Persistent sparing of action conceptual processing in spite of increasing disorders of action production: A case against motor embodiment of action concepts

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ABSTRACT

In this study, we addressed the issue of whether the sensorimotor processes that underpin the control of voluntary movements (i.e., actions) are causally involved in representing and processing action related concepts like concepts of actions (e.g., jumping or drinking) and concepts of manipulable objects (e.g., a hammer or a fork). We carried out a single-case, longitudinal study of an individual (JR) suffering from a progressive brain degeneration causing severe disorders of action production. The patient was examined four times during a three-year period (T1 to T4) so as to record the progression of his abilities in both action production and conceptual processing of visually-presented actions and objects. Over the same period, a voxel-based morphometric analysis of brain MRI was performed to determine the modification of grey matter volume in brain regions that sustain action production. The analyses of MRI showed increasing bilateral atrophy over time in both cortical and subcortical regions involved in the sensorimotor control of voluntary movements, notably, the superior parietal cortex, the primary motor and premotor cortex, the inferior frontal gyrus, and the basal ganglia. At the same time, the longitudinal behavioral pattern revealed a clear-cut dissociation: the patient presented increasingly severe action production disorders from T1 to T4 whereas his performance in tasks assessing conceptual processing of actions and of manipulable objects remained remarkably stable and within the range of performance of control participants during the same period. These findings indicated that action concept processing hinges on cognitive and neural resources that are mostly distinct from those underlying the sensorimotor control of actions – a case against motor embodiment of action related concepts.

Keywords. Concepts; Conceptual processing; Actions; Manipulable objects; Embodied cognition; Corticobasal degeneration; Apraxia; Movement disorders; Motor disorders.

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A fundamental and long-standing issue of cognitive science concerns the nature of the relationships between the perceptual, conceptual, and motor processes that underlie human intelligent behavior: to what extend are these processes functionally separable? how do they interface with each other? to what extend do they overlap? In recent years, because of the growing influence of the "embodied" or "grounded" cognition framework, a lot of empirical work related to this issue has concentrated on a particular proposal, which is a central tenet of the embodied framework, and according to which conceptual processes are not functionally separable from perceptual and motor processes, the former being rooted in the latter — a view that stands in sharp contrast to more classical approaches of cognition positing functionally separable representational and processing levels for conceptual and perceptual or motor functions.

In the neuropsychological study reported here, we sought empirical evidence pertaining to this issue by addressing the particular case of conceptual processing of actions (e.g., jumping or drinking) and of man-made objects that are being frequently manipulated (e.g., hammer or fork). The specific question we asked was to what extent action conceptual processing is *dependent on* the cognitive and neural processes that control the production of voluntary body movements.

The production of voluntary movements, i.e., motor acts or actions, engages a complex set of processes that translate an action goal into kinematic patterns and muscle commands while integrating visual information from the peri-personal space and sensory information on the body parts' state as well as stored representations based upon prior sensorimotor experience. Such sensorimotor integration relies on an action production system comprising multiple parallel parietal-frontal and cortico-subcortical circuits, whose respective contribution is still poorly understood, but certainly entail the motor cortex (primary motor, premotor, and supplementary motor areas), the inferior frontal lobe, the superior and inferior parietal cortex, and the basal ganglia, as well as the somatosensory cortex (e.g., Andersen & Cui, 2009; Cisek & Kalaska, 2010; Gallivan & Culham, 2015; Leiguarda & Marsden, 2000; Rizzolatti, Cattaneo, Fabbri-Destro, & Rozzi, 2014).

In classical theories of conceptual representation and processing, the sensorimotor processes that control action production are functionally separable from conceptual processes that give meaning to actions (e.g., what are their typical cause and consequences) and objects (e.g., what are their typical

functions). They are conceived of as an output component that is connected to but is not overlapping with the conceptual processing system (e.g., Hillis, Rapp, Romani, & Caramazza, 1990; Humphreys, Riddoch, & Quinlan, 1988; Pylyshyn, 1984; Rothi, Ochipa, & Heilman, 1997; Tyler & Moss, 2001; Warrington & Shallice, 1984). In contrast, within grounded theories of conceptual processing, the sensorimotor processes controlling action production are *constitutive of* the conceptual processing of actions and action related objects like tools or other manipulated objects, as well as of words or sentences expressing them. Indeed, in this view, action related concepts are partly or even primarily represented by the cognitive and neural circuitry that controls action production.

The grounded approach to concepts has been articulated in several ways varying greatly on the importance of the contributing role ascribed to perceptual or sensorimotor processes in conceptual processing (see for reviews, Binder & Desai, 2011; Kiefer & Pulvermüller, 2012; Meteyard, Cuadrado, Bahrami, & Vigliocco, 2012; Wilson, 2002). Here we addressed specifically the stronger and most influential proposals, namely, those advanced within the "Perceptual Symbol Systems" theory (Barsalou, 1999; Barsalou, Simmons, Barbey, & Wilson, 2003; Kiefer & Barsalou, 2013), the « Distributed Neuronal Assemblies » theory (Pulvermüller, 1999, 2001, 2005 ; Pulvermüller & Fadiga, 2010), and the "Neural Parameters Simulation" theory (Gallese & Lakoff, 2005). Although these proposals were developed within quite different theoretical frameworks, they all actually ascribe to the circuitry that controls action production, not only a necessary but also a primary functional role in conceptual processing of actions and action related objects, words, or sentences.

With the "Perceptual Symbol Systems" theory, Barsalou (1999; see also Barsalou et al., 2003; Kiefer & Barsalou, 2013) proposes a general framework of how the brain could implement a conceptual system that represents types, supports categorization, and produces categorical inferences by using sensory and motor mechanisms only and no additional (e.g., amodal) representational system. The primary thesis is that the sensory and motor systems not only represent perceived entities, they also serve to conceptualize them through the formation of "symbols" and "simulators" operating as follows. During perception, configurations of neurons in sensory and motor regions of the brain capture information about the properties of perceived entities and events in the environment and in the individual's body. Selected aspects of perceived experience, those on which selective attention

focused on, are then stored in long-term memory. These records later function as symbols. "Perception" and "perceived experience" refer here to any modality, not only vision and other sensory modalities but also proprioception and introspection. As a result, various types of perceptual symbols are stored: symbols of shapes and colors from vision, symbols of sounds and speech from audition, symbols for hand movements and body positions from proprioception, and so forth. Related perceptual symbols become organized into a "simulator" that enables the cognitive system to integrate the various perceptual symbols and construct "simulations" of an object or event in its absence, that is, to represent conceptual knowledge of some *kind* of object or event.

One important aspect of this theory is that perceptual symbols become established in the same brain areas as the perceptual states that produced them: visual symbols in visual areas, auditory symbols in auditory areas, and proprioceptive symbols in motor areas. In that way, a common representational system underlies both perception and conception. For Barsalou (1999), this aspect of the theory provides an explanation for the pattern of category-specific conceptual deficits reported in lesion studies, because damage to a given sensory or motor region is expected to disrupt the conceptual processing of categories that rely on it during the perceptual or motor processing of its instances: damage to visual areas disrupts the conceptual processing of categories whose exemplars are primarily processed by vision (e.g., animals), and damage to motor and somatosensory areas disrupts the conceptual processing of categories mainly defined by motor and somatosensory properties (e.g. tools).

As for the « Distributed Neuronal Assemblies » theory (Pulvermüller, 1999, 2001, 2005; Pulvermüller & Fadiga, 2010), it provides a neuronal account of how word phonological forms and their meanings, i.e., concepts, are processed and represented in the brain's sensory and motor circuitries. The theory is based on the Hebbian learning rule stating that when correlated neuronal activity is present in a large number of neurons in different cortical areas, some of these neurons eventually develop into an anatomically and functionally connected group of cell assemblies. Thus, during language learning, speech articulation and the coincident acoustic signal it produces result in correlated neuronal activity within primary and higher-order motor, somatosensory, and auditory cortices, which eventually develops into a distributed functional assembly within the so-called

perisylvian cortex. This assembly represents the word phonological form. Then, because word forms are frequently produced when objects to which they refer are perceived or when body movements of the actions to which they refer are carried out by the infant, the perisylvian assembly connects to neurons in the sensory and motor cortices co-activated during perception and action, to develop into a higher-order assembly. Once such an assembly has formed, input to either its form or semantic part is sufficient for « igniting » the entire assembly which, on the cognitive level, corresponds to the perception of a meaningful stimulus and activation of its associated conceptual knowledge.

One consequence of the formation of functional assemblies, is that distinct cortical topographies develop for words and concepts referring to action or to perception. Words whose meanings are mostly related to the visual modality (e.g., highly imageable nouns, like animal names), would consist of a perisylvian assembly linked to neurons in primary and higher-order visual cortices while action related words (typically, verbs, but also names of tools) would be represented by a functional assembly linking the perisylvian assembly to motor programs in motor and premotor cortices. Cortical topographies of category-specific semantic assemblies would even be more fine grained. Due to the somatotopic organization of the motor and premotor cortex, action words that refer to actions performed with different muscles (e.g., to smile, to sign, to kick) develop into topographically distinct neuronal assemblies in perisylvian (face-related words), lateral (arm-related words), or dorsal (leg-related words) motor and premotor cortex. That these « category-specific semantic circuits » (Pulvermuller & Fadiga, 2010) distributed in the motor cortex are crucial for processing action related concepts and words is explicitly underlined by Pulvermuller and his colleagues. Furthermore, because they are thought to be « necessary for, and make an important contribution to, semantic processing » (Pulvermuller & Fadiga, 2010 :357), the theory also provides a natural account for category-specific conceptual deficits observed in brain-damaged individuals.

Gallese and Lakoff (2005; see also Gallese, 2000)'s theory of grounded concepts was especially elaborated with respect to action concepts, although it could also be extended to object and even abstract concepts. The strong claim made by these authors is that the sensorimotor system underpinning the control of action not only driven the representation of action concepts but provides the full structure and *content* of action concepts. The structure of action concepts should include the

semantic role (Agent-Action-Objet-Location), the aspectual (Initial condition-Starting phase-Central Phase-Purpose and Manner-Final State), and the hierarchical category structures. It is claimed that the information structure needed to characterize this conceptual content is fully available at the neural level *inside* the sensorimotor system and, therefore, does not need to be duplicated outside that system.

This central tenet of the theory of concepts is founded on a well-articulated neuroscientific theory of action, that describes how three parallel parietal-premotor cortical circuits (i.e., F4-VIP, F5ab-AIP, and F5c-PF) work in concert not only to control action, but also to create an integrated representation of actions together with the objects acted on and the locations toward which actions are directed. Notably, the theory assumes that these circuits are structured by neural networks of functional clusters called "schemas", which implement the parameters of motor acts and their values. Thus, for instance, the neural parameters of role (Agent-Object-Location), manner (e.g., level of force, effector, direction of motion), and temporal phases (e.g., Initial, Central, and Final phase) of motor acts are built into our neural structure. Each time an action is performed (but also, perceived or imaged via "simulation"), it makes use of the same neural parameters, specified with the parameter values appropriate to the context (e.g., high level of force if object is heavy). The choice of parameter values thus determines, at a lower-level of the structure, the most suitable motor programmes for interacting properly with the objects. Because the schemas have the internal relational structure required by action concepts, they are suited for both acting and conceptualizing actions, by means of "simulation". Conceptualizing "grasping", for instance, requires the simulation of the act of grasping by using the same functional clusters as those used in the actual action of grasping.

