Table S1. CNV breakpoints, gender, age at time of analysis, age of seizure onset, and AEDs for individuals with 4p deletions and no other clinically reportable CNVs (henceforth designated "individuals with only 4p deletions."). All coordinates are given in hg19/GRCh37.

Patient	CNV coordinates (hg19)	Deletion size (Mbp)	Gender	Age (years)	Seizures: age of onset (months)	Seizure medications (AEDs)
1	chr4: 68345-32587789	32.5	F	3.8	5	Phenobarbital
2	chr4: 68345-22799761	22.7	F	14.8	11	For SE: Diazepam. Carbemazepine, Topiramate
3	chr4: 68345-19797868	19.7	M	7.2	5	Diazepam and Lorazepam for SE. Levitiracetam, Topiramate, and Clonazepam in combination. Levitiracetam only.
4	chr4: 68345-19258986	19.2	M	16.5	6	Chlorazepate Dipotassium and Lacosamide and "many others."
5	chr4: 68345-18958105	18.9	F	2.8	16	For SE: Levitiracetam, Diazepam, rectal Diazepam. For seizure control: Levitiracetam, rectal Diazepam
6	chr4: 68345-16452492	16.4	F	38.0	5	Phenobarbitol, Valproate. Weaned off all seizure meds at

						age 21
7	chr4: 68345-15891049	15.8	F	8.0	17	Phenobarbitol, Diazepam. Has been seizure free for past two years. Ketogenic diet.
8	chr4: 68345-15338783	15.3	M	4.0	No answer[1]	Lamotrigine
9	chr4: 68345-15067905	15.0	F	26.5	14	Phenobarbital, Valproic acid.
10	chr4: 1025119-15582327	14.6	M	3.7	18	Advised not to medicate due to lack of seizures.
11	chr4: 68345-13578589	13.5	F	20.5	8	Diazepam for SE. Phenobarbital, Phenobarbital/Valproate, Valproate/Clonazepam, Valproate/Levitiracetam, Levitiracetam only since July 2006.
12	chr4: 49450-11487322	11.4	F	1.0	No answer[1]	Levitiracetam, Valproate, Levocarnitine
13	chr4: 68345-10621914	10.6	F	7.5	9	Topiramate, Levitiracetam, Lamotrigine. Phenobarbital
14	chr4: 68345-10255806	10.2	F	5.0	6	Diazepam, Midazolam, Propanolol for SE. Phenobarbital, Clonazepam, Oxcarbazepine,

						Clonazepam, Ethosuximide, Gabapentin, Phenytoin, Valproic acid, Felbamate, Topiramate, Zonisamide, Lacosamide, Levitiracetam. Clobazam Lorazepam.
15	chr4: 68345-9785068	9.7	F	9.0	16	For SE: Lorazepam, Diazepam, Phenytoin. For other seizures: Carbemazepine, Levitiracetam. Seizure free for three years
16	chr4: 68345-7670607	7.6	M	6.0	No answer[1]	No answer
17	chr4: 965069-7686694	6.7	M	1.5	n/a[2]	n/a
18	chr4: 68345-6335151	6.3	F	2.3	14	Levitiracetam, Diazepam
19	chr4: 68345-6146360	6.1	F	3.5	9	Diazepam, Docosahexaenoic acid
20	chr4: 68345-5595216	5.5	F	22.0	No answer[1]	Phenobarbital, Valproate from 24 mo to 7 yr
21	chr4: 1701018-7102682	5.4	F	10.0	n/a[2]	n/a
22	chr4: 68345-5418070	5.3	F	18.0	11	Carbemazepine

23	chr4: 113981-5087478	5.0	M	11.0	12	Diazepam in case of emergency but never used
24	chr4: 1682255-6055232	4.4	M	8.0	n/a[2]	n/a
25	chr4: 68345-4426571	4.4	M	15.0	24	No answer
26	chr4: 68345-4288168	4.2	M	20.0	24	No answer
27	chr4: 68345-4214933	4.1	M	5.0	42	Levetiracetam
28	chr4: 68345-3956051	3.9	F	5.0	10	Diazepam
29	chr4: 68345-2283825	2.2	F	6.7	No answer[1]	Levitiracetam, Topiramate, Lamotrigine, Lorazepam, Clonazepam, Phenytoin, Diazepam
30	chr4: 68345-2115175	2.0	F	9.0	No answer[1]	Levitiracetam, Lamotrigine Phenobarbitol
31	chr4: 68345-2110649	2.0	M	11.3	No answer[1]	Valproate
32	chr4: 68345-2009432	1.9	F	15.0	No answer[1]	Topiramate, Levitiracetam, Clobazam, Ketogenic diet

