

Supplementary Material

Pharmacological Strategy for Congenital Myasthenic Syndrome with *CHRNE* Mutations: A Meta-Analysis of Case Reports

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Supplementary Tables

Supplementary Table S1. Overview of effect of pharmacologic treatment in *CHRNE*-mutated fast-channel syndrome.

Case	onset(year)	Age(year)	treatment	Effect	Mutation
1[1]	0	8	AChEI	+	c.163T>C
2[2]	0.6	2	AChEI AChEI +BA	++ +++	c.43T>C; c.113C>A
3[3]	0	5	AChEI	+	c.523G>A; c.544A>T
4[4]	0	21	AChEI PDN AChEI +PDN others	+ ++ + -	c.362C>T; c.1233C>T
5[5]	0	4	AChEI	+	c.362C>T; c.428C>T
6[6]	early childhood	39	AChEI	+	c.382T>A; c.1254ins18
7[7]	N.M*	N.M	AChEI	+++	c.610G>A
8[7]	N.M	N.M	AChEI	+++	c.712C>T
9[7]	N.M	N.M	AChEI	+++	c.778C>A; c.965G>A

Effect: (-) no effect; (+) partial, incomplete, moderate, modest or mild effect; (++) beneficial, positive or clear effect; (+++) remarkable, dramatical or satisfying effect. *NM: not mentioned

Supplementary Table S2. Overview of effect of pharmacologic treatment in *CHRNE*-mutated slow-channel syndrome.

Case	Onset(year)	Age(year)	Treatment	Effect	Mutation
1[7]	0	34	BA + FLX	++	c.865C>A (heter)
2[8]	0	16	QUIN	+++	p.L269F
3[8]	0	22	QUIN	++	p.T264P
4[9]	2.5	29	AChEI	-	c.846G>T
5[10]	0	15	AChEI FLX	+++ +	c.805C>T (heter*)
6[11]	17	27	QUIN AChEI	+ +	c.775G>C (heter)
7[11]	childhood	53	QUIN AChEI	+ +	c.775G>C (heter)
8[11]	childhood	28	QUIN AChEI	+ +	c.775G>C (heter)
9[11]	N.M	24	QUIN AChEI	+ +	c.775G>C (heter)
10[12]	2	19	QUIN	++	p.V259L
11[12]	0	15	QUIN	++	p.V259L
12[12]	0	20	AChEI FLX	- ++	p.L269F
13[12]	0	18	AChEI FLX	- ++	p.L269F
14[13]	6	N.M**	AChEI FLX others	++ + +++	c.833_835delCTC
15[14]	2	6	AChEI +DAP BA	+ ++	c.850A>C (heter)
16[15]	0	21	AChEI	+	c.854T>C
17[16]	4	21	AChEI FLX	- +	c.865C>T (heter)
18[16]	11	24	FLX	+	c.865C>T (heter)
19[17]	13	60	BA	+	c.721C>T (heter)
20[17]	19	31	BA + FLX	+	c.721C>T (heter)

Effect: (-) no effect; (+) partial, incomplete, moderate, modest or mild effect; (++) beneficial, positive or clear effect; (+++) remarkable, dramatical or satisfying effect. *heter: heterogeneous; **NM: not mentioned.

Supplementary Table S3. Overview of effect of pharmacologic treatment in *CHRNE*-mutated primary AChR deficiency.

