Neuroscience and Biobehavioral Reviews 80 (2017) 673–687

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Review article

Losing ground: Frontostriatal atrophy disrupts language embodiment in Parkinson's and Huntington's disease

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ARTICLE INFO

Keywords:
Frontostriatal circuits
Parkinson's disease
Huntington's disease
Embodied cognition
Action language
Motor-language coupling
Syntax

ABSTRACT

Within the language domain, movement disorders triggered by frontostriatal damage are characterized by deficits in action verbs, motor-language coupling, and syntax. However, these impairments have not been jointly interpreted under a unifying rationale or integratively assessed in terms of possible clinical implications. To bridge these gaps, here we introduce the "disrupted motor grounding hypothesis", a new framework to conceive such impairments as disturbances of embodied mechanisms (high-order domains based on the recycling of functionally germane sensorimotor circuits). We focus on two relevant lesion models: Parkinson's and Huntington's disease. First, we describe the physiopathology of both conditions as models of progressive frontostriatal impairment. Then, we summarize works assessing action language, motor-language coupling, and syntax in samples at early and preclinical disease stages. To conclude, we discuss the implications of the evidence for neurolinguistic modeling, identify key issues to be addressed in future research, and discuss potential clinical implications. In brief, our work seeks to open new theoretical and translational avenues for embodied cognition research.

1. Introduction

Frontostriatal circuits are neuronal pathways that connect the frontal lobes with the basal ganglia. Specifically, they originate in prefrontal and motor regions and project to the striatum, followed by the globus pallidus, the substantia nigra, and then the thalamus, with feedback loops leading from the latter structure back to the prefrontal cortex (Alexander and Crutcher, 1990; Alexander et al., 1986; Tekin and Cummings, 2002) –see Fig. 1A for details. The main innervations to the basal ganglia are glutamatergic (predominantly from prefrontal cortical areas) and dopaminergic (from the substantia nigra and the ventral area). Further inputs to these circuits are serotoninergic, cholinergic, and noradrenergic. The activity of these pathways modulates several higher-order processes and, more particularly, motor function (Packard and Knowlton, 2002).

More specifically, the frontostriatal network is comprised of highly interactive cortico-subcortical loops running in parallel through the basal ganglia (Alexander et al., 1986); –see Fig. 1B. First, the motor loop, via the putamen to the supplementary motor area, receives input from the premotor, primary motor, and somatosensory cortices. As specified below, this circuit is crucially involved in the initiation, coordination, and other aspects of bodily motion. Second, the associative loop, with inputs from the dorsolateral prefrontal and the lateral orbitofrontal cortices to the head of the caudate nucleus, and outputs leading back from the basal ganglia via the thalamus, is mainly implicated in executive and other high-order cognitive functions (Krack et al., 2010; Monteiro and Feng, 2016). Finally, in the limbic loop, the ventral striatum receives its main input from the medial orbitofrontal cortex and the amygdala, and, in turn, projects back to these areas via the medial dorsal nucleus of the thalamus. The latter circuit is implicated in emotional processing, motivational states, and reward-based learning, so it is not directly relevant for the processes targeted in this work. Furthermore, the basal ganglia may be divided into (i) a direct pathway, which runs from the striatum directly to the output nuclei

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http://dx.doi.org/10.1016/j.neubiorev.2017.07.011
Received 24 January 2017; Received in revised form 25 July 2017; Accepted 27 July 2017
Available online 02 August 2017

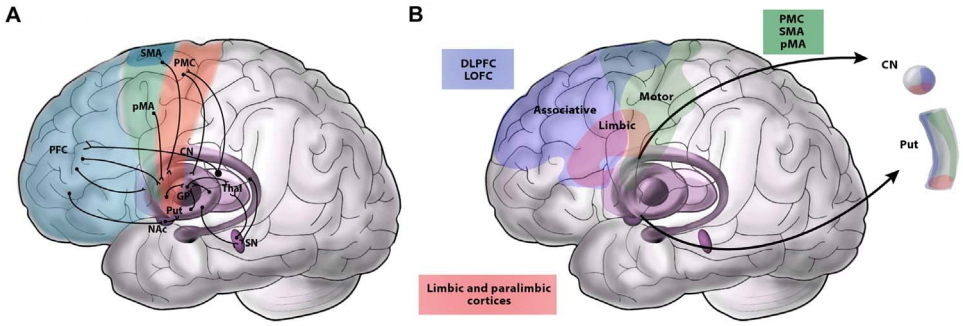

Fig. 1. (A) Schematic representation of frontostriatal circuits. The striatum (which comprises the caudate nucleus, the putamen, and the nucleus accumbens) receives inputs from a range of cortical areas, including various motor and frontal regions. Connections between such regions and striatal structures comprise three distinct circuits (Tekin and Cummings, 2002). On the one hand, the motor circuit originates from neurons in the supplementary cortex, the premotor area, and the primary motor cortex. These areas project to the putamen, followed by the globus pallidus and the substantia nigra pars reticularis. The globus pallidus connects to the ventrolateral nucleus of the thalamus, which projects back to the motor cortex. On the other hand, the associative circuit originates in the prefrontal cortex –particularly, in the dorsolateral prefrontal and lateral orbitofrontal cortices. These areas project to the caudate nucleus and the anteromedial portion of the putamen (Krack et al., 2010; Monteiro and Feng, 2016). Then, neurons in these sites project to the globus pallidus and the rostrolateral substantia nigra pars reticularis, and then project back via the anterior nucleus of the thalamus. Finally, in the limbic circuit, the lateral orbitofrontal cortex and the amygdala project to the ventral striatum, including the nucleus accumbens, while projections from the latter to the cortex are mediated by the medial dorsal nucleus of the thalamus (Krack et al., 2010; Monteiro and Feng, 2016). The panel omits non-frontal projections from the basal ganglia, including links to the somatosensory cortex, the inferior and middle temporal gyrus, the parietal lobe, the cerebellum, and the thalamus (Leh et al., 2007). Circles represent the origin of connections and hooks indicate their terminal site. **(B)** Schematic representation of the overlap among the three frontostriatal circuits. Frontostriatal networks comprise three functionally distinguishable circuits. The associative circuit (including the dorsolateral prefrontal cortex, lateral orbitofrontal cortices, the caudate nucleus, the putamen, the globus pallidus, the substantia nigra, and the anterior nuclei of the thalamus) is critical for executive and other high-order cognitive functions. The limbic circuit (spanning the hippocampus, the amygdala, the paralimbic and limbic cortices, the ventral protion of the caudate and putamen, the nucleus accumbens, the substantia nigra, the globus pallidus, and the mediodorsal nucleus of the thalamus) is implicated in emotional processing, motivational states, and reward-based learning. The motor circuit (comprising premotor, primary motor, and somatosensory cortices, the posteriolateral putamen, the globus pallidus, the substantia nigra, and the ventrolateral thalamus) subserves the initiation, coordination, sequencing, selection, and control of bodily movements. Image based on Monteiro and Feng (2016), with permission. SMA: supplementary motor area; pMA: premotor area; PMC: primary motor cortex; CN: caudate nucleus; NAc: nucleus accumbens; SN: substantia nigra; Thal: thalamus; Put: putamen; GP: globus pallidus; DLPFC: dorsolateral prefrontal cortex; LOFC: lateral orbitofrontal cortex; PFC: prefrontal cortex.

(intern segment of the globus pallidus and the substantia nigra pars reticulate); and (ii) an indirect pathway, which connects the input to the output via the external segment of the globus pallidus and the subthalamic nucleus.

In particular, the frontostriatal motor loop comprises putative substrates of bodily movement, playing critical roles in motor learning (Andalman and Fee, 2009; Lehericy et al., 2005; Turner and Desmurget, 2010), sequential motor control (Alexander and Crutcher, 1990; Alexander et al., 1986; Graybiel, 2008; Marsden and Obeso, 1994), response vigor (Turner and Desmurget, 2010), and action selection (Grillner et al., 2005; Houk et al., 2007). Indeed, the disruption of these circuits is a hallmark of various neurodegenerative movement disorders, as clearly seen in Parkinson's disease and Huntington's disease (PD and HD, respectively) (Beste et al., 2011; Zgaljardic et al., 2003). Both syndromes are associated with basal ganglia atrophy, dysfunctional frontobasal connections, and altered dopamine levels (Helie et al., 2015), and they afford some of the most compelling evidence on the links between frontostriatal circuitry and bodily motion: while PD involves symptoms such as resting tremor, postural instability, and bradykinesia (Helmich et al., 2012; Rosin et al., 1997), HD is mainly characterized by overshooting choreic movements (Ross and Tabrizi, 2011).