Evidence cited in support of the view that the sensorimotor processes that control action production are constitutive of conceptual processing mainly comes from neurostimulation studies and lesion studies.[1] Thus, studies using transcranial magnetic stimulation (TMS) found that the stimulation of cortical motor areas has a significant effect on the processing of action related words. For instance, in Pulvermüller and colleagues (Pulvermüller, Hauk, Nikulin, & illmoniemi, 2005)'s study, single-pulse TMS was applied to the hand and leg sector of the left primary motor cortex of participants while they performed a lexical decision task including verbs referring to hand (e.g., grasp) or leg (e.g., walk) actions. Participants responded faster to hand-related verbs when the hand area was stimulated

whereas stimulation on the leg sector resulted in faster responses for leg-related verbs. Likewise, Willems and colleagues (Willems, Labruna, D'Esposito, Ivry, & Casasanto, 2011) found that repeated trains of TMS applied to the left premotor cortex prior to a lexical decision task accelerated participants' responses for verbs referring to actions (e.g., write) but not for abstract verbs (e.g., wander). It is worth noting that the effects reported in these studies were seen in response latencies of the order of 30 milliseconds, not in response accuracies. Hence, the contribution of the primary motor and premotor cortex could consist, at best, in enhancing the efficiency of the lexico-semantic processing of stimulus words. Although consistent with the view that motor processes are causally involved in the processing of action concepts, it is not clear that such evidence indeed points to their major contribution (Dreyer et al., 2015).

Evidence coming from lesion studies in fact was cited as stronger evidence for the primary role of the sensorimotor circuitry in the processing of action concepts. Here evidence is related to the patterns of conceptual deficits observed in individuals who had lesions in brain regions that impinge on the circuitry responsible for the control of action. Thus, neuropsychological studies have reported that, after a left-hemispheric stroke affecting the primary motor cortex or the inferior frontal and/or parietal lobe, individuals presenting with spatio-temporal disorders in producing actions or using tools (i.e., so-called ideomotor apraxia) were impaired in retrieving conceptual knowledge specifically for actions and/or tools and action related words (Buxbaum, Kyle, &Menon, 2005; Buxbaum & Saffran, 2002; Negri et al., 2007; Papeo, Negri, Zadini, & Rumiati, 2010; Pazzaglia, Pizzamiglio, Pes, & Aglioti, 2008; Pazzaglia, Smania, Corato, & Aglioti, 2008). Were cited as particularly compelling, the patterns of action verb deficits observed in individuals with various types of degenerative brain diseases that affect predominantly (albeit diversely) the motor system. For example, individuals with the motor-neuron disease, a condition characterized by progressive atrophy in the primary motor and premotor cortex (e.g., Agosta et al., 2007), were reported who were more impaired when processing verbs (referring to actions) than nouns (referring to objects) in an associative semantic task, a picture naming task, or a word-to-picture matching task (Bak, O'Donovan, Xuereb, Boniface, & Hodges, 2001; Bak & Hodges, 1997, 2004; Grossman et al., 2008; Hillis, Oh & Ken, 2004; Hillis et al., 2006). Similar patterns of verb deficit in lexico-semantic tasks were reported in patients presenting with the

progressive supra-nuclear palsy (Bak et al., 2006; Daniele, Giustolisi, Silveri, Colosimo, & Gainotti, 2004; Daniele et al., 2012; Cotelli et al., 2006), which mainly affects the basal ganglia, the cerebellum, and the frontal lobes (e.g., Cordato et al., 2002), and in patients with corticobasal degeneration (Cotelli et al., 2006; Silveri & Ciccarelli, 2007; Stamenova, Roy, & Black, 2011; Spatt, Bak, Bozeat, Patterson, & Hodges, 2002), characterized by lesions involving the premotor, parietal, and subcortical motor system (e.g., Dickson et al., 2002). Parkinson's disease, causing dysfunction of the basal ganglia-thalamo-frontal motor circuit (e.g., Gelb, Oliver, & Gilman, 1999), was also reported to be associated with deficits in naming pictures of actions (Albani, Pignatti, Mauro, & Semenza, 2010; Bertella et al., 2002; Cotelli et al., 2007; Rodríguez-Ferreiro, Menéndez, Ribacoba, & Cuetos, 2009; Pignatti, Ceriani, Bertella, Mori, & Semenza, 2006) or in processing verbs in a lexical decision task (Boulenger et al., 2008).

However, while pervasive, the interpretation of these findings is limited in an important way by the brain lesions being typically widespread and, in fact, not circumscribed to the sensorimotor curcuitry for action production. Therefore, it is not clear whether the action or verb deficit observed in these cases was indeed the direct consequence of the sensorimotor lesion or, instead, the result of other impaired but functionally separate, processes. In most cases, especially in the neurodegenerative conditions, the patient's pathological profile included other cognitive disorders like visuo-perceptual deficits, aphasia, or executive disorders, which are each likely to influence negatively the performance of brain-damaged patients in picture or word processing tasks, especially with pictures of actions or with action verbs. Action pictures have higher visual and interpretative demands than object pictures (see, for example, d'Honincthun & Pillon, 2008) and verbs have lower imageability and higher morphosyntactic complexity than nouns (see, for example, Bird, Howard, & Franklin, 2000; Luzzatti, Raggi, Zonca, Pistarini, Contardi, & Pinna, 2002; see for reviews, Mätzig, Druks, Masterson, & Vigliocco, 2009; Pillon & d'Honincthun, 2010).[2] Besides, a number of exceptions to this pattern were recorded. In studies using a multiple-case (Negri et al., 2007; Papeo et al., 2010; Pazzaglia, Pizzamiglio et al., 2008; Pazzaglia, Smania et al., 2008) or a single-case methodology (Bartolo, Cubelli, Della Sala, Drei, & Marchetti, 2001; Chainay & Humphreys, 2003; Cubelli, Marchetti, Boscolo, & Della Sala, 2000; Graham, Zeman, Young, Patterson, & Hodges, 1999; Rapcsak, Ochipa,

Anderson, & Poizner, 1995; Rumiati, Zanini, Vorano, & Shallice, 2001), some individual cases presented no conceptual deficit for actions or manipulable objects despite their presenting with disorders of action production. These exceptions, however, could be viewed as nil effects and, therefore, weaker evidence compared to the evidence provided by the general pattern. Thus, the failure to observe a conceptual deficit could be due to poor sensitivity of the conceptual assessments in case of participants having only a mild conceptual deficit and/or high premorbid abilities, or to participants not having lesions affecting the sensorimotor circuitry indeed.

The neuropsychological study to be reported here was aimed to seek novel evidence relevant to the issue of the role of the action production system in conceptual processing with a design that was likely to overcome the difficulties raised by previous neuropsychological studies.

We carried out a longitudinal single-case study of an individual, JR, who was diagnosed with a progressive brain disease that affects predominantly the action production system, that is, corticobasal degeneration (CBD). The patient was examined four times during a three-year period so as to record the progression of his abilities in both action production and action conceptual processing as well as of the loss of grey matter volume within brain regions including the action production system. The advantages of this empirical approach are threefold.

First, CBD is a progressive neurodegenerative disease invariably associated with progressive action production disorders that however appear within a wide spectrum of clinical presentations also including cognitive symptoms like executive dysfunction, aphasia, visuo-perceptual and conceptual deficits (see Boeve, Lang, & Litvan, 2003; Dickson et al., 2002). In such a context, like in most focal or degenerative conditions studied so far, evidence based on associations of deficits in action production and action conception could be spurious (i.e., due to distinct, unrelated, impaired processes). Examining in an individual the progressive emergence and evolution of deficits in both domains provides a means to examine the functional, i.e., causal, relationships between both deficits (e.g., Code, Tree, & Mariën, 2015).

Second, whatever the associated signs, the characteristic features of CBD are progressive movement abnormalities associated with a progressive asymmetric but bilateral frontal, parietal, and basal ganglia atrophy (e.g., Borroni et al., 2008; Dickson et al., 2002; Kouri et al., 2011). Thus, in that

condition, brain atrophy affects most if not all the cortical and subcortical areas housing the neural circuitry responsible for action control, which warrants the relevance of the pathological condition for the issue investigated here.

Third, the design of a single-case, longitudinal study enables to assess concept processing in a *within-patient* design and, thereby, to gain more power to detect even subtle degradations of conceptual knowledge than in case-control studies, whatever the premorbid performance of the patient. In addition, to insure sensitivity and specificity of the conceptual assessment, a large number of stimuli of actions (total number of 76 items) and of manipulable objects (88 items in total) as well as matched sets of non-action-related stimuli (i.e., animals, plants, and non-manipulable objects) were used in several tasks (picture naming, word-picture matching, or semantic association task).

CASE DESCRIPTION

JR is a right-handed man with a Master's Degree in engineering (17 years of formal education) who worked as an international consultant in a bank company. He was 81 years-old when the study began, in July 2009, and 84 when the study ended in 2012. JR presented himself for the first time to the hospital in November 2008. At this time, he complained of walking difficulties and of difficulties to execute fine movements with his left hand (e.g., buttoning his shirt), which he reported to have increased since January 2008. The neurological examination noted the presence of a slight left limb dystonia. A brain MRI performed in January 2009 showed a frank diffuse cortico-subcortical atrophy with clear parietal and slight right hemisphere predominance (see Figure 1, Panel A). A neuropsychological examination carried out in May 2009 concluded that JR had bilateral but left predominant limb apraxia but no other sign of cognitive dysfunction. On the basis of the insidious unilateral onset, asymmetric course, and gradual progression of JR's limb apraxia and limb dystonia, JR's condition was diagnosed as probable corticobasal degeneration (CBD) by an experimented neurologist and according to international descriptions (Rinne, Lee, Thompson, & Marsden, 1994). One month after the diagnosis, in June 2009, JR volunteered to participate in this study. In June 2010,

given his increasing gait impairment, JR was prescribed PROLOPA 3x125 mg/day. In September 2010, the treatment, that was inefficient, was augmented to PROLOPA 3x250mg/day; it was stopped in December 2010 because still inefficient. The resistance of JR's movement disorder to dopaminergic medication was a further argument for the diagnosis of probable CBD.

Detailed neuropsychological examination was carried out at the 4 periods corresponding to those chosen for the experimental study (T1-T2-T3-T4; see next section). The battery of neuropsychological tests included a general measure of JR's cognitive functioning, as well as of memory (auditory-verbal and visuo-spatial short-term, long-term, and working memory), executive functions, spatial abilities, visuo-perceptual skills, and visual processing (see tests in Table 1). We also included a short language examination battery (see Table 2). As shown in Table 1, JR's performance remained in the normal range over the three-year period in most of the neuropsychological tests. Nonetheless, his performance was impaired in the Stroop task, his responses being significantly slower than control subjects in the reading condition, already from T1, and in all the other conditions from T3. Moreover, interference indexes (interference condition minus naming condition) showed impaired processing either in accuracy or speed at T1, T2, and T3. The indexes were in the normal range at T4, but this could be due to JR being very slow in responding at that moment. In the Trail Making Test, JR also made significantly more errors than controls at T3 and could not terminate the task at T3 and T4. However, his impaired performance was likely due to impaired retrieval of the sequence of the alphabet itself. When asked to recite the alphabet after the Trail Making Test at T3 and T4, JR forgot many letters and was unable to reach the end of the alphabet. As regards visual processing, access to the structural description of objects (objet/non-object decision task) was slightly impaired at T3 ($z = -2.4$) but better at T4 ($z=-1.9$) when the results to all subtests were pooled together. Finally, as shown in Table 2, JR showed no language impairment over the period of investigation. However, he became unable to write at T3.