Case	Onset(year)	Age(year)	Treatment	Effect	Mutation
1-30[7]	N.M	N.M	AChEI	++	CHRNE (details not known)
31[14]	0.1	26	AChEI	+	c.655_665del
32[14]	1	38	AChEI	+	c.786C>G
33[14]	0.1	26	AChEI	+	c.911T>G
34[18]	1.5	55	AChEI	++	c.1101insT
35[19]	N.M*	29	AChEI	+	c.1206ins19
36[19]	N.M	16	AChEI	+	c.70insG
37[19]	N.M	12	AChEI	+	c.70insG; g.IVS7+2T>C
38[19]	N.M	20	AChEI	+	c.1276delG
39[19]	N.M	19	AChEI	+	c.1276delG
40[19]	N.M	13	AChEI	+	c.59ins5
41[20]	N.M	N.M	AChEI	++	c.1369delG
42[20]	N.M	N.M	AChEI	++	1369delG; p.Y15H
43[20]	N.M	N.M	AChEI	++	1369delG; p.R311Q
44[20]	N.M	N.M	AChEI	++	1369delG; c.509insA
45[20]	N.M	N.M	AChEI	++	p.R311Q
46[21]	0	6	AChEI	+	c.553del7; g.IVS9-1G>C
47[21]	0	18	AChEI	+	c.553del7
48[21]	0	10	AChEI	+	c.553del7
49[21]	0	39	AChEI	+	c.553del7
50[21]	0	16	AChEI	+	c.553del7
51[21]	0	30	AChEI	+	c.553del7; c.1021ins20
52[21]	0	8	AChEI	+	c.553del7; c.1098insG
53[21]	0	10	AChEI	+	c.460G>T
54[21]	0	33	AChEI	+	c.470del13; g.IVS4-2A>C
55[22]	0	23	PDN AChEI	- ++	c.511A>T
56[22]	0	19	PDN AChEI	- ++	c.511A>T
57[22]	0	16	PDN AChEI	- ++	c.511A>T
58[23]	0	59	AChEI	+	g.IVS6-1G>C
59[23]	0	23	AChEI	+	g.IVS9-1G>A
60[23]	0	2.5	AChEI	+	g.IVS10-9_c.1167dup16
61[23]	0	6	AChEI	+	c.1259_g.IVS11+15del23; c.1033delG
62[23]	0	44	AChEI	+	c.857G->T; c.734C>T
63[24]	early childhood	18	AChEI	++	c.911delT; g.IVS5-16G>A
64[25]	2	14	AChEI	++	c.855C>T
65[26]	0.6	21	AChEI + DAP	++	c.1293insG
66[26]	0	23	AChEI	++	c.1293insG
67[26]	0.3	18	AChEI	++	c.1293insG
68[26]	0	9	AChEI	++	c.1293insG
69[26]	0	37	AChEI + DAP	++	c.1293insG
70[26]	0	8	AChEI	++	c.1293insG

71[26]	0	22	AChEI	++	c.1293insG
72[26]	4	41	AChEI	++	c.1293insG
73[26]	N.M	20	AChEI	++	c.1293insG
74[26]	4	17	AChEI	++	c.1293insG
75[26]	0	13	AChEI	++	c.1293insG
76[26]	0	13	AChEI	-	c.1293insG
77[26]	0.3	5	AChEI	++	c.1293insG
78[27]	0	14	AChEI	++	c.1369delG; p.R311Q
79[27]	0	48	AChEI	++	c.1369delG
80[27]	0	24	AChEI	+	c.1369delG; c.509insA
81[27]	1	74	AChEI	++	c.1369delG; p.R311Q
82[27]	3	80	AChEI	+++	c.1369delG; p.R311Q
83[27]	0	53	AChEI	+++	p.R64X; p.R311Q
84[28]	5	56	AChEI	+	c.24T>G; c.874_876del3
85[29]	5	26	AChEI	++	c.70insG; c.127ins5
86[29]	4	23	AChEI	++	c.70insG; c.127ins5
87[29]	8	17	AChEI	++	c.70insG
88[29]	5	19	AChEI	++	c.70insG
89[29]	1	23	AChEI	++	c.70insG
90[29]	0	18	AChEI	++	p.L11P
91[29]	5	N.M	AChEI	++	c.1293insG
92[29]	childhood	33	AChEI	++	c.1293insG
93[29]	0	7	AChEI	++	c.1293insG; c.70insG
94[29]	0	12	AChEI	++	c.70insG; p.S235L
95[29]	1	32	AChEI	++	c.70insG
96[29]	0	19	AChEI	-	c.70insG
97[29]	1	15	AChEI	-	c.70insG
98[29]	0	33	AChEI	++	p.R286M
99[29]	3	16	AChEI	++	p.R286M
100[30]	0	21	AChEI	++	c.123_127dup5
101[30]	0.4	17	AChEI	++	c.123_127dup5
102[30]	0.4	13	AChEI	++	c.123_127dup5
103[31]	0	63	AChEI + BA	+	c.1293insG
104[32]	0.4	56	AChEI + DAP BA PDN others	+ +++ +++ -	c.127ins5; c.1293insG
105[32]	0.3	35	PDN BA AChEI + DAP	- +++ +	p.C142Y
106[33]	0	49	AChEI others	++ -	c.845C>G; c.798_800del
107[34]	3	13	AChEI	+++	CHRNE (details not known)
108[34]	5	5	AChEI	+++	CHRNE (details not known)
109[34]	0	33	AChEI	+++	CHRNE (details not known)
110[35]	N.M	14	BA AChEI + DAP	+++ +	c.554-560del; c.IV58-1G>A
111[35]	N.M	18	BA AChEI + DAP	+++ +	c.554-560del; c.IV58-1G>A

