The Role of the Cerebellum in Dynamic Changes of the Sense of Body Ownership: A Study in Patients with Cerebellar Degeneration

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Abstract

■ The sense of the body is deeply rooted in humans, and it can be experimentally manipulated by inducing illusions in at least two aspects: a subjective feeling of ownership and a proprioceptive sense of limb position. Previous studies mapped these different aspects onto anatomically distinct neuronal regions, with the ventral premotor cortex processing subjective experience of ownership and the inferior parietal lobule processing proprioceptive calibration. Lines of evidence suggest an involvement also of the cerebellum, but its precise role is not clear yet. To investigate the contribution of the cerebellum in the sense of body ownership, we applied the rubber-hand illusion paradigm in 28 patients affected by neurodegenerative cerebellar ataxia, selectively involving the cerebellum, and in 26 age-matched control participants. The rubber hand illusion is established by synchronous stroking of the participants' real unseen hand and a visible fake hand. Short asynchronous stroking does not bring about the illusion. We tested the subjective experience of the illusion, evaluated through a questionnaire and the proprioceptive drift of the real unseen hand toward the viewed rubber hand. In patients with cerebellar ataxia, we observed reduced sense of the subjective illusory experience specifically after synchronous stroking. In contrast, the proprioceptive drift was enhanced after synchronous and after asynchronous stimulation. These findings support the contention that the mechanisms underlying the presence of the illusion and the proprioceptive drift may be differently affected in different conditions. Impairment of the subjective sense of the illusion in cerebellar patients might hint at an involvement of cerebellar-premotor networks, whereas the proprioceptive drift typically associated with synchronous stroking appears to rely on other circuits, likely involving the cerebellum and the parietal regions. ■

INTRODUCTION

The sense of control and ownership of our body is so automatic and familiar that it is hardly ever questioned. However, in some pathological conditions (like in asomatognosia), the patients do not recognize their own limbs as part of their body (Babinski, 1914). Recent research has begun to investigate how the sense of body arises or is impaired. The rubber hand illusion (RHI; Botvinick & Cohen, 1998) allows to manipulate the experience of ownership of the body experimentally. The RHI is established by synchronous stroking of the participants' unseen hand and a visible artificial hand. After a few seconds of stroking, the individual has the illusion that the artificial hand belongs to his own body (Botvinick & Cohen, 1998). The RHI arises from a multisensory stimulation in which visual, tactile, and proprioceptive information is integrated and combined with the participant's own body representation (Tsakiris, 2010). In this situation, the vision of the artificial hand being stroked induces the need to reconcile the mismatch between the seen and the felt location of the stroking by recalibrating one's own limb position toward the rubber hand (for a review, Ramakonar, Franz, & Lind, 2011). This illusion allows investigating two different aspects of body ownership: the subjective feeling of ownership and a proprioceptive sense of limb position. The neural underpinnings of these two aspects rely on different brain regions: The ventral premotor cortex and its connections are thought to process the illusory feeling (Zeller, Gross, Bartsch, Johansen-Berg, & Classen, 2011; Ehrsson, Spence, & Passingham, 2004), whereas the inferior parietal lobule (Kammers et al., 2009), the right posterior insula, and the frontal operculum (Tsakiris, Hesse, Boy, Haggard, & Fink, 2007) process the drift.

The cerebellum is involved in multisensory processing and receives information by many sensory modalities, including vision and proprioception (Hagura et al., 2009; Glickstein, 2000; Donga & Dessem, 1993). Furthermore, it seems to be crucially involved in the sense of body ownership (Ehrsson, Holmes, & Passingham, 2005; Ehrsson et al., 2004), although its precise and causal contribution

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remains unknown. In healthy participants, cerebellar activation correlates with the ownership ratings, indicating a role of this structure in the illusory feeling (Ehrsson et al., 2004, 2005). In addition, activation in the cerebellum was found before the illusion onset, and this was suggested to be related to a recalibration process that precedes the illusion (Ehrsson et al., 2004). However, whether the cerebellum is directly involved in the proprioceptive drift, typically occurring during the RHI, remains an open question, despite the evidence showing that the cerebellum is involved in processing kinaesthetic information and in updating limb position (Roth, Synofzik, & Lindner, 2013; Hagura et al., 2009; Proske & Gandevia, 2009; Naito et al., 2005) and that damages to this structure result in poor limb coordination, such as ataxia and dysmetria (Bastian, 2011).

To investigate the specific and causal role of the cerebellum in the sense of body ownership, we studied the RHI in a large sample of patients with a rare disease characterized by pure cerebellar neurodegeneration, measuring both the subjective illusory feeling of ownership and the proprioceptive drift. Studying patients with selective cerebellar pathology, without involvement of the motor and sensory systems, may help to infer the causal contribution of the cerebellum to the specific subcomponents of the sense of body ownership. On the basis of the correlative observations of cerebellar activation linked to ownership feelings (Ehrsson et al., 2004, 2005) and on the known role of the cerebellum in processing proprioceptive information (Hagura et al., 2009; Proske & Gandevia, 2009), we hypothesize that both subcomponents of body ownership illusion may distinctly be affected in degenerative ataxia.