EXPERIMENTAL STUDY

General Method

The patient was examined 4 times during a three-year period (T1: summer 2009; T2: summer 2010; T3: summer 2011, and T4: spring 2012). At each period, four sets of evaluations were performed: (i) Evaluation of brain atrophy progression, including measures of grey matter volume loss in several regions of interest with voxel-based morphometric analysis of brain MRI; (ii) Testing of simple and complex movement production; (iii) Assessment of conceptual processing of actions and of manipulable objects as well as matched sets of non-action-related stimuli, with 2 picture naming tasks; (iv) Assessment of both gesture processing and conceptual processing with an identical set of instrumental actions and manipulable objects. In addition to these tests, at T4, a timed picture naming task with actions and manipulable objects was presented to the patient.

Behavioral tests took place at patient's home in sessions lasting between 60 and 90 minutes. Most of the tasks presented to him were also presented to healthy, control participants, who differed across the tasks. All participants had a normal or corrected to normal vision and no history of psychiatric or neurological disorder. More detailed characteristics of the different control groups of participants will be specified with the tasks in which they participated.

We used Crawford and Howell's (1998) modified *t*-test to establish whether JR's performance differed significantly from that of the control group and we used Crawford and Garthwaite's (2007) Bayesian Standardized Difference Test (BSDT) to test whether the discrepancy in JR's performance between two sets of items was significantly different from the discrepancy between them in the control group. We also used the McNemar statistics (McNemar, 1947) to test whether JR's performance at different tests or sets of items significantly decreased over time.

The study was approved by the biomedical ethic committee of the *Cliniques universitaires Saint-Luc* (Brussels) and all participants gave written informed consent prior to the study.

Brain atrophy progression

Method

The patient underwent a clinical MRI in 2008 (T1), and he was then enrolled in the study including a follow-up MRI in 2010 (T2), 2011 (T3) and 2012 (T4). FLuid Attenuated Inversion Recovery (FLAIR) images were obtained in the axial plane in 2008 and 2011. Axial diffusion and T2*-weighted images, as well as axial and coronal T2-weighted images, were also acquired in 2008. For the follow up, 3D heavily T1-weighted images were obtained at 3T (Achieva, Philips Healthcare, Eindhoven, The Netherlands) with a 32 channels phased array head coil. The anatomical 3D sequence consisted in a gradient echo sequence with an inversion prepulse (Turbo Field Echo –TFE) acquired in the axial plane using the following parameters: TR/TE/flip angle = 9.1 ms/4.6 ms/8°, 150 slices, slice thickness = 1 mm, in-plane resolution = 0.81 x 0.95 mm^2 (acquisition) reconstructed in 0.75 x 0.75 mm^2, FOV = 220 x 197 mm^2, acquisition matrix = 296 x 247 (reconstruction 320^2), SENSE factor = 1.5 (parallel imaging).

The images were first visually assessed by an experienced neuroradiologist. Then, volume- and surface-based analyses (FreeSurfer; Martinos Center for Biomedical Imaging, Boston, MA, USA) were used to measure JR's grey matter volume loss in several regions of interests (ROIs) from T1 to T4. The whole brain was segmented by completing the FreeSurfer image analysis pipeline which is documented and freely available for download online (http://surfer.nmr.mgh.harvard.edu/). The final segmentation is based on both a subject-independent probabilistic atlas and subject-specific measured values. The atlas is built from a training set, i.e., a set of 40 subjects whose brains (surfaces or volumes) have been labelled by hand. The technical details of these procedures were described in prior publications (Fischl et al., 2002; Fischl et al.,2004; Ségonne et al., 2004).

The volumetric analyses focused on 22 ROIs, i.e., 16 (8 right and 8 left) cortical regions within the parietal and frontal lobes and the 6 (3 right and 3 left) structures of the basal ganglia (i.e., putamen, pallidum, caudate). The ROIs identified within the parietal lobes were the supramarginalis gyrus, inferior parietal lobe, and superior parietal lobe. Within the frontal lobes, the ROIs were the precentral gyrus, pars triangularis and pars opercularis, the superior frontal lobe, and the caudal middle

frontal gyrus (see Figure 1, Panel B). These ROIs involve cortical and subcortical structures that are known to sustain the control of voluntary movements (e.g., Johnson-Frey, 2004; Rizzolatti & Luppino, 2001) and whose damage results in action production disorders (e.g., Buxbaum, Shapiro, & Coslett, 2014; Goldenberg & Spatt, 2009; Haaland, Harrington, & Knight, 200; Leiguarda & Marsden, 2000). Notably, they encompass the brain areas that were explicitly stated as being part of the shared neural substrate for action control and action conception within the theories addressed here. Specifically, the precentral gyrus, superior frontal lobe, and caudal middle frontal gyrus house the primary motor and premotor cortex, deemed crucial for action control and action verb conceptual processing within the « Distributed Neuronal Assemblies » theory (Pulvermüller, 1999, 2001, 2005 ; Pulvermüller & Fadiga, 2010). The superior parietal lobule, pars triangularis, and pars opercularis encompass, with the motor and premotor cortex, the parietal-frontal circuits serving both action control and action conceptualization within the "Neural Parameters Simulation" theory (Gallese & Lakoff, 2005).

The grey matter volume loss measured in JR from T1 to T4 was then compared to the volume loss of age-matched, healthy individuals, estimated from the annual rate of atrophy reported by Fjell et al. (2009) in healthy elderly subjects and multiplied by 2.6 years (corresponding to the delay between T1 and T4),

Results

Transversal and sagittal sections of JR's brain from T1 to T4 are displayed on Figure 1, Panel A. At T1, the neuroradiologist described a moderate bilateral parietal atrophy, with a thinning of the pre- and postcentral gyri and an enlargement of the subarachnoïd spaces at the vertex, particularly in the parietal area. There was a slight enlargement of the precentral sulcus, a more prominent enlargement of the central sulcus, and even more of the postcentral sulcus. There was also a widening of the right superior frontal sulcus and of the intraparietal sulcus, especially at the right side. No other lesion was noted, and the patient had no vasculo-ischemic lesion (leucoaraïosis rated as 1/9 according to the Manolio's scale). At T2, this regional atrophy had slightly worsened, and a new enlargement of the right sylvian fissure was observed. At T3 and T4, a diffuse atrophy could be observed with two areas being particularly affected: (i) a bilateral parietal atrophy with a right dominance and a slow worsening

since T1, and (ii) a rapidly progressive perisylvian atrophy (principally at the right side), mainly characterized by an atrophy of the inferior frontal gyrus and of the right temporal lobe encompassing the parahippocampic gyrus but not the hippocampus.

As shown in Figure 1, Panel B, volume- and surface-based analyses showed that grey matter volume loss in JR from T1 to T4 largely exceeded that of age-matched healthy individuals in most of the ROIs. Volume loss was the largest in the basal ganglia (mean = -6.06%) followed by the posterior frontal ROIs (mean = -4.88%) and the parietal ROIs (mean = -2.73%). In the basal ganglia, the volume loss exceeded largely the normal rate in all the ROIs except in the left pallidum and there was a right hemisphere predominance. In the posterior frontal ROIs, the largest volume loss was observed in the left precentral gyrus. Finally, volume loss in the parietal ROIs concerned mainly the left and right supramarginal gyri and the left superior parietal lobe, the right inferior parietal and superior parietal lobes showed less volume loss.

Discussion

At T1, JR presented with diffuse bilateral brain atrophy with right parietal predominance. From T1 to T4, he presented grey matter volume loss in most of the ROIs investigated. The atrophy affected mostly the bilateral superior, inferior, and posterior frontal cortex, the left superior parietal cortex, and the basal ganglia, a pattern that is typically found in CBD (Dickson et al., 2002). Four regions did not show abnormal volume loss throughout the study: the inferior parietal lobes, the right superior parietal lobe, the right caudal middle frontal gyrus, and the left pallidum. The relative preservation of the inferior parietal lobes is, again, typical of this condition (Dickson et al., 2002). However, whether the brain regions that showed no clear volume loss throughout the three-year period of the study were functional is difficult to know. Since JR presented already diffuse atrophy at T1, at least some of these regions may have underwent atrophy before the study began. Furthermore, decreases of metabolism may be present in regions where no atrophy was found. In any case, these neuroanatomical analyses clearly showed, from T1 to T4, a significant progression of the atrophy in both cortical and subcortical regions involved in the sensorimotor control of voluntary movements, notably, in cortical areas comprising the primary motor and premotor cortex as well as the parietal-frontal circuits defined as

shared neural substrate for action control and action conception in Pulvermüller's and Gallese and Lakoff's theories.

Action production

Simple movements

Method. The following 3 tests were presented to JR at T1 and T4 by an experienced occupational therapist: (i) the "Jamar Hydraulic Hand Dynamometer" test, that evaluates handgrip strength; (ii) the "Box and Block Test" (Mathiowetz, Volland, Kashman, & Weber, 1985), which tests gross hand dexterity by scoring the number of blocks of 1 cm (3/8 in.) the patient is able to grasp with one hand in the ipsilateral compartment of a box, displace over a 15.2 cm (6 in.) partition, and then release in the contralateral compartment of the box in 60 sec; (iii) the "Purdue Pegboard Test" (Tiffin & Asher, 1948), which assesses finger dexterity by scoring the maximal number of small pegs that the patient is able to insert into the small holes of a board in 30 seconds using only one hand.

Results. As shown in Table 3, JR's hand and finger dexterity was impaired at T1, decreased from T1 to T4 and was always worse for the left than the right hand. In contrast, his grip strength was in the normal range and showed no sign of asymmetry at T1, although it subsequently decreased predominantly for the left hand, that was selectively impaired at T4.

Complex movements

Method. JR's performance in the following tasks was compared to that of 15 right-handed elderly control participants (eight men; mean age = 68.4 years) whose performance was reported in Peigneux et al. (2001). The tasks were presented to JR at each period of assessment. They aimed to assess the production of manual gestures by imitation and on verbal command. In the gesture imitation task, JR was asked to imitate 20 skilled and 20 novel unimanual gestures. Skilled gestures were those implied in actions like shaving, drinking, or hammering. Skilled and novel gestures were matched in movement components (whole limb or hand/finger complex), kinematic (dynamic or static gestures),

and global complexity. Each trial started with the video display of a gesture that JR was asked to watch carefully "in order to reproduce exactly the same arm, hand, and finger movements and positions". Imitation was allowed when the video clip ended. The task eliciting gesture production on verbal command probed the same 20 unimanual, skilled gestures. Here, the examiner orally named the to-be-mimed gesture (e.g., "combing") and JR was asked to mime it as well as possible. Finally, a gesture recognition task was also administrated to allow proper interpretation of performance in the imitation task. In this task, the patient was presented with the video clip of 60 gestures (40 unimanual and 20 bimanual), equally divided in known and novel gestures. The patient was asked to decide, for each gesture, whether it referred to a known or an unknown gesture. The order of passation of the production tasks, hands, and sets of items is shown in Table 4 between brackets. JR's performance was videotaped and analyzed according to Peigneux and Van der Linden's (2000) scheme (adapted from Rothi et al., 1997) which distinguishes content, spatial, temporal, and "other" errors. A gesture was considered incorrect if it involved any of these types of errors.

