CEREBELLAR LESIONS AT A YOUNG AGE PREDICT POORER LONG-TERM RECOVERY

Pierre-Aurélien Beuriat, Irene Cristofori, Nathalie Richard, Lara Bardi, Celia Loriette, Alexandru Szathmari, Federico Di Rocco, Pierre Leblond, Didier Frappaz, Cécile Faure-Conter, Line Claude, Carmine Mottolese and Michel Desmurget.

SUPPLEMENTARY MATERIAL

Inclusion criteria.

Being older than six years at the time of evaluation. Two main reasons account for the implementation of this inclusion criterion. First, the Purdue Pegboard Test, used to evaluate fine motor coordination, provides no normalized data for preschool children (Lafayette Intruments, 2012). Second, we were worried about test reliability in light of previous studies suggesting a high degree of inconsistency of response from test to retest in young children (Vane and Motta, 1980).

Suffering no transient post-operative complications capable of interfering with recovery, including mutism. Two main reasons account for the implementation of this inclusion criterion. First, group-pairing would have been difficult considering that CM (i) is much more commonly observed in children (around 25 %) than adults (roughly 1 %) (Catsman-Berrevoets and Patay, 2018) and (ii) is associated with lesions at numerous sites along the dento-thalamo-cortical pathway (Tamburrini *et al.*, 2015; Catsman-Berrevoets and Patay, 2018) -although other hypotheses exist (Lanier and Abrams, 2017)-. Second, the follow-up duration would have been impacted and difficult to interpret considering that CM duration is variable and lasts from a few days up to several months and even years in some cases (Catsman-Berrevoets and Patay, 2018). This would have been all the more problematical for the present study that CM duration has been reported to increase with age (Catsman-Berrevoets and Aarsen, 2010)."

Supplementary table 1. Characteristics of the patients (N = 45) and statistical differences between the three age group for these characteristics (last column).

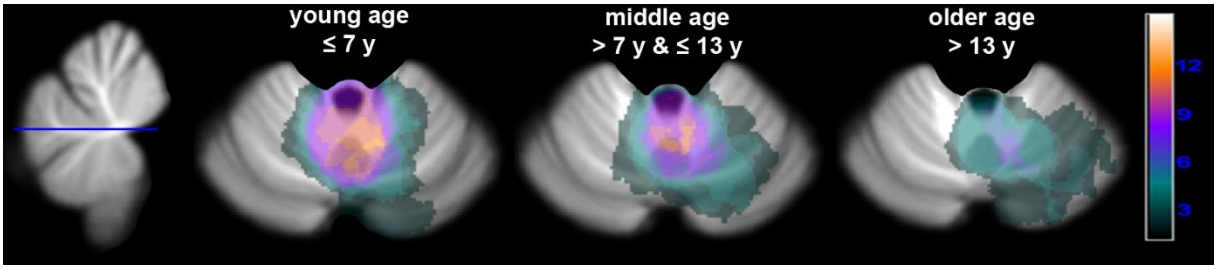
Parameters	**Measures**	**Age-group differences**
Sex Male Female	number (%) 21 (47 %) 24 (53 %)	Maracuillo multiple proportion test non-significant (all $p > .05$)
Age at surgery (years) Young (≤ 7) Middle (> 7 & ≤ 13) Old (> 13)	number (%) / mean/ range 15 (33 %) / 4.6 / 0.9 - 6.9 15 (33 %) / 10.0 / 7.3 - 12.5 15 (33%) / 20.9 / 13.5 - 39.8	ANOVA significant ($F_{(2,42)} = 32.4$; $p < .00001$)
Follow-up Delay from surgery to assessment (years)	mean (SD) / median 5.0 (2.9) / 4.2	ANOVA non-significant ($F_{(2,42)} = 1.25$; $p > .25$)
Radiotherapy Yes No	number (%) 25 (56 %) 20 (44 %)	Maracuillo multiple proportion test non-significant (all $p > .05$)
Tumor type Malignant (medulloblastoma, ependymoma) Benign (pilocytic astrocytoma, hemangioblastoma, ganglioglioma)	number (%) 25 (56 %) 20 (44 %)	Maracuillo multiple proportion test non-significant (all $p > .05$)
Tumor volume and location Volume (mm^3) Location Vermis Vermis extending to the hemisphere	mean (SD) / median 42 (31) / 36 number (%) 11 (24 %) 34 (76 %)	ANOVA non-significant ($F_{(2,42)} = 0.88$; $p > .42$) Maracuillo multiple proportion test* non-significant (all $p > .05$)
Deep Nuclei Preserved Lesioned	number (%) 24 (53 %) 21 (47 %)	Maracuillo multiple proportion test non-significant (all $p > .05$)