33	chr4: 68345-1740152	1.7	F	6.0	No answer[1]	Topiramate, Oxcarbazepine, Lamotrigine, Levitiracetam, Valproic Acid, Ketogenic diet, Diazepam
34	chr4: 750979-2009432	1.3	F	11.0	n/a[2]	n/a
		Average size: 9.6			Average age of onset (months): 13.4 +/- 8.7	

[1]Age of onset was not provided; patient is known to have seizures. [2]Patient does not have seizures, therefore age of onset is not applicable (n/a). SE, status epilepticus.

Table S2. CNV breakpoints, gender, age at time of study, and age of seizure onset for individuals with a 4p deletion and a second clinically reportable CNV. All coordinates are given in hg19/GRCh37.

Patient	4p CNV coordinates (hg19)	4p deletion size (Mbp)	Additional CNV coordinates (hg19)[1]	Additional CNV size (Mbp)	Pathogenicity of second CNV	Sex	Age (years)	Age at seizure onset (months[2])	Seizure medications (AEDs)
35	chr4:68345-33934217	33.9	chr19:56455446-57033092 (dup)	0.58	VOUS	F	0.9	6	Levitiracetam
36	chr4:68345-23113681	23.0	chr2:110873834-110980107 (del)	0.11	VOUS; Joubert carrier due to *NPHP1* deletion	F	27.0	16 years old, initially associated with menarche	For SE: rectal Diazepam. Remains on Valproate but has not had seizure for several years
37	chr4:68345-22970801	22.9	chr16:21931247-22442007 (del)	0.51	Pathogenic: 16p12.2 microdeletion syndrome. This syndrome is associated with high penetrance and variable expressivity and includes the following: DD,ID, autism, microcephaly, congenital heart defects, hypotonia, seizures.[2–6]	M	4.5		Levitiracetam, Topiramate
38	chr4:68345-21981129	21.9	chr1:246840624-249224684 (dup)	2.4	VOUS: case reports associate 1q44 trisomy with ID, speech delay, facial features, heart defects, macrocephaly, ASD,	M	23.0	9	ATCH injections for infantile spasms, Diazepam for SE. Clonazepam,

					seizures[7,8]AM				Topiramate, Lamotrigine, Diazepam, Phenytoin, Phenobarbital, Levitiracetam, Tiagabine, Gabapentin, Carbamazepine
39	chr4:5762133-26720441	21.0	chr4:5488819-5760770 (dup)	0.27	VOUS: This is a duplication adjacent and distal to the deletion in 4p16.1. NB: Due to the CMA results, this individual's diagnosis was changed from WHS to proximal 4p deletion syndrome.	M	25.0	18	Valproate
40	chr4:68345-17983528	17.9	chr4:17983558-18562949 (dup)	0.58	VOUS, likely benign	M	6.7	6	Lorazepam for SE. Valproate, Rufinamide, Clonazepam, Levitiracetam, Phenobarbital, Primidone, Topiramate, Lorazepam, Diazepam, Clobazam, Vigabatrin, Zonisamide, Ketogenic diet.
41	chr4:68345-15305951	15.2	chr4:15310408-17226923 (dup)	1.9	VOUS	F	14.0	8	Topiramate and Clonazepam for SE. Phenobarbital, Clonazepam, Carbamazepine, Topiramate
42	chr4:68345-	9.4	chr8:158048-	7.0	VOUS	M	20.0	7	Diazepam, and Lorazepam for SE.