METHODS

Participants

We recruited 28 patients (9 women and 19 men, mean age = 49.32 ± 14.15 years) affected by pure neurodegenerative cerebellar ataxia, without involvement of the motor and the sensory systems (such as somatosensory and visual systems), from the outpatient clinic of the Neurology Institute Carlo Besta in Milan, Italy. All the patients presented symptoms and signs of cerebellar dysfunction, such as gait ataxia, four-limb dysmetria, mild dysarthria, and mild lateral gaze-evoked nystagmus. All the patients included in the study presented diffuse cerebellar atrophy at MRI. Neurophysiological investigations, including electromyography, peripheral nerve conduction, somatosensory and motor-evoked potentials of the four limbs, and visual-evoked potentials did not disclose any abnormality. No patient had cognitive impairment at clinical evaluation.

Twelve participants of 28 had a positive family history for ataxia, and 16 of 28 were sporadic. In seven participants with positive family history, a genetic diagnosis was identified (five participants from three families were SCA28, and two participants from one family were SCA15). In all the other participants, both sporadic and with family history, we did not identify a genetic cause of the disease. Genetic tests for SCA1-SCA2-SCA3-SCA6-SCA7-SCA17-DRPLA-SCA15-SCA28 were performed, and all the secondary causes of cerebellar ataxia were excluded, such as metabolic alterations, vitamin E deficiency, and malabsorption.

All patients underwent neurological examination, and the severity of ataxia was evaluated by using the Scale for the Assessment and Rating of Ataxia (SARA; Schmitz-Hubsch et al., 2006). This clinical scale comprises a total of eight items, three of them being strictly related to the evaluation of the upper limbs coordination, that is, finger chase, finger-to-nose test, and fast alternating hand movements. Disease duration ranged from 1 to 52 years (mean = 20 ± 13.4 years). Further details are presented in Table 1.

We applied the same task also to 26 age-matched healthy participants (13 women and 13 men, mean age = 49.3 ± 17.7 years). Age was not significantly different between the two groups (independent samples *t* test, $t(52) = 0.003$, $p = .997$). All participants were right-handed (Edinburgh Handedness Inventory; Oldfield, 1971). Patients have been informed on the nontherapeutic nature of the test, and local ethical committee approval was obtained.

Procedure

The procedure was performed as described previously (Fiorio et al., 2011). In brief, a realistic reproduction of a hand was placed on a table, directly in front of the participant and at a fixed distance from the participant's real hand (20 cm medial to the real hand). The rubber hand was always to the left of the participant's right hand or to the right of the participant's left hand. Only the rubber hand was visible, whereas the participant's own hand was placed on the table and covered with a black cloth. The participant was asked to focus on the rubber hand, while two paintbrushes were used to stroke both the rubber hand and the participant's hidden hand either synchronously or asynchronously for 2 min, in separated sessions. The illusion is expected to occur only following synchronous stroking, whereas identical asynchronous stroking should have no effect (Botvinick & Cohen, 1998). Both hands were tested in all participants in a counterbalanced order, and each experimental condition (synchronous and asynchronous) was performed once in each hand. Before and after each stimulation session, participants had to indicate the position of their index finger by reporting the corresponding number on a ruler positioned in front of them. The ruler onset and offset numbers changed every time to avoid response biases. During the proprioceptive judgment, the rubber hand and the participants' hand were out of view (Figure 1).

Table 1. Demographic and Clinical Information about the Patients Group

n	*Sex*	*Age*	*Duration (years)*[a]	*Severity*[b]	*Type*[c]
1	F	44	8	10.5	Sporadic
2	M	64	30	11	Positive familiar history
3	M	27	15	6	Positive familiar history
4	F	56	35	10	Sporadic
5	M	63	8	14	Sporadic
6	F	49	27	9	SCA28
7	M	48	30	13	SCA28
8	M	49	30	12	Sporadic
9	F	44	28	14	Sporadic
10	M	60	12	11	Sporadic
11	F	44	7	2	Sporadic
12	M	73	36	31	Sporadic
13	M	51	11	6	Positive familiar history
14	F	35	8	8	Sporadic
15	M	72	52	11	SCA28
16	M	64	44	15	SCA28
17	M	37	19	8	SCA28
18	M	51	10	11	SCA15
19	M	23	4	2	SCA15
20	F	47	32	9	Sporadic
21	F	34	14	12	Sporadic
22	M	48	8	5.5	Sporadic
23	M	22	1	6.5	Sporadic
24	M	69	29	16	Sporadic
25	M	33	13	10	Sporadic
26	M	63	6	5	Sporadic
27	F	57	32	10	Positive familiar history
28	M	54	10	4	Positive familiar history

[a]Years from disease onset.

[b]Total severity score at the SARA.

[c]SCA28 and SCA15 = definite genetic mutation; Positive familiar history = familiarity without definite genetic mutation; Sporadic = no familiarity and no genetic mutation.

