with an incidence of 1/80,000 to 1/100,000 live births.[1,2] It is characterized by complex malformation of the midbrain-hindbrain, with the so-called molar tooth sign on axial imaging.[3] This results from vermian hypoplasia, a deep interpeduncular fossa, and thickened, elongated, and abnormally horizontal superior cerebellar peduncles.[3] Joubert syndrome is clinically characterized by hypotonia evolving into ataxia and developmental delay[4] and is associated with the variable involvement of other organs and systems, mainly the eyes and kidneys.[5] Genetic heterogeneity mirrors the clinical heterogeneity of Joubert syndrome.[5] Radiologic-genotype correlation in Joubert syndrome is difficult because of the low estimated prevalence.[6] The morphological appearance in Joubert syndrome patients shows great variability, even among Joubert syndrome siblings. The largest imaging review of 75 Joubert syndrome patients found intrafamilial variability in imaging appearance on conventional magnetic resonance imaging (MRI) sequences and no distinct neuroimaging features between the genotypes.[6]

Diffusion tensor imaging (DTI) technique has given an insight into the underlying complex fiber tract abnormalities in Joubert syndrome. The concept of axonal migration and failure of decussation of fiber tracts in Joubert syndrome may be influenced by specific gene mutation, and it is plausible to speculate a possible correlation. The aim of the study was to evaluate the course of white matter tracts by performing DTI in two Joubert syndrome patients in comparison to age-matched controls.

Patient and Materials

Two children with Joubert syndrome after parental consent were recruited into the study—a 4-month-old boy (patient A) and a 10-year-old

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TABLE.
Distribution of Patients with Joubert Syndrome

Patients	Age/sex	Clinical Presentation	Medical History	Renal or Ocular Findings
A	4-month-old boy (MRI with DTI acquisition)	Oculomotor dyspraxia, ataxia and gross motor developmental delay.	Parental consanguinity. The child was born at term by Cesarean section without complication. The parents recall nystagmus being present in the first days of life.	Normal funduscopic examination. Normal abdominal ultrasound with no hepatic or renal abnormalities.
B	10-year-boy (MRI with DTI acquisition)	Hypotonia, motor delay, ataxia, conjugate oculomotor apraxia	Normal term pregnancy and with no neonatal complications. Retrospectively, the parents noted pauses and in coordination with his breathing during the first month.	Bilateral optic nerve hypoplasia and electroretinogram evidence of retinitis pigmentosa. Normal abdominal ultrasound with no hepatic or renal abnormalities.

Abbreviations:
DTI = Diffusion tensor imaging
MRI = Magnetic resonance imaging

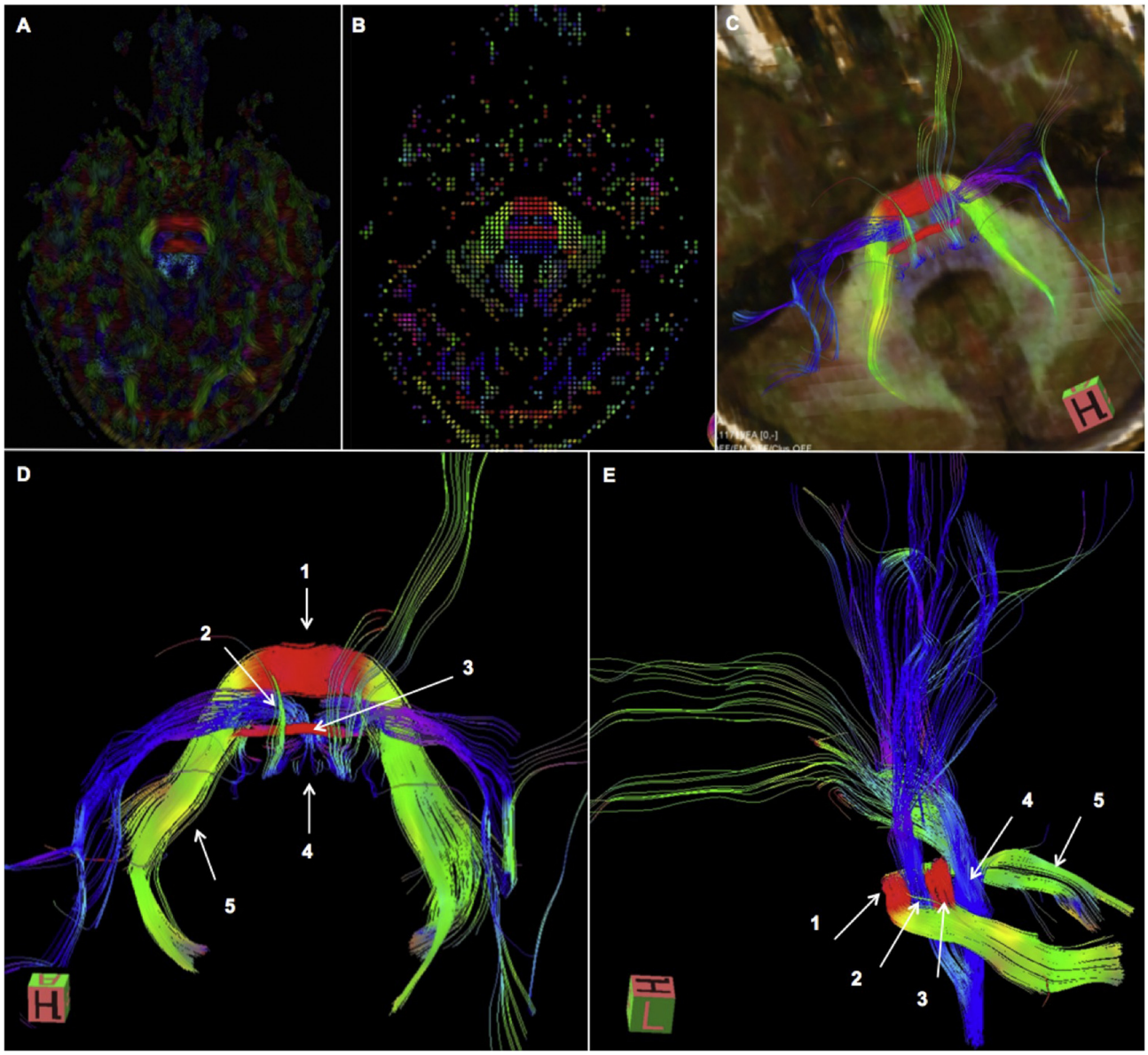

FIGURE 1.
In a healthy subject, axial color-coded fractional anisotropy map (A), tensor map (B) tractography superimposed on the anatomical dataset (C), and three-dimensional tractography projection views (D, E) at the level of mid pons demonstrate normal laminar appearance of the major fiber tracts. 1 = ventral ponto-cerebellar tract (red); 2 = corticospinal tracts (blue); 3 = dorsal pontocerebellar (red); 4 = pontine tegmental tract (blue); 5 = middle cerebral peduncle (green).