Also, as stated above, frontostriatal pathways subserve high-order cognitive functions, such as decision making, attention, working memory, reward monitoring, motivation, and error monitoring (Beste et al., 2008; Dubois and Pillon, 1996; Enzi et al., 2012; Owen, 2004). More particularly, within the language domain, they play critical roles in three functions, namely: (i) action language (verbal expressions denoting bodily motion) (Bak, 2013; García and Ibáñez, 2016; Hochstadt et al., 2006; Pulvermüller, 2005, 2013), (ii) motor-language coupling (the integration of action-verb information with ongoing motor actions) (Cardona et al., 2013; García and Ibáñez, 2014), and (iii) syntax (grammatical patterning of words and phrases) (Ullman, 2004, 2008). Indeed, these three domains are distinctively compromised in both PD and HD, even in early and preclinical stages (e.g., Abrevaya et al., 2017; García et al., 2017c; Melloni et al., 2015).

Although informative reviews of such clinical findings are available (e.g., Bak, 2013; Cardona et al., 2013; Damasio, 1989; Dominey et al., 2003; Glenberg and Kaschak, 2002; Pulvermüller, 1999), they have addressed only selected subsets of the evidence with a restricted theoretical focus and without jointly considering both PD and HD as complementary frontostriatal lesion models. Also, no work so far has offered a unified review of these three impaired domains across both conditions (in fact, no previous review exists of the evidence from motor-language coupling tasks in these two populations). Moreover, no attempt has yet been made to synergistically interpret such patterns under a unifying theoretical rationale, or to delineate possible clinical applications of the findings considering the patients' overall cognitive status and the sensitivity of these domains to tap deficits in asymptomatic subjects at risk for either disease. The present review aims to bridge all these gaps by conceiving of the three functional specializations above as embodied mechanisms, that is, high-order systems grounded in functionally germane sensorimotor circuits.

Our rationale runs as follows. In line with the neuronal recycling framework (Dehaene and Cohen, 2007), we contend that, as individuals develop linguistic skills, the circuits which represent and coordinate motoric information become recycled to subserve functionally akin linguistic operations. Thus, specific frontostriatal pathways critical for mapping, integrating, and sequencing hierarchically organized movement patterns emerge as functionally apt bases for lexico-semantic mapping of movement (action language), integrating verbal and motor information (motor-language coupling), and sequencing hierarchically organized lexical patterns (syntax).

First, during verbal processing, motor circuits are differentially recruited to map action semantics. For example, linguistic stimuli referring to actions preferentially performed with a particular part of the body (e.g., the verbs *lick*, *pick*, and *kick*) activate motor and premotor areas, even in a somatotopic manner (Pulvermüller, 2005, 2013). Crucially, however, these circuits evince no such fine-grained distinctions for meanings related to other bodily modalities, such as olfactory (González et al., 2006) or taste-related (Barrós-Loscertales et al., 2012) meanings. Thus, in the development of semantic skills, they seem to have been specifically recycled to subserve action-related meanings.

Second, frontostriatal networks have a crucial role in integrating action routines with high-order processes. For example, gait can be disturbed by cognitive tasks like mental tracking (Al-Yahya et al., 2011). More particularly, in tasks which require manual responses during processing of action sentences, specific motor hubs exchange

information with cortical regions involved in abstract semantic processes (Ibáñez et al., 2013). This functional property is proposed to support motor-language coupling at large.

Finally, frontostriatal circuits, as key substrates of procedural memory, are critical in any form of processing that requires sequencing structurally organized patterns of information (Janata and Grafton, 2003; Packard and Knowlton, 2002). As captured by well-established neurocognitive models of language (e.g., Hagoort, 2013; Kotz et al., 2009; Ullman, 2001), one of the defining characteristics of syntactic processes, at the phrasal, clausal, or sentential levels, is that they involve grammatically constrained linearization of words and recognition of the structural relations between them. These operations are the foundation of multiple syntactic phenomena, such as subject-verb agreement, phrase structure parsing, participant role assignment, topicalization, establishment of long-distance dependencies, and other forms of sentential hierarchy building (e.g., identification of subject-relative and object-relative sentences). Despite their functional specificities, all these functions involve unification of sequentially organized information within hierarchical structural constraints. Thus, they are proposed to rely on circuits specialized for such forms of processing (Hagoort, 2013; Kotz et al., 2009; Ullman, 2001).

By the same token, deficits in the above domains following frontostriatal atrophy in PD and HD are not merely arbitrary anatomo-clinical correspondences; rather, they can be viewed as *dysfunctions of functionally recycled motor mechanisms*. Thus, we propose to interpret them under the "disrupted motor grounding hypothesis" (DMGH), a theoretically-driven framework to conceive high-level impairments in neurological disorders.[1] Importantly, this conceptual recast could foster cross-fertilization between the embodied cognition framework, neuropsychology, and clinical neuroscience, with two main implications. From a theoretical perspective, available and prospective findings can promote breakthroughs for neurolinguistics and cognitive neuroscience at large. From a clinical perspective, the detection of embodied domains which are convergently targeted by frontostriatal physiopathology could contribute to the characterization of cross-domain impairments in early disease stages and, more importantly, to the consolidation of sensitive prodromal biomarkers.

First, we describe the physiopathological stages of PD and HD as models of progressive frontostriatal impairment. Second, we review multiple studies assessing action language, motor-language coupling, and syntax in patient samples at various disease stages (although the bulk of the evidence comes from PD, the few studies conducted on HD offer convergent and complementary insights). Finally, in the Discussion, we jointly discuss and interpret the three patterns of impairment, considering their implications for neurolinguistic modeling, the key unresolved issues that should be addressed in future research, and the potential clinical applications derivable therefrom. In brief, our work seeks to foster open new theoretical and translational avenues for embodied cognition research.

2. The progression of frontostriatal damage in PD and HD

The physiopathology of PD and HD is characterized by progressive atrophy of frontostriatal networks. This process begins with nigral degeneration in PD and with neostriatal abnormalities in HD, eventually compromising multiple connections between the basal ganglia and cortical structures. In both diseases, such disruptions entail partially overlapping motor and cognitive symptoms, as detailed below.

[1] While this framework focuses on the role of motor networks in the three reviewed domains, brain regions implicated in other modalities play important roles in the embodiment of other high-order information. For example, words denoting fear, small, color, and form are grounded in regions specialized for emotion (Naccache et al., 2005), olfaction (González et al., 2006), chromatic perception (Simmons et al., 2007), and shape recognition (Wheatley et al., 2005), respectively.

2.1. Physiopathological and cognitive changes in the course of PD

Affecting one out of 100 individuals above the age of 60, PD is the most prevalent neurodegenerative movement disorder worldwide (Samii et al., 2004). It is associated with progressive atrophy of dopaminergic neurons in the substantia nigra and Lewy body inclusions (Rodriguez-Oroz et al., 2009). The vast majority of cases represent sporadic forms of the disease, often associated with environmental factors, such as poor nutrition, generating epigenetic changes in the DNA (e.g., methylation, demethylation, acetylation) (Landgrave-Gomez et al., 2015). However, PD may also be triggered by genetic mutations in various target loci (Nalls et al., 2014), including PARK1 and LRRK2. Mutations in both genes are related with nigral neuronal loss and late dominant inherited forms of the disease, typically manifesting around age 60 (Trinh and Farrer, 2013).

Degeneration of dopaminergic neurons in the substantia nigra pars compacta reduces dopamine innervation to the striatum. This loss typically starts posteriorly, affecting the motor loop via the putamen and resulting in characteristic motor symptoms, such as akinesia, bradykinesia, resting tremor, muscle rigidity, and postural instability (Braak et al., 2003). Then, as progressive atrophy affects more anterior regions of the striatum in the course of the disease, patients exhibit emotional and cognitive impairments, including executive deficits.

