

Magnetic resonance imaging findings in children with spasms nutans

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Abstract

Background

Spasmus nutans (SN) is a rare pediatric ophthalmologic syndrome characterized by nystagmus, head bobbing, and abnormal head positioning. Historically, SN has been associated with underlying optic pathway gliomas (OPG); however, evidence of this association is based primarily on a small number of isolated case reports. Prior retrospective analyses have found the rate of OPG to be <2%, but these studies only intermittently used neuroimaging with computed tomography, which has limited sensitivity for detection of small lesions in the optic pathway. The purpose of this study was to investigate the association of SN with intracranial abnormalities, particularly OPG, using magnetic resonance imaging of the brain and orbits.

Methods

Neuroradiology databases at three institutions spanning January 2010 to May 2016 were queried for examinations ordered for evaluation of SN; MRI examinations of the brain and/or orbits were included and evaluated for OPG and other structural abnormalities. Medical records were reviewed to confirm a diagnosis of SN, presence of other underlying neurological disease, or preexisting diagnoses.

Results

A total of 40 patients with eligible MRI examinations were identified. None had optic nerve pathway gliomas. Two children had optic nerve hypoplasia; no other patients had optic pathway abnormalities. None had intracranial or orbital masses. MRI examinations were normal in 25 patients.

Conclusions

This series represents the largest collection of MRI examinations for SN in the literature to date

and shows no association between OPG and SN. In children presenting with SN but no other findings concerning for OPG or neurological abnormalities, neuroimaging may not be required.

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Spasmus nutans (SN) is a rare pediatric ophthalmologic syndrome that was first described in the English-language literature in 1901 is defined by the triad of nystagmus, head-nodding or titubation, and anomalous head position, such as torticollis, with onset in the first year of life.¹ The nystagmus is typically intermittent, of small amplitude and high frequency, variably disconjugate or disjunctive, greater in the abducting eye, and may have a vertical component. Head nodding is irregular and may have horizontal and vertical components. Strabismus and amblyopia may coexist, and SN may also be associated with or a mimicker of underlying retinal pathology.^{2,3} Historically, however, SN has been associated with underlying optic pathway gliomas, prompting contrast-enhanced neuroimaging to become a common component of its diagnostic work up.⁴⁻⁷ However, the evidence of this association is based primarily on a small number of isolated case reports dating back to the 1970s.^{6,8-12}

Several prior retrospective studies of children with SN-like nystagmus have found no increased incidence of optic pathway gliomas, with rates ranging from <2% to 9%.¹³⁻¹⁵ However, most of these studies suffered from small series sizes and used only lower-resolution computed tomography (CT). We performed a systematic analysis of a cohort of 40 children diagnosed with SN and subsequently undergoing magnetic resonance imaging (MRI) with the goal of evaluating the prevalence of intracranial abnormalities, particularly optic pathway gliomas.

Subjects and Methods

This study was approved by the local institutional review boards of Emory University, Indiana University, and Johns Hopkins University. Neuroradiology databases of Children's Hospital of Atlanta, Riley Hospital for Children, and Johns Hopkins Children's Center spanning the period from January 2010 to May 2016 were queried for examinations ordered for evaluation of SN using searches for "spasmus nutans" as well as associated misspellings, including "spasms" and

“mutans.”

All patients with MRI ordered for SN were included. Clinical diagnosis of SN was made prior to imaging by pediatric ophthalmologists or neurologists. Electronic medical records, when available, were examined for concomitant underlying neurological disease; for known, preexisting systemic disorders, including genetic syndromes and chromosomal abnormalities; and for symptoms consistent with SN (nystagmus, head nodding, and anomalous head position). Additionally, available ophthalmology notes were examined for signs of underlying intraorbital or optic pathway abnormality, such as reduced visual acuity and strabismus. Age at symptom onset was also collected when available.

Brain and orbit MRI studies were performed according to institutional protocols using 1.5 or 3.0 T clinical MR scanners. At minimum, imaging protocols included standard brain MRI sequences such as sagittal T1-weighted spin echo (SE) or 3D T1 gradient echo (GRE), axial T2-weighted fast spin echo and T2 fluid-attenuated inversion recovery and, if contrast was administered, postcontrast coronal and axial T1 SE or sagittal 3D T1 GRE. The majority of patients had dedicated orbital MRI sequences such as thin-slice coronal T2 turbo-spin echo and fat-suppressed contrast-enhanced T1 SE. MRI examinations were considered eligible for inclusion when the optic apparatus could be properly assessed. All available MRI studies were evaluated for optic pathway gliomas and other structural brain abnormalities by a subspecialty certified neuroradiologist with 6 years of experience in pediatric neuroimaging (BPS).