	9501651		7112571 (dup)						Phenytoin, Phenobarbital, Valproate, Carbamazepine. Has been off seizure meds since age 15
43	chr4:68345-7442049	7.4	chr8:146082484-146295771 (dup)	0.21	VOUS	M	12.0	9	Diazepam, Fosphenytoin for SE. Phenytoin, Topiramate, Clonazepam, Lamotrigine, Carbamazepine, Phenobarbital, Valproate, Zonisamide, Oxcarbazepine
44	chr4:68345-6257188	6.2	chr3:124342797-124394169 (del)	0.051	VOUS; Deletion includes the *KALRN* gene[9]AM	M	5.0	12	Valproic acid
45	chr4:68345-4165335	4.1	chr8:158048-6999114 (dup)	6.8	VOUS	M	2.0	16	Valproic acid
46	chr4:68345-3941740	3.9	chr12:173786-8393815 (dup)	8.2	Pathogenic: 12p trisomy syndrome. 12p trisomy syndrome is characterized by seizures, DD, and hypotonia, unique facial features , and hearing loss[10]AM	F	3.0	No answer	Diazepam, Clobazam, Vigabatrin
47	chr4:68345-3927887	3.9	chr12:173786-8393815 (dup)	8.2	Pathogenic: 12p trisomy syndrome. 12p trisomy syndrome is characterized by seizures, DD, and hypotonia, unique facial features , and hearing loss[10]AM	F	19.5	8	Diazepam, Phenobarbital, Phenytoin, Levitiracetam, Valproic acid with Phenytoin, Topiramate

48	chr4:68345-2437290	2.4	chr22:42932261-51197838 (dup)	8.3	Pathogenic: Phelan-McDermid Syndrome. DD, hypotonia, ASD, and absent or delayed speech	F	22.0	15	Lorazepam for SE, Levitiracetam
		Average size of 4p deletion (Mbp): 13.8		Average size of additional CNV (Mbp): 3.2				Average age of onset (months), excluding Patient 36 as an outlier: 10.4 +/- 4.2	

[1]For additional CNVs, deletion (del) or duplication (dup) of the region is indicated in parentheses following the CNV coordinates. [2]Age of seizure onset of Patient 36 is given in years. Abbreviations: VOUS, variant of unknown significance, ABN, abnormal CNV, ID, intellectual disability, DD, developmental delay, ASD, autism spectrum disorder

Table S3: Calculation of Two-tailed Fisher's Exact test

	751 kbp terminal region intact	751 kbp terminal region deleted
Seizures: No	5	0
Seizures: Yes	0	29

Table S4. Coordinates for all deletions helping to define a seizure susceptibility region (see Figure 1b). "SEIZURE REGION" is the candidate 197 kbp seizure susceptibility region, the SRO between patients described in Izumi et al (2010) and Zollino et al 2014). WHS Critical regions are labeled "WHSCR" and "WHSCR2," respectively. Patient identifiers are in parentheses and correspond to the number given to them in their respective papers (cited). For example, "Zollino 2014 (3 and 4)" is the label for deletion shared by siblings, patients 3 and 4 in Zollino et al., 2014[11]. All coordinates are given in hg19/GRCh37. Some deletion sizes from older reports had to be inferred because the mapping of breakpoints was done using FISH probes and not by microarray analysis.

	Coordinates	**Seizures?**
SEIZURE REGION	chr4:367691-564593	
Izumi 2010[12]	chr4: 367691-1948108	Yes
Zollino 2014 (3 and 4)[11]	chr4:71552-564593	Yes

Van Buggenhout 2004 (6)[13]	chr4:0-300000	No
34	chr4:750979-2009432	No
18	chr4:965069-7686694	No
10	chr4:1025119-15582327	No
Zollino 2014 (2)[11]	chr4:1079721-1919855	No
Van Buggenhout 2004 (3)[13]	chr4:1283478-2833478	No
Shimizu 2013 (13)[14]	chr4:1339023-10645858	No
24	chr4:1682255-6055232	No
21	chr4:1701018-7102682	No
Andersen 2014 (1)[15]	chr4:1743630-2120247	No
Zollino 2014 (1)[11]	chr4:1778765-2909499	No
Okamoto 2013[16]	chr4:1822203-1931042	No

Andersen 2014 (2)[15]	chr4:1827029-1997169	No
Andersen 2014 (3)[15]	chr4:1828867-3724595	No
Van Buggenhout 2004 (4)[13]	chr4:1880226-3505324	No
Rauch 2001[17]	chr4:1906575-2093987	No
Maas 2008 (17)[18]	chr4:2700000-14800000	No
Van Buggenhout 2004 (1)[13]	chr4:0-3679582	No
Van Buggenhout 2004 (5)[13]	chr4:0-3505324	Yes
Van Buggenhout 2004 (2)[13]	chr4:0-2351677	Yes
Bayindir 2013[19]	chr4:68345-1729442	Yes
33	chr4:68345-1740152	Yes
23	chr4:113981-5087478	Yes

LETM1	chr4:1813206-1857974	
WHSCR2	chr4:1345236-1945236	
WHSCR1	chr4:1945236-2110236	

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