The progression of the above physiopathological process involves several stages (Braak et al., 2003). In stage 1, α-synuclein and Lewy body inclusions appear in the dorsal motor nucleus of the vagal nerve and olfactory bulb, progressing rostrocaudally up the brainstem. In stage 2, alterations are evident in the raphe and the locus coeruleus. At this point, subjects are asymptomatic and cannot be diagnosed through routine neurological examination. Nigral degeneration, together with the mesocortical and thalamic atrophy, starts in stages 3 and 4. These changes signal the onset of the symptomatic phase, characterized by gradual appearance and worsening of motor impairments such as resting tremor, postural instability, and bradykinesia (Helmich et al., 2012; Rosin et al., 1997). Finally, in stages 5 and 6, damage extends to the neocortex, including prefrontal structures, motor, and sensory areas (Braak et al., 2003; Rodriguez-Oroz et al., 2009).

Beyond these histological features and associated movement abnormalities, patients may present psychiatric symptoms (e.g., depression, sleep disorders) and cognitive decline. Indeed, executive, attentional, and mnemonic deficits are associated with reduced frontostriatal activity (Lewis et al., 2003) and loss of striatal white matter tracts (Melzer et al., 2013). Moreover, degraded connections between prefrontal and striatal (i.e., external and internal capsule) structures further compromise cortical functions in the disease (Melzer et al., 2013). Depending on the severity of these impairments, PD patients may present with mild cognitive impairment (MCI), a form of higher-order disability falling below criteria for dementia (Emre et al., 2007; Litvan et al., 2012). In sum, the disruption of frontostriatal mechanisms characterizes the physiopathology of PD since early and even preclinical stages, compromising both motor and high-level cognitive functions grounded in such circuitry.

2.2. Physiopathological and cognitive changes in the course of HD

HD is an inheritable autosomal dominant disorder caused by an expansion of CAG repeats in the huntingtin gene, placed in the short arm of the chromosome 4; whereas 36–40 repeats are related to incomplete penetrance, 41 or more repeats imply full penetrance (Walker, 2013). Mutations in this gene cause aggregation of the huntingtin protein and compromise the latter's functions, such as axonal transport, intracellular signaling, protein interactions, and avoidance of stress-induced apoptosis (Bossy-Wetzel et al., 2008). In particular, these physiopathological mechanisms severely affect neurons connecting the striatum with the globus pallidus and the substantia nigra in the basal ganglia (Tabrizi et al., 2009; Walker, 2013).

In pre-manifest stages of HD, although subjects do not evince typical motor signs (Stout et al., 2011), structural changes can be observed in the basal ganglia, including atrophy of the caudate and putamen (Tabrizi et al., 2009). If present, changes in motor skills, personality (e.g., mood changes, anxiety, depression), processing of reward and punishment, and high-order cognition (e.g., multitasking, executive skills) during this stage are only subtle (Baez et al., 2015; Enzi et al., 2012; Thompson et al., 2002; Walker, 2013) –although they can approximate those of symptomatic subjects in specific domains, such as negative emotion recognition (Baez et al., 2015) or moral emotion processing (Baez et al., 2016). Later on, since early clinical stages, functional frontostriatal connections become weaker as neurodegeneration progresses (Harrington et al., 2015), disrupting corticostriatal loops (Watkins et al., 2000). Concomitantly, grey matter loss spreads to the cingulate, precentral, and prefrontal cortices, and even extends to temporal, parietal and occipital regions, a pattern that is exacerbated in late stages (Tabrizi et al., 2009).

Such corticostriatal abnormalities are associated with psychomotor, reward, and executive deficits (Enzi et al., 2012; Montoya et al., 2006). Indeed, the disconnection of corticostriatal white matter tracts contributes to the first clinical signs of the disease (Kloppel et al., 2008). Increasingly abnormal choreiform movements associated with HD, as well as motor incoordination, dystonia, bradykinesia, and characteristic psychiatric symptoms (Ross and Tabrizi, 2011) would result from hyperactivity in the direct pathway due to the selective loss of neurons in the indirect pathway, which normally inhibits the globus pallidus and substance nigra output via GABAergic projections to the subthalamic nucleus (Ross and Tabrizi, 2011). Of note, overt motor abnormalities may sometimes be accompanied, and in certain cases even preceded, by psychiatric symptoms. These usually consist in apathy and depression, but they may also involve manic and psychotic signs (Martinez-Horta et al., 2016; McColgan et al., 2017). Additional cognitive dysfunctions include memory deficits, executive dysfunction, and impairments in cognitive flexibility and speech (Stout et al., 2011). In short, HD is also characterized by frontostriatal alterations since early and preclinical stages, with behavioral and cognitive manifestations which go beyond strictly motor signs.

3. Evidence for the DMGH from PD and HD

As shown in Section 2, frontostriatal abnormalities are a hallmark of both PD and HD since early and preclinical stages. Following the DMGH, then, linguistic mechanisms rooted in such circuitry should yield differential or selective deficits since the very onset of physiopathology. That is, atrophy patterns compromising motor network integrity should particularly disturb functionally akin mechanisms: in patients with problems to *map*, *integrate*, and *sequence* motor information, linguistic deficits should be salient in tasks requiring verbal *mapping of movement* (action language), *integration of verbal and motor information* (motor-language coupling), and *sequencing of lexical patterns* (syntax). Moreover, if these impairments are truly associated with frontostriatal damage, as opposed to alterations in other regions as atrophy progresses, they should even be triggered by incipient degeneration of the circuit's subcomponents, such as the substantia nigra in preclinical PD or the caudate and the putamen in preclinical HD. Below we review critical evidence to test these conjectures, considering our three target domains in turn.

3.1. Disruptions of action language

Action language comprises verbal stimuli denoting or implying motor actions. In healthy individuals, processing of words and sentences denoting movements of specific body parts activates somatotopic regions of the motor cortex (e.g., the verb *kick* differentially engages leg-related motor regions) (Arevalo et al., 2012; Aziz-Zadeh et al., 2006; Hauk et al., 2004; Postle et al., 2008; Tettamanti et al., 2005), while also triggering more widespread activity throughout motor networks at large (Arevalo et al., 2012; de Zubicaray et al., 2010; Kemmerer and Gonzalez-Castillo, 2010). Notably, although subcortical portions of frontostriatal pathways do not seem to be differentially related to action semantics in healthy subjects (Jirak et al., 2010), their disruption does entail distinctive difficulties in such a domain (for a discussion, see Section 4.1). Though the bulk of evidence comes from PD patients, incipient evidence shows similar impairments in HD, even preclinically (see Appendix, Table 1 in Supplementary material).

In a study on early PD, Boulenger et al. (2008) assessed lexical decision on nouns and action verbs while patients were “on” and “off” L-dopa. Dopaminergic treatment selectively influenced reaction times for the latter word class. Further evidence from lexical decision ruled out the possibility that such an effect was driven by verbs at large. Indeed, lexical access in non-demented PD patients is more markedly impaired for action verbs (*grasp*, *squeeze*) than for abstract verbs (e.g., *depend*, *improve*) (Fernandino et al., 2013a).

Word production is also differentially impaired for action verbs in early PD. For example, these patients evince specific difficulties for such a word class during picture naming tasks (Bertella et al., 2001; Cotelli et al., 2007; Péran et al., 2009). Furthermore, they make more grammatical errors and show poorer overall performance in verb generation relative to noun generation (Crescentini et al., 2008; Péran et al., 2003; Rodríguez-Ferreiro et al., 2009). Interestingly, whereas action naming is compromised alongside naming of other categories in PD patients with MCI, the former skill is selectively disturbed in patients with a preserved cognitive status (Bocanegra et al., 2017; Bocanegra et al., 2015).