Results

A total of 40 patients (21 males) with MRI of the brain and/or orbits ordered for evaluation of SN were included: 31 at Children’s Hospital of Atlanta, 4 at Riley Hospital for Children, and 5 at Johns Hopkins Children’s Center. The median age at time of imaging was 16.3 months

(interquartile range, 17.4 months).

Of 13 children with complete ophthalmology notes available, 5 had clinically isolated SN. Four children had decreased visual acuity, 4 had esotropia, 1 child had astigmatism, 1 had retinal dystrophy, and 1 had familial exudative vitreoretinopathy. No patient had relative afferent pupillary defect or optic disk pallor.

Of the 31 patients for whom medical records at the time of SN diagnosis were available, 16 had no previously known underlying disease or developmental delay at the time of imaging; 15 did have significant, systemic, nonocular diagnoses, including trisomy 21 (7), cerebral palsy (2), developmental delay of unknown etiology (5) and a 1p36 chromosomal deletion syndrome (1).

On imaging review, 25 patients (63%) had normal, age-appropriate MRI examinations. No patients had optic pathway gliomas. Two patients had bilateral optic nerve hypoplasia (Figure 1); no other patients had any optic pathway abnormalities. Intracranial abnormalities were found in 15 patients (Table 1).

Of the 16 known developmentally normal, otherwise healthy children, 11 had normal MRI examinations. The abnormal findings included mild ventriculomegaly, periventricular nodular heterotopia, large subarachnoid spaces, and a complex pineal cyst. There was no significant difference between the frequency of abnormal MRI examinations in otherwise healthy children compared to children with known delays ($P = 0.38$).

Discussion

Spasmus nutans can be confused with other entities. The nystagmus of SN is asymmetric—even monocular—pendular, low amplitude, and high frequency.^{14,16} Symptoms most commonly arise between 6 and 36 months of age and typically resolve within several years without harm to

visual acuity, although subclinical nystagmus can be noted as many as 7 years after diagnosis.¹⁷⁻
¹⁹ Antony and colleagues⁷ presented cases of children “misdiagnosed” with SN who were ultimately found to have intracranial tumors; one also had persistent, severe failure to thrive, another, low body weight–to–head circumference and optic disk pallor.⁷ Head nodding or head titubation may be seen in other diseases including rhombencephalosynapsis, Joubert syndrome, “bobble-head doll” syndrome, congenital nystagmus, shuddering attacks, and *STXBPI* encephalopathy.²⁰ Differentiation between head nodding or head titubation in SN and head movements in other disorders is usually possible based on the clinical characteristics of the head movements and additional neurological findings.

When optic pathway gliomas have been found with SN as an early symptom, it has usually been in the setting of other symptoms or signs considered red flags. Kiblinger and colleagues¹⁵ found 2 cases of optic gliomas in 20 imaged children; however, both of these children presented with SN at a later age than the average presentation, and neither child had the classic SN triad; both were noted to have optic disk pallor on their initial examination, and one had been previously diagnosed with neurofibromatosis.¹⁵ In addition, the spontaneous resolution of SN with age is well compatible with the lack of an underlying structural abnormality and might rather reflect either structural maturation of the brain or “full calibration” of eye movements, although spontaneous resolution of SN does not preclude the absence of an underlying lesion.¹¹

This study of 40 children with a diagnosis of SN evaluated with MR imaging shows that there is no apparent association between optic pathway gliomas and SN. The absence of underlying gliomas is consistent with prior series of SN that have included neuroimaging—almost exclusively CT—which reported a prevalence of optic pathway gliomas in zero of 14

patients¹⁴ and zero of 41 patients.¹³

Our data suggests that although some patients with SN may have underlying structural abnormalities found on imaging, the risk of optic gliomas in children without other neurological deficits or signs concerning for intracranial mass lesions is very low. Using the simplistic assumption that the next patient enrolled in our cohort would have an optic glioma—as was assumed in a prior study¹³—would result in an incidence of one in 41, or 2.4%. Similarly, by the binomial exact test, the association between SN and optic pathway gliomas is low, with a 95% confidence interval for nonassociation of 0.91-1.00; larger studies are warranted for further, more detailed statistical analysis.

