

## Separate Pathways for Automatic and Intentional Visuo-Manual Reach Transformations: New Perspectives for Hemiparesia Rehabilitation Using Moving Objects

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### Abstract

Reaching implies effector and target locations to be computed and updated continuously all along the visuo-motor transformation process, before and during movement execution, aiming in making these instantaneous locations coincide spatially. So instead of a neuro-anatomical dissociation between areas devoted to motor planning versus control, there might be 1) an automatic pathway of visual-to-motor transformation which relies on a comparison at the level of oculo-centric coordinates between visual target and hand locations from multimodal sources of information and 2) intentional pathways relying on the allocentric comparison between visual locations of the hand and of the target. Converging evidence from patients with optic ataxia, neuroimaging and transcranial magnetic stimulation techniques, and investigations in primates, has led to ascribe the automatic pathway to the direct connection between the medio-dorsal occipito-parietal cortex (the caudal part of the superior parietal lobule) and the dorsal premotor cortex (and further the primary motor cortex). Studies involving patients with visual agnosia (infero-temporal cortex), Parkinson disease (basal ganglia) or neglect (inferior parietal lobule) have put forward a more diffuse putative neural substrate for the intentional visual-to-motor pathway. If most strokes affect the intentional motor function while preserving the automatic pathway of visual-to-motor transformation, we propose a new rehabilitation method for hemiparesia relying on the stimulation of the automatic pathway using moving rather than stationary objects. Preliminary data are included.

**Keywords:** Hemiparesia Rehabilitation; Rehabilitation; Transformation; Optic ataxia

### Optic Ataxia: Deficit of Visual-to-Motor Transformation Based on Which Source of Information and in Which Reference Frame?

Optic ataxia is the typical deficit for reach-and-grasp to visual objects following focal lesion of the superior parietal lobule and the intraparietal sulcus, with deficits when the healthy hand reaches in the contralesional visual field (isolated field effect) and when the contralesional hand reaches in the healthy visual field (isolated hand effect) and major deficit when they use the contralesional hand to reach into the contralesional visual field [1], in absence of primary visual (the patient can see, and describe the visual world, binocular vision is unaffected), motor (the patient can move the two arms freely) and proprioceptive (the patient can match joint angles between the two arms) deficits. Besides this combination of field and hand effects, the issue of the presence of reaching error in central vision [2] seems to be linked with the presence or absence of visual feedback from the hand (closed-loop versus open-loop conditions, respectively). Blangero et al. have observed the appearance of additional visual pointing errors in the whole space [3], when the ataxic hand points in open-loop condition (reaching toward a point of light in full darkness). Since vision of the hand can partly compensate these “hand effect” errors, we postulated that they mainly correspond to impaired localization of the

hand based on non-visual, possibly proprioceptive, signals. This interpretation was reinforced by the results of a proprioceptive pointing task showing that two unilateral optic ataxia patients were seriously impaired when pointing with their healthy hand toward their ataxic hand in the dark while maintaining central eye fixation, in absence of primary proprioceptive deficits: these patients can reproduce imposed arm postures as well as they can grasp their thumb or point to their nose [3]. The mislocalisation of the ataxic hand thus constitutes a specific “high-level” deficit in the proprioception-to-motor transformation, which can account for the “hand effect”. The computation of eye-centred proprioceptive localization has been evidenced in patients and in healthy subjects [3,4]. Accordingly, the observed reduction of reaching accuracy in absence of visual feedback of the hand could be attributed to an impaired ability to determine the position of the ataxic hand in extrapersonal eye-centred coordinates using proprioceptive information, to be compared with visual target location, also in eye-centred coordinates. Consistently, the qualitative assessment of reaching errors due to the field effect (errors observed in contralesional visual space, independently of the hand used) also reflect a deficit of visual target localization in an eye-centred reference frame: they depend on the position of the gaze [5] and do not vary with head or body orientations [6]. A recent study examined the performance of 7 unilateral optic ataxia patients reaching to visual targets displayed on a 2D matrix [7]. The error vectors produced in the contralesional field were systematically directed toward the central fixation point, and were better explained along polar coordinates

centred on the gaze than along cartesian coordinates. This error pattern of the field effect was strongly consistent and reproducible in the 7 unilateral patients of the study, confirming that optic ataxia patients express misreaching errors when an eye-centred reference frame is used to encode the movement. Optic ataxia would thus produce errors as soon as visual-to-motor transformation occurs in eye-centred coordinates [4,8] in the whole space (including central vision) when the ataxic hand is used (hand effect) in the dark and unilaterally (if the hand or the target location is encoded in the contralesional visual field) in lighting conditions [9,10].