* A MANOVA was also performed on the MNI coordinates (x, y, z) of the center of gravity of the lesions. Results failed to reveal any difference between age-groups ($F_{(6,80)} = 1.57$, $p = .17$)

Supplementary table 2. Summary of statistical results. Significant differences are highlighted in bold ($p < .05$). Duncan significant difference test was used for post-hoc comparisons (Winer, 1971). Interactions between factors were not detailed but summarized within a single line (interactions) considering that no interaction reached significance level. hrQoL: Health-related Quality of Life; PS: Performance Status; ICARS: International Cooperative Ataxia Rating Scale; Pegboard Purdue Test: PegBoard; FSIQ: Full Scale Intelligence Quotient.

			hrQoL	**PS**	**ICARS**	**PegBoard**	**FSIQ**
Age at surgery	ANOVA		**$F_{(2,31)}$= 4.50 p= .019**	**$F_{(2,31)}$= 3.68 p= .037**	**$F_{(2,31)}$= 4.62 p= .018**	**$F_{(2,31)}$= 3.34 p= .048**	**$F_{(2,31)}$= 4.39 p= .021**
	post-hoc	*young vs middle*	***p = .008***	***p = .026***	***p = .006***	***p = .022***	***p = .010***
		young vs old	***p = .026***	***p = .043***	***p = .022***	***p = .019***	***p = .023***
		middle vs old	*p = .533*	*p = .747*	*p = .498*	*p = .862*	*p = .671*
Nuclei preserved	ANOVA		$F_{(1,31)}$= 1.46 p= .236	**$F_{(1,31)}$= 5.60 p= .024**	**$F_{(1,31)}$= 7.97 p= .008**	**$F_{(1,31)}$= 16.00 p= .0004**	**$F_{(1,31)}$= 16.66 p= .0003**
Radiation therapy	ANOVA		**$F_{(1,31)}$= 4.34 p= .045**	$F_{(1,31)}$= 1.31 p= .261	$F_{(1,31)}$= 2.43 p= .130	**$F_{(1,31)}$= 4.84 p= .035**	$F_{(1,31)}$= 0.02 p= .894
Lesion volume	ANOVA		$F_{(1,31)}$= 2.99 p= .094	$F_{(1,31)}$= 0.46 p= .502	$F_{(1,31)}$= 0.01 p= .935	$F_{(1,31)}$= 0.58 p= .451	$F_{(1,31)}$= 3.61 p= .067
Delay to assessment	ANOVA		$F_{(1,31)}$= 0.41 p= .526	$F_{(1,31)}$= 0.41 p= .525	$F_{(1,31)}$= 0.39 p= .535	$F_{(1,31)}$= 0.01 p= .932	$F_{(1,31)}$= 1.60 p= .216
Interactions	ANOVA		all ps > .335	all ps > .240	all ps > .245	all ps > .355	all ps > .130

Supplementary figure 1. Regional distribution of lesions for each age-group of the patient sample. Lesions have been mapped on cerebellar horizontal sections using the SUIT Atlas (level of sections is shown by the blue line on the right sagittal view). For the sake of legibility, all left-sided lesions have been flipped to the right. The regional frequency of brain lesions in each cerebellar area is expressed by the color scale.



References

Catsman-Berrevoets C, Patay Z. Cerebellar mutism syndrome. In: Manto M, Huisman T, editors. Handbook of Clinical Neurology: Elsevier; 2018. p. 273-88.

Catsman-Berrevoets CE, Aarsen FK. The spectrum of neurobehavioural deficits in the Posterior Fossa Syndrome in children after cerebellar tumour surgery. Cortex 2010; 46: 933-46.

Lafayette Intruments. Purdue Pegboard Test, User Instruction Manual. 2012.

Lanier JC, Abrams AN. Posterior fossa syndrome: Review of the behavioral and emotional aspects in pediatric cancer patients. [Review]. Cancer 2017; 123: 551-9.

Tamburrini G, Frassanito P, Chieffo D, Massimi L, Caldarelli M, Di Rocco C. Cerebellar mutism. [Review]. Childs Nerv Syst 2015; 31: 1841-51.

Vane J, Motta R. Test response inconsistency in young children. J Sch Psychol 1980; 18: 25-33.

Winer BJ. Statistical principles in experimental design. New York: Mc Graw-Hill; 1971.