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 the developmental processes culminating in articulate speech and language. Neural and genetic substrates of this disorder may inform the ontogeny 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 VIIa 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:
Jos Egger, Willem Verhoeven, Joep Tuurtings, Nicole De Leeuw
Objectives: The 22q11.2 deletion syndrome (22qDS), mostly caused by a submicroscopic deletion (LCR-D) encompasses the FOXP2 gene, 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.
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Gene expression, antisense processing, and splicing in a patient with Noonan syndrome
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Quality of life in adults with Noonan syndrome
Ellen Wingbermuhle, Floor Nobbe, Renee Roelofs, Ineke Van der Burgt, Roy Kessels, Jos Egger
Objective: Noonan syndrome (NS) is a genetic disorder related to mutations in the RAS-MAPK pathway. Cardinal features include short stature, facial dysmorphism, congenital heart defects, subtle cognitive deficits and a slightly lowered mean IQ (= 90). These characteristics may bring about lowered levels of quality of life (QoL). In this study, QoL was evaluated in adults with NS.
Authors: Forty-five adult patients with NS and 26 IQ-matched, healthy controls completed the Dutch version of the Lancashire Quality of Life Profile (LQoLP), a comprehensive structured interview covering nine domains of QoL, as well as global measures on wellbeing. Groups were compared using ANOVA and chi-square tests.
Results: Patients with NS demonstrated significantly lower levels of QoL on two out of four general outcome measures (Happiness with life and Cantril’s ladder, p<0.05). Contrary to the controls, the majority of patients did not have a relationship (p<0.05). A history of being bullied in youth was more prevalent in the NS group (p<0.01) and patients presented with significantly lower levels of self-esteem (p<0.05). No difference was found in satisfaction with health, in spite of the medical burden in the NS group.
Conclusions: The QoL profile of adult NS patients differs from that of controls with respect to both subjective measures, such as happiness with life and self-esteem, and objective measures, like relationship status. Lowered QoL in NS may be moderated by neurocognitive deficit, such as slower speed of information processing and alexithymic traits, which have been demonstrated in this group before.
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