### **Effect of Time and Instruction: Automatic versus Intentional Visual-to-Motor Transformations**

All sources of sensory information are not present immediately for visuo-manual transformation. In particular, localization of the visual target and of the hand from central vision is provided late, allowing the allocentric/relative visual localization of hand and target only at the end of motor execution, when the visible hand is approaching the visual target. This visual target-hand allocentric comparison can therefore be used to amend the trajectory only for slow movements. In fact, people rarely look at their hand and often start their reaches before to fovealise the visual target [11]. Only patients with optic ataxia, exhibiting a misreaching deficit consecutive to dorsal stream damage, have been shown to repetitively look at their hand [10] and systematically start their movement only when visual target is seen in central vision [12]. This highlights the major contribution of peripheral vision but also of visual updating processes to the goal and effector specification and the crucial role of online movement correction in reaching.

Considering the inaccuracy of peripheral vision and the inaccuracy of the primary saccade towards a peripheral target [13], Goodale et al. [14] and Pélissier et al. [15] hypothesized that the target updating at the end of the saccade allows both a secondary saccade for the foveal capture of the visual target, and a locking of the unseen hand guidance to the target [16,17]. They designed real-time psychophysical paradigm in which target was displaced unexpectedly during the primary saccade and visual reafference of the hand was provided (closed loop) or not (dynamic open loop). The experimental apparatus used in this series of studies allowed the subject to see the visual target but not the hand [17]. The major results were that: 1) no subject was able to report the target jump; 2) the gain of the primary saccade remained unchanged and the corrective saccade was modified in amplitude and direction but not delayed; 3) the hand movement was corrected toward the new target location in open-loop as well as in closed-loop condition; 4) the durations of perturbed and unperturbed reaching movements, as well as their velocity and acceleration profiles, were similar, with a single peak velocity profiles. Thus, introduction of a small artificial perturbation of target location (target jump) at the end of the primary saccade, when visual location of the target is updated from more accurate perifoveal information, is simply included in the natural visual updating process of target location relative to hand during motor execution.

In order to highlight that in response to a consciously perceived target jump the flexible automatic correction of the ongoing reaching movement is also involved and even overrides the voluntary processes under speed constraints, Pisella et al. [18] performed an experiment in which they put in conflict the demonstrated automatic visuo-manual guidance toward a target jump and the explicit instruction given to this target jump occurrence. Subjects had to point to visual targets

presented on a touch screen placed in the fronto-parallel plane and arm responses were programmed and executed in free vision. In a restricted number of trials (20%), the target could be randomly displaced a few degrees apart at hand movement onset. Since this target jump was consciously perceived, the paradigm allowed experimenters to provide different instructions to the subjects. In separate sessions, subjects had to correct their movement to compensate for the target location change ('location-go') or instead immediately stop their response in-flight ('location-stop'). Subjects produced a large number of online corrections in the 'location-go' condition, but surprisingly, also produced a significant number of inappropriate online corrections in the 'location-stop' condition. This failure to completely suppress the inappropriate response indicated that flexibility can be generated in an automatic mode that escapes conscious and voluntary processes [18]. Interestingly, in the location-go condition, movements corrected toward the new target location resulted from a mixture of fast on-line corrective processes (with movement duration in the confidence interval of unperturbed movements) and slow intentional corrective processes (implying movement lengthening). Consistently, the movements which were corrected against the instruction in the location-stop condition were only of the first type, i.e. not producing movement lengthening with respect to the confidence interval of movement duration for unperturbed trials (Figure 1).