Results. The results are displayed in Table 4. Already at T1, JR was impaired in imitating skilled gestures with his left hand and in performing skilled gestures on verbal command with both hands. JR's impaired performance in gesture imitation cannot be ascribed to gesture recognition difficulties since his performance in the gesture recognition task was within the normal range at every period. Moreover, his performance in imitating novel gestures was preserved at T1, as indicated by his z score. From T1, JR's performance decreased sharply (and significantly in most tasks) throughout the subsequent periods of assessment. From T3, his performance became significantly impaired in all the production tasks, types of gestures, and hands. At T4, he was unable to perform any gesture with his left hand and, with his right hand, he accurately executed only 25% and 35% of skilled gestures on imitation and on verbal command, respectively. As shown in Table 5, JR's gesture production errors were mainly spatial errors with some temporal errors. No content errors were observed, except a partial perseveration in the imitation of right hand gestures at T4. The spatial errors consisted mainly in wrong position and orientation of the hands with respect to the body and poor coordination of the movements of different fingers; incorrect gestures were also due to wrong digital configurations, wrong articulator (e.g., hammering movement done by shoulder rather than elbow and wrist

movements), or reduced movement amplitude. The temporal errors concerned mainly movement slowing and speed irregularities.

Daily activities

Method. Two questionnaires were presented to JR in 2009, 2011, and 2012, in which he was asked to report on his functional independence in daily activities: (i) the index of independence of the "Activities of Daily Life" (ADL, Katz, Ford, Moskowitz, Jackson, & Jaffe, 1964) included 6 activities (bathing, dressing, going to the toilet, transferring, continence, and feeding), scored from 1 to 4 (where 1 = independent and 4 = total dependence); (ii) the "Instrumental Activities of Daily Living Scale" (IADL, Lawton & Brody, 1969) was composed of 8 activities (telephoning, shopping, food preparation, housekeeping, laundering, use of transportation, use of medicine, and financial behavior), rated from 1 to 3 (where 1 means no particular difficulty, 2 a need of help and 3 means a total inability).

Results. JR was independent for all daily activities at T1 (ADL=6; IADL=11). At T3, he needed help for most activities such as to wash the lower part of his body, to dress, to stand up, to go to the toilet, to prepare food, to do housekeeping, and to use means of transportation (ADL=10; IADL=14). At T4, he needed help for all the activities and started to use a rolling chair (ADL=16; IADL=20).

Interim result summary and discussion

At T1, although still independent in his everyday-life activities, JR already presented with movement disorders, which then progressively increased to become very severe at T4 by affecting all his daily activities and functional independence. Although part of the movement disorders certainly were directly linked to corticospinal or basal ganglia deficit (rigidity and dystonia, postural imbalance, and gait disorder), the formal praxis tests unambigously indicated a progressive increase of the cortical signs typically observed in that condition, that is, limb apraxia, "the neurological disorder of learned

purposive skill that is not explained by deficits of elemental motor or sensory systems" (Rothi, & Heilman, 1997: 3).

JR's gestural difficulties likely resulted from the combination of two sets of symptoms, which have been labelled "limb-kinetic" apraxia and "ideomotor apraxia", respectively, in previous studies of CBD, and are both typically observed in this condition (e.g., Osiurak & Le Gall, 2012; Stamenova, Roy, & Black, 2009). Limb-kinetic apraxia is characterized by the loss of hand and finger dexterity confined to finger and hand contralateral to the lesion, with preservation of power and sensation; it is thought to result from frontal lobe damage centred on the premotor cortex, associated with parietal and/or basal ganglia involvement (Leiguarda & Marsden, 2000). It affects all types of gestures, skilled or novel, elicited on verbal command or imitation. Ideomotor apraxia, on the other hand, is characterized by temporal (e.g., irregular speed) and spatial (e.g., abnormal hand/arm configuration) errors in performing manual actions involving or not an object. Unilateral lesions of the left hemisphere in right-handed patients produce bilateral deficits. Ideomotor apraxia is likely caused by lesions centred in the left supramarginal gyrus and the superior parietal lobe and/or the underlying white matter, which may interrupt corticocortical and corticosubcortical connections, notably with the premotor cortex (Leiguarda & Marsden, 2000).

The pattern of distribution of cortical atrophy and of the resulting gesture disorders observed in JR was consistent with the neuroanatomical and behavioral descriptions of both these higher-order motor disorders. In particular, the asymmetric pattern of overall performance for the gestures performed with the left hand (more impaired) and the right hand, observed since the first examination, was consistent with the initially predominant right-hemisphere involvement, which caused unilateral left limb-kinetic features that combined with ideomotor features resulting from the left-hemisphere atrophy, whereas right hand gestures were affected by ideomotor features mainly.

Hence, the results of the brain's volumetric analyses and of the behavioral praxis tests provided converging evidence for an increasing dysfunction of both the premotor cortex and the parietal-frontal circuits that control action production. It is also worth emphasizing that no evidence was found for visuoperceptual difficulties in gesture recognition during the same period.

Conceptual processing of actions and of manipulable objects vs. matched sets of non-action-related stimuli

To assess conceptual processing of various categories of stimuli in JR, we choose to use the picture naming task. There is broad agreement that naming a visual stimulus entails not only that it has been accurately recognized but also comprehended, in the sense that associated conceptual knowledge of the category of actions or objects (i.e., the concept) to which it belongs have been successfully (albeit mostly implicitly) retrieved from memory. Moreover, it is widely if not unanimously considered as the most sensitive task to detect even subtle impairment of conceptual processing (e.g., Pobric, Jefferies, & Ralph, 2007; Woollams, Cooper-Pye, Hodges, & Patterson, 2008).[3]

At each period of evaluation, JR was presented with 2 picture naming tasks composed of various sets of stimuli: (i) the "Actions, Manipulable objects, Plants, and Animals" (AM/PA) naming task, which included two categories of action-related stimuli (human actions and manipulable objects) and two categories of non-action-related stimuli (plants and animals); (ii) the "Actions/Objects" (A/O) naming task, which included pictures of human actions, manipulable objects, and non-manipulable objects (See the list of items in Appendix A.).

Method

Participants. The AM/PA picture naming task was presented to JR and to 12 control participants matched with him in gender, age [mean = 70.33; modified t (11) = 1.23, p = 0.24], and years of education [mean = 14.42; modified t (11) = 1, p = 0.34]. All control participants achieved at least 21/22 on a shortened, twenty-two item version of the MMSE (mean = 21.5). The A/O naming task was presented to JR and to a group of 8 younger control participants [mean = 62.62; modified t (7) = 10.87, $p < 0.01$] matched with him in gender and years of education [mean = 16.25; modified t (7) = 1, p = 0.35], taken from a previous study (Vannuscorps & Pillon, 2011).

Material. The picture stimuli used in both the AM/PA and the A/O naming task were color photographs with no context. The photographs of actions depicted all the persons, objects, or

instruments typically involved in the action. The characteristics of nouns and verbs corresponding to these stimuli in terms of spoken word frequency, concept familiarity, imageability, and age of acquisition, when available, are displayed in Table 6.

The AM/PA naming task included 94 picture stimuli divided in 46 action-related (24 human actions and 22 manipulable objects)[4] and 48 non-action-related (24 plants and 24 animals) stimuli. Human actions were performed with various body parts (mostly upper limbs but also mouth and whole body). Manipulability of the objects was estimated by three independent judges who were asked to tell whether these objects, embedded in a larger set of 120 objects, entailed manipulation, that is, whether the utilization of the object entailed specific and fine hand movements (Saccuman et al., 2006). The 22 manipulable objects reached 100% agreement across the judges. The four categories of items were matched for spoken name frequency [F (3, 90) = 1.39, p = 0.25], age of acquisition [F (3, 90) = 1.14, p = 0.34], concept familiarity [F (3, 90) < 1], and imageability [F (3, 90) = 2.40, p > 0.05].

The material of the A/O naming task included 32 pictures of human actions performed with various body parts, 16 pictures of manipulable objects, and 16 pictures of non-manipulable objects. Manipulability of the objects was estimated by three independent judges who were asked to tell whether a pre-selected set of 60 objects entailed manipulation, i.e., whether the utilization of the object entailed specific and fine hand motion (Saccuman et al., 2006). Only items unanimously judged as manipulable or non-manipulable were selected. The three sets of items were matched in concept familiarity [F (2, 61) = 1.28, p = 0.29]. However, actions had significantly lower imageability and higher spoken word frequency than both categories of objects [all ts (30) > 2.2; all ps < 0.01], which did not significantly differ with respect to these variables, however [both ts (30) < 1.2; both ps > 0.2].

Procedure. Participants were presented with all the photographs of a given task in a single session. They were asked to name them within 20 seconds. The naming of actions was elicited by the beginning of a sentence, i.e., "*il ou elle est en train de"* which requires being completed by the infinitive form of a verb ("*en train de* $Verb_{inf}$" is the French equivalent of English "$Verb_{ing}$"). Each task was preceded by a few examples to familiarize the patient with the task.

Results

Only the expected name was considered as a correct response. In the AM/PA naming task, the data from one control participant were excluded due to abnormally high error rate in the "plant" category (58% of erroneous responses). The results are displayed in Figure 2, Panel A.

In the AM/PA naming task, JR's performance in naming actions and manipulable objects was within the normal range of performance at T1 [both modified *t*s (10) > 0; both *p*s > 0.3] and remained within the normal range in all the following periods of assessment [all modified *t*s (10) > -0.2; all *p*s > 0.2]. Actually, JR's performance did not significantly change over time (both McNemar tests, $\chi^2 <$ 1.33; both *p*s > 0.25). Unexpectedly, JR's performance was consistently and significantly below the control group's performance in naming animals [all modified *t*s (10) < -2.55; all *p*s < 0.05]. In naming plants, JR's performance was impaired at T2 [modified *t* (10) = -2.59, *p* < 0.05] but was within the normal range at the three other periods [all modified *t*s (10) = -1.26, all *p*s > 0.2]. His performance for plants did not significantly change from T1 to T4 (McNemar tests, $\chi^2 = 2.25$; both *p*s > 0.1), but it changed significantly for animals (McNemar tests, $\chi^2 = 6.12$; both *p*s = 0.01). In the A/O naming task, JR's performance was within the range of controls' performance for the three categories of stimuli and at the 4 periods of assessment [all modified *t*s (7) > -1; all *p*s > 0.3]. Furthermore, his performance did not significantly decrease from T1 to T4 for any of these three categories (all McNemar tests, $\chi^2 <$ 0.25; all *p*s > 0.6).

Discussion

In contrast to movement disorders that progressively increased throughout the period of the study, JR performed within the normal range, at every time period, in the picture naming tasks assessing conceptual processing of actions and manipulable objects. Throughout the study, JR was always as accurate as the control participants in naming actions and manipulable objects. As regards non-action-related stimuli, we found that, unexpectedly, JR's performance was impaired in naming animals and, to a lesser extent, plants, although it was not impaired in naming non-manipulable objects. Whether this pattern indicated a true category-specific deficit for animals and plants affecting either the structural or the conceptual level of processing (e.g., Capitani, Laiacona, Mahon & Caramazza, 2003)

or only low personal familiarity with these categories of stimuli is unclear. Answering this question would have required additional testing, which was beyond the scope of this study.

Gesture and conceptual processing tested with the same set of actions and manipulable objects

The previous tasks aimed to follow up the pattern of JR's performance in action production and in action conceptual processing over time. However, in these tasks, both cognitive domains were not probed with an equivalent set of actions and objects. The purpose of the following tasks was to test JR's performance over time in both domains in relation with an identical set of actions and objects. In addition, the design included tasks which aimed to assess, for the same items, the processing of motor acts without requiring actual movement execution, on the one hand, and the explicit retrieval of conceptual knowledge without requiring actual naming, in the other hand.

