

Table e-1. Pediatric Cerebral Performance Category¹¹

Score	Category	Description
1	Normal	Normal; at age-appropriate level; school-age child attending regular school classroom.
2	Mild disability	Conscious, alert, and able to interact at age-appropriate level; school-age child attending regular school classroom but grade perhaps not appropriate for age; possibility of mild neurological deficit.
3	Moderate disability	Conscious; sufficient cerebral function for age-appropriate independent activities of daily life; school-age child attending special education classroom and/or learning deficit present.
4	Severe disability	Conscious; dependent on others for daily support because of impaired brain function.
5	Coma or vegetative state	Any degree of coma without the presence of all brain death criteria; unaware, even if awake in appearance, without interaction with environment; cerebral unresponsiveness and no evidence of cortex function; possibility of some reflex response, spontaneous eye-opening and sleep-wake cycles.
6	Brain death	Apnea, areflexia, and/or electroencephalographic silence.

Table e-2. Description of neuropsychological assessment

Test	Domain	Description
CANTAB		
Spatial span	Executive functions	White squares on the screen briefly change color in a variable sequence. Participants must remember the sequence and touch squares in the same order. The sequence length is growing throughout the test.
Stockings of Cambridge	Executive functions	Three colored balls are displayed on the screen. The participant must move the balls in the lower display to match the arrangement in the upper display.
Intra-extra dimensional set shift	Executive functions	Participants must first use feedback to learn a rule involving two dimensions. When feedback implies that the rule has changed, the participant must shift attention to the previously irrelevant dimension.
Paired associated learning	Visual memory	Boxes are displayed on the screen and automatically opened in a random order and show a number of patterns. Thereafter all patterns are consecutively shown in the center of the screen. The participant must select the box where the figure was located.
Reaction time	Attention	The participant must hold down a button until a yellow spot appears on the screen and then touch the yellow spot.
Additional tests		
Dutch dot cancellation test	Speed and sustained attention	Twenty-four dotted figures on 33 lines are shown. The participant must strikethrough certain figures as rapidly as possible.
Rey Auditory Verbal Learning Test (RAVLT)	Verbal memory	Fifteen words are repeated over 5 different trials. Participants must repeat the words every trial, and recall them 30 min later.
Boston naming test	Word finding	The participant must name line drawings.
Word Generation (NEPSY II)	Executive functions	The participant must name as many animals as possible in 60 sec.
Token test	Word comprehension	There are multiple colored circles and squares shown on the table. The participant must perform certain tasks, i.e. 'place the green circle on the red square'.

Abbreviations: CANTAB = Cambridge Neuropsychological Test Automated Battery.

Table e-3. Demographics and follow-up characteristics

No	Sex, age (years)	Prodromal phase	Symptoms during disease course	Treatment	Max. PCPC	Hospital stay (days)	Age at FU	FU (months)	PCPC FU	Current complaints
1	F, 17	Headache	Hyperactivity, aggression, suspicious, disinhibition, memory disorder, mutism, TCS, bradycardia, hypotension	MP, IvIg Resection OT	4	27	18	15	1	No complaints
2	F, 17	Headache	TCS, focal seizures, hallucinations, cognitive decline	MP, IvIg	3	3	23	69	2	Easily irritated and angry, fatigue, difficulties concentrating
3	F, 17	Headache, nausea	Anxiety, confusion, cognitive decline, focal seizures, mutism, dystonia, indifference	MP	4	67	25	91	2	Unemployed due to fatigue, word finding difficulties, inactive
4	M, 6	Upper respiratory tract symptoms	TCS, status epilepticus, indocile, hallucinations, insomnia, dystonia, catatonia, fluctuations in saturation	MP, IvIg, Rituximab	4	64	8	27	3	Fatigue, tantrums, dyslexia, concentration problems
5	F, 3	Upper respiratory tract symptoms	Hemiparesis, hallucinations, focal seizures, insomnia, indifference, cognitive decline, dystonia, chorea, mutism	MP, IvIg, Plex, Rituximab	5	55	6	25	1	Obsessive behavior, hypersensitive, irritable, tantrums
6	F, 14	No	Focal seizures, childish behavior, disorientation, mutism, dyskinesia, hyperhidrosis, blood pressure fluctuations, hypoventilation	MP, IvIg, Plex	5	56	16	34	4	Spasticity, vocal cord paralysis, memory deficits
7	F, 17	Blurred vision	Anxiety, decorum loss, aggressive, insomnia, mutism, TCS, catatonia, weight loss, apathy	MP, IvIg	4	103	23	77	1	Attention disorder
8	F, 17	No	Collaps after use of cannabis, mutism, childish behavior, affective disorder, apathy,	MP, IvIg, Rituximab	4	31	18	10	1	No complaints