#### **Upper panel**

In the Location-Go condition [18] the instruction is compatible with the on-line automatic guidance toward the displaced target. Subjects produced both slow and fast motor corrections (lengthening or not, respectively, the movement duration with respect to the confidence interval of unperturbed trials).

#### **Middle panel**

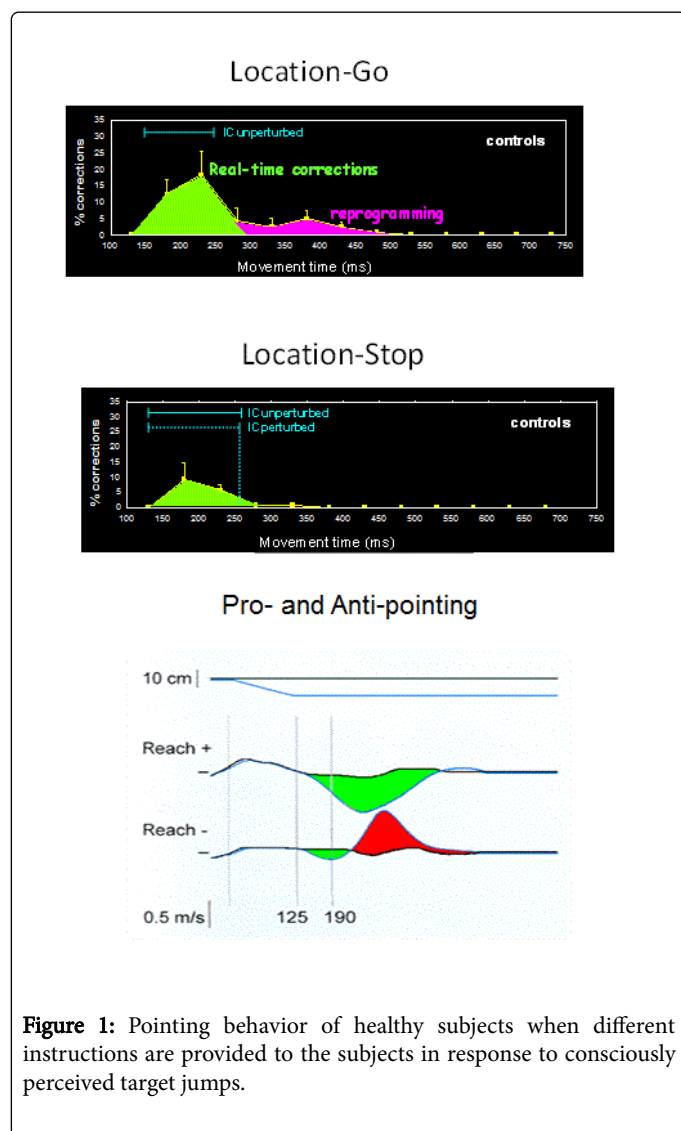
In the Location-Stop condition [18] the instruction was incompatible with the on-line automatic guidance toward the displaced target. Subjects were able to stop their ongoing movement in response to target jump only for movement durations longer than 250 ms. Faster movements did not reach the target where it was before movement onset but at the displaced target location. These motor corrections were not instructed but irrepresible, automatically elicited by the target displacement, and were all produced without in the time range of unperturbed trials (fast on-line corrections).

#### **Lower panel**

In the reach+ (Pro-pointing) and the reach- (Anti-pointing) tasks, the instruction was either to go toward the displaced target (compatible with automatic guidance) or to go away (to the other side), respectively. When the target jumps to the right (horizontal left/right position are represented on the vertical axis), the horizontal component of the trajectory is first automatically biased toward the side of the target in both reach+ and reach- tasks (trajectory correction highlighted in green with a latency of about 130 ms), followed later (with a latency longer than 200 ms) by an horizontal deviation toward the opposite side. This paradigm also allowed the authors [19] to distinguish between fast uninstructed hence automatic corrections versus slow intentional modification of ongoing movement.