Method

An identical set of 50 manipulable objects were used as stimuli in the following tasks: (i) an object/gesture matching task; (ii) a task eliciting gesture production from the name of the object; (ii) a picture naming task; (iii) a picture association task assessing, in one condition, knowledge of the gesture associated with the conventional use of each object and, in another condition, knowledge of the function of the object, i.e., what it is used for, its conventional usage. Further to the object stimuli, both the picture naming task and the gesture production task on verbal command probed a set of 20 instrumental actions (i.e., actions performed with an instrument or tool). The list of the 50 object and 20 action items are provided in Appendix B.

The object/gesture matching task aimed to assess the sensorimotor functions underlying the production of learned manipulation gestures without requiring overt movement execution. In this task, the patient was presented with a picture of an object and then with 2 video clips showing an agent pantomiming the use of an (absent) object; he had to tell which pantomime was appropriate for the object. We assumed that performing this task requires some kind of first-person mental rehearsal of

the manipulation gestures associated with the pictured object, which have then to be compared with the visual percepts extracted from the manipulation pantomimes. Given ample evidence that covert (imagined) first-person gesturing with an object mostly relies on the same neural processes as actual gesturing (e.g., Jeannerod, 2001), the task allowed us to assess the sensorimotor functions entailed in the production of manipulation gestures in a condition uncontamined by the effects of execution.

Four video clips were created for each of the 50 manipulable objects. One video clip presented the gesture implied in the correct use of the object, another the gestures implied in the use of a semantically-related item (semantic foil, e.g., the foil for the hammer was the pantomime of a screwdriver), another corresponded to the use of the object with a wrong digital configuration (digital configuration foil, e.g., hammering with only two fingers holding the hammer), and another to the use of the object with a spatially or temporally wrong movement (movement foil, e.g., hammering with faster up than down movements). Three lists were created, each containing a clip of the 50 correct pantomimes associated with a clip of one of their three foils. The different kinds of foils were similarly distributed in the three lists (in each list, 17 foils of one kind and 18 of the two other kinds). The three lists were proposed to JR in three different sessions. A trial comprised the following sequence of events: (1) The photograph of an object was displayed on a computer screen until the patient agreed to move to the next step; (2) Two video clips showing a man pantomiming the use of an (absent) object were subsequently presented on the left and right side of the screen. The left video clip was launched first by the experimenter and, when it was terminated, the right one was launched. JR was asked to decide which video clip depicted the correct manipulation gesture for the previously-presented object. He was also asked to wait the end of the second video clip before responding. There was no time limit and JR was allowed to watch again any video clip as many times he wanted.

In the task eliciting gesture production on verbal command, JR was asked to pantomime the use of the same 50 objects and to pantomime 20 instrumental actions from their spoken name with his right (less affected) hand. His performance was videotaped and analyzed according to Peigneux and Van der Linden's (2000) scheme. This task has not been presented to a control group and not presented to JR at T4.

In the picture naming task, JR was presented with the 50 manipulable objects and the 20 instrumental actions in a single session and asked to name them. This task has not been presented to a control group.

The picture association task was presented to JR and to a group of 8 younger control participants [mean = 62.62; modified t (7) = 10.87, $p < 0.01$] matched with him in gender and years of education [mean = 16.25; modified t (7) = 1, $p = 0.35$], taken from a previous study (Vannuscorps & Pillon, 2011). This task was composed of a pictured material used in two conditions. In the "gesture" condition, the material was used to assess, again, the sensorimotor functions underlying the production of learned gestures without requiring overt movement execution. (Like in the object/gesture matching task, we assumed that the "gesture" condition of this task entails mentally rehearsing the learned gestures.) In the "function" condition, the same material was used to assess the explicit retrieval of knowledge about the function of the same objects. Participants were presented with a picture of a manipulable object (probe item) with, below it, an array of 3 pictures of other manipulable objects. In the "gesture" condition, they were asked to point to the object that is conventionally used with hand movements similar to those used for the probe; in the "function" condition, they were asked to point to the object that, within the array, has a function similar to that of the probe. The same probe items and the same array of choices were displayed in the same order in both the "gesture" and the "function" conditions. This allowed us to match perfectly the material used in both conditions. Thus, in both the "gesture" and the "function" conditions, the probe item (e.g., a cigarette lighter) was presented with, below it, a picture of an object that is manipulated in a similar way (e.g., a chronometer), a picture of an object having a similar function (e.g., a match), and a visually-related object (e.g., a salt shaker).[5] The probe objects, the gesture and function targets, and the visually-related foils were matched in imageability [F (2, 47) < 1], age of acquisition [F (2, 47) < 1], and familiarity [F (2, 47) < 1]. The participants underwent the "gesture" and "function" conditions in an ABBA order.

Results and discussion

Gesture processing. The results are displayed in Figure 3, Panel A. In the object/gesture matching task, a significant decrease of performance was observed (McNemar $chi^2 = 3.76$, $p = 0.05$). In this

task, JR made numerous errors that consisted in choosing the finger configuration foil (8%, 14%, and 26% of the trials at T1, T3, and T4, respectively) or the movement foil (12%, 28%, and 32% of the trials at T1, T3, and T4, respectively), but rarely the semantic foil (4%, 6%, and 4% of the trials at T1, T3, and T4, respectively). The increase of errors on finger configuration and movement foils from T1 to T4 was significant (both McNemar $\chi^2 > 5$, $p < 0.05$).

In the "gesture" condition of the picture association task, JR's performance was in the normal range at T1 [modified t (7) = -1, $p = 0.35$], almost significantly below the controls' at T2 [modified t (7) = -1.97, $p = 0.09$], and significantly below the controls' at T3 and T4 [both modified ts (7) = -6.28; both ps < 0.001]. This decrease of performance was significant (McNemar test, $\chi^2 = 6.67$, $p < 0.01$).

In the gesture production task on verbal command, 13 objects whose pantomime needed a stand-up position (e.g., the rake, the fork) were removed from the analysis due to JR's balance problems. At T1, JR performed correctly 70% of the gestures but only 19% at T3, a decrease of performance that was significant (McNemar test, $\chi^2 = 15.43$, $p < 0.01$). In all sessions, errors were mainly spatio-temporal inaccuracies (65% at T1; 89% at T2; 95% at T3) such as abnormal hand/finger or shoulder/wrist/elbow configuration, or wrong spatial orientation of hand movements. With the set of instrumental action items, JR's performance was already poor at T1 (70%) and then decreased from T1 to T3 (McNemar test, $\chi^2 = 3.5$, $p = 0.06$).

These results demonstrated progressively increasing dysfunction of the sensorimotor processes entailed in the production of learned manipulation gestures, in particular, of the functions computing the spatial and temporal aspects of manipulation gestures. Moreover, the results from the two "covert" gesturing tasks showed that this increasing dysfunction could not be ascribed to peripheral execution disorders only.

Conceptual processing. As displayed in Figure 3, Panel B, at T1, JR named correctly 82% of the manipulable objects, and his performance slightly increased from T1 to T4 (84%). Likewise, with the set of instrumental actions, JR's naming performance was relatively high at T1 (85%) and was higher at T3 and T4 (90%). In the "function" condition of the picture association task with manipulable objects, JR's performance was always within the normal range of performance [all modified ts (7) > -

1.6; all *p*s > 0.15] and did not significantly decrease between 2009 and 2012 (McNemar test, $\chi^2 < 1.12$, $p > 0.25$).

The results of this set of tests confirmed the pattern of dissociation observed with the previous tests: over time, the processing of learned gestures associated to actions and objects significantly deteriorated in JR while, during the same period, conceptual processing of the same actions and objects remained stable and seemingly unaffected by the disease.

Timed picture naming of actions and of manipulable objects at T4

Although conceptual processing for actions and objects was seemingly unaffected in JR throughout the longitudinal study, the patient could nevertheless have experienced difficulties in the naming tasks that would be apparent only in the speed of response, not in response accuracy. To address this issue, JR was presented with a timed version of the AM/PA picture naming task three months after the end of the longitudinal study.

Method

This task was presented to JR and to 8 age, gender, and education-matched control participants [mean age = 76.25; modified *t* (7) < 1; mean education = 16.87; modified *t* (7) < 1]. These control participants were members of the "University for the Elderly", had a preserved cognitive functioning (all MMSE ≥ 28), a normal visual acuity (Parinaud's test), normal visuo-perceptive abilities (Birmingham Object Recognition Battery, Riddoch, & Humphreys, 1993: test 7: all = 25/25; test 8: all = 25/25; test 11: all ≥ 30/32), and performed above the mean performance of their age category in a standardized object naming task (de Partz, Bilocq, De Wilde, Seron, & Pillon, 2001; all *z* > 0). Furthermore, none of these controls had movement production complaints. Participants were presented with the stimuli of the AM/PA picture naming task in the same session and were asked to name them as fast and as accurately as possible. A fixation point was presented in the center of a computer screen

for 200 ms; then the screen was cleared for 500 ms and the stimulus was displayed until the voice key was triggered. The next trial began after an interval of 1000 ms. The experiments were controlled by the E-Prime software (Psychological Software, 2002, Pittsburgh, PA). The participants were equipped with a sensitive built-in microphone connected with an RT-measuring PST (Psychology Software Tool) serial response box. Malfunctioning of the voice key and participants' responses were checked by the experimenter.

Results and discussion

Trials with malfunctioning of the voice key were first removed (Controls = 3.19%; JR = 9.57%). Response latencies were visually checked for abnormally fast or slow response latency and latencies below 300 msec or above 5000 msec were removed from the analyses (Controls = 1.14%; JR = 2.78%). The results (see Figure 4) showed that JR's performance did not significantly differ from the controls' for any of the four categories of items, neither in accuracy [all modified *t*s (7) > -0.90; all *p*s > 0.30] or in speed [all modified *t*s (7) < 1.88; all *p*s > 0.1]. In addition, the discrepancy in JR's accuracy and speed between action-related (Actions & Manipulable objects) and non-action-related (Plants & Animals) items never significantly differed from that found in control participants (all *BSDT, ps* > 0.15). The results of this additional naming task therefore corroborated the findings from the longitudinal study: JR had no detectable conceptual impairment with actions or manipulable objects even when, in the course of the disease, the action production disorders were very severe.

GENERAL DISCUSSION

In this study, we have reported on the three-year pattern of evolution of brain atrophy and movement disorders, along with performance in conceptual processing of actions and of objects, in a patient (JR) diagnosed with CBD, a progressive brain disease known to affect predominantly the action production system. The pattern of evolution showed a clear-cut dissociation. Over the period of investigation, images of JR's brain showed a progressively increasing volume loss of grey matter in brain regions

involving the sensorimotor circuitry controlling action production, which was associated with progressively increasing disorders in producing voluntary movements. On the other hand, over the same period, the patient's performance in conceptual processing of actions and of manipulable objects remained consistently in the normal range of performance. Importantly, the design of this study allowed us to demonstrate that JR retained normal ability to retrieve the concepts of the same actions he lost the ability to perform and of the same familiar objects he could not utilize anymore.

This pattern of dissociation is at odds with the predictions derived from the strong views of conceptual grounding addressed in this study, namely, those advanced within the "Perceptual Symbol Systems" theory (Barsalou, 1999; Barsalou et al., 2003; Kiefer & Barsalou, 2013), the « Distributed Neuronal Assemblies » theory (Pulvermüller, 1999, 2001, 2005 ; Pulvermüller & Fadiga, 2010), and the "Neural Parameters Simulation" theory (Gallese & Lakoff, 2005). Within these theories, the sensorimotor functions and neural substrate that control the production of voluntary movements not only have a necessary, but also a primary functional role in the conceptual processing of actions and action related objects. Actually, conceptual processing *depends on* that cognitive and neural circuitry. Hence, damage to it should result in a deficit in processing action related concepts in addition to disorders of action production.