112[35]	N.M	36	BA AChEI + DAP	+++ +	c.554-560del
113[35]	N.M	32	BA AChEI + DAP	+++ +	c.554-560del
114[35]	N.M	53	BA AChEI + DAP	+++ +	c.972+1G>T
115[35]	N.M	15	BA AChEI + DAP	+++ +	c.1267-32_1319del
116[36]	4	34	AChEI	+++	CHRNE (details not known)
117[36]	6	N.M	AChEI	+++	CHRNE (details not known)
118[37]	N.M	4	AChEI + DAP	++	c.1327delG
119[37]	N.M	5	AChEI + DAP	++	c.295C>T
120[38]	0.1	20	AChEI	+	c.1267delG
121[38]	9	16	AChEI	+	c.1267delG
122[38]	0.1	8	AChEI	+	c.1267delG
123[38]	1	8	AChEI	+	c.1267delG
124[38]	2	34	AChEI	+	c.1267delG
125[38]	2	30	AChEI	+	c.1267delG
126[38]	0.1	30	AChEI + DAP	++	c.1267delG
127[38]	0.1	32	AChEI + DAP	+	c.1267delG
128[38]	0.5	20	AChEI + DAP	++	c.1267delG
129[39]	2	17	AChEI	+	c.183_187dup5
130[40]	0.1	4	BA	+++	c.475A>C
131[40]	1	20	AChEI	-	c.704C>T; c.475A>C
132[40]	1	13	AChEI	-	c.704C>T; c.475A>C
133[41]	0.4	21	AChEI	++	c.130insG; c.1353insG
134[41]	0.1	19	others	++	c.130insG; c.1353insG
135[41]	0.1	53	AChEI + DAP	++	c.1353insG
136[41]	0.1	8	AChEI	++	c.1353insG
137[41]	0	4	AChEI	++	c.865C > T
138[42]	N.M	N.M	AChEI BA	++ +++	c.43T>C; c.113C>A
139[43]	N.M	30	AChEI + BA	++	c.130dupG
140[43]	N.M	29	AChEI + BA	++	c.130dupG
141[43]	N.M	12	AChEI + BA	++	c.130dupG
142[43]	N.M	28	AChEI + BA	++	c.130dupG
143[43]	N.M	19	AChEI + BA	++	c.130dupG
144[43]	N.M	13	AChEI + BA	++	c.130dupG
145[43]	N.M	32	AChEI + BA	++	c.130dupG (heter**)
146[43]	N.M	12	AChEI + BA	++	c.130dupG
147[43]	N.M	37	AChEI + BA	++	c.130dupG
148[43]	N.M	10	AChEI + BA	++	c.130dupG
149[43]	N.M	25	AChEI + BA	++	c.130dupG
150[43]	N.M	4	AChEI + BA	++	c.130dupG
151[43]	N.M	34	AChEI + BA	++	c.130dupG
152[43]	N.M	14	AChEI + BA	++	c.130dupG
153[43]	N.M	64	AChEI + BA	++	c.130dupG; c.803-2A>G
154[43]	N.M	54	AChEI + BA	++	c.130dupG; c.803-2A>G

155[43]	N.M	8	AChEI + BA	++	c.130dupG
156[43]	N.M	16	AChEI + BA	++	c.130dupG; c.858_859dup
157[43]	N.M	7	AChEI + BA	++	c.130dupG; c.858_859dup
158[43]	N.M	38	AChEI + BA	++	c.130dupG
159[43]	N.M	21	AChEI + BA	++	c.130dupG
160[43]	N.M	28	AChEI + BA	++	c.130dupG
161[43]	N.M	43	AChEI + BA	++	c.130dupG
162[43]	N.M	34	AChEI + BA	++	c.130dupG
163[43]	N.M	38	AChEI + BA	++	c.130dupG
164[43]	N.M	18	AChEI + BA	++	c.130dupG
165[43]	N.M	27	AChEI + BA	++	c.130dupG
166[43]	N.M	34	AChEI + BA	++	c.130dupG
167[43]	N.M	19	AChEI + BA	++	c.130dupG
168[43]	N.M	5	AChEI + BA	++	c.130dupG; c.422T>A
169[44]	0.2	3	AChEI + PDN	++	c.295C>T; c.442T>A
170[45]	0.3	2	AChEI others	++ ++	c.1327delG
171[45]	1	2	AChEI	++	c.1327delG
172[45]	1.3	4	AChEI	++	c.3G>A
173[46]	1	12	AChEI	++	c.452_454delAGG
174[46]	1	8	AChEI	++	IVS7+2T>C(c.802+2T>C)
175[46]	1.2	6	AChEI BA	+ +++	c.865C>T; c.872C>G
176[47]	0.2	0.5	others	+++	c.973G>T
177[48]	0.2	35	AChEI BA	+++ +++	c.712C>T
178[48]	0.4	34	BA others	++ +	c.712C>T
179[48]	1.5	25	AChEI	+++	c.610G>A

Effect: (-) no effect; (+) partial, incomplete, moderate, modest or mild effect; (++) beneficial, positive or clear effect; (+++) remarkable, dramatical or satisfying effect. *NM: not mentioned; ** heter: heterogeneous.

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