A similar type of study, also addressing the question of the relationship between automatic behavior and intention, was

undertaken by Day and Lyon [19]. These authors also studied subjects' behavior in response to consciously perceived target jumps (Figure 1). In response to target jumps that could be triggered at movement onset with a low probability, subjects were required to either follow the target jump (Pro-pointing task named "Reach +") or to point at the opposite side (anti-pointing task named "Reach -"). In the former task the earliest reaction time to adjust the trajectory toward the displaced target was about 125 ms whereas in the anti-pointing task, the earliest trajectory adjustment in the opposite direction were observed later (200 ms on average), preceded by an initial automatic correction in the wrong direction (toward the target) with a similar latency as in the reach + task. So, independent on the instruction given to the subject, the earliest reaction to the target jump was to guide an automatic corrective response toward the displaced target. Then, in the anti-pointing task, slower intentional corrections could be driven away from the target displacement.



**Figure 1:** Pointing behavior of healthy subjects when different instructions are provided to the subjects in response to consciously perceived target jumps.

In sum, in most of the classical double step studies in which the target perturbation was not produced during saccadic orienting [18-21], 1) the target jump was consciously detected; 2) a mixture of automatic and voluntary corrections of ongoing movements in response to perturbations were observed (Figure 1); 3) the voluntary

corrections were characterized by late integration to the ongoing movement of additional sub-movements with their own velocity peak(s) and an increase of total movement duration; 4) conversely, the fast automatic corrections were characterized by an early, smooth and compulsory integration of target displacement to the ongoing movement, independent on the instruction provided to the subject (Go, Stop, Antipointing).

## Neurophysiological Substrates of Automatic Versus Intentional Visual-to-Motor Transformations and Rehabilitation Perspectives of the Motor Function

Triggering the target jump during saccadic orienting allowed Prablanc and colleagues (review in 2014) to cancel the consciousness of the target jump and therefore to isolate the automatic correction processes. Testing patients with optic ataxia in target jump paradigms, conversely, allowed to isolate the intentional processes: they have been shown not to be able to amend their reach on-line, and only exhibit movement corrections toward displaced visual targets when they were instructed (location-go condition), involving movement lengthening [18] and multiple peaks [21]. This led Rossetti et al. [22] to propose the reliance of the fast automatic visual-to-motor transformation on the direct connection demonstrated in monkey between area within the occipito-parietal sulcus (caudal part of the superior parietal lobule) and the dorsal premotor cortex (PMd), directly connected to the motor cortex [23]. The dorsal premotor cortex is a key structure for online visuomotor guidance [24-27]. Moreover, area V6A is a bimodal visual/somatosensory area involved in the control of both reaching and grasping movements, with a major role of gaze-centred reference frame [28].

The reliance of the fast automatic visual-to-motor pathway on the neural substrate whose damage causes optic ataxia has been further demonstrated by the preservation of fast automatic corrections in patients with neglect consecutive to damage sparing the superior parietal lobule and medial occipito-parietal junction [29], as well as in patients with lesion of the dorso-lateral prefrontal cortex [30] and in patients with Parkinson disease [31]. Conversely, Desmurget et al. also reported that patients with Parkinson disease were impaired at generating intentional corrective reaching sub-movements to large target perturbations. These latter study confirmed that the two extreme types of corrections of an ongoing goal-directed limb response (automatic, fast on-line and smooth corrections versus intentional, slow and large corrections) rely on different neural substrates [32] and indicate that the basal ganglia may be involved specifically in the second type. In addition, the findings of Thaler and Goodale [33] about a different role of visual feedback for the control of target-directed and allocentric movements is consistent with the idea that these two types of movements may be mediated by different networks, as they have distinct representations. This network fits well with the larger network involved in the generation of externally- (versus internally-) guided movements [34]. The involvement of the cerebellum in the automatic network was suggested by the neuroimaging study of Desmurget et al. [35], and the involvement of the superior colliculus by a studies in animal [36,37]. The crucial involvement of the superior parietal lobule has been demonstrated by the lesion studies in optic ataxia patients [18,21,38] and by a study of transcranial magnetic stimulation [39]. In contrast, when grasping movements have to be reprogrammed (slow intentional corrections), a related TMS approach showed that inhibition of the planned action was activated by PMv-M1 connections [40].