Additional evidence comes from fluency tasks. Herrera and Cuetos (2012) studied phonological (letters beginning with F), semantic (animals or supermarket objects), and verb (infinitive form of action verbs) fluency in early PD patients while “on” versus “off” L-dopa. Compared to controls, patients exhibited deficits in all three categories irrespective of medication. More importantly, while patients could only access high-frequency verbs during the “off” phase, their performance on action verbs at large was similar to controls upon dopamine restoration.

The neural mechanisms subserving action-verb processing in PD have been specified via neuroimaging evidence. While action-verb generation in healthy individuals recruits the left inferior and superior parietal cortex, PD patients process show a distinct involvement of the prefrontal cortex, Broca's area, and the anterior cingulate cortex (Péran et al., 2009). Also, as shown by Abrevaya et al. (2017), PD patients and controls recruit similar circuits for noun listening (Fig. 2A), but each group relies on different networks for processing action verbs. In healthy subjects, this lexical category elicits major connectivity between the primary motor area, and left anterior regions (inferior frontal gyrus) implicated in action imitation and observation (Decety et al., 1997). Instead, in PD patients, action verbs engaged long-range connections between the primary motor cortex and bilateral posterior areas (median cingulate and paracingulate gyri) involved in amodal semantics (Fig. 2B). Notably, the recruitment of such alternative pathways positively correlates with basal ganglia atrophy (Fig. 2C). Accordingly, frontostriatal damage seems to involve a selective recruitment of non-canonical (motor) circuits for action-verb processing.

Moreover, action-language deficits in PD are not restricted to single-word processing. Indeed, non-demented patients show significant comprehension difficulties for sentences with action verbs (e.g., *The woman is pinching my cheeks*) (Fernandino et al., 2013b). Notably, this selective deficit emerges even for sentences denoting actions through idiomatic constructions (e.g., *The business is pinching pennies*) (Fernandino et al., 2013b) –Fig. 2D. Such impairments have also been evinced through naturalistic tasks. García et al. (2016b) evaluated spontaneous narratives of PD patients via computerized tools. Analysis of semantic fields revealed that the conceptual make-up of the patients' texts, relative to those of controls, relied less heavily on action-related meanings. Notably, this was the case although both groups produced

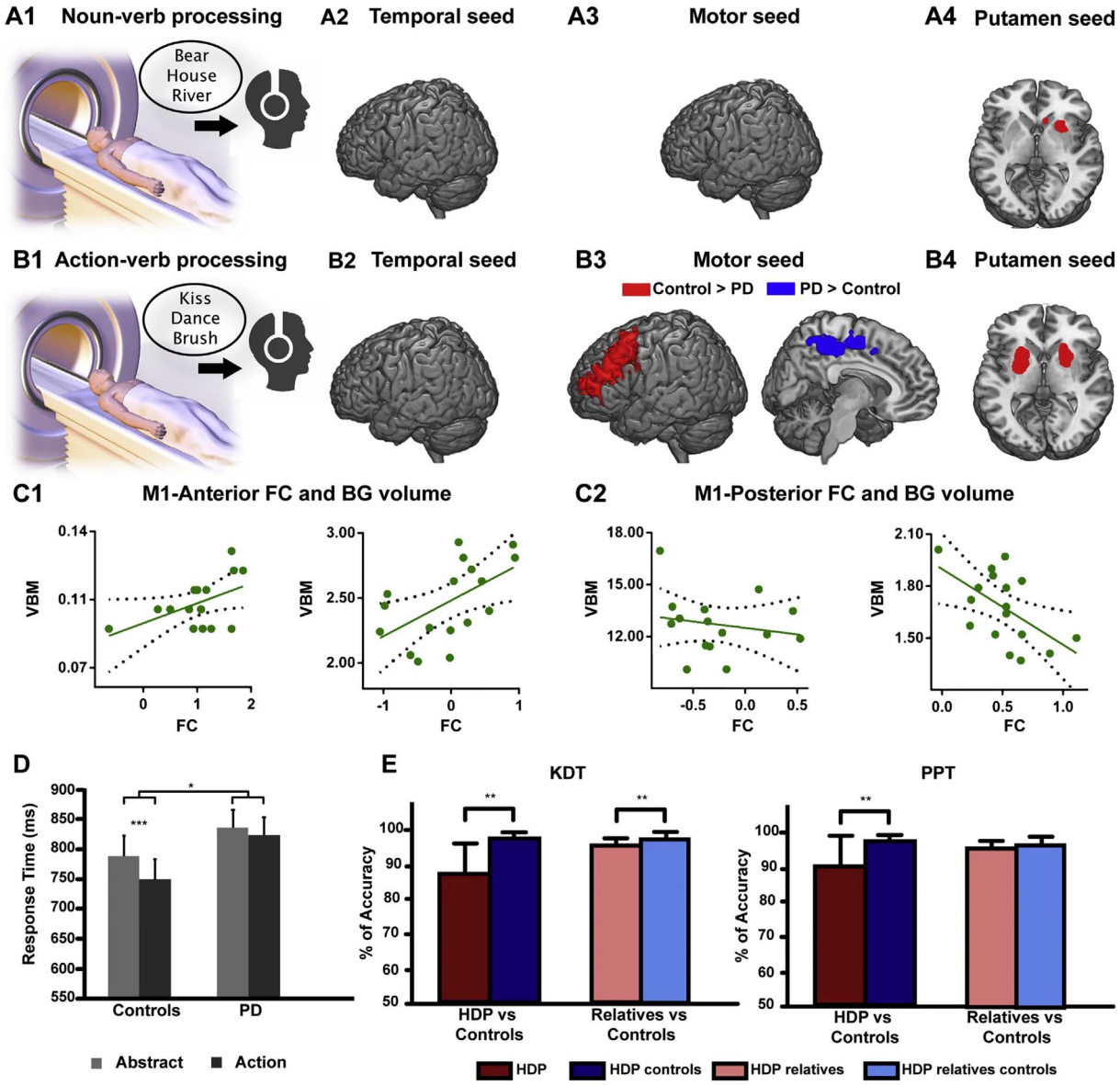

Fig. 2. Disruptions of action language in Parkinson's and Huntington's disease. (A, B, C) Paradigm and results from Abrevaya et al. (2017). **(A1)** Subjects listened to non-manipulable concrete nouns inside the MRI scanner. **(A2–A4)** Seed analysis differences between controls and patients during noun processing. **(B1)** Subjects listened to action verbs inside the MRI scanner. **(B2–B4)** Seed analysis differences between controls and patients during action-verb processing. Red colors indicate clusters where connectivity with the respective seed was significantly higher ($p < 0.05$, FWE corrected at cluster level) for controls than for patients. Blue colors indicate clusters where connectivity with the respective seed was significantly higher ($p < 0.05$, FWE corrected at cluster level) for patients than for controls. **(C1–C2)** Correlations between BG volume and M1 functional connectivity during action-verb processing, for controls and patients. Scatterplots depict the dispersion of correlation results. PD: Parkinson's disease patients; FC: functional connectivity; BG: basal ganglia; VBM: voxel-based morphometry. **(D)** Results from Fernandino et al. (2013b). Response times to action and abstract verbs in a lexical decision task. Error bars represent the standard error of the mean. The single asterisk (*) indicates $p < 0.005$; the triple asterisk (***) indicates $p < 0.005$. **(E)** Results from García et al. (2017b). Kissing and Dancing Test (KDT) and Pyramids and Palm Trees in Huntington's disease patients (HDP) and asymptomatic relatives vs. controls. Y axis shows the proportion of correct responses. Statistically significant differences between groups are indicated by asterisks (*). Panels A, B, and C: Reprinted with permission from Abrevaya et al. (2017); Panel D: Reprinted with permission from Fernandino et al. (2013b); Panel E: Modified with permission from García et al. (2017b). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

similar numbers of action verbs. In a similar vein, evidence from naturalistic reading tasks (García et al., 2017a) shows that deficits in the appraisal of action meanings prove uniquely *sui generis* in patients with and without MCI, and that they emerge selectively in the latter group. What is more, such a disturbance was the only discourse-level pattern that robustly classified PD-MCI patients from controls, and it even superseded a sensitive executive battery in discriminating between PD-nMCI and controls (García et al., 2017a).