After the proprioceptive judgment, participants were asked to rate on a numerical rating scale the degree of agreement or disagreement (from 0 = *completely disagree* to 10 = *completely agree*) with nine sentences assessing the subjective experience of feeling ownership over the rubber hand (adapted from Botvinick & Cohen, 1998). More precisely, three statements are thought to be directly representative of the presence of the illusion (Botvinick & Cohen, 1998), addressing illusory touch and feeling of ownership. In particular, Statement 1 (S1) refers to an illusory localization of touch ("It seemed as if I were feeling the touch of the paintbrushes in the location where I saw the rubber hand touched"), S2 refers to a causal link between vision and touch ("It seemed as though the touch I felt was caused by the paintbrushes touching the rubber hand"), and S3 more directly refers to the illusory feeling of ownership ("I felt as if the rubber hand was my own hand"). Conversely, the other six statements were only inserted as catch trials (Botvinick & Cohen, 1998) and will not be further analyzed (S4: "It felt

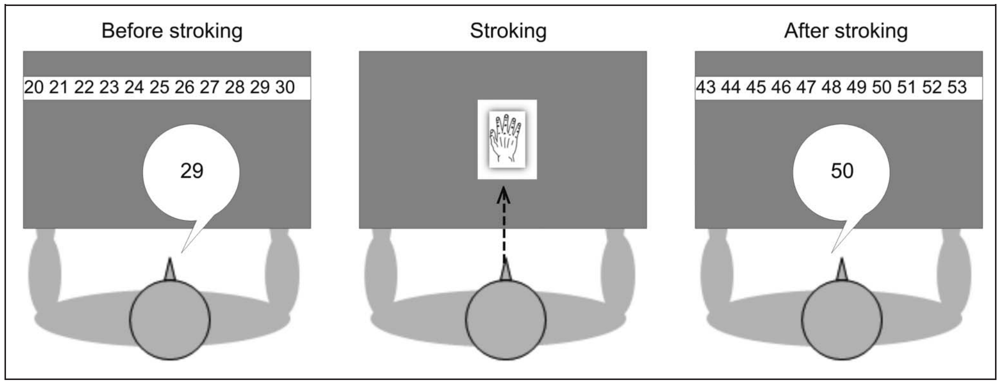

Figure 1. Time line of the experimental sessions. Before stroking, participants had to judge the position of their index finger by verbally reporting the corresponding number on a ruler positioned in front of them. Participants' hands were out of sight. During stroking, participants could see only the rubber hand in front of them, and they were touched on their own unseen hand, either synchronously or asynchronously. After stroking, participants had to report again the number on the ruler corresponding to the position of their index finger. Following synchronous stroking, there is usually a drift in the perceived position of the hand toward the position previously occupied by the rubber hand. The onset of the ruler was changed at each measurement to avoid response biases.

as if my hand were drifting toward the rubber hand"; S5: "It seemed as if I might have more than one hand or arm"; S6: "It seemed as if the touch I was feeling came from somewhere between my own hand and the rubber hand"; S7: "It felt as if my hand were turning 'rubbery'"; S8: "It appeared as if the rubber hand were drifting towards my hand"; S9: "The rubber hand began to resemble my own hand"). The sentences were read aloud by the experimenter in a randomized order of presentation across participants.

Data Handling and Analysis

Severity scores at the three subscales of the SARA (finger chase, finger-to-nose test, and fast alternating movements) were analyzed comparing the left and the right limb by means of paired-samples *t* tests.

Judgments given to the three statements of the questionnaire strictly related to the illusory localization of touch (S1), to the illusory vision–touch causal link (S2), and to the illusory feeling of ownership (S3) have been analyzed by means of mixed design ANOVAs with Group (cerebellar patients and control participants) as between-participant factor and Stroking (synchronous vs. asynchronous) and Side (right vs. left hand) as within-participant factors.

To compute the proprioceptive drift, we subtracted the proprioceptive judgment regarding the hand position after stroking (final) from the proprioceptive judgment before stroking (baseline). This difference represents the "proprioceptive drift," that is the proprioceptive displacement of the real hand toward the rubber hand (Tsakiris & Haggard, 2005). Because the drift could occur either toward or away from the rubber hand, we decided not to consider the absolute value of the drift, but the mean value computed by taking into account also the drift direction. Data were analyzed by means of a mixed-design ANOVA with Group as between-participant factor and Stroking and Side as within-participant factors. The Spearman correlation coefficient was applied to assess any correlation between severity of disease in the group of cerebellar patients and the proprioceptive drift after the synchronous and the asynchronous stroking.

Post hoc comparisons have been made by means of *t* tests applying the Bonferroni correction for multiple comparisons where necessary. In all the analyses, $p < .05$ were considered significant.