Another argument to say that optic ataxia errors are linked to a deficit of fast visual-to-motor transformation comes from the effect of introducing a delay between target presentation and movement onset. A series of experiments investigating delay effects in optic ataxia [41-45] have shown a remarkable paradoxical improvement of pointing performance. Moreover, if the visual target is shown at a location, then hidden for 2 seconds and shown at a displaced location when the go-signal is provided, control subjects are able to quickly (during the movement reaction time) update target location and guide their reaching straight toward the new target location, as if no target had been presented 2 seconds earlier. Patients with optic ataxia were not able to perform this fast visuo-motor updating: their movement started toward the previous, memorized, target location and was amended late during the ongoing trajectory. Conversely, patient with lesion of the infero-temporal cortex (visual agnosia patient DF) could correctly reach-and-grasp visual objects she could not describe, but lost this preserved motor ability when her action was delayed by only 2 seconds [33]. Rossit et al. [46] have also shown this pattern of impaired delayed but preserved immediate grasping in a neglect patient, whose occipito-parietal lesion spared the medio-dorsal occipito-parietal cortex but also the infero-temporal cortex.

Our interpretation is that this intentional pathway relies on the slower signals available and on the slower reference frame to compute, which is the visual-visual comparison of target and hand locations in allocentric coordinates [32,47]. The studies of the visuo-motor abilities of patient DF [33,48] have suggested that the ventral stream of visual processing (the infero-temporal cortex) is the neural substrate for visual allocentric coordinates. Moreover, it has been shown in monkey that the inferotemporal cortex projects onto the dorsal striatum and ventral pre-frontal cortex, which in turn projects on the ventral premotor cortex and the motor cortex [49,50], representing the putative slow intentional visual-to-motor pathway [51].

In sum, one can put forward that most cortical and subcortical strokes causing hemiparesia may affect the upper limb intentional motor function in various ways but preserve the automatic visual-to-motor pathway by sparing the short (probably monosynaptic) connection between parieto-occipital junction and dorsal premotor cortex [23,51]. This opens rehabilitation perspectives for hemiparesia. Indeed, fast automatic and intentional routes both converge toward the primary motor area the recruitment of the automatic visuo-motor pathway could help maintaining some muscular activity in hemiparetic patients to avoid spasticity, or it could constitute an interesting and less effortful alternative way to stimulate the recovery of hand movements following anterior damage. While classical motor neurorehabilitation methods are mainly based on the training of intentional and effortful movements [52], the potential for rehabilitation of hemi-paretic patients through the use of automatic reaching pathways stimulated by moving objects has begun to be evaluated [53].

### **Kinematic Analysis of Reach-to-Grasp Movement Before and After Rehabilitation Using Moving Objects**

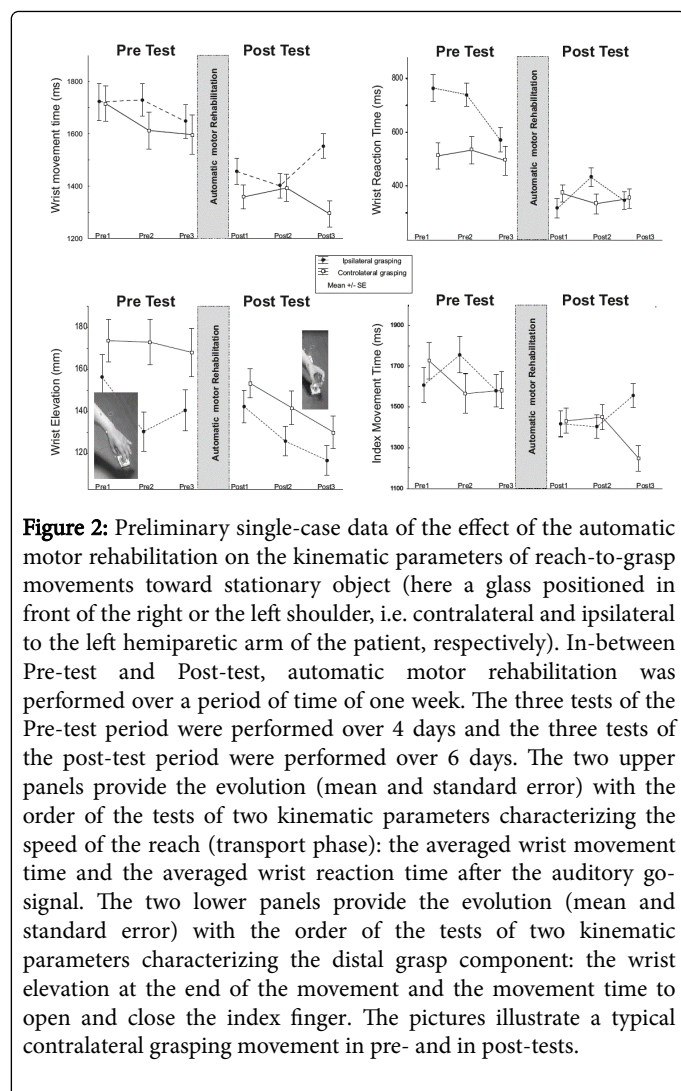
These latter experiments [18,19] have highlighted that target displacement is a sufficient condition to elicit irrepresible fast automatic visuo-manual guidance. Consequently, we decided to design different situations using target displacement in order to stimulate the preserved automatic visuo-motor pathway in patients with hemiparesia at movement initiation and at movement execution stages. First, we reproduced a target displacement at movement onset. In the two other tasks, we speeded the movement initiation. In the second

