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Brief Communications

Ipsidirectional impairment of prism adaptation after unilateral lesion of anterior cerebellum

Abstract—In a patient with damage of the left cerebellar cortex (SCA territory), the authors tested four combinations of exposure to optical shift (leftward prisms, right hand; rightward prisms, right hand; leftward prisms, left (ataxic) hand; rightward prisms, left (ataxic) hand). He adapted to rightward but not leftward prisms, independent of which hand was used during exposure. This suggests a role of anterior cerebellar cortex in the computation or compensation of ipsidirectional visual error.

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L. Pisella, PhD; Y. Rossetti, MD; C. Michel, PhD; G. Rode, MD; D. Boisson, MD; D. Pélisson, PhD; and C. Tilikete, MD;

Cerebellar dysfunction classically affects the accuracy of the ipsilateral (ataxic) arm, causing kinetic tremor for slow movements and hypermetric errors for fast goal-directed movements.¹ Lesion studies have suggested that the cerebellum also plays a crucial role in adaptation to prisms shifting laterally the visual field,² especially the posterior cerebellar cortex.^{3,4} The prism-adaptation procedure involves visuomanual pointing with the hand and targets visible through displacing prisms (exposure). The potential link between the ipsilateral motor impairment and the prism-adaptation impairment remains ambiguous: Limb inaccuracy can occur with no effect on prism-adaptation ability but prism-adaptation impairment has been observed with the ataxic hand after unilateral lesion of the posterior cerebellum.^{3,4} The cerebellum receives limb proprioceptive and corollary discharge information and also visual input from the mossy fibers that could serve as an error signal.⁴ However, the direction of the visual error with respect to the lesion side has not been considered as a crucial factor for the ability to adapt to prisms after unilateral cerebellar damage.

The aim of this study was to study the lateralization of cerebellar function in prism adaptation in a patient with unilateral lesion of the anterior cerebellar cortex. We measured the after effects of prism adaptation in the four conditions of exposure combining the potential effects of the hand used (left hand

vs right hand) and of the direction of the prismatic deviation (leftward prisms vs rightward prisms).

Methods. This study was conducted with the informed consent of the patient, in agreement with French law (March 4, 2002) and the Declaration of Helsinki.

Case report. A 42-year-old man was admitted for acute vertigo and ataxia. Both the clinical and MRI pictures (figure 1) were compatible with a stroke in the territory of the left superior cerebellar artery (SCA).⁵ This was confirmed by a control MRI performed 4 months later. At the time of the testing, 2 months post-stroke, clinical examination disclosed a persistent left superior limb ataxia including slight dysmetria and adiadochocinesia. Visual field, visual acuity, and oculomotor examinations were normal.

Design. The testing included a pretest, a prism-adaptation procedure, and a posttest (details previously reported^{6,7}). The four conditions of 15-degree prism-adaptation exposure were performed in the following order: leftward prisms, right hand (day 1); rightward prisms, right hand (day 3); leftward prisms, left hand (day 6); rightward prisms, left hand (day 7). The comparison of the end points in the pretest and posttest allowed quantification of the magnitude of adaptive after effects.

Statistics. A factorial three-way analysis of variance was performed with session (pre vs post), hand (left vs right), and prism direction (leftward vs rightward) as independent variables and open-loop target pointing error (degree) with exposed hand as the dependent variable. Scheffé's post hoc tests were then used to compare pairs of conditions.

Results. *Pointing accuracy and variability.* Mean accuracy and error variability did not appear different for the right and left (ataxic) hands (see pretests, figure 2). Indeed, 1) the movement speed spontaneously adopted by the subject elicited kinetic tremor instead of hypermetric errors and 2) kinetic tremor has been shown to be reduced in the open-loop condition.⁸ During exposure, the pointing movements were accurate from the beginning, prismatic deviation eliciting curved trajectories as often when visual feedback is available.