RESULTS

Clinical and demographic information of patients is provided in Table 1. Total mean ataxia severity score was 10.1 ± 1.1 (mean ± *SEM*; Table 1). On average, severity scores at the finger chase were somewhat higher for the left (1.25 ± 0.13) than for the right (1.04 ± 0.14) limb (paired samples *t* test, $t(27) = -2.7$, $p = .011$). Similarly, also the scores at the finger-to-nose test were somewhat higher for the left (0.82 ± 0.07) than for the right (0.61 ± 0.09) limb (paired samples *t* test, $t(27) = -2.3$, $p = .031$). Hence, a stronger impairment localized on the left limb was found in our sample regarding these two items. Scores were comparable for the left and the right limb in the fast alternating hand movements (left limb: 0.82 ± 0.12, right limb: 0.82 ± 0.13; $t(27) = 0$, $p = 1$). By averaging the three subscores, a tendency toward significance remained, with the left limb (0.97 ± 0.08) being numerically more impaired (paired samples *t* test, $t(27) = -2.02$, $p = .053$) than the right limb (0.83 ± 0.09). On clinical examination, all the patients presented with overshooting in the evaluation of dysmetria.

Questionnaire Ratings Related to Illusory Body Ownership Feeling

The factor Stroking was significant in the first three statements: S1-illusory localization of touch, $F(1, 52) = 89.87$, $p < .001$; S2-illusory vision–touch causal link, $F(1, 52) = 39.79$, $p < .001$; and S3-illusory feeling of ownership, $F(1, 52) = 34.48$, $p < .001$. This effect was because of higher scores after synchronous (S1: 7.3 ± 0.5; S2: 5.5 ± 0.5; S3: 3.4 ± 0.5) than asynchronous stroking

(S1: 2.7 ± 0.5; S2: 2.0 ± 0.4; S3: 1.1 ± 0.3). This finding only suggests that the paradigm was suitable to induce the experience of ownership after synchronous and not after asynchronous stroking. It does not inform, however, on the potential differences between the two groups. The factor Group was significant only in S3-illusory feeling of ownership, $F(1, 52) = 7.75$, $p = .007$, because of overall higher scores given by control participants (3.2 ± 0.5) than patients (1.3 ± 0.5), whereas it was not significant in S1-illusory localization of touch ($p = .282$) and in S2-illusory vision–touch causal link ($p = .108$). Again, this finding does not inform about group differences that are specific to the illusion. More interestingly, the interaction Group × Stroking was significant in S2-illusory vision–touch causal link, $F(1, 52) = 7.77$, $p = .007$, and in S3-illusory feeling of ownership, $F(1, 52) = 5.36$, $p = .025$, but not in S1-illusory localization of touch, $F(1, 52) = 1.92$, $p = .172$. Post hoc comparisons revealed that control participants gave significantly higher scores in S2-illusory vision–touch causal link (6.9 ± 0.6) and S3-illusory feeling of ownership (4.9 ± 0.7) than cerebellar patients (S2-illusory vision–touch causal link: 4.1 ± 0.7; S3-illusory feeling of ownership: 2.0 ± 0.6) only after synchronous stroking (S2: $p = .006$; S3: $p = .004$), whereas no difference between the two groups emerged in S1-illusory localization of touch (controls: 7.4 ± 0.7; patients: 7.2 ± 0.7, $p = .833$). These findings hint at a specific reduction of the illusory causal link between the seen and the felt touch (S2) arising after synchronous stroking and more importantly to a reduction in the illusory feeling of ownership (S3) in cerebellar patients compared with control participants. Interestingly, the illusory localization of touch (S1) appeared to be preserved in cerebellar patients. Moreover, the mean scores of healthy controls in the current study are in line with those of previous studies conducted by our group (Fiorio et al., 2011) and other groups (Ionta, Sforza, Funato, & Blanke, 2013; Guterstam, Petkova, & Ehrsson, 2011), using similar scales and stimuli. The triple interaction Group × Stroking × Side was not significant (S1: $p = .296$; S2: $p = .526$; S3: $p = .357$). A display of the results can be found in Figure 2.