The outcome of this study conflicts with a number of previous neuropsychological reports that were cited as evidence that lesions to the sensorimotor circuitry underpinning action control did result in a conceptual deficit for actions, action related objects, or action related words (i.e., verbs). Thus, individuals with left-hemispheric stroke in premotor or parietal areas as well as patients with various types of degenerative brain diseases predominantly affecting the motor system — including corticobasal degeneration, like in the present case — showed impaired performance with actions or action related objects and words in picture naming, word-to-picture matching, lexical decision, or semantic association tasks (see Introduction). However, as we noted, the causal relationship between lesions to the sensorimotor circuitry and impaired action/verb processing in these tasks is questionable because the lesions were typically not circumscribed to the sensorimotor system. As a result, the patients' pathological profile invariably included other cognitive disorders like visuo-perceptual deficits, aphasia (mostly, anomia), and executive disorders. These disorders were overlooked in the

interpretation of the patient's performance while they are each likely, and in fact are known, to influence negatively, and specifically, the performance of brain-damaged patients with action pictures or verbs.

Thus, there is evidence that naming or comprehending visually-presented actions is more demanding on executive resources than naming objects. For instance, Rhee and colleagues (Rhee, Antiquena, & Grossman, 2001) and Silveri and colleagues (Silveri, Salvigni, Cappa, Della Vedova, & Puopolo, 2003) provided evidence for a significant correlation between a disproportionate deficit in action naming (Silveri et al., 2003) or action comprehension (Rhee et al., 2001) and executive resource limitation in patients with the frontal variant of frontotemporal dementia (see also Grossman et al., 2008, for similar evidence with patients with amyotrophic lateral sclerosis). Also, evidence was provided that the use of static, instead of dynamic, depictions of actions to probe action naming and comprehension was causally related to a seemingly disproportionate deficit in verb naming and comprehension in a patient with reduced executive resource (d'Honincthun & Pillon, 2008; see also den Ouden, Fix, Parrish, & Thompson, 2009). Furthermore, there are numerous reports of anomic individuals that were specifically impaired in naming action pictures, that is, in producing verbs, in the spoken or the written modality only. In these cases, therefore, the specific verb naming deficit did not arise from an impairment in action concept processing but, instead, from a deficit in retrieving the phonological or the orthographical form of words from a specific grammatical category (see for reviews, Pillon & d'Honincthun, 2010; Shapiro & Caramazza, 2003). Hence, a deficit in naming pictures of actions may have various functional causes, not only an impairment in processing action concepts, but also a limitation of executive resource or a verb specific lexical deficit. The present study was not subjected to these potential confounds, since the patient presented with a selective, in fact, isolated, deficit in action production, without any evidence of executive deficit or anomia during the entire period of the longitudinal investigation.

The results reported here corroborated the description of individual cases of patients who, following a left-hemispheric stroke or a neurodegenerative disease, performed within the normal range in naming pictures of action or of manipulable objects despite their mild to severe action production disorders (Bartolo et al., 2001; Chainay & Humphreys, 2003; Cubelli et al., 2000; Graham et al., 1999;

Negri et al., 2007; Ochipa, Rothi, & Heilman, 1994; Papeo et al., 2010; Pazzaglia, Smania, et al., 2008; Pazzaglia, Pizzamiglio, et al., 2008; Rapcsak et al., 1995 ; Rumiati et al., 2001; Tessari, Canessa, Ukmar, & Rumiati, 2007). Nevertheless, these observations were somewhat limited because failing to detect a naming deficit can be due to the sensitivity of the naming test being inappropriate to the patients (e.g., too familiar items or poorly demanding task given the premorbid abilities) or to the action disorder not being caused by a lesion affecting the sensorimotor circuitry itself. The present study was less exposed to these limitations.

First of all, the design enables to rule out that we failed to detect a subtle impairment because JR had presented exceptionally good premorbid conceptual abilities or, its corollary, because control participants had exceptionally poor performance. JR's naming performance was compared either to highly-educated *younger* participants (in the A/O naming task and in the picture association task) or to age-matched individuals attending the "University of the Elderly" (in the "AM/PA" timed naming task) and who performed above the mean performance of their age group in naming pictures of objects in a standardized naming test. Also, if JR's unimpaired performance in comparison to control participants were due to one of these reasons, his performance in conceptual processing tasks still should have decreased throughout the three-year period of testing if the neural system controlling action indeed supported conceptual processing of actions and of manipulable objects. Second, there are reasons to believe that the tasks and measures used here were appropriate and sensitive enough to disclose a mild conceptual impairment if present. As we mentioned before, the picture naming task is a sensitive task to disclose even mild conceptual impairments and we found that JR performed several picture naming tasks not only with normal accuracy but also at normal speed. Moreover, his performance was not impaired either in a more explicit conceptual task, in which he was asked to retrieve explicitly conceptual knowledge about objects, that is, what they are used for. Finally, it is unlikely that action concept processing was spared in JR because brain's atrophy did not affect the sensorimotor circuitry itself or did not affect critical brain structures within that circuitry. The results of the voxel-based morphometric analyses clearly showed significant and increasing atrophy in cortical areas comprising the primary motor and premotor cortex as well as the parietal-frontal circuits defined as shared neural substrate for action control and action concept processing within

Pulvermüller's, and Gallese and Lakoff's theories. Moreover, as evidenced by the behavioral results, brain atrophy in those areas actually had significant functional consequences, that is, a growing breakdown of critical sensorimotor functions such as those involved in the computation of the spatial and temporal aspects of gesture production and in the proper selection of finger and hand motor programmes.

On these grounds, the outcome of this study allows us to conclude that the sensorimotor circuitry that controls action production does not contribute in any significant way to (at least) those kinds of conceptual processes that are required to name or to understand the name (in word-picture verification tasks; Cf. footnote 1) of visually-presented actions and of manipulable objects, or to retrieve information about what these objects are used for. Thus, the evidence reported here strongly favors theories that posit functionally independent systems for action control and action conception.

Besides evidence provided by the study of patients with action production disorders, like the present one, other kinds of evidence support the view that the systems for action control and action conception are relatively autonomous one from the other. For example, we (Pillon & d'Honincthun, 2011) reported on the case study of an individual (GC) who, after extensive left temporal damage due to herpes simplex virus encephalitis, was left with severe anomia and speech comprehension difficulties at the age of 37. The study occurred 10 years post onset and we observed that the patient still presented a severe conceptual deficit for various sets of items, including actions and manipulable objects. Thus, the patient's performance was severely impaired in naming pictures or videos of actions, in naming pictures of objects, in understanding the names of actions or objects (in word-picture verification tasks), and in answering yes/no questions about actions' and objects' semantic features. In contrast, the patient had spared visuo-perceptual and visuo-praxic abilities, evidenced by his well above average drawing skills (see examples in Pillon & d'Honincthun, 2011; Figure 2). Also, he performed within the normal range in a standardized test of discrimination between visually-presented skilled or novel gestures and in several tasks in which he was asked to imitate the gestures implied by the same actions or manipulable objects he could not process conceptually. This pattern showed that even persistent disorders in conceptual processing of actions and of manipulable objects had no significant impact on the ability to recognize and perform the skilled movements associated with these

actions or objects. At the same time, it is striking that those visual and sensorimotor processes underpinning the residual recognition and production of skilled movements in that patient, did not seem to have assisted in any significant way the recovering of conceptual information about familiar actions or objects over time. Therefore, it appears that preserved sensorimotor as well as visuo-perceptual processes are far from being sufficient to drive the "re-learning" of action related concepts after brain damage, which, at the very least, points to distinct cognitive and neural resources being recruited in sensorimotor, perceptual, and conceptual processing.[6]

In addition, there are suggestions that congenitally altered sensorimotor experience does not hamper in any significant way conceptual development or action-related concept acquisition. In two previous studies, we investigated the conceptual processing of actions and of manipulable objects in a 51 year-old man, DC, who was born without upper limbs (i.e., bilateral upper limb aplasia due to thalidomide-related embryopathy) and never wore a prosthesis (Vannuscorps et al., 2013, 2014; see also Vannuscorps & Caramazza, 2016). This condition prevented him to perform manual actions or to manipulate familiar objects from birth, although some manual actions and some objects could be performed or used with his feet, mouth, or whole body. We assessed conceptual processing of actions and of manipulable objects in DC with several picture or video naming tasks. We surmised that if sensorimotor processes were constitutive of action-related concept acquisition, DC should have richer concepts and therefore should be more efficient for actions and objects he had already realized or used, even idiosyncratically, in comparison with those he did not. We found that DC was as efficient (accurate and fast) as normally-limbed participants in naming actions or manipulable objects, whether or not he had already performed or used them. Thus, although DC was deprived of sensorimotor experience for a number of actions and objects from birth, the conceptual representations he acquired were seemingly as rich and/or as efficient as those acquired by normally-limbed individuals. These findings thus pointed out to the relative autonomy of conceptual development vis-à-vis idiosyncratic sensorimotor experiences, as already evidenced by studies having investigated object and action concepts in congenitally blind individuals (Bedny & Saxe, 2012).

As a final matter, we would like to make clear that the conclusion we drawn from this study, namely, that action control and action conception mainly relies on independent functional systems,

does not undermine the grounding approach to cognition as a whole — it applies specifically to the issue of how the cognitive and neural systems responsible for action control and action conception are functionally related[7]. Moreover, this conclusion does not preclude that the sensorimotor (or perceptual) circuitry could play a significant role in other cognitive domains, say, spatial or numerical processing, working memory, or decision making, or in any task — including conceptual tasks — that calls upon imagery, memory, or prediction of motor acts. Actually, in the conceptual domain, our findings are consistent with what Meteyard and colleagues (2012) called « secondary embodiment ». That is, even if the conceptual system is functionally independent of the system controlling action production, it is directly linked to it by non-arbitrary connections. Therefore, when a concept of action or of manipulable object is being processed, activation automatically flows from the conceptual to the action production system. In that way, while performing a task involving action related stimuli, both conceptual and sensorimotor information is automatically activated, even if sensorimotor information is not required or relevant for the task. Sensorimotor information can then facilitate or interfere on performance depending on the congruency between the output of both the conceptual and the action production systems (Hauk & Tschentsher, 2013).

Our findings are compatible also with a « weak embodiment » view, to continue borrowing Meteyard and colleagues' formulations. Here the idea is that sensorimotor information activated within the action production system while conceptual processing takes place is *constitutive of the meaning* of actions, even if not *central* to that meaning. Sensorimotor content would *add* meaning without being *essential* to the meaning content required, for example, in the kind of tasks that were used in this study. Thus, sensorimotor content would not be necessary for categorizing and naming an action or retrieving knowledge about the function of an object. However, it could add relevant information in more demanding conceptual tasks, for example, when action stimuli are unfamiliar or visually ambiguous (Vannuscorps et al., 2013). Certainly, the sensorimotor content also has an impact on the phenomenological experience associated with viewing, naming, and (feeling of) knowing what an action or an object is. However, at present, it is unclear whether distinct *a priori* predictions could be drawn from that « weak embodiment » view compared to the « secondary embodiment » view, and how both positions could be empirically distinguished.