The above findings highlight the semantic nature of action-verb processing deficits in PD. Compatibly, patients are impaired in processing action-related concepts even in non-verbal tasks. This has been mainly shown through the picture versions of the Pyramids and Palm Trees (PPT) test and the Kissing and Dancing Test (KDT), which assess conceptual associations between object and action pictures, respectively. For example, (Ibáñez et al., 2013) found that early PD patients showed specific deficits on the KDT despite presenting a well-preserved cognitive profile. Moreover, even when both tasks are compromised in PD patients, only KDT deficits emerge irrespective of executive dysfunction (Bocanegra et al., 2015). Notably, this is the case for samples with and without MCI, suggesting that action-verb difficulties constitute a selective *sui generis* deficit present before full-blown frontostriatal alterations (Bocanegra et al., 2017).

Finally, although much scanter, evidence from HD underscores the sensitivity of action-semantic tasks to tap very subtle frontostriatal

damage. Specifically, whereas patients with a confirmed diagnosis are impaired in both the PPT test and the KDT, asymptomatic first-degree relatives evince selective deficits in the latter, irrespective of their cognitive status (García et al., 2017b) –Fig. 2E. Given the autosomal dominant nature of HD, this evidence suggests that action-semantic tasks may index incipient disruptions of frontostriatal networks even before the underlying physiopathological process triggers clinically visible symptoms.

In sum, action language and action semantics seem to be selectively or differentially impaired following frontostriatal atrophy. Moreover, incipient evidence suggests that at least some of those deficits could be primary in nature (i.e., not epiphenomenal to more general cognitive dysfunction) and detectable even before the onset of clinical stages –although more studies are needed in this regard (see Section 4.3). As shown in the following section, similar findings stem from studies assessing the integration of action language and bodily movements in PD and, less abundantly, in HD.

3.2. Disruptions of motor-language coupling

Motor-language coupling refers to the situated integration of verbal processes and deliberate bodily movements (García and Ibáñez, 2014). In particular, processing of hand-action verbs in the company of ongoing manual actions systematically yields inhibitory or facilitatory effects in healthy subjects (García and Ibáñez, 2016). To assess whether this natural coupling is disrupted by frontostriatal damage, a number of studies have assessed PD samples through the action-sentence compatibility effect (ACE) paradigm, and one of them has done so considering both HD patients and subjects at risk for such a disease (see Appendix, Table 2 in Supplementary material).

The ACE paradigm taps the ability to integrate action-verb comprehension with manual actions. Typically, the execution of specific movements (e.g., towards or away from the body) is significantly modulated by concurrent processing of sentences denoting directionally compatible actions (Borreggine and Kaschak, 2006). In one version of this task, participants listen to sentences involving actions typically performed with an open hand (OH, e.g., *clapped*) or a closed hand (CH, e.g., *hammered*), as well as neutral sentences denoting non-manual actions (e.g., *visited*). Immediately upon comprehension of each sentence, participants press a button with a pre-assigned hand-shape (open or closed). The combination of sentence type and response type generates compatible (OH sentence and OH response, or CH sentence and CH response), incompatible (OH sentence and CH response, or vice versa), and neutral (neutral sentence with either response) trials. In healthy individuals, the ACE manifests as shorter reaction times for the compatible than the incompatible condition (Aravena et al., 2010). At a neural level, the effect involves bidirectional modulations of motor and language areas: motor preparation affects verbal processing (as indexed by an N400 at the left inferior frontal and middle/temporal gyri), and language processing activity affects movement-related areas (as indexed by a motor potential at primary and premotor cortices) (Ibá & ez et al. 2013).

Ibá & ez et al. (2013) first administered the task to early PD patients, (during the “on” phase of levodopa or a dopamine agonist) and matched controls. Despite their relatively preserved motor and cognitive repertoire, the patients showed a diminished ACE, even when tested on medication. Furthermore, ACE performance correlated with KDT scores. Importantly, the deficit was independent from general cognitive impairment or executive dysfunction (Fig. 3A).

Importantly, this abnormality is not caused by *any* movement disorder. Cardona et al. (2014) administered the ACE task to early PD patients and two samples featuring peripheral (i.e., musculoskeletal) movement disorders: neuromyelitis optica and transverse myelitis patients. While the ACE was abolished in PD patients, it emerged normally in the other two groups, indicating that such a disruption is specifically triggered by frontostriatal damage.

More recently, Melloni et al. (2015) replicated the finding of an abolished ACE in early PD patients and showed that it was accompanied by aberrant fronto-temporal connectivity at high and low frequencies (Fig. 3B). Such results suggest that functional connectivity in PD can be modulated by cognitive load during motor-language coupling. Furthermore, the patients showed reduced modulations of the motor potential in compatible trials. Remarkably, such electrophysiological abnormalities were predicted by overall basal ganglia atrophy, further highlighting the intimate links between motor-language coupling and frontostriatal integrity.

Finally, Kargieman et al. (2014) applied the ACE paradigm in two groups: one composed of patients genetically and clinically diagnosed with HD, and another one comprising asymptomatic subjects with a positive history of HD to the first-degree of consanguinity. Each group was matched in sex, age, and years of education with healthy controls. Results showed that the ACE was impaired not only in the patients, but also in the asymptomatic relatives. This suggests that motor-language coupling deficits may appear even 10 years before motor symptoms become manifest, opening a promising avenue for early detection of incipient frontostriatal damage in subjects at risk for motor diseases (Figs. 3C and D). However, so far, Kargieman et al.'s is the only study exploring this issue. More research is thus needed before this claim can be firmly embraced (for further insights, see Section 4.2 below).

In short, the natural integration of action-verb information and congruent manual movements seems to be distinctively disrupted by frontostriatal degeneration. Although scant, the available evidence further suggests that this alteration may be independent from more general cognitive disturbances and observable before subjects reach clinical stages (see Section 4.3). As shown below, such findings are complemented by others from studies assessing syntactic skills in PD and HD.

3.3. Disruptions of syntax

As described in the Introduction, syntax involves multiple operations which involve sequencing, hierarchization, and unification lexical patterns (Ullman, 2004, 2008). In healthy subjects, syntactic computation engages left striatal circuits alongside perisylvian regions, particularly during local phrase structure building (Friederici et al., 2003b) and even when sentences are made up of pseudowords (Moro et al., 2001). As we argued at the outset, such linguistic operations correspond with broad functions of frontostriatal hubs implicated in homologous motor patterns. In healthy individuals, syntactic processing is grounded in movement-related regions, such as the motor cortex, Broca's area, and the basal ganglia (Ullman, 2004, 2008). This domain, too, is distinctively compromised in PD and HD patients (see Appendix, Table 3 in Supplementry material).

In early stages of PD, patients are impaired in processing sentences of varied syntactic complexity, as observed in both monolingual (Angwin et al., 2006; Lieberman et al., 1992) and bilingual (Zanini et al., 2004) samples. For example, they exhibit disproportionate deficits when parsing non-canonical sentences, such as those with raised subjects –e.g., *Music is easy for Jacob to play* (Kemmerer, 1999). Other studies on PD have also reported impairments for processing passive sentences (Colman et al., 2006; Hochstadt et al., 2006) and center-embedded (specially, object-relative) subordinate clauses –e.g., *The man that the woman touched was tall* (Angwin et al., 2005, 2006; Grossman et al., 2000, 2002; Lee et al., 2003).

Significant deficits also emerge in tasks tapping comprehension of implied and metaphorical meanings evoked by sentences (Berg et al., 2003; Monetta and Pell, 2007). Moreover, they are evident in the production of spontaneous discourse. For example, Murray (2000) found that non-demented PD and HD patients produced a smaller proportion of grammatical sentences than controls during a narrative task. In the same vein, Murray and Lenz (2001) reported reduced syntactic complexity during conversational discourse in PD patients.