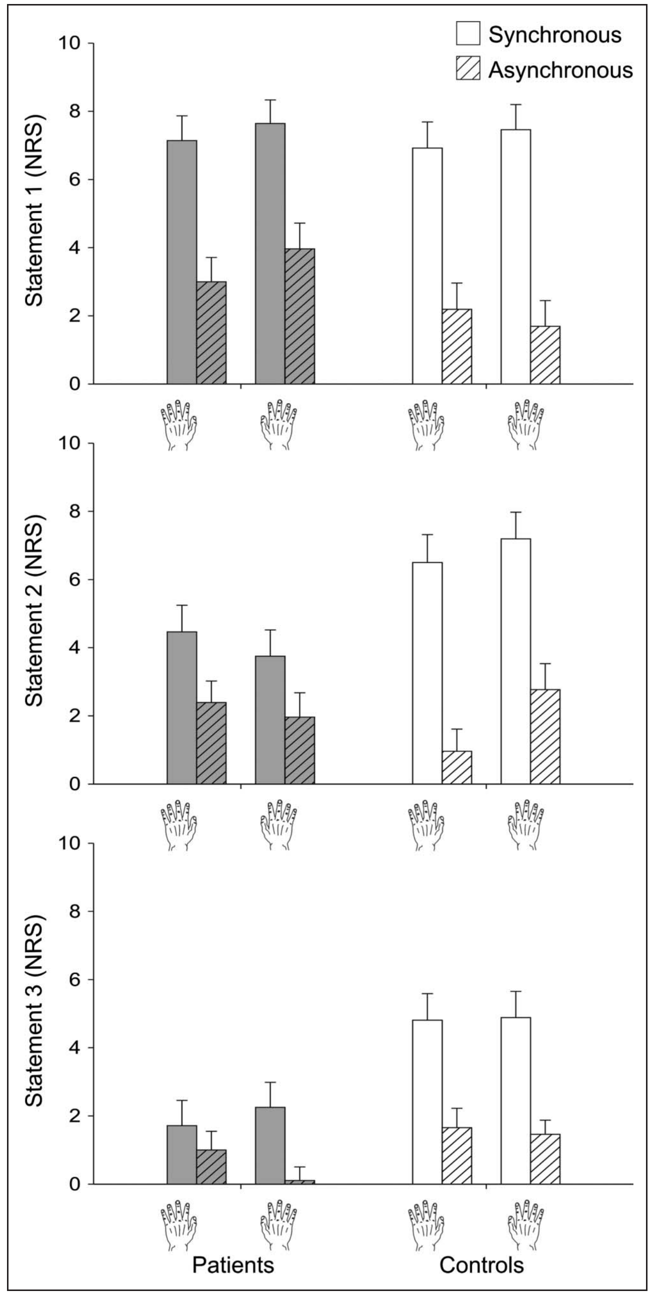

Figure 2. Questionnaire ratings of the two groups on the left and right hands after synchronous and asynchronous stroking in the three statements related to the subjective experience of feeling ownership over the rubber hand (S1, S2, S3). Subjective ratings at S2 and S3 are higher in controls than in patients after synchronous stroking. Error bars represent standard errors.

Proprioceptive Drift

Preliminary analyses showed that before stroking the difference between the hand position reported by the participants and the actual hand position measured by the experimenter was not significantly different in the two groups (independent samples t test, right hand: $t(52) = 1.33$, $p = .189$; left hand: $t(52) = -0.35$, $p = .728$).

Results of evaluation of the proprioceptive drift are displayed in Figure 3A and B. ANOVA revealed that the factor Stroking was significant, $F(1, 52) = 13.05$, $p = .001$, because of greater proprioceptive drift after the synchronous (2.5 ± 0.33) than the asynchronous (1.11 ± 0.22) stroking. This finding suggests that the paradigm was adequate to induce more pronounced limb recalibration after synchronous than asynchronous stroking. Group was also significant, $F(1, 52) = 5.77$, $p = .020$, because of greater drift in patients (2.3 ± 0.27) than controls (1.32 ± 0.29). This finding suggests that in general cerebellar patients presented more proprioceptive displacement than control participants, independent from the stroking condition (synchronous or asynchronous). The other factors and interactions, in particular the interaction Group × Stroking ($p = .511$) and the triple interaction Group ×

Stroking × Side (p = .716) were not significant, suggesting that the enhanced proprioceptive drift presented by cerebellar patients might be a general effect of the cerebellar degeneration and not specifically related to the RHI.

In the group of patients, no significant correlation was found on either hand between the severity of ataxia and the amount of drift after synchronous (right hand: Spearman's rho = 0.171, p = .385; left hand: Spearman's rho = 0.157, p = .425) or asynchronous stroking (right hand: Spearman's rho = −0.262, p = .178; left hand: Spearman's rho = 0.142, p = .472), indicating that the enhanced proprioceptive drift was unrelated to the severity of disease.

DISCUSSION

The results of this study show that patients affected by pure cerebellar disease exhibited an abnormal pattern of behavioral response on the RHI paradigm. Although the subjective feeling of the illusion was weakened, the proprioceptive drift was present and indeed enhanced. These observations have important implications for the neurobiological mechanisms underlying the RHI.