Adaptive after effects. Presence of adaptation is demonstrated by significant difference between pointing error in the pretest and posttest (figure 2). Based on a three-way interaction session $\times$ prisms $\times$ hand ($F(1,72) = 10.8$; $p < 0.01$), Scheffé's post hoc tests were performed and showed a lack of adaptation to leftward prismatic deviation (right-hand exposure: 1.1 degrees of adaptive after effects, left hand: 0.9 degree; both $p > 0.3$) and adaptation to rightward prismatic deviation (right-hand exposure: 8.2 degrees

From Espace et Action, UMR Unité 534 (Drs. Pisella, Rossetti, Michel, Rode, Boisson, Pélisson, and Tilikete), INSERM, Université Claude Bernard Lyon-I, Institut Fédératif des Neurosciences Lyon, Lyon, France; Hospices Civils de Lyon (Drs. Rossetti, Rode, Boisson, and Tilikete), Université Claude Bernard Lyon-I, Service de Rééducation Neurologique de l'Hôpital Henry Gabrielle, Service de Neuro-Ophthalmologie de l'Hôpital Neurologique, Lyon, France.

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Address correspondence and reprint requests to Dr. Laure Pisella, INSERM U534, Espace et Action, 16 avenue Lépine, 69676 Bron Cedex, France; e-mail: pisella@lyon.inserm.fr

Figure 1. The horizontal section (A) and a series of sagittal sections (B) through the patient's brain, visualized with structural MRI. The sagittal sections are presented (from bottom to top) from the median one to the most left lateral one. The lesion included culmen and lingula of the left anterior lobe of the cerebellum, superior part of the left brachium conjunctivum, and left dentate nucleus.

of adaptive after effects, left hand: 5.8 degrees; both $p < 0.000001$), irrespective of the hand used. The magnitude of after effects in normal adaptation ranges between one-third and one-half of the optical deviation.⁷

Awareness for the prismatic deviation. During the first exposure condition (day 1: leftward prisms, right hand), the patient did not make any spontaneous comment about the leftward optical deviation and correlatively showed no significant adaptation. By contrast and like healthy subjects, the patient expressed his surprise about the rightward optical deviation when performing the first pointing movements of the following exposure condition on day 3 (rightward prisms, right hand).

Discussion. This study shows the lack of adaptation specific to prism direction after lesion in the SCA territory, independent on the arm used for prism exposure. Impaired adaptation with such topography appears contradictory with a previous anatomic study³ that observed impaired adaptation with the ataxic arm in five patients with a lesion in the territory of the posterior inferior cerebellar artery (PICA) but preserved adaptation in three patients with a lesion in the SCA territory. However, these authors tested the two hands but only one (left) prismatic deviation. Consequently, only one among their

Figure 2. Columns represent the means and SDs of the final errors (degrees) for the 10 open-loop target pointing performed with the exposed hand and without goggles before (pretest session) and after (posttest session) each of the four combinations of prismatic deviation and hand exposure in the patient. The pointing error carried a minus sign for leftward and a plus sign for rightward errors. The mean pointing values are significantly modified between the pretest and the posttest in the two conditions of rightward prismatic deviation, attesting for prismatic adaptation. By contrast, they are not modified significantly for the conditions of leftward prismatic deviation.

three patients with SCA topography was tested with prisms deviating in the ipsilesional direction. Contrary to the present case, this patient (WD) with a lesion in the left cerebellar hemisphere showed adaptation to left-deviating prisms. Note that WD also presented a lesion in the PICA territory that was asymptomatic for prism adaptation with the ataxic arm, suggesting that his SCA lesion might also be asymptomatic for an unknown reason. The present case does not invalidate the previous findings of impaired prism adaptation specific to the use of the ataxic arm after cerebellar lesions of topography different from that of our patient.^{3,4} In particular, the lack of prism adaptation was reported only with the ataxic arm in one monkey whose lesion involved the caudal part of the cerebellum (dorsal paraflocculus and uvula).⁴