task, we presented a target in peripersonal space which is moving away from the body: the task is to reach it before it escapes from the reaching space. In the third task, we used two visual objects: the stationary one having to be reached before the moving one enters in collision to the stationary one: as soon as the subject has reached the stationary one, the movement of the other (moving) object is stopped. We implemented these three tasks with a system developed by Schenk et al. [54] allowing the experimenter to produce a great variety of real object movements along a flat-table surface, using a linear positioning system displacing a sled beneath the table surface and a magnetic coupling transferring the sled's movement to the target object on the tabletop. Preliminary results of this rehabilitation have been published in French [44,53], including a single-case who was assessed with kinematic analysis presented below in details.

The three tasks with moving objects were performed at each rehabilitation training session (five sessions performed at Day 5, Day 8, Day 9, Day 10 and Day 11, with a week-end in-between days 5 and 8). Before and after these tasks, a different clinician from the one who performed the rehabilitation sessions recorded the kinematic parameters of the reach-and-grasp movements toward stationary objects. This measure of hemiparesia was also performed in a different environment (not on the table which was used for the training) and with different objects: a glass positioned in the right or in the left hemispace (in front of the right or the left shoulder). This same assessment was performed and compared three times before (pre-test: Pre1: Day 1, Pre2: Day 3 and Pre3: Day 4, with a week-end in-between days 1 and 3) and three times after (post-test: Post1: Day 12, Post2: Day 15, Post3: Day 16, , with a week-end in-between days 12 and 15) the rehabilitation. The repetition of pre- and post-tests aimed at evaluating potential spontaneous recovery of the movement at regular time with repetition of the same gesture. Kinematic parameters characterized the duration of the transport phase (reaction time and movement time of the wrist) and its quality (as illustrated on figure 2, the more elevated is the wrist, the less functional is the grasp), and the duration of the distal grasping phase of the gesture indicated by the duration of the fingers' opening (index movement time) [55-57].

A 63-year-old right-handed man with chronic hemiparesia of the left upper limb without sensorial deficit was involved in this protocol of automatic motor rehabilitation. He initially presented left hemiplegia following a right lenticular vascular ischemic accident. Following stroke, the patient received physiotherapy and occupational therapy at the hospital. Back home, he received weekly physiotherapy. However, 15 months after stroke he suffered from spasticity on his left arm and still a severe left hemiparesia.

The first result was the feasibility of the automatic motor rehabilitation. We observed that the patient complained about spasticity and pain while performing the movements toward stationary object and therefore struggled to finish the 56 movements toward the glass required for the assessment of his motor ability (pre-test sessions). However, he could perform 126 movements by session during the rehabilitation with moving objects. In addition to the fact that the three tasks of the automatic motor rehabilitation can be taken as a game, the temporal constraint probably allowed the movements to rely on more automatic and less effortful processes. The subjective report of the patient was that the movements toward the glass were performed with less difficulty and complaint in the post-test than in the pre-test, but still with more difficulty and complaint than the three tasks of the rehabilitation sessions with moving objects.