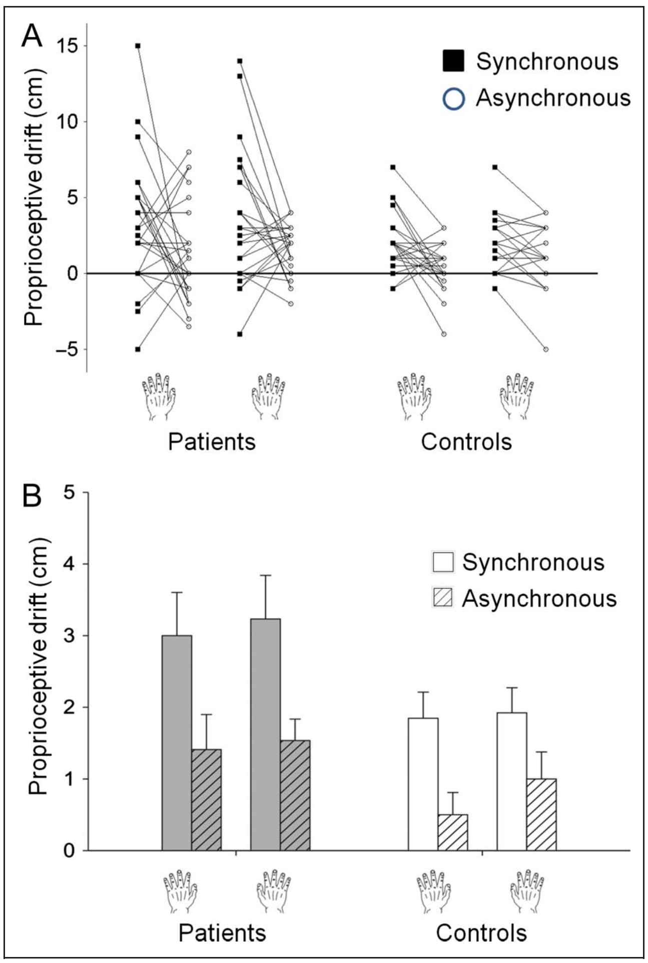

Figure 3. (A) Individual values of proprioceptive drift of the left and right hand toward the rubber hand, in patients and controls. Black squares represent the drift after synchronous stroking and white circles after asynchronous stroking. (B) Mean proprioceptive drift of the left and right hand toward the rubber hand. The group of patients (gray bars) presents overall higher drift compared with control participants (white bars). Error bars represent standard errors.

Illusory Feeling

Impairment in the subjective feeling of the illusion, evidenced by the different scores given by control participants and cerebellar patients at statements related to the illusory causal link between vision and touch (S2) and to the illusory feeling of ownership (S3), suggests that the cerebellum is involved in this subcomponent of the RHI.

Interestingly, no difference was found between patients and controls in regard to S1 ("It seemed as if I were feeling the touch of the paintbrushes in the location where I saw the rubber hand touched"), which implies the illusory localization of touch in the spatial position where the visual stimulus is perceived. At first sight, this statement appears to be very similar to S2 ("It seemed as though the touch I felt was caused by the paintbrushes touching the rubber hand"), in that both refer to illusory touch and to a fusion of two sensory modalities, that is, vision and touch. However, whereas S1 is bound to the spatial dimension, as if vision and touch would share the same location, S2 refers to a causal link between vision and touch, as if the visual stimulus were the cause of the tactile one. Hence, we hypothesize that, although the cerebellar damage did not impair the ability to spatially combine vision and touch during the RHI, it reduced the ability to perceive a causal link between the two sensory modalities. Of note, asking whether the felt touch was caused by the seen paintbrush implies the recognition of a sequential link in which one effect (the felt touch) occurs after a cause (the seen paintbrush). Hence, the low scores of cerebellar patients at S2 could be related to a reduced ability to elaborate the temporal association between two successive sensory events (Ivry & Spencer, 2004; Richter et al., 2004; Timmann et al., 2004; Gerwig et al., 2003).

More importantly, a striking difference between patients and controls emerged for S3 ("I felt as if the rubber hand was my own hand"), which is the only one directly related to the illusory feeling of embodiment of the rubber hand. Previous neuroimaging studies implicated the bilateral ventral premotor cortex (Ehrsson et al., 2004) and the bilateral cerebellum (Ehrsson et al., 2005) in the illusory ownership feeling. The present study may suggest that an intact ventral premotor cortex is not sufficient to generate an intact illusion, a conclusion supported by a recent study indicating that disruption of the anatomical projections onto the ventral premotor cortex may generate failure of the RHI (Zeller et al., 2011). By using transneuronal retrograde tracers in the monkey brain, it has been demonstrated that the cerebellum has connections to several cortical areas (Strick, Dum, & Fiez, 2009; Dum & Strick, 2003; Dum, Li, & Strick, 2002) including, after a relay in the thalamus, the ventral premotor cortex (Ramnani, 2012; Middleton & Strick, 1998, 2000). Hence, it is possible that the cerebellar degeneration has impaired a cerebello-ventral premotor cortex connection, thus hindering the subjective experience of the illusion. Two mechanisms could be put forward to explain the relation between the reduced functioning of this circuit and the reduced experience of illusory feeling at the RHI: one related to the perception of synchrony and one related to the integration of the ongoing sensory information with the inner body model.

With regard to the first point, as suggested in previous studies (Ehrsson et al., 2004, 2005; Botvinick & Cohen, 1998), the sense of body ownership might derive from a multisensory integration of synchronous visual, tactile, and proprioceptive information. Suitable candidate areas for this multisensory integration are the ventral premotor cortex and the cerebellum (Gentile, Petkova, & Ehrsson, 2011; Ehrsson et al., 2004, 2005). Although it remains unclear whether the ventral premotor cortex is at all differently activated in cerebellar patients than in healthy controls, we suggest that the cerebellar degeneration has impaired the perception of synchrony of the sensory signals, resulting in impaired multimodal integration occurring in the cerebello-ventral premotor cortex circuit and required to generate the illusory feeling of ownership. Different lines of evidence hint at the involvement of the cerebellum in temporal elaboration of sensory events (Ivry, 1996). Activation of the posterior cerebellum (and the ventral premotor cortex) is associated with the prediction of the timing of perceptual events (O'Reilly, Mesulam, & Nobre, 2008) and, in particular, detecting temporal synchrony between multimodal sensory inputs (Bushara, Grafman, & Hallett, 2001). In patients with degenerative cerebellar ataxia, an MMN study pointed to a predominant failure in generating precisely timed perceptual expectancies (Moberget et al., 2008). Therefore, cerebellar damage through degenerative disease could have impaired the ability to perceptually synchronize the different sensory inputs deriving from the body. This assumption implies that the perception of synchrony may be a necessary condition to interpret the multimodal integration leading to the subjective feeling of ownership. This reasoning gains strong support from a recent behavioral study in healthy participants (Rohde, Di Luca, & Ernst, 2011), demonstrating that, although a proprioceptive drift could be obtained even after asynchronous stroking, the subjective feeling of ownership required synchronous stroking to occur.