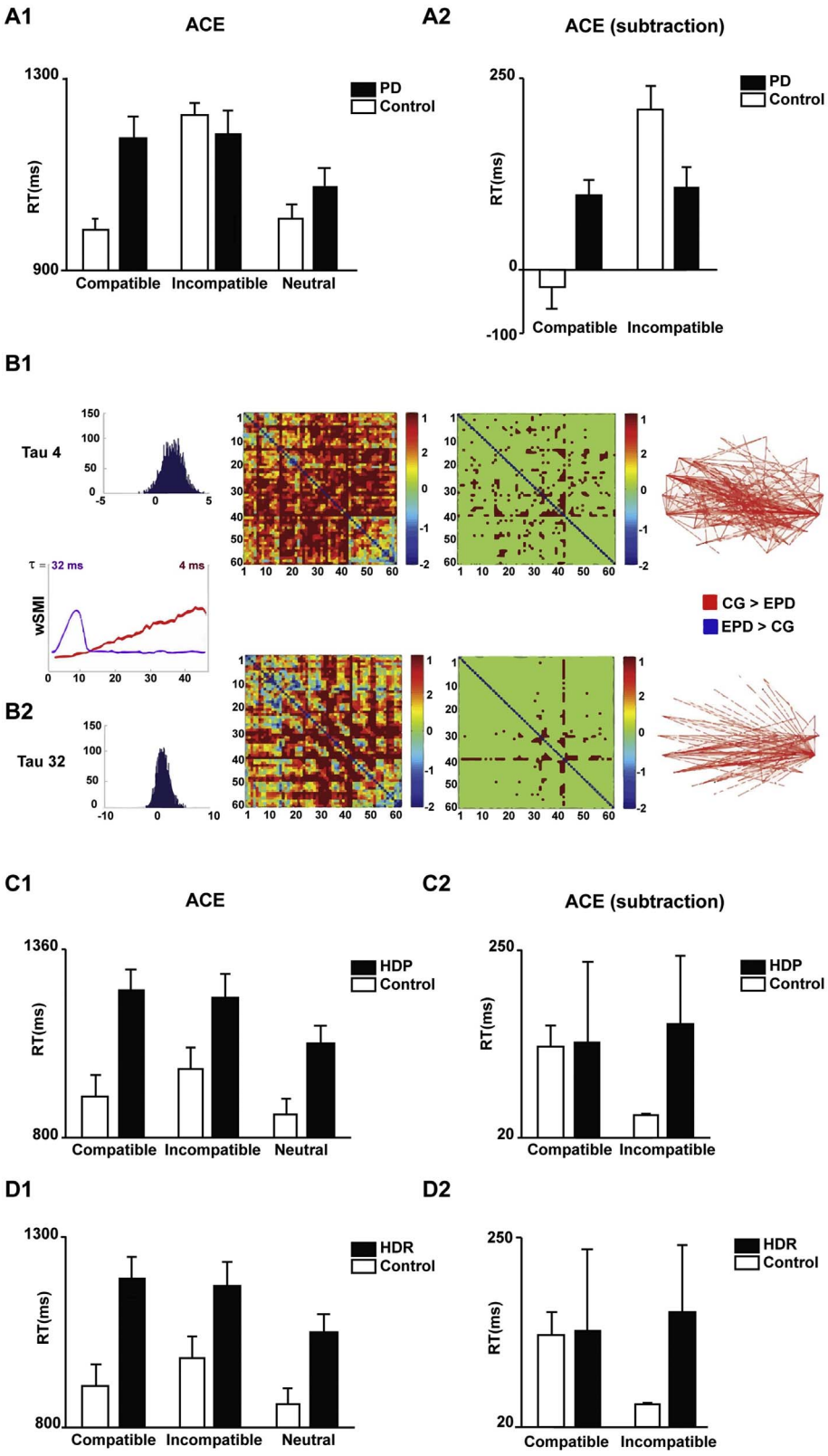

Fig. 3. Disruption of motor-language coupling in Parkinson's and Huntington's disease. (A) Results from Ibá & ez et al. (2013). ACE in Parkinson's disease (PD). (A1) Mean reaction times from compatible, incompatible, and neutral trials for PD and control participants. Control group participants show a classic ACE, whereas the ACE was absent for PD participants. **(A2)** ACE subtraction; group comparison of ACE normalized by subtracting the mean reaction time of the neutral trials from those of the compatible and incompatible trials. **(B)** Results from Melloni et al. (2015). **(B1)** Global broadcasting of information across distant cortical regions, as asssessed with the Weighted Symbolic Mutual Information (wSMI) metric. Two-tailed *t*-tests on the wSMI matrices of each group were obtained upon subtracting the correlation matrices of the incongruent and congruent conditions. The Frequency Specificity Graph shows the sensitivity of wSMI to pure-frequency signals. The value of τ makes the wSMI measure sensitive to different frequency ranges (τ = 4 ms is specific for frequencies among 11–40 Hz and τ = 32 ms is specific for frequencies ranging between 1 and 11 Hz). (B1) Analysis for tau = 4 ms (> 11 Hz): (i) histogram showing the number of occurrences (y axis) of the *t*-values (x axis); the distribution of these values exhibits a positive trend, indicating that information sharing is larger for controls than early PD (EPD) patients; (ii) correlation matrix of raw *T*-value; (iii) masked correlation matrix: *T*-values were corrected with an alpha level set at $p < 0.01$; non-significant values were assigned a value of 0; (iv) connectivity map of significant connections only across the scalp indicating that controls presented higher information sharing at fronto-temporal regions. **(B2)** Analysis for tau = 32 ms (specific for 1–11 Hz): (i) histogram showing the number of occurrences (y axis) of the *t*-values (x axis); the distribution of these values exhibits a positive trend, indicating that information sharing is larger for controls than EPD patients; (ii) correlation matrix of raw *T*-value; (iii) masked correlation matrix: *T*-values were corrected with an alpha level set at $p < 0.001$; non-significant values were assigned a value of 0; (iv) connectivity map of significant connections only across the scalp indicating that controls presented higher information sharing mainly at bilateral temporal regions. (C, D) Results from Kargieman et al. (2014). Action compatibility effect (ACE) in Huntington's disease patients (HDPs) and asymptomatic relatives (HDRs). **(C1)** Mean reaction time from compatible, incompatible, and neutral trials for HDP. Unlike controls, HDPs did not show an ACE. **(C2)** ACE subtraction; group comparison of the ACE normalized by subtracting the mean reaction time of the neutral trials from those of the compatible and incompatible trials. **(D1)** Mean reaction times for HDRs. Unlike controls, HDRs did not show an ACE. **(D2)** ACE subtraction, calculated as in A2. In all panels, the bars depict the SD. Panel A: modified with permission from Ibá & ez et al. (2013); Panel B: reprinted with permission from Melloni et al. (2015); Panels C and D: modified with permission from Kargieman et al. (2014).

Similar results were obtained by Reddy et al. (2016). However, differential syntactic performance in PD may also involve an overuse of specific grammatical features, such as subordinating conjunctions (García et al. 2016b).

A debate has emerged on whether syntactic impairments in PD are strictly linguistic or secondary to executive dysfunction. On the one hand, some studies have attributed morphosyntactic deficits in PD to deficits in selective attention (Lee et al., 2003) or other executive resources, such as working memory (Angwin et al., 2006; Hochstadt et al., 2006). On the other hand, individuals with PD appear to have morphosyntactic impairments regardless of the presence of non-linguistic cognitive alterations (Longworth et al., 2005; Terzi et al., 2005).

Against this background, recent evidence suggests that the role of executive deficits in syntactic difficulties depends on the specific grammatical demands of the task. In a study by Sambin et al. (2012), HD patients could normally process center-embedded and right-branching relative clauses (e.g., *The girl who watches the dog is green* vs. *The girl watches the dog which is green*) despite their differential demands on working memory. However, they failed to acknowledge that names and pronouns cannot be co-referential in sentences such as *He smiled when Paul entered*. Thus, the authors concluded, this specific syntactic deficit is not a byproduct of working memory impairment. Similarly, Bocanegra et al. (2015) documented syntactic deficits in PD patients with and without MCI, but noted that these depended on executive skills only when syntactic comprehension demands were high (namely, when stimuli featured embedded clauses, as in *The woman who is fat is kissing her husband*). This result was replicated in patients featuring both sporadic and genetic forms of the disease (García et al., 2017c). In sum, then, at least some grammatical dysfunctions following frontostriatal damage may occur in a *sui generis* fashion (i.e., they are not secondary to extralinguistic deficits).