A visual cerebellar lateralization is thus demonstrated here that adds to the well-known motor lateralization. The cerebellum is conceived as a sensorimotor correlation storage area that integrates the motor output (efference) and the visual error resulting from this output (visual reafference). This integration may be performed in two steps. A first integration in a spatial reference frame, independent from the arm, relies on the SCA territory. A second integration in a body reference frame, specific to the arm, relies on the PICA territory.^{3,4} According with this second integration, prism adaptation with the head fixed is known to be restricted to the exposed arm.⁷

To our knowledge, only one other anatomofunctional study has compared adaptation to rightward and leftward prismatic deviations.⁹ In this study, deficit in adaptation was observed after inactivation of the ventral premotor area in monkeys only when

vision was shifted contralesionally. Because connections between the cerebellum and the cerebral cortex are crossed, this makes a consistent cerebrocerebellar lateralized network for the computation and integration of directional visual error in prism adaptation. Further studies should similarly evaluate the implication of the temporoparietooccipital junction in this network suggested by partial results of prism adaptation after a cerebral lesion.^{6,7} Interestingly, we recently collected imaging data¹⁰ that confirm the role of the anterior part of the right cerebellar hemisphere together with the left cerebral hemisphere in the beneficial effect of adaptation to rightward prisms in hemineglect.⁶ The present case study brings the crucial information that this part of the cerebellum is necessary for prism adaptation.

Finally, the spontaneous comments of the patient during prism exposure suggested that the cerebellum is involved in one component necessary for awareness of the prismatic deviation. However, this aspect is not specific to the present case; patients with hemineglect are also unaware of the prismatic deviation but largely adapt to right prisms.⁶ We suggest that the anterior cerebellum is crucial both for adaptation to and awareness of the optical deviation just because it computes the visual error signal.

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References

1. Bonnefoi-Kyriacou B, Legallet E, Lee RG, Trouche E. Spatio-temporal and kinematic analysis of pointing movements performed by cerebellar patients with limb ataxia. *Exp Brain Res* 1998;119:460–466.

2. Weiner MJ, Hallett M, Funkenstein HH. Adaptation to a lateral displacement of vision in patients with lesions of the central nervous system. *Neurology* 1983;33:766–772.
3. Martin TA, Keating JG, Goodkin HP, Bastian AJ, Thach WT. Throwing while looking through prisms. I. Focal olivocerebellar lesions impair adaptation. *Brain* 1996;119:1183–1198.
4. Baizer JS, Kralj-Hans I, Glickstein M. Cerebellar lesions and prism-adaptation in macaque monkeys. *J Neurophysiol* 1999;81:1960–1965.
5. Barth A, Bogousslavsky J, Regli F. The clinical and topographic spectrum of cerebellar infarcts: a clinical-magnetic resonance imaging correlation study. *Ann Neurol* 1993;33:451–456.
6. Rossetti Y, Rode G, Pisella L, et al. Hemispatial neglect and prism-adaptation: when adaptation to rightward optical deviation rehabilitates the neglected left side. *Nature* 1998;395:166–169.
7. Pisella L, Michel C, Gréa H, Tilikete C, Vighetto A, Rossetti Y. Preserved prism-adaptation in bilateral optic ataxia: Strategic versus adaptive reaction to prisms. *Exp Brain Res* 2004;156:399–408.
8. Haggard P, Jenner J, Wing A. Coordination of aimed movements in a case of unilateral cerebellar damage. *Neuropsychologia* 1994;32:827–846.
9. Kurata K, Hoshi E. Reacquisition deficits in prism-adaptation after muscimol microinjection into the ventral premotor cortex of monkeys. *J Neurophysiol* 1999;81:1927–1938.
10. Luaute J, Michel C, Rode G et al. Cerebral plasticity induced by prismatic adaptation in neglect patients. A PET study. Presented at the 3rd World Congress in Neurological Rehabilitation, Venice, 2002.

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