Finally, even stronger views of embodiment could handle with the findings of this study but only with great expense — that is, either by abandoning some of their central assumptions or by adding new hypotheses on how neural representations and neural processes are related. For instance, within a distributed view of embodiment, one may assume multiple and distributed grounding systems in the brain for action (and other kinds of) concepts. Thus, the sensorimotor circuitry involved in action control would just be *one* of the grounding systems for action concepts, these concepts being also grounded in perceptual (visual and auditory) systems. Under this view, the sparing of action concepts in JR is accounted for by their being also represented within the perceptual system, which indeed appeared relatively preserved in JR. (Note however that within some theories, like Gallese and Lakoff's, action control and action perception systems share their neural substrate.) However, abandoning the notion that action concepts mostly depend on the brain's motor system, as opposed to vision related concepts for instance, would considerably weaken the explanatory power of conceptual grounding theories, notably in respect to category-specific conceptual deficits, which were naturally *predicted* by the current strong views of concept grounding. Another logical possibility, for reconciling strong views of concept grounding with our findings, would be to assume that only the *representational* substrate is shared by action control and action conception, not the neural machinery that retrieves these representations for acting *versus* conceiving. In that case, strong grounding theories would lose one of their most attractive aspect — parsimony — and should develop articulated and testable hypotheses on how such functionally independent machineries are realized by the cognitive and neural systems.

In conclusion, the neuropsychological study reported herein added novel evidence to the view that the cognitive and neural circuitry that controls the production of actions has, at best, a very limited functional role in the representation and processing of action concepts. Our findings showed that processing concepts of actions and concepts of manipulable objects hinges on cognitive and neural resources that are distinct from those underlying the control of voluntary movements – a case against motor embodiment of action related concepts. These findings are not inconsistent with the grounded approach of cognition as a whole, but should encourage to articulate detailed hypotheses about which cognitive components are dependent on the brain's sensory and motor systems and which are

relatively autonomous from them, in a way that accounts for the remarkable plasticity and creativity of human cognition and behavior.

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Figure captions

Figure 1. (A) Transversal (*top*) and sagittal (*bottom*) sections of JR's brain at the four periods of testing (T1, T2, T3, and T4). (B) JR's percentage of volume loss between T1 and T4 in ROIs within the left and right hemisphere. Bars in light grey represent the normal volume loss in the same ROIs in healthy elderly control participants (Mean age= 75.6) calculated from the annual rate reported by Fjell et al. (2009).

Figure 2. JR's and control participants' percentage of correct responses in two picture naming tasks: (A) "Actions & Manipulable objects/Plants & Animals" (AM/PA) picture naming task. (B) "Actions and Objects"(A/O) picture naming task. JR's results are displayed for the four periods of testing (T1 to T4). Error bar = range.

Figure 3. JR's percentage of correct responses at the various tasks assessing gesture processing (A) and conceptual processing (B) with the same set of manipulable objects and instrumental actions, at the four periods of testing (T1 to T4).

Figure 4. JR's and control participants' percentage of correct responses (A) and mean response latency (B) in the "Actions & Manipulable objects/Plants & Animals" (AM/PA) timed picture naming task performed at the last period of the investigation (T4). Error bar = range.

Table 1. Neuropsychological examination in patient JR from T1 to T4.

TESTS	T1		T2		T3		T4	
	JR's score	**JR vs. controls**	**JR's score**	**JR vs. controls**	**JR's score**	**JR vs. controls**	**JR's score**	**JR vs. controls**
GLOBAL FUNCTIONING								
Minimal Mental State Examination (MMSE) [1]	30	n.a	29	n.a	30	n.a	28	n.a
SHORT TERM MEMORY								
Number span forward	5	*z* = -0.91	6	*z* = 0	5	*z* = -0.91	5	*z* = -0.91
Spatial Span forward [2]	5	*z* = -1	6	*z* = -0.33	n.a	n.a	6	*z* = -0.33
WORKING MEMORY								
Number span backward	5	*z* = 0.82	5	*z* = 0.82	5	*z* = 0.82	5	*z* = 0.82
Spatial Span backward [2]	5	*z* = 0	3	*z* = -1	n.a	n.a	5	*z* = 0
LONG TERM MEMORY								
RL/RI [3]								
Free recall 1	11	*z* = 1.58	7	*z* = -0.26	8	*z* = 0.20	11	*z* = 1.58
Free recall 2	11	*z* = 0.88	12	*z* = 1.32	7	*z* = -0.89	10	*z* = 0.44
Free recall 3	13	*z* = 1.16	8	*z* = -1.08	12	*z* = 0.71	13	*z* = 1.16
Delayed recall	11	*z* = 0.30	5	***z* = -2.42**	9	*z* = -0.60	13	*z* = 1.18
Doors Test [4]								
Part A	12	P99	10	P75	9	P50	11	P90 - 95
Part B	6	P75	9	P95-P99	5	P50	5	P50
Total	18	P90	19	P95	14	P50	16	P75
EXECUTIVE FUNCTIONS								
Trail Making Test [5]								
Duration A	62	*z* = 0.72	52	*z* = 0.17	65	*z* = 0.89	n.a	n.a
Duration B	133	*z* = 0.29	97	*z* = - 0.41	Impossible		n.a	n.a
Duration B – A	71	*z* = 0.05	45	*z* = -0.6	n.a		n.a	n.a

Errors A	0	*z* = 0.13	0	*z* = 0.13	0	*z* = 0.13	n.a	n.a
Errors B	0	*z* = 0.33	4	*z* = -4.73	Impossible		n.a	n.a
Errors B – A	0	*z* = 0.41	4	*z* = -7.13	n.a		n.a	n.a
Fluency								
Letter fluency (P)	22	*z* = 0.01	19	*z* = -0.27	24	*z* = 0.2	14	*z* = -0.75
Category fluency (Animals)	27	*z* = -0.07	31	*z* = 0.41	34	*z* = 0.78	33	*z* = 0.67
Stroop Test [5]								
Duration								
Naming	81	*z* = -1.33	82	*z* = -1.41	90	***z* = -2.08**	121	***z* = -4.67**
Reading	59	***z* = -2.5**	58	***z* = -2.33**	65	***z* = -3.5**	81	***z* = -6.17**
Interference	171	*z* = -1.5	166	*z* = -1.34	200	***z* = -2.41**	201	***z* = -2.44**
Errors								
Naming	1	***z* = -3.14**	0	*z* = 0.31	0	*z* = 0.31	0	*z* = 0.31
Reading	1	***z* = -7.54**	0	*z* = 0.15	0	*z* = 0.15	0	*z* = 0.15
Interference	5	***z* = -7.05**	3	***z* = -3.97**	1	*z* = -0.89	0	*z* = -0.64
Interference index								
Duration	90	*z* = -1.28	84	*z* = -1.04	110	*z* = -2.08	80	*z* = -0.88
Errors	4	*z* = -5.10	3	*z* = -3.71	1	*z* = -0.93	0	*z* = 0.46
SPATIAL ABILITIES								
Line bisection [6]								
20 cm	-4 mm	*z* = - 0.74	-4 mm	*z* = - 0.74	+5 mm	*z* = - 0.96	+5mm	*z* = - 0.96
5 cm	+0.5 mm	*z* = - 0.2	0 mm	*z* = 0.06	0 mm	*z* = 0.06	+1mm	*z* = - 0.56
Bell test [6]								
Duration	183	*z* = -0.82	126	*z* = 0.15	200	*z* = -1.11	163	*z* = -0.47
Miss	2	*z* = 0.24	1	*z* = 0.69	1	*z* = 0.69	2	*z* = 0.24
VISUAL PROCESSING								
B.O.R.B [7]								
Minimal feature view	25	*z* = 0.85	23	*z* = -0.15	25	*z* = 0.85	25	*z* = 0.85
Object/Non-Object decision								

A: Hard	26	z = -0.45	24	z = -1.36	24	z = -1.36	25	z = -0.91
B: Hard					22	z = -0.72	22	z = -0.72
B: easy					28	z = -1.79	28	z = -1.79
A: Easy					27	z = -0.79	29	z = 0
Global performance					101	**z = -2.4**	104	z = -1.9

[1] Folstein, Folstein, & McHugh (1975); French norms from Derouesné, Poitreneau, Hugonot, Kalafat, Dubois & Laurent (1999); [2] Smirni, Villardita, & Zappala (1983); [3] Van der Linden, Coyette, Wyns, Calicis, and Le groupe "Mémoire" du GRECO (2004); [4] Baddeley, Emslie, and Nimmo-Smith (1994); [5] Reitan (1955); French norms from Meulemans (2008); [6] Gauthier, Dehaut & Joanette (1989); French norms from Rousseaux et al. (2001); [7] Riddoch and Humphreys (1993). In bold, $p < 0.05$.

Table 2. Language examination in patient JR from T1 to T4.

TESTS	T1	T2	T3	T4
REPETITION				
Regular nouns	20	20	20	19
Regular verbs	20	20	20	20
Pseudo-words	16	20	20	19
READING				
Regular nouns	20	20	20	20
Regular verbs	20	20	20	20
Irregular nouns	20	18	18	20
Pseudo-words	19	17	19	19
WRITING				
Regular nouns	20	20	n.a	n.a
Regular verbs	20	20	n.a	n.a
Irregular nouns	17	19	n.a	n.a
Pseudo-words	20	20	n.a	n.a
AUDITORY LEXICAL DECISION TASK				
Nouns	36/36	36/36	n.a	36/36
Pseudo-nouns	34/36	34/36	n.a	34/36
Verbs	36/36	36/36	n.a	36/36
Pseudo-verbs	33/36	36/36	n.a	36/36
PICTURE NAMING TASK				
Lexis[1]	54/64 (z = 0.6)			51/64 (z = 0)

[1]de Partz, Bilocq, De Wilde, Seron, & Pillon (2001).

Table 3. Tests of simple movement production in patient JR in T1 and T4.

TESTS	T1		T4	
	JR's score	JR vs. controls	JR's score	JR vs. controls
Strength (Jamar hand dynamometer)[1]				
Right hand	35 kg	z = -1.46	30kg	z = -1.7
Left hand	30 kg	z = -1.47	1.5kg	z = **-3.15**
Hand dexterity (Box & Block Test)[2]				
Right hand	43	z = **-2.82**	23	z = **-5.63**
Left hand	30	z = **-3.73**	10	z = **-6.11**
Finger dexterity (Purdue Pegboard)[3]				
Right hand	9	z = **-3.45**	6	z = **-5.05**
Left hand	5	z = **-5.69**	1	z = **-8.47**

[1] Mathiowetz, Kashman, Volland, Weber, Dowe & Rogers (1985); [2] Mathiowetz, Volland, Kashman, & Weber (1985); [3] Tiffin & Asher (1948). In bold, $p < 0.05$.

Table 4. Tests of complex movement production in patient JR from T1 to T4. Percentage of correct responses by condition.