**Figure 2:** Preliminary single-case data of the effect of the automatic motor rehabilitation on the kinematic parameters of reach-to-grasp movements toward stationary object (here a glass positioned in front of the right or the left shoulder, i.e. contralateral and ipsilateral to the left hemiparetic arm of the patient, respectively). In-between Pre-test and Post-test, automatic motor rehabilitation was performed over a period of time of one week. The three tests of the Pre-test period were performed over 4 days and the three tests of the post-test period were performed over 6 days. The two upper panels provide the evolution (mean and standard error) with the order of the tests of two kinematic parameters characterizing the speed of the reach (transport phase): the averaged wrist movement time and the averaged wrist reaction time after the auditory go-signal. The two lower panels provide the evolution (mean and standard error) with the order of the tests of two kinematic parameters characterizing the distal grasp component: the wrist elevation at the end of the movement and the movement time to open and close the index finger. The pictures illustrate a typical contralateral grasping movement in pre- and in post-tests.

Figure 2 provides the mean and standard error of the kinematic parameters of the movements successfully guided toward the glass for the three pre- and the three post-tests. These kinematic parameters were analyzed with a factorial ANOVA with three factors: the test (Pre versus Post), the order of the tests (1, 2 or 3) and the side where the glass was positioned (ipsilateral or contralateral to the hemiparetic arm). The statistical significance was set at  $p < 0.01$ . There was a main effect of Side on wrist movement time, reaction time and elevation (all  $F(1,164) > 6.9$ ;  $p < 0.01$ ) showing that reaching the glass in the right space with the left hemiparetic hand took longer and led to a grasp with an abnormal elevation (grasp “from above”, as can be seen on figure 2). Wrist movement time was significantly shorter in the post-test than in the pre-test (main effect of Test:  $F(1,164) = 58.3$ ,  $p < 0.001$ ) without interaction of Order or Side. Wrist reaction time was also improved after the automatic motor rehabilitation (main effect of Test:  $F(1,164) = 100.7$ ;  $p < 0.001$ ) with a Test X Side interaction ( $F(1,164) = 11.8$ ;  $p < 0.01$ ) showing that the benefit was larger for ipsilateral grasping, which was also the slower condition. The analysis of two parameters revealed that the automatic motor rehabilitation positively facilitated the speed of the transport phase toward the glass, while the repetition of the gesture with time has no effect (no effect of order). Concerning the distal grasping component, the abnormal wrist

elevation exhibited by the patient while grasping the glass in the pre-test, especially in the contralateral side, was corrected after the automatic motor rehabilitation: the glass was more functionally grasped (see picture on figure 2). This was also shown by a significant main effect of Test on the wrist elevation ( $F(1,164) = 17.6$ ;  $p < 0.001$ ), without interaction of order or side. While there was this significant effect of Test, there was no significant effect of order ( $F(2,164) = 4.1$ ;  $p > 0.01$ ), showing that simply repeating the gesture toward the stationary object did not change the quality of the grasp, while the automatic motor rehabilitation allowed this change. Note that because of this unusual final hand posture, the marker of the index finger was lacking in 20 trials of the pre-test sessions (because it was hidden by the wrist for the camera positioned above). However, we had enough data from this marker to analyze the index movement time, which reflected the time to open the fingers during the ongoing movement and to close the fingers on the glass. This time was significantly reduced after the automatic motor rehabilitation (main effect of Test:  $F(1,144) = 24.5$ ;  $p < 0.001$ ), with no interaction of Order and Side.

In sum, this single case report is encouraging since it suggests that both proximal and distal components of reach-to-grasp movements can potentially benefit from the automatic motor rehabilitation procedure, with a benefit in time and in the functional quality of the grasp. Further investigations in a large group of patients are ongoing and will be necessary to confirm this benefit and whether it is dependent on the site of lesion causing the hemiparesia.

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