Supplementary Table 1: Clinical Details of Individuals with FBXO11 variants										
	P1	**P2**	**P3**	**P4**	**P5**	**P6**	**P7**	**P8**	**P9**	**P10**
Gender	Male	Female	Male	Female	Female	Male	Female	Male	Male	Female
Age at last investigation	12 years	N/A	26 years	15 years	12 y 4 m	5	4 years	7 years	4 years old	16 years old
variant description NM_001190274.1	deletion exons 11-23 plus *MSH6*	c.1676G>A p.(Gly559Asp)	c.1967A>G p.(Asn656Ser)	c.2655G>C; p.(Arg885Ser)	c.2440A>G (p.Met814Val)	c.983C>G (p.Ser328*)	c.657C>G (p.Tyr219*)	c.2747C>T, p.(Ala916Val)	c.11_14del, p.(Val4Glufs*161)	c.11_14del, p.(Val4Glufs*161)
Methods	duo GS	trio GS	trio ES	trio ES	trio ES	Singleton ES	trio ES	trio ES	trio ES	trio ES
Inheritance/ De novo?	unknown	de novo	de novo	de novo	de novo	Unknown - not maternally inherited	Inherited (father)	de novo	inherited (father)	inherited (father)
ACMG criteria	2A-2E - +1.00	PM2. PP3, PP2,PM6	PM2, PP3, PP2	PM2, PP3, PP2, PM6	PM2, PP2, PM6	PVS1, PM2	PS4, PVS1, PM2	PS4, PM1, PP2, PM2, PM6	PVS1 and PM2	PVS1 and PM2
ACMG classification	pathogenic	Likely pathogenic	Likely pathogenic	likely pathogenic	Variant of uncertain significance	likely pathogenic	Pathogenic	likely pathogenic	likely pathogenic	likely pathogenic
Contributor classification	pathogenic	likely pathogenic	Likely Pathogenic	likely pathogenic	likely pathogenic	likely pathogenic	Pathogenic	likely pathogenic	likely pathogenic	likely pathogenic
Other variants	N/A	N/A	N/A (reportedly normal)	N/A	*HIVEP2*:c.1543G>A (p.Glu515Lys)	N/A	NRXN2:c.1487C>A (p.T496N) DLGAP2:c.902A>G (p.D301G)	N/A	N/A	N/A
B. weight	3.490 kg (-0.11SD)	3.0 kg (-0.81SD)	N/A (reportedly normal)	4.18 kg (+1.65SD)	3.68 kg (+0.56SD)	3.61 kg (+0.51SD)	2.53 kg (-1.70SD)	N/A	2.88 kg (-1.22SD)	3.35 kg (-0.14SD)
B. weight (SD)	-0.11	-0.81	N/A (reportedly normal)	1.65	0.56	0.51	-1.7		-1.22	-0.14
B. length	52.5 cm (+0.9SD)	48 cm (-0.65SD)	N/A (reportedly normal)	54 cm (+1.65SD)	48 cm (-0.65SD)	48 cm (-0.81SD)	45 cm (-2SD))	N/A	48 cm (-0.81SD)	50 cm (+0.2SD)
B. length (SD)	0.96	-0.65	N/A (reportedly normal)	1.65	-0.65	-0.81	-2		-0.81	0.2
B. OFC	34.5 cm (-0.61SD)	32 cm (-1.9SD)	N/A (reportedly normal)	N/A	N/A	34 cm (-0.83SD)	30.5 cm (-2.92SD)	N/A	33 cm (-1.27SD)	34 cm (-0.54SD)
B. OFC (SD)	-0.61	-1.9	N/A (reportedly normal)			-0.83	-2.92		-1.27	-0.54
Weight	39 kg (-0.24SD)	17 kg (+1SD)	72 kg (0.18SD)	59 kg (+0.45SD)	49 Kg (+0.58SD)	20kg (+0.51SD)	13.6kg (-1.34SD)	29 kg (+1,34 SD)	17.7 kg (+0.60SD)	76 kg (+1.43SD)
Weight (SD)	-0.24	1	0.18	0.45	0.58	0.51	-1.34	1.34	0.6	1.43
Height	144 cm (-0.69SD)	103 cm (+1SD)	166cm	170 cm (+1.25SD)	158 cm (+0.95SD)	112cm (+0.68SD)	94cm (-1.60SD)	121.5cm (-0.04SD)	112 cm (+2.30SD)	157cm (-0.80SD)
Height (SD)	-0.69	1	-1.47	1.25	0.95	0.68	-1.6	-0.04	2.3	-0.8
OFC	51.5cm (-1.54SD)	46 cm (-2.5SD)	57cm (+1.32SD)	N/A	52 cm (-0.85SD)	49.5cm (-1.08SD))	45cm (-2.98SD)	50.5cm (-1.13SD)	48.7cm (-1.17SD)	52.5cm (-1.69SD)
OFC (SD)	-1.54	-2.5	1.32		-0.85	-1.08	-2.98	-1.13	-1.17	-1.69
Walking at age	13 months	16 months	12 months but unstable till 3 years	Average - but always a bit clumsy	14 months	24 months	28 months	17 months	18 months	18 months
first words at age/speech abilities	first words > 24 months; now makes simple/incomplete sentences	10 words at 24 months; now makes sentences	3 years	Average	4 years	Delayed- unable to recall age, unclear speech, has made good progress with speech therapy	24 months	>24 months	language delay, short sentences	firts words -11 months, then language delay. At 5 years : association of three words
DD/ID severity	mild	Mild	mild	Mild	Moderate-severe	Mild	Mild	mild	mild	mild