Additional evidence has revealed some neurological markers of syntactic alterations in PD. Friederici et al. (2003a) found that the P600, a specific marker of late syntactic integration and repair processes, was abnormally modulated during sentence processing in PD, while the N400 and the LAN (indexing semantic and early grammatical processes, respectively) were similar to those of controls. The authors concluded that basal ganglia damage specifically affects late syntactic processes, without compromising earlier, automatic aspects of sentence parsing. Another study showed that these alterations may involve not just the basal ganglia, but also its extended cortical projections. Specifically, Grossman et al. (2003) found that PD patients had less striatal, anteromedial prefrontal, and right temporal activation when processing long sentences, suggesting that impaired sentence comprehension in PD may reflect disturbances of a large-scale network (Fig. 4A). Moreover, neuroimaging evidence shows that selective rule application impairments in HD correlate with striatal atrophy, as indexed by bicaudate ratios Teichmann et al. (2006).

The sensitivity of syntactic tasks to tap the integrity of frontostriatal circuits is further emphasized by research on preclinical samples. For example, asymptomatic relatives of HD patients are selectively impaired in syntactic tasks requiring the establishment of long-distance dependencies (García et al., 2017b) (Fig. 4B). Also, García et al. (2017c) reported that, relative to matched controls, asymptomatic individuals with mutations in PD-related genes manifested selective deficits in a syntactic task requiring the identification of functional roles of noun phrases within predicates (Fig. 4C). Notably, in the latter two studies, such patterns emerged in the absence of executive deficits, highlighting the strictly grammatical nature of the dysfunction. Moreover, the very tasks revealing deficits in each group were spared in the other. Considering that preclinical atrophy is mostly nigral in PD and predominantly neostriatal in HD, this double dissociation suggests that specific subportions of the basal ganglia could play distinct roles in specific syntactic functions (see Section 4.1).

By the same token, De Diego-Balaguer et al. (2008) studied the learning of a simplified artificial language in HD patients at different disease stages and pre-symptomatic subjects with confirmed HD-related genetic mutations. As compared with healthy subjects, late-stage patients showed deficits in both rule and word learning, whereas early-stage patients were predominantly impaired in the former skill. More strikingly, although pre-symptomatic individuals were unimpaired in general language tests, they exhibited specific difficulties in transferring newly learnt grammatical rules. This finding complements evidence that morphological processing in pre-symptomatic HD patients is characterized by rule-application alterations, such as over-suffixation and over-regularization (Nemeth et al., 2012).

All in all, syntactic processes in PD and HD are systematically related to frontostriatal alterations. Furthermore, some studies indicate that such deficits can emerge in the absence of other cognitive deficits and, more notably, before the onset of clinical symptoms (see Sections 4.1, 4.2 and 4.3 below). While more research is needed to comprehensively test these incipient patterns, extant findings highlight their potential relevance to forge useful links between the embodied cognition framework, clinical neuroscience, and neuropsychology, as discussed below.

4. Discussion

Traditionally, descriptions of linguistic deficits in PD and HD mainly emphasized changes in articulation and other motoric aspects of verbal production (Cummings et al., 1988). However, as seen in this review, at least three high-order language domains (action-verb processing, motor-language coupling, and syntax) seem to be distinctively compromised after frontostriatal disruptions. Although the evidence mainly comes from PD, the more sparse research on HD shows considerable convergence. Importantly, these deficits have been reported even in preclinical stages. Such findings align with the DMGH, highlighting the possibilities of for more direct dialogue between the embodied cognition framework, neuropsychology, and translational neuroscience. At the same time, the evidence expounds the limitations of the hypothesis, paving the way for a new, promising research agenda. Next, we address these issues, identifying theoretical insights, challenges for future research, and potential clinical implications.

4.1. Insights for neurolinguistic modeling

Our review indicates that linguistic subsystems specialized for the lexico-semantic mapping of movement, the integration of verbal and motor information, and the sequencing of hierarchically organized lexical patterns become distinctively dysfunctional upon compromise of frontostriatal networks, which are critical for mapping, integrating, and sequencing hierarchically organized movement patterns. This threefold pattern aligns with the embodied cognition framework, which has compellingly shown that high-order mental systems are grounded in sensorimotor systems mediating our interactions with the world (Barsalou, 1999; Gallese and Lakoff, 2005; Pulvermüller, 2005, 2013). More particularly it supports the DMGH, as postulated at the outset. In other words, we propose that the reason why these seemingly unrelated domains become consistently compromised in PD and HD is that they depend on the functional recycling (Dehaene and Cohen, 2007) of frontostriatal motor loops.

The evidence broadly aligns with recent neurolinguistic models focused on the biological basis of action language (Pulvermüller, 2005, 2013), motor-language coupling (Cardona et al., 2013; García and Ibáñez, 2016), syntactic mechanisms (Ullman, 2004, 2008), and even with overall accounts of the organization of the linguistic system (Ardila et al., 2016; Hagoort, 2013; Hagoort and Indefrey, 2014). Moreover, some of the above findings motivate refinements of the neural substrates proposed in these models. In particular, results from preclinical samples emphasize the critical dependence of all three domains on the substantia nigra and the neostriatum, given that atrophy in prodromal stages of PD (Braak et al., 2003) and HD (Halliday et al., 1998) is typically confined to those structures, respectively. Such findings move beyond coarse-grained models which posit an undifferentiated role of the entire frontobasal circuitry to specific linguistic domains, such as syntax (Ullman, 2001) –for additional insights, see Section 4.2 below.

Our review also extends models of the neural organization of lexico-semantics at large and action language in particular. For example, the declarative/procedural model posits that the lexico-semantic system in its entirety relies on extra-striatal regions subserving declarative memory (Ullman, 2001, 2004, 2008). This paper shows that action verbs, and possibly other lexical categories evoking motor-related meanings, are crucially grounded in frontostriatal networks. Also,