With regard to the second point, according to a neurocognitive model suggested by Tsakiris (2010), the sense of ownership over the rubber hand depends not only on the integration of the ongoing synchronized visuo-tactile stimuli but also on matching them with the preexisting body representation, so as to update the body model to the new sensory information. A recent study by Roth et al. (2013) suggests that the cerebellum is strongly involved in updating sensory predictions. Hence, failure to update the current sensory signals to the inner body model because of cerebellar degeneration could be expected to finally result in reduced feeling of ownership. Again, given the documented central role of the ventral premotor cortex in the illusory feeling of ownership (Zeller et al., 2011; Ehrsson et al., 2004, 2005), it appears reasonable to speculate that correct functioning of the connections between the cerebellum and the ventral premotor cortex is required.

Proprioceptive Drift

Overall, the cerebellar patients exhibited larger proprioceptive drift than the controls. On the one hand, this finding suggests that the capacity for proprioceptive recalibration is preserved and is in line with a recent report showing that sensory recalibration in response to a misalignment between vision and proprioception (somewhat analogous to the RHI) is present in patients with cerebellar ataxia (Block & Bastian, 2012). On the other hand, however, it should be noted that the significant factors Group and Stroking and the lack of significant Group by Stroking interaction found in our study indicate that (a) cerebellar patients had overall more drift than controls, (b) the proprioceptive drift was generally greater after synchronous than asynchronous stroking, and (c) the group difference in drift was not related to a specific stroking condition (synchronous or asynchronous). The fact that patients presented overall more drift than controls suggests that the proprioceptive recalibration was possible (even if faulty), despite the cerebellar degeneration. Larger drift in the patients hints at an involvement of the cerebellum, but one that is quite distinct from the involvement in producing the illusory feeling. In cerebellar patients, a certain amount of drift was observed even after asynchronous stroking, although to a lesser extent than after synchronous stroking. The fact that asynchronous and synchronous stimulations are associated with smaller or larger proprioceptive displacements suggests that the evaluation of the relative timing of signals was at least partially retained in our cerebellar patients. We suggest that the larger proprioceptive drift associated with synchronous stimulation is likely mediated outside the cerebellum. Block and Bastian (2012) suggested that visual-proprioceptive realignment depends on brain areas entailed in the posterior parietal cortex. Also in regards to the proprioceptive drift associated with synchronous stimulation at the RHI task, it has been suggested that posterior parietal cortex allows the recalibration of the coordinate systems that results in the proprioceptive drift (Brozzoli, Gentile, & Ehrsson, 2012; Tsakiris, 2010; Makin, Holmes, & Ehrsson, 2008). The inferior parietal lobule may also be a candidate region for this function. Evidence for this can be derived from a TMS study in healthy participants revealing disruption of proprioceptive drift by stimulation of the inferior parietal lobule (Kammers et al., 2009). We propose that this specific recalibration process occurring in parietal regions is functional in cerebellar patients. The cerebellar neurodegeneration may have caused a general tendency to overrecalibrate (in a way similar to the clinical manifestation of overshooting, see below), and by virtue of the connections between the cerebellum and the parietal cortex (Clower, West, Lynch, & Strick, 2001), it may have added further shift even to the limb displacement dependent on synchronous stimulation, which is selectively elaborated in the parietal cortex (Brozzoli et al., 2012; Kammers et al., 2009; Makin et al., 2008). Hence, the cerebello-parietal connections may modulate the amount of drift, regardless of the stroking condition.

The question remains on the mechanisms contributing to the overall enhanced drift presented by cerebellar patients. One possibility is to associate the enhanced drift to the pathophysiology implicated in the clinical motor deficit. Clinically, all the patients in our study presented with the hypermetric form of dysmetria, that is, they displayed overshooting while reaching toward a target. Therefore, one might speculate that proprioceptive scaling is directly related to cerebellar dysmetria as evident in the clinical motor tests. However, severity scores were not correlated with the amount of drift. This observation suggests only an indirect relationship between the motor disorder and the amount of perceptual drift. In other words, although the enhanced drift seems to reflect the same quality of dysfunction as evident in the motor domain (both indicating overshoot, rather than a mixture of undershoot and overshoot), the amount of drift is not associated to the amount of clinical dysmetria, and this is in line with the notion that the two forms of dysmetria (cognitive and motor) derive from different underlying mechanisms or circuits. In this regard, evidence suggests that, although the anterior cerebellar lobe is mainly implicated in motor control, the posterior lobe is involved in nonmotor higher-order functions (Salmi et al., 2010; Stoodley & Schmahmann, 2010; Schmahmann, 2004). Current pathophysiological models define dysmetria of movement as caused by deficient feed-forward control in timing agonist versus antagonist activation, thus resulting in over- or undershooting (Manto et al., 2012). To explain the "cognitive dysmetria" observed in our study, we hypothesize a form of perceptual overshooting occurring during the recalibration of limb position. Namely, although in our task no movement was present, to inertly shift the real hand toward the rubber hand, a displacement of the real hand should occur during the stroking period. This covert displacement may resemble the characteristics of overt movement execution (i.e., overshooting), thus resulting in an overall enhanced drift. A qualitative inspection of Figure 3 suggests that, on average, both groups drifted in a positive direction (toward the rubber hand) even after asynchronous stroking. This might be because of a natural bias toward the central positions during fingertip position estimates (Fuentes & Bastian, 2010).

