

Supplementary Note

Clinical description of patients with the 17q21.31 deletion

Patient 1

The chromosomes of this 3 year-old-girl were analyzed prenatally and found to be normal. She was born at 35 2/7 weeks gestation with a birth weight of 2078 g (10th centile) and head circumference of 30.4 cm (5th centile). She was severely hypotonic and her development was considerable delayed: sitting at 3 years and no words at 3 years and 1 month. Magnetic Resonance Imaging (MRI) of the brain at 1 year of age showed widened ventricles and periventricular white matter changes. Electromyography (EMG) was normal, but Brainstem Evoked Response Audiometry (BERA) was abnormal. At 3 months she was treated for a congenital hip dysplasia. Diagnostic testing including DNA analysis for myotonic dystrophy, Spinal Muscular Atrophy (SMA), Prader-Willi syndrome, metabolic screening in blood and urine revealed no abnormalities.

On physical examination at the age of 3 years and 1 month, her height was 95 cm (40th centile), weight 12.5 kg (10th centile for height) and head circumference 49.5 cm (50th centile). She had a long hypotonic face with frontal bossing and bitemporal narrowing, ptosis, blepharophimosis, upward slanting palpebral fissures, epicanthal folds, large low set ears with hypoplastic crus superior, low nasal bridge, bulbous nasal tip, long columella, triangular nostrils, high palate with broad gums and a broad chin (**Fig. 1e**). Her broad thorax had wide-space nipples and a mild pectus excavatum. She had long fingers, narrow long feet with long toes and hyperlaxity of the joints (Beighton score of 6/8). She was good natured with normal eye contact.

Patient 2

This 17-year-old, moderately mentally retarded woman was born at 38 weeks gestation in breech position with a caesarian section and she had a birth weight of 1980 g (<3rd centile). In the first 3 weeks she received nasal catheter feeding because of low glucose levels and phototherapy because of hyperbilirubinaemia. She was hypotonic and started walking and speaking after the age of 2 years. She had an IQ of 48 points and attended special schooling. From the age of 1.5 to 3.5 years she had epileptic insults for which antiepileptic drugs were used. An MRI of the cerebrum showed wide ventricles, especially of the temporal horn of the lateral ventricles. In addition, routine chromosome analysis, metabolic screening in blood and urine and EMG, revealed no abnormalities. She developed a scoliosis at 13 years of age. She had normal hearing but mildly impaired vision (+4/+4).

On physical examination at the age of 17 years, she had a low-normal height of 160.8 cm (10th centile). Her weight was 51.2 kg (50th centile for height) and head circumference 53 cm (10th centile). She had a long hypotonic face with ptosis, blepharophimosis, upward slanting palpebral fissures, large ears with hypoplastic crus superior, tubular pear-shaped nose with high nasal bridge and long columella, short philtrum, 2 missing upper teeth, everted lower lip and broad chin (**Fig. 1f**). She had a thoracal scoliosis with a lumbar hyperlordosis. Her hands and fingers were long and slender with a simian crease in the left palm. Her feet had high arches with hallux valgus bilaterally and mild hammer toes. The lower part of the limbs were slender and there was a mild general decrease of strength. In addition, she had mild hyperlaxity of the finger joints (Beighton score of 2/9), and numerous moles on the skin. She had nasal speech and an amiable nature.

Patient 3

This 26-year-old, moderately mentally retarded male was born after an uneventful pregnancy at term with a normal birth weight of 3120 g (50th centile) but a large head circumference of 37.5 cm (>97th centile). He was notably hypotonic and computed tomography imaging of the brain at 4 months of age showed a communicating hydrocephaly without increased intracranial pressure. Both Somatosensory Sensory Evoked Potentials (SSEP) and BERA studies were abnormal at 6 months but normalized later in life. His development was retarded, walking at 3 years of age and he attended special school. He had an IQ of 40 points at the age of 18 years. He was operated on inguinal hernia and cryptorchidism. A scoliosis developed at 13 years of age. Diagnostic test including routine chromosome, *FMRI* analysis and metabolic screening in blood and urine revealed no abnormalities.

On physical examination at the age of 26 years, he had a low-normal height of 173 cm (10th centile), and a large head circumference of 63 cm (>97th centile). His weight was 68 kg (70th centile for height). He had a long narrow face with a high, broad forehead, blepharophimosis, strabismus divergence, large ears with hypoplastic crus superior and large lobules, tubular pear-shaped nose with bulbous tip and long columella, high palate with broad gums and diastemia frontal upper teeth, and a large broad chin (**Fig. 1g**). The thorax was flat and broad with wide-spaced nipples and a scoliosis.

His hands and fingers were long and hyperlax (Beighton score of 4/9). His feet had high arches with hallux valgus bilaterally and his skin revealed numerous moles. He had nasal speech and a friendly nature.