			fever, cognitive decline, TCS							
19	F, 13	Headache, nausea	More emotional, anxiety, childish behavior, cognitive decline, less spontaneous speech, TCS, catatonia	MP, IvIg Resection OT	4	34	17	45	1	More irritable, sometimes word finding problems, forgetful
10	F, 4	No	Focal seizure, hemiparesis, obsessive behavior, emotional fluctuations, confusion, chorea, insomnia, mutism	MP, IvIg	4	58	10	69	1	Dyslexia, word finding problems
11	F, 9	Headache	More emotional, aggressive, agitated, hallucinations, mutism, cognitive decline, insomnia, catatonia, cardiac arrhythmia, hypoventilation	MP, IvIg, Plex, Rituximab Resection OT	5	111	13	45	1	Word finding difficulties
12	F, 17	No	Anxiety, problems in organization, insomnia, dyskinesia, psychosis, loss of decorum, fever, cognitive decline, mutism, TCS, hypoventilation	MP, IvIg, Plex	5	67	20	34	2	no job because of fatigue, depression
13	F, 17	No	Loss of decorum, insomnia, agitation, delusions, hallucinations, focal seizures, TCS, cognitive decline, mutism, catatonia, dyskinesia	MP, Plex	5	57	21	51	1	No complaints
14	F, 16	Herpes encephalitis	Decreased consciousness, obsessive behavior, aggression, disinhibition, dyskinesia, dystonia, mutism, fever	MP, IvIg, Rituximab	5	34	18	17	3	Impulsive
15	F, 16	Headache	TCS, childish behavior, disinhibition, aggression, cognitive decline, mutism	MP, Rituximab	4	27	17	6	1	Indecisive, anxiety

16	F, 14	No	TCS, psychosis, bradyphrenia, insomnia, dystonic posture	MP	4	3	15	14	2	Impulsive, anxiety, Indecisiveness
17*	F, 15	Headache	TCS, focal seizures, hallucinations, anxiety, less spontaneous speech	MP	4	67	18	34	1	Anxiety with agoraphobia
18*	M, 7	Herpes encephalitis	Dyskinesia, cognitive decline, mutism, TCS, focal seizures, insomnia	IvIg	5	106	12	50	4	Refractory epilepsy, cognitive decline
19*	M, 1	Herpes encephalitis	Status epilepticus, childish behavior, chorea, mutism, cognitive decline	MP, IvIg Plex Rituximab	5	137	4	41	3	Cognitive decline, Unable to walk, dysphasia
20*	F, 14	Headache	Status epilepticus, aggressive, disinhibition	MP	5	12	15	7	1	No complaints
21*	M, 14	Headache	Hemichorea, less spontaneous speech, catatonia, behavior disorder	MP, IvIg, Rituximab	5	47	15	5	1	No complaints
22*	M, 7	Headache, fever	Cognitive decline, behavior disorder, speech disorder	MP, IvIg, Rituximab	4	8	9	23	3	irritable, insecure

* Only completed the questionnaires.

Abbreviations: PCPC= Pediatric Cerebral Performance Category, FU= Follow-up, TCS= Tonic-clonic seizures, MP= Methylprednisolone, IvIg = Intravenous immunoglobulins, OT= Ovarian teratoma, Plex = Plasmapheresis.