Dissecting the Subjective Feeling of Ownership and the Proprioceptive Drift

Two previous studies (Fiorio et al., 2011; Kammers et al., 2009) showed that the proprioceptive drift can be reduced in the presence of normal illusory body ownership feelings. In one study, inhibiting cortical activity of the inferior parietal lobe by TMS resulted in reduced proprioceptive drift but preserved the subjective feeling of ownership over the rubber hand (Kammers et al., 2009). A similar pattern was observed in patients with focal hand dystonia (Fiorio et al., 2011). Combined, these previous observations showed that the proprioceptive drift and illusory feeling of ownership are not strictly associated, suggesting that they are likely related to different underlying neural mechanisms and circuits. Against this background, this study provides independent and complementary evidence for dissociate mechanisms underlying the two components. As a matter of fact, the presence of the drift in our patients would discard the initial hypothesis that the cerebellum has a specific role in the recalibration of limb position associated with the RHI. That the proprioceptive drift after synchronous stroking is preserved in cerebellar patients suggests, instead, that it is not a cerebellum-dependent process but is selectively elaborated in other brain areas (e.g., the inferior parietal lobule, Kammers et al., 2009, or the posterior parietal cortex, Brozzoli et al., 2012). Conversely, the cerebellum seems to be selectively involved in the subjective feeling of ownership at the RHI, in line with a neuroimaging study (Ehrsson et al., 2005). As previously stated, perception of synchrony is fundamental for the subjective feeling of ownership, but not for the proprioceptive drift (Rohde et al., 2011) that can be automatically driven by visual dominance over somatosensation (Hagura et al., 2007, 2009; Holmes, Snijders, & Spence, 2006; Newport, Hindle, & Jackson, 2001; Pavani, Spence, & Driver, 2000; Botvinick & Cohen, 1998) and occurs independently from the illusory sense of ownership (Rohde et al., 2011; Holmes et al., 2006). Hence, failure to perceive synchronized signals impacts on the subjective feeling of ownership rather than on the proprioceptive drift. In addition, fundamental for the lack of illusory feeling of ownership in cerebellar patients could be the impairment in updating the inner body model with the ongoing synchronized sensory signals (Tsakiris, 2010).

The evidence derived from our data leads to the suggestion that the cerebellum could be differently involved in the circuits subtending the two components of the illusion: A direct casual role could be hypothesized for the cerebello-ventral premotor cortex circuit in regards to the illusory feeling of ownership, whereas an indirect and only modulatory role could be thought for the cerebello-parietal circuit in regards to the proprioceptive drift. This theoretical speculation, however, requires further studies to be experimentally confirmed. As noted above, we hypothesize that two distinct cerebellar circuits are involved in the experience of body ownership and proprioceptive drift. Following this hypothesis, one could predict that these different behavioral aspects of the RHI are differently affected by lesions in specific parts of the cerebellum. Our hypothesis would receive strong support if an ongoing study in patients with cerebellar strokes were to provide evidence for a double dissociation of both behavioral aspects.

We previously found impairment of the RHI in patients suffering from focal hand dystonia (Fiorio et al., 2011). In focal dystonia, the drift of the affected hand was reduced, whereas the illusory feeling of ownership was retained (Fiorio et al., 2011). This study shows enhanced, but not reduced, proprioceptive drift in cerebellar patients. This finding seems to indicate that if the cerebellum is involved in the pathogenesis of dystonia, as suggested by some reports (Argyelan et al., 2009), then the nature of involvement in dystonia is very different from that in cerebellar ataxia.

Concluding Remarks

In conclusion, this study has provided novel evidence that (a) the cerebellum is involved in the ownership-feeling component of the RHI; (b) the cerebellum is involved in scaling a general proprioceptive drift, unrelated to the presence of the ownership-feeling; and (c) the mechanism sustaining illusory feeling of body ownership and proprioceptive drift are distinct.

The absence of a detailed mapping of the cerebellar damage, which is only possible in focal lesion studies, does not allow us to appreciate the selective contribution of the anterior and posterior circuits to the sense of body ownership. Nevertheless, the strength of this study is that it presents data from a large number of patients affected by a rare disease, characterized by a selective damage to the cerebellum, without the involvement of the motor or sensory systems (such as somatosensory and visual systems). This reinforces the inference about the prominent role of the cerebellum in the subjective sense of body ownership.

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