Tests	T1	T2	T3	T4	T1/last session McNemar test χ^2
GESTURE RECOGNITION TASK					
Discrimination[1]	92% (*z* = 1.22)	95% (*z* = 1.91)	92% (*z* = 1.22)	82% (*z* = -0.87)	2.5
PRODUCTION BY IMITATION					
Skilled gestures					
Uni-manual - Right hand (3)	75% (*z* = -1.81)	60% (*z* = -3.74)	55% (*z* = -4.39)	25% (*z* = -8.13)	5.78*
Uni-manual - Left hand (5)	60% (*z* = -3.74)	40% (*z* = -6.33)	10% (*z* = -10.20)	n.t.	8.1**
Novel gestures					
Uni-manual - Right hand (4)	40% (*z* = -1.03)	30% (*z* = -1.68)	20% (*z* = -2.32)	10% (*z* = -2.97)	3.12•
Uni-manual - Left hand (6)	45% (*z* = -0.71)	30% (*z* = -1.68)	10% (*z* = -2.97)	n.t.	5.14*
PRODUCTION ON VERBAL COMMAND					
Uni-manual - Right hand (1)	70% (*z* = - 5.16)	70% (*z* = -5.16)	55% (*z* = -9.04)	35% (*z* = -14.20)	4*
Uni-manual - Left hand (2)	55% (*z* = - 9.04)	35% (*z* = -14.20)	20% (*z* = -18.07)	n.t.	3.27•
TOTAL GESTURE PRODUCTION					
Uni-manual - Right hand	62% (*z* = -2.37)	53% (*z* = -3.44)	50% (*z* = -3.87)	24% (*z* = -7.26)	15.61**
Uni-manual - Left hand	53% (*z* = -3.44)	35% (*z* = -5.81)	13% (*z* = -8.61)	n.t.	30.03**

Brackets = Order of passation. [1] In comparison to 10 control participants. n.t. = not tested. • $p < 0.1$; * $p < 0.05$; ** $p < 0.01$

Table 5. Tests of complex movement production in patient JR from T1 to T4. Distribution of errors by condition.

	T1				T2				T3				T4			
	Content Errors	**Temporal Errors**	**Spatial Errors**	**Other**	**Content Errors**	**Temporal Errors**	**Spatial Errors**	**Other**	**Content Errors**	**Temporal Errors**	**Spatial Errors**	**Other**	**Content Errors**	**Temporal Errors**	**Spatial Errors**	**Other**
PRODUCTION BY IMITATION																
Skilled gestures																
Uni-manual - Right hand	0%	20%	80%	0%	0%	40%	60%	0%	0%	18%	82%	0%	4%	22%	74%	0%
Uni-manual - Left hand	0%	33%	58%	8%	0%	29%	65%	6%	0%	23%	74%	3%	0%	0%	0%	100%
Novel gestures																
Uni-manual - Right hand	0%	22%	74%	4%	0%	17%	83%	0%	0%	33%	67%	0%	0%	6%	82%	12%
Uni-manual - Left hand	0%	13%	67%	20%	0%	20%	76%	4%	0%	14%	77%	9%	0%	0%	0%	100%

PRODUCTION ON VERBAL COMMAND																
Uni-manual - Right hand	0%	0%	83%	17%	0%	17%	83%	0%	0%	25%	62.5%	12.5 %	0%	24%	70%	6%
Uni-manual - Left hand	0%	0%	91%	9%	0%	27%	67%	6%	0%	32%	64%	4%	0%	0%	0%	100%

Table 6. Mean and standard deviation of the spoken word frequency, concept familiarity, imageability, and age of acquisition for the various subsets of items in the naming tasks used in the study.

Naming task	N	Spoken word frequency [1]	Familiarity [2]	Imageability [3]	Age of acquisition [3]
Actions & Manip. objects/Plants & Animals (AM/PA)					
Actions	24	6.93 (8.54)	2.87 (0.81)	4.22 (0.34)	2.38 (0.57)
Manipulable objects	22	5.59 (6.19)	2.79 (1.06)	4.41 (0.38)	2.69 (0.71)
Plants	24	6.82 (7.27)	2.87 (0.76)	4.51 (0.40)	2.52 (0.56)
Animals	24	10.36 (10.76)	2.67 (0.81)	4.44 (0.43)	2.44 (0.57)
Actions/Objects (A/O)					
Actions	32	40.61 (61.94)	3.20 (0.61)	3.75 (0.46)	n.a.
Manipulable objects	16	5.63 (8.12)	2.79 (0.64)	4.56 (0.56)	n.a.
Non-manipulable objects	16	11.25 (16.80)	3.01 (1.33)	4.62 (0.32)	n.a.
Items probed in movement and conceptual processing					
Objects	50	11.39 (25.28)	2.86 (1.07)	4.29 (0.53)	2.77 (0.66)
Actions	20	39.22 (94.81)	n.a.	n.a.	n.a.

[1] Number of lemma occurrences per million in a corpus of subtitles of films (New, Brysbaert, Pallier & Veronis, 2007); [2] From Alario and Ferrand (1999), Bonin, Peereman, Malardier, Meot and Chalard (2003), and Bonin et al. (2004) for the items of the "AM/PA" picture naming task; rated on a five point scale (1=low, 5=high familiarity) by 20 subjects (mean age=35.95) for the items of the "A/O" picture naming task. [3] From Alario and Ferrand (1999), Bonin, Peereman et al. (2003), and Bonin et al. (2004). n.a=non-available.

Apprendix A. Conceptual processing of actions and of manipulable objects vs. matched sets of non-action-related stimuli. List of items in the 2 naming tasks (a) Actions, Manipulable objects, Plants, and Animals (AM/PA) (B) Actions/Objects (A/O).

Actions & Manip. Objects/plants & animals (AM/PA)			**Actions/objects (A/O)**	
Actions	Salt shaker	Strawberry	**Actions**	**Manipulable objects**
To paint	Pencil	Clover	To pinch	Stopwatch
To saw	Comb	Rose	To nail	Set square
To draw	Compass	Spruce	To pierce	Rake
To typewrite	Dart	Palm	To sprinkle	Guitar
To erase	Tambourine	**Animals**	To wax	Spade
To pour	Nail file	Mosquito	To mix	Spud
To embrace	Violin	Spider	To collect	Rifle
To sign	Harmonica	Slug	To tickle	Hammer
To knit	Envelope	Shark	To press	Ruler
To grate	Key	Oyster	To saw	Revolver
To spray	Doll	Lizard	To paint	Screwdriver
To nail	Compass	Pigeon	To slap	Trumpet
To plug	Top	Mole	To cover with plastic	Synthesizer
To spit	**Plants**	Crab	To spray	Mower
To bite	Celery	Rooster	To cumple	Shovel
To lick	Peach	Boar	To applaud	Compass
To sew	Artichoke	Goose	To dance	**Non manipulable objects**
To blow	Onion	Chicken	To sing	Chair
To swim	Pepper	Shrimp	To crawl	Truck
To crawl	Pumpkin	Donkey	To kneel	Houseboat
To yawn	Mushroom	Beaver	To stretch	Balloon
To sneeze	Cactus	Duck	To lick	Seaplane
To shout	Asparagus	Deer	To run	Catamaran
To ski	Carrot	Hedgehog	To slide	Pouffe
Manipulable objects	Peanut	Doe	To hide	Van
Syringe	Chestnut	Lamb	To flight	Sink
Cigar	Nuts	Rabbit	To spit	Submarine
Stethoscope	Fern	Ladybug	To parade	Hang-glider
Whistle	Pineapple	Chick	To ski	Couch
Rake	Holly		To skate	Paragliding
Tie	Watermelon		To shout	Armchair
Ladle	Grapes		To whisper	Bathtub
Padlock	Cherry			Boat

Appendix B. Gesture processing and conceptual processing tested with the same set of actions and manipulable objects. List of the 50 manipulable objects and 20 instrumental actions used in the various tasks.

Manipulable Objects		Actions
Screwdriver	Magnifying glass	To screw
Pliers	Guitar	To nail
Hammer	Lighter	To cut
Scisors	Bulb	To vaccum up
Thermos	Bell	To rake
Frying pan	Ruler	To sew
Clothes peg	Maracas	To file
Trumpet	Flashlight	To saw
Vacuum cleaner	Pitcher	To shoot
Rake	Whistle	To staple
Fork	Helm	To erase
Bow	Keyboard	To pour
Needle	Key	To typewrite
Sword	Compass	To trace
Phone	Cigar	To throw
Nail file	Catapult	To draw
Saw	Chopper	To chop
Revolver	Pencil	To comb
Stapler	Ping-pong racket	To plug
Tommy gun	Ax	To paint
Boomerang	Accordion	
Spoon	Comb	
Gum	Plug	
Piano	Zipper	
Harmonica	Brush	

FOOTNOTES

[1] We do not mention here evidence from neuroimaging, neurophysiological, and behavioral studies demonstrating that motor processes are automatically activated when actions or manipulable objects or words referring to them are processed in tasks that do not envolve any intention to act (see for reviews, Aziz-Zadeh & Damasio, 2008; Culham & Valyear, 2006; Fischer & Zwaan, 2008; Lewis, 2006; Watson, Cardillo, Ianni, & Chatterjee, 2013; Willems & Hagoort, 2007). As it is now widely acknowledged, whereas such evidence supports the view that motor processes are automatically engaged when action concepts are retrieved, it does not constitute evidence that motor processing is *constitutive of* concept processing (e.g., Chaterjee, 2010; Csibra, 2008; Hauk & Tschentscher, 2013; Hickok, 2009; Kiefer & Barsalou, 2013; Mahon & Caramazza, 2008; Vannuscorps, Andres, & Pillon, 2013, 2014).

[2] In a number of reports, it was even unclear whether the deficit was specific to action pictures or verbs, because no data was provided about the patients' performance with matched sets of non-action-related stimuli like animals, plants, or non-manipulable objects (e.g., Albani et al., 2010; Bertella et al., 2002; Cotelli et al., 2006; Pignatti et al., 2006; Spatt et al., 2002; Silveri & Ciccarelli, 2007; Stamenova et al., 2011). Moreover, in most reports, it was not established whether the deficit was conceptual in nature, affecting specifically actions as a conceptual category, or was caused by the lexical retrieval of verbs, as a grammatical category of words, being impaired (see for discussion, Pillon & d'Honincthun, 2010).

[3] In addition, we had included word/picture verification tasks in the protocol of investigation. We did so in order to be able to determine whether a naming deficit, if present, was due to an impairment at the word production level or at the conceptual level of processing entailed in the naming task. Because no naming deficit was observed in JR whatever the set of stimuli or the period of assessment, and since the word-picture verification task is known to be less sensitive to detect a mild/moderate conceptual impairment than the naming task, we decided not to report here the results of the

word/picture verification tasks, for the sake of brevity. Needless to say, the results obtained in the word-picture verification tasks led to the same conclusions as those drawn from the naming tasks.

[4] Initially, the task was composed of 24 manipulable objects but 2 objects were discarded because the 3 judges disagreed about their manipulability.

[5] However, in 28% of the trials, the same picture served as the target response for both the "movement" and the "function" conditions, the two other pictures in the array being two visually-related foils. These trials were included in order to discourage the participants to discard the picture he chosen in the first presentation of the probe when presented with it the second time.

[6] GC's pattern of recovery over time could only be inferred *a posteriori*. Of course, further studies focusing on the follow up of functional recovery across domains after a stroke are needed.

[7] Also, we would like to make clear that our conclusion does not concern other issues that are related but (in our opinion) should be treated as independent from that issue, like the organization of conceptual knowledge in the brain (e.g., Caramazza & Shelton, 1998; Patterson et al., 2007; Binder et al., 2009) and the modality-specific vs. amodal nature of conceptual representations (e.g., Barsalou, 1999; Machery, 2007; Mahon & Caramazza, 2008). Thus, for example, our findings are *not* inconsistent with the view that the organization of conceptual knowledge in the brain is *driven* by the sensory and motor processing channels (e.g., Warrington & Shallice, 1984) and, in particular, with the proposal that the neural substrate underpining action control and action conceptual processing are adjacent (Martin, 2007). They do, however, contradict the view that both kinds of processes depend on the same neural circuitry.