This study has several limitations, including those inherent to its retrospective design. One institution contributed the majority of patients (31). Not all patients underwent dedicated orbital MRI, and there was some heterogeneity in sequences used. However, all MRI examinations were considered of sufficient quality to properly assess the brain and optic apparatus. Not all patients had detailed ophthalmology notes available for review; thus the misdiagnosis of SN rather than another eye-movement disorder cannot be entirely ruled out, especially in children with underlying systemic disorders associated with nystagmus, including as trisomy 21.²¹⁻²⁴ Lastly, the clinical diagnosis of SN may have been variable, given its low prevalence.

This series further confirms that neuroimaging—often requiring sedation given the young age of the patients in question—is not always necessary as part of initial diagnostic work-up in children diagnosed with or being evaluated for spasmus nutans. Based on our findings, we believe a period of watchful waiting prior to imaging is reasonable in children with clinical diagnosis of spasmus nutans but no additional concerning findings on physical examination or

history.

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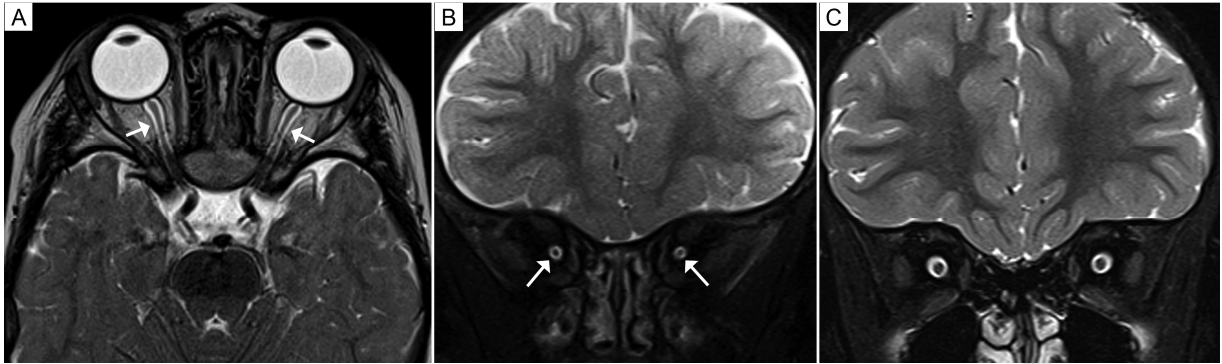
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Legends

FIG 1. Optic nerve hypoplasia, found in 2 patients, was the most common intracranial abnormality in our study cohort and the only optic pathway abnormality. Its association with spasmus nutans has not been established. Axial (A) and coronal (B) T2-weighted magnetic resonance images show symmetrically diminished caliber of the optic nerves (arrows) with normal signal intensity, consistent with hypoplasia. Coronal (C) T2-weighted image of a different patient shows, for comparison, normal-sized optic nerves.

Table 1. Intracranial abnormalities on magnetic resonance imaging ordered for children with suspected spasmus nutans

MRI findings	Medical history, if known
Agensis (partial) of posterior body and splenium of corpus callosum, malrotated hippocampi	Trisomy 21, premature
Brachycephaly, mild-to-moderate ventriculomegaly	Developmental delay
Bulging at lateral aspect of bilateral globes	Otherwise healthy; known history of familial exudative vitreoretinopathy
Complex pineal cyst without hydrocephalus	Otherwise healthy
Corpus callosum thinning	Global developmental delay, premature
Corpus callosum thinning, mild ventriculomegaly, diminished periventricular white matter	1p36 chromosomal deletion, resultant seizure disorder
Frontal lobe: large subarachnoid spaces	Otherwise healthy
Intraventricular hemorrhage/germinal matrix hemorrhage (mild, chronic)	Unknown
Optic nerve hypoplasia, bilateral	Global developmental delay
Periventricular leukomalacia (mild)	Unknown
Periventricular nodular heterotopia	Otherwise healthy
Ventricles, prominent, and bilateral optic nerve hypoplasia	Unknown
Ventriculomegaly (mild)	Otherwise healthy
Ventriculomegaly with paucity of white matter without gliosis	Developmental delay, premature



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