reasoning (p=0.016) and visual memory (p=0.014). Within the NS/FS group there was a lower neurodevelopmental level in children with history of infantile spasms (p=0.026).

**Conclusions:** Patients with nonsense or frameshift variants show a lower neurodevelopmental level; however, a history of infantile spasms modulates this genotype-phenotype relationship.

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**Neocerebellar abnormalities in a neonate with the FOXP2 mutation**

Georgios P.D. Argyropoulos, Rachael Elward, Maneet Saini, Mortimer Mishkin, Faraneh Vargha-Khadem

**Objective:** A dominantly inherited verbal and orofacial dyspraxia in half the members of the multi-generational ‘KE family’ is linked to a mutation in FOXP2, the first gene implicated in developmental processes culminating in articulate speech and language. Neural and genetic substrates of this disorder may inform the ontology and developmental trajectory of human speech. FOXP2 expression is known to occur strikingly early during embryonic development and is prominent in the human, rodent and avian olivo- and ponto-cerebellar circuits. Indeed, imaging studies from our laboratory on affected KE family members aged 9-77 years have previously reported structural and functional abnormalities in the cerebellum as well as other cortical and subcortical structures. However, up to now, it had not been possible to document the emergence of FOXP2-dependent abnormalities in the brain of affected neonates from this large pedigree.

**Methods:** We analysed structural T1- and T2-weighted magnetic resonance images acquired from a neonate with the FOXP2 mutation, his unaffected twin, and 12 healthy control neonates (6-16 weeks-old). We used voxel-based morphometry and volumetry to investigate grey- and white-matter abnormalities in the affected neonate.

**Results:** We report a marked reduction of neocerebellar lobule Vlla Crus I in the affected member as compared to his unaffected sibling and unrelated controls.

**Conclusions:** FOXP2 mutation is associated with cerebellar Crus I volume reduction from the early stages of neonatal life, consistent with the gene’s expression in the human embryonic cerebellum. These findings highlight the significance of cerebellar abnormalities in developmental orofacial dyspraxia in the pre-linguistic infant.

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**Genetic subtyping and its implications for clinical management: The case of 22q11.2 syndrome**

Jos Egger, Willem Verhoeven, Joep Tuerli, Ellen Weiβermühlle, Roy Kessel, Jos Egger

**Objective:** 22q11.2 deletion syndrome (22qDS), mostly caused by chromosomal microdeletions, affects 1 in 4,400 newborns. A variety of clinical problems have been associated with the deletion, such as heart defects, subtle cognitive dysfunctions, and psychiatric conditions. Recent work has established that these phenotypes are modulated by the genetic substrates of this disorder. Here, we report a marked reduction of neocerebellar lobule VIIa, Crus I in the affected member as compared to his unaffected sibling and unrelated controls.

**Methods:** We used voxel-based morphometry and volumetry to investigate grey- and white-matter abnormalities in the affected neonate.

**Results:** We report a marked reduction of neocerebellar lobule Vlla Crus I in the affected member as compared to his unaffected sibling and unrelated controls.

**Conclusions:** FOXP2 mutation is associated with cerebellar Crus I volume reduction from the early stages of neonatal life, consistent with the gene’s expression in the human embryonic cerebellum. These findings highlight the significance of cerebellar abnormalities in developmental orofacial dyspraxia in the pre-linguistic infant.

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**Quality of life in adults with Noonan syndrome**

Ellen Weiβermühlle, Floor Nobbe, Renée Roelofs, Ineke Van der Burgt, Roy Kessel, Jos Egger

**Objective:** Noonan syndrome (NS) is a genetic disorder related to mutations in the RAS-MAK pathway. Cardinal features include short stature, facial dysmorphism, congenital heart defects, subtle cognitive dysfunctions, and autism spectrum disorders. The *MAPK1* gene is associated with specific heart defects and the presence of anxiety disorders. The relatively rare *CRKL* gene, and the cartilaginous *DMP1* gene, are thought to contribute to the clinical spectrum. Here, we report a marked reduction of neocerebellar lobule VIIa Crus I in the affected member as compared to his unaffected sibling and unrelated controls.

**Methods:** We used voxel-based morphometry and volumetry to investigate grey- and white-matter abnormalities in the affected neonate.

**Results:** We report a marked reduction of neocerebellar lobule Vlla Crus I in the affected member as compared to his unaffected sibling and unrelated controls.

**Conclusions:** FOXP2 mutation is associated with cerebellar Crus I volume reduction from the early stages of neonatal life, consistent with the gene’s expression in the human embryonic cerebellum. These findings highlight the significance of cerebellar abnormalities in developmental orofacial dyspraxia in the pre-linguistic infant.

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**Intelligent development in Noonan syndrome: A longitudinal study**

Renée Roelofs, Nikki Janssen, Ellen Weiβermühlle, Roy Kessel, Jos Egger

**Objective:** While cognitive impairments in adults with Noonan syndrome (NS) seem to be limited to a low-average intelligence and slower processing speed, studies in children with NS have demonstrated more extensive cognitive problems (e.g. deficits in language, memory, attention, and executive functioning). This longitudinal study is the first to investigate intellectual development in patients with NS. Although childhood IQ is expected to be lower than adult IQ, it is assumed to be a significant predictor of adult intelligence.

**Participants and Methods:** Sixteen patients with NS underwent intelligence assessment in childhood and in adulthood, using Wechsler’s intelligence scales. IQ scores and Wechsler standard scores achieved in childhood and adulthood were compared. Childhood verbal and performance IQ (VIQ/PIQ) were included as predictors in multiple regression analyses for adult IQ and index scores.

**Results:** Compared with childhood scores, adult full-scale IQ (FSIQ) and PIQ significantly increased (FSIQ: *(t*)= 2.88, *p*= .01, *η*² = .36; PIQ: *(t*)= 5.49, *p* < .001, *η*² = .67). Adult PIQ was higher than VIQ (*(t*)= -2.23, *p* = .04, *η*² = .25). Childhood PIQ and VIQ together predicted all adult IQ and index scores (adjusted *R*² > .62, *p* < .01), except for processing speed.

**Conclusions:** In accordance with the hypothesis, childhood IQ significantly predicted adult intelligence in patients with NS. PIQ advanced to a normal level in adulthood, while VIQ did not develop proportionately, resulting in a discrepancy between adult PIQ and VIQ. This may suggest a delay in the development of executive functioning in patients with NS, which seems to be outgrown in adulthood.

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