Table e-4. Patients assessed by neuropsychological testing compared to the other patients

	NPT group (n = 16)	Other patients (n = 12)	p-value
Female gender			
< 12 years	3/4	1/5	0.20
≥ 12 years	12/12	5/7	0.12
Age at onset in years, median [IQR, range]	16 (10-17, 4-17)	11 (7-15, 1-16)	0.059
Maximum PCPC			0.67
3; moderate disability	1	0	
4; severe disability	9	7	
5; coma/vegetative state	6	5	
First-line immunotherapy (%)	16/16	12/12	
Second-line immunotherapy (%)	7/16	6/12	1.00

Abbreviations: NPT= neuropsychological testing, PCPC = Pediatric cerebral performance category, IQR= interquartile range.

Table e-5. Results of the neuropsychological assessment

Domain - test – measure	N	Z-score	P-value	95% CI
CANTAB				
Executive functions - spatial span - span length	16	-0.54	0.016 [†]	-1.61 to -0.19
Executive functions - stocking of Cambridge - problems solved in minimal moves	16	-0.30	0.27	-0.86 to 0.26
Executive functions - intra-extra dimensional set shift - total errors	14 ^a	-0.27	0.32	-0.84 to 0.30
Visual memory - paired associated learning - total errors	15 ^a	-0.90	0.016 [†]	-1.61 to -0.19
Attention – reaction time - mean simple reaction time	11 ^b	-0.32	0.37	-1.07 to 0.43
Additional tests				
Sustained attention - Dutch dot cancellation test - S.D. reaction time*	16	-2.10	< 0.0001	-2.71 to -1.4
Speed – Dutch dot cancellation test - reaction time	16	-1.53	0.002 [#]	-2.40 to -0.66
Long-term verbal memory -RAVLT - total recall*	15	-0.76	0.031	-1.29 to -0.07
Short-term verbal memory -RAVLT– trial 1-5	15 ^a	-0.76	0.023 [†]	-1.40 to -0.15
Word finding - Boston naming test - total score	16	-0.78	0.019 [†]	-1.40 to -0.15
Executive functions – Word generation- Total score	15 ^a	-0.14	0.60	-0.71 to 0.42
Word comprehension -token test - total score	16	0.57	0.044 [†]	0.17 to 1.13

*Primary outcome measures.

[†]Secondary outcome measures with $p_{\text{uncorrected}}$ between 0.05 and 0.005, should be considered carefully.

[#]Secondary outcome measure with $p\text{-value} < 0.005$.

^aResults of patient of whom the test was aborted earlier are not shown.

^bNo normative data available for children < 14 years of age.

Abbreviations: S.D.= standard deviation, RAVLT= Rey Auditory Verbal Learning Test.

Table e-6. Results of the questionnaires

Questionnaire - measure	N	Z-score	P-value	95% CI
PedsQL – Self-report^a				
Physical functioning	21	-0.58	0.11	-1.28 to 0.13
Emotional functioning	21	-0.57	0.12	-1.30 to 0.17
Social functioning	21	-0.83	0.013 [†]	-1.46 to 0.20
School functioning	21	-0.76	0.056	-1.53 to 0.023
Total functioning*	21	-0.86	0.032	-1.64 to -0.08
PedsQL – MFS – Self-report^a				
General fatigue	21	-1.03	0.003 [†]	-1.66 to -0.41
Sleep fatigue	21	-0.54	0.069	-1.130 to 0.05
Cognitive fatigue	21	-0.80	0.019 [†]	-1.46 to -0.14
Total fatigue*	21	-0.96	0.008 [†]	-1.64 to -0.28
BRIEF – Self-report^{ab}				
Inhibition	19	-0.26	0.27	-0.74 to 0.22
Cognitive flexibility	19	0.33	0.22	-0.22 to 0.88
Emotional Control	19	0.19	0.45	-0.34 to 0.73
Initiation	6 ^c	0.083	0.89	-1.35 to 1.51
Working memory	19	0.24	0.23	-0.17 to 0.65
Planning and organization	19	0.23	0.38	-0.30 to 0.75
Monitoring	19	0.15	0.58	-0.41 to 0.70
Behavior Rating Inventory	19	-0.06	0.84	-0.52 to 0.63
Metacognition Index	19	0.24	0.35	-0.28 to 0.77
Total	19	0.18	0.45	-0.31 to 0.68
SDQ – Self-report^{a,d}				
Total difficulties	10	0.002	0.94	-0.06 to 0.07
Emotional symptoms	10	0.40	0.40	-0.13 to 0.93
Behavior problems	10	-0.20	0.59	-1.01 to 0.61
Hyperactivity-inattention	10	-0.21	0.22	-0.68 to 0.25
Peer problems	10	0.06	0.06	0.73 to 0.85
Prosocial behavior	10	0.39	0.39	-0.03 to 0.95