IQ/DQ	N/A	N/A	WISC IV - borderline to mild ID	Total IQ: 70; Verbal 77; speed 64, executive 88	N/A	FSIQ 71-83 (5th precentile)	N/A	IQ of 75, follows special needs school	N/A	NA
any regression	no	no	no	no	no	no	no	no	no	Yes
Seizures (onset) (type)	no	no	no	6 years, Focal	Episodes of disconnection with clonic movements of the right corner of the mouth, drooling	no	no	episodes of staring	no	no
MRI anomalies	no	biometries generally below the 3rd percentile, with aspecific bilateral and symmetrical	no	Partial incomplete inversion of left hippocampus	Cerebellar vermis hypoplasia/atrophy. Thick, mild dysplastic corpus callosum	no	hypotrophy of the white matter, T1 and T2 signal hyperintensities	N/A	no	no
Hypotonia	Yes	no	yes	no	Yes	Yes	Yes begins in the neonatal period	no	Yes	Yes
Sleeping difficulties	yes	no	yes	Difficulty falling asleep. Melatonin	Frequent awakenings during the night	Sleep dysregulation	Yes	no	N/A	N/A

Behavioural anomalies	Tantrums, compulsions (food intake), aggressivity	hyperactivity, hypersensitivity, aggressiveness, concentration difficulties, tiredness, impulsiveness	concentration difficulties, uninhibitions, anxiety, executive dysfunction	can be aggressive	Outbreaks of irritability and self-aggression triggered by certain sounds (episodes more frequent in the last 4-5 years). Screams of excitement/surprise, and and loses muscle tone, falling to the ground. Puts objects in her mouth, smells everything	ADHD diagnosed, behavioural dysegulation, periodic aggressive behaviour, at other times very loving and kind.	aggressiveness	temper tantrums, poor attention but no formal diagnosis of ADHD. Wants to control other children	no	no
Cardiac Malformations	no	no	no	N/A	no	no	bicuspid aortic valve	no	no	no
Renal malformation	no	no	no	N/A	no	no	no	no	no	no
Genital malformation	no	no	no	no	no	no	no	hypospadia and cryptorchidism	no	no
vision	strabismus	bilateral ptosis + astigmatism	normal	Normal	Divergent strabismus. Normal vision	Normal	Normal	Normal	Normal	Normal
hearing	Normal	Normal	normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
microcephaly	Yes	Yes	no	Not measured - but does not look like it	Yes	Yes, relative	Yes	no	Yes	Yes
dental	Normal	Normal	dental malocclusion	Normal				Normal	Normal	Normal
nose	bulbous nose	normal	bulbous nasal tip, low hanging columella	Broad nasal tip; convex nose	N/A	N/A	marked nasal tip, anteverted nose, depressed nasal bridge	normal	normal	normal
philtrum	long and smooth	long and smooth	normal	Short	N/A	N/A	N/A	Normal	Normal	Normal
other	thin upper lip	thin upper lip, large, protruding ears	narrow upslanting palpebral fissures	N/A	N/A	Thin upper lip, macrotia (+1.8SD)	round face, bilateral epicanthus, arched eyebrow, microstomia	round face with long palpebral fissures, thin upper lip, relative large ears,	N/A	N/A
Abnormalities of hands and feet	no	no	no	Feet: broad with space between the toes	Fetal finger pads	talipes, unusual palmar creases	valgus feet	mild clinodactyly dig 5 at the hands and a mildly dysplastic nail at dig 5 of	no	no
Cleft lip or palate	no	no	no	no	no	no	no	no	no	no
Skeletal anomalies	Hyperlaxity	distal hyperlaxity	scoliosis	no	no	N/A	gibbosity, isolated hemivertebra T9 , butterfly vertebrae	no	no	no
recurrent infections/otitis media	yes	no	no	no	no	no	no	no	No	no
Other anomalies	N/A	plagiocephaly, hypertrichosis of back and legs	hypertrichosis, severe hyperhidrosis, sleep apnea and sleep walking	N/A	N/A	generalised joint hypermobility	4 years : walks on 400m only, doesn't run et jump, daily tasks are delayed. father	frequent reflux when young	No	No