*Primary outcome measures.

[†]Secondary outcome measures with $p_{\text{uncorrected}}$ between 0.05 and 0.005, and should be considered carefully.

^a Only for patients aged > 4 years.

^b For the results of the youngest patients no normative data were available

^c Only for patients aged 17 years or older.

^d Only for children aged 11 to 17 years.

Abbreviations: PedsQL = Pediatric Quality of Life, MFS= Multidimensional FatigueScale, BRIEF = Behavior Rating Inventory of Executive Function, SDQ = Strengths and Difficulties Questionnaire.

Table e-7. Results of the questionnaires completed by parents

Questionnaire - measure	N	Z-score	P-value	95% CI
PEDSQL – Parent Proxy-report^a				
Physical functioning	15	-1.12	0.087	-2.42 to 0.18
Emotional functioning	15	-0.82	0.024 [†]	-1.51 to -0.13
Social functioning	15	-1.19	0.009 [†]	-2.04 to -0.34
School functioning	15	-0.87	0.047 [†]	-1.73 to -0.01
Total functioning	15	-1.34	0.004 [#]	-2.15 to -0.52
PEDSQL – MFS- Parent Proxy-report^a				
General fatigue	15	-0.80	0.054	-1.61 to 0.01
Sleep fatigue	15	-0.59	0.15	-1.44 to 0.25
Cognitive fatigue	15	-0.80	0.032 [†]	-1.52 to -0.08
Total fatigue	15	-0.90	0.025 [†]	-1.67 to -0.13
BRIEF Parent Proxy-report^b				
Inhibition	13	0.26	0.52	-0.61 to 1.13
Cognitive flexibility	13	0.77	0.065	-0.05 to 1.56
Emotional Control	13	0.65	0.077	-0.08 to 1.38
Working memory	13	0.62	0.064	-0.04 to 1.27
Planning and organization	13	0.25	0.30	-0.24 to 0.74
Behavior Rating Inventory	13	0.45	0.16	-0.20 to 1.11
Metacognition Index	13	0.42	0.15	-0.18 to 1.02
Total	13	0.58	0.075	-0.07 to 1.24
SDQ Parent Proxy-report^c				
Total difficulties	10	1.02	0.012 [†]	0.28 to 1.77
Emotional symptoms	10	1.05	0.054	-0.02 to 2.12
Behavior problems	10	0.85	0.039 [†]	0.06 to 1.24
Hyperactivity-inattention	10	0.21	0.65	-0.80 to 1.22
Peer problems	10	0.69	0.11	-0.20 to 1.59
Prosocial behavior	10	-0.54	0.32	-1.72 to 0.63

[#] Secondary outcome measures with $p_{\text{uncorrected}} < 0.005$

[†] Secondary outcome measures with $p_{\text{uncorrected}}$ between 0.05 and 0.005, and should be considered carefully.

^a Only completed by parents of children currently 4- 17 years.

^b Only completed by parents of children currently 6-17 years.

^c Only completed by parents of children currently 4-16 years.

Abbreviations: PedsQL = Pediatric Quality of Life, MFS= Multidimensional FatigueScale, BRIEF = Behavior Rating Inventory of Executive Function, SDQ = Strengths and Difficulties Questionnaire.