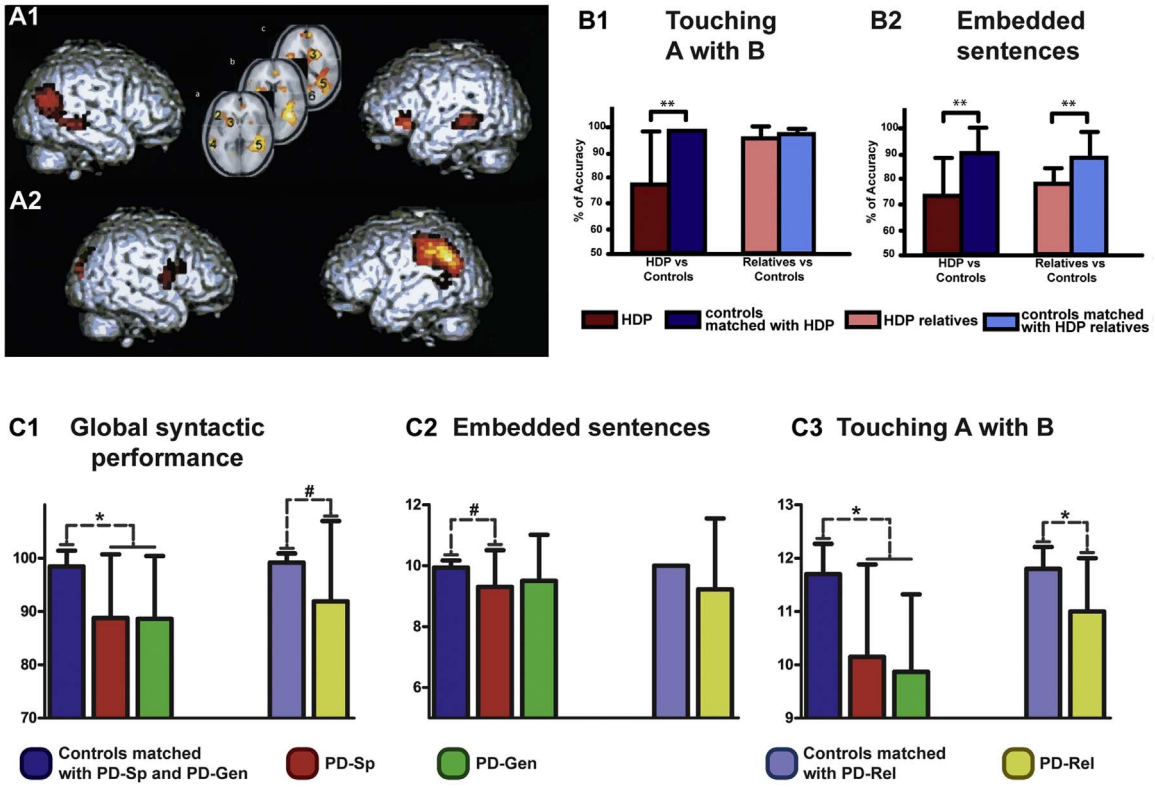

Fig. 4. Disruption of syntax in Parkinson's and Huntington's disease. **(A)** Results from Grossman et al. (2003). Regional activation patterns in direct contrasts of PD patients and healthy seniors. **(A1)** Areas of reduced activation in PD patients relative to healthy seniors for object-relative long-linkage sentences, including lateral views and representative transaxial views (left hemisphere on the left) at z = 0 mm (a), z = +8 mm (b), and z = +16 mm (c). 1 = bilateral anteromedial prefrontal region; 2 = left ventral inferior frontal region; 3 = bilateral striatum; 4 = left posterolateral temporal region; 5 = right posterolateral temporal region; 6 = bilateral occipital region. **(A2)** Areas of increased activation in PD patients relative to healthy seniors for object-relative long-linkage sentences. **(B)** Results from García et al. (2017b). **(B1)** Performance on the Touching-A-with-B test by Huntington's disease patients (HDPs), Huntington's disease relatives (HDRs), and their matched controls. **(B2)** Performance on embedded sentences task by HDPs, HDRs, and their matched controls. Error bars represent SDs. Statistically significant differences are indicated by **. **(C)** Results from García et al. (2017c). Performance of sporadic PD patients (PD-Sp), genetic PD patients with parkin or dardarin mutation (PDGen), and asymptomatic first degree relatives of the latter with similar mutations (PD-Rel), relative to controls, on global syntactic performance (A), the "Embedded sentences" test (B), and the "Touching A with B" test (C). # indicates statistical differences at $p < 0.05$. * indicates statistical differences at $p < 0.05$ after a covariance test adjusted for executive functions scores. Black vertical bars indicate standard deviations. The y-axis in each panel shows the numerical scores of the corresponding test, except for "Global syntactic performance", which is represented in percent values. Panel A: reprinted with permission from García et al. (2017b); Panel B: reprinted with permission from Grossman et al. (2007); Panel C: reprinted with permission from García et al. (2017c).

robust accounts of action language have emphasized the role of *cortical* motor networks in grounding relevant semantic information (e.g., Pulvermüller, 2005, 2013). Though fully compatible with this view, our review shows that action semantics is also critically subserved by the basal ganglia, and even some of its subportions in particular (García et al., 2017b; Kargieman et al., 2014). It follows that (i) semantic processing, in general, spreads beyond declarative memory circuits; and that (ii) the embodied foundations of action language, in particular, involve widespread networks cutting across relevant cortical *and* subcortical hubs. Interestingly, neuroimaging studies in healthy samples (e.g., Hauk et al., 2004; Kemmerer et al., 2008; Van Dam et al., 2010) and relevant meta-analytical research (Jirak et al., 2010) indicates that basal ganglia circuits are not differentially recruited during processing of action verbs relative to other linguistic units. This suggests that subcortical components of frontostriatal pathways, when fully preserved, may support general lexico-semantic functions (Crosson et al., 2003), which are accompanied by fine-grained contributions of cortical motor areas more specialized for action semantics (Pulvermüller, 2005, 2013). However, as seen in Section 3.2, basal ganglia damage may in fact selectively disrupt action semantics. Indeed, selective deficits of action semantics may be triggered even when only certain subportions of the basal ganglia are compromised in preclinical disease stages (García et al., 2017b; García et al., 2017c). Taken together, these strands of evidence suggest that abnormal signaling from such subcortical structures may compromise the operation of their frontal connections, indirectly triggering the selective deficits observed in PD and HD. However, specific studies should be conducted to test how subcortical and cortical components of frontostriatal networks interact during to action semantics, considering both healthy subjects and patient populations.

Furthermore, frontostriatal networks seem to constitute a key hub for the *convergence* of linguistic and motor information. In daily life, verbal processes do not occur in the context of a static body, and movements are oftentimes accompanied by linguistic contexts. These co-occurring phenomena modulate each other in reciprocal ways, as recently captured by a network-based model (García and Ibáñez, 2016). The finding that such cross-domain synergies are systematically disrupted in PD and HD, but not in movement disorders resulting from extra-striatal abnormalities (Cardona et al., 2014), point to the basal ganglia and their frontal connections as an association area merging linguistic and non-linguistic signals.

This review also recasts the debate on the relationship among frontostriatal networks, syntactic processing, and executive functions. In particular, frontostriatal regions are implicated in both syntactic (Friederici et al., 2003b; Moro et al., 2001) and executive (Braver et al., 2001; Gelfand and Bookheimer, 2003; McNab and Klingberg, 2008; Menon et al., 2000) processing, but the interaction between such domains remains unclear. Based on individual studies from PD and HD, some authors have argued for a dependence of syntax on extralinguistic mechanisms (e.g., working memory), while others have framed

atrophied regions as playing domain-specific roles in grammatical processing –see Section 3.3. However, neither overarching answer seems adequate. Indeed, the engagement of executive mechanisms during syntactic parsing depends on the specific grammatical demands of the task at hand. For example, Bocanegra et al. (2015) and García et al. (2017c) reported that syntactic deficits in PD are explained by executive deficits only when the stimuli involved long-distance dependencies. Similarly, Sambin et al. (2012) found that the difficulties of HD patients to block incorrect name-pronoun co-reference were not secondary to working memory deficits. Accordingly, the recruitment of executive functions subserved by the basal ganglia during sentence processing cannot be framed as an all-or-nothing problem. Only certain grammatical operations seem to crucially rely on executive resources for adequate task completion.

The relationship between frontostriatal networks and syntax is neither straightforward nor monolithic. Certain syntactic functions, such as processing of object-relative clauses or of the so-called Principle C, can become disproportionately impaired in PD (García et al., 2017c), and HD (García et al., 2017b), respectively. Indeed, in preclinical PD, incipient atrophy of the substantia nigra (Rodriguez-Oroz et al., 2009) has been linked to impairments in functional-role assignment (a predominantly sequential form of syntactic processing), with no concomitant deficits in parsing of long-distance dependencies (which distinctly taxes hierarchical processing mechanisms) (García et al., 2017c). Instead, preclinical HD patients, characterized by more focal neostriatal atrophy (Tabrizi et al., 2009), exhibit the exact opposite pattern. This aligns with computational evidence that different subportions of the striatum play distinct roles during linguistic processing, including specializations of specific cortico-striatal pathways for syntactically complex sentences (Szalisznyó et al., 2017). Thus, although the evidence does not warrant strict attributions of specific syntactic subdomains to different putative regions, it seems that not all frontostriatal hubs contribute equally to all syntatic processes. In this sense, it has been proposed that Brodmann area 44 would be a key contributor to the processing of complex hierarchical structures (Zaccarella and Friederici, 2016), while certain substructures of the basal ganglia (e.g., the substantia nigra) would be more critically involved in sequential than in hierarchical processing (García et al., 2017b). While these possibilities remain speculative, the evidence does suggest that specific patterns of atrophy may lead to differential patterns of disturbed and spared syntactic functions. Further research is needed to clarify the role of each subportion of motor networks in specific syntactic domains.

Note that, in stating that frontostriatal networks are critical to ground action verbs, motor-language coupling, and syntax, we are not claiming that they are the sole substrates of these domains. Indeed, all three functions also recruit additional areas. For example, the thalamus, the cerebellum, and temporal regions have been acknowledged as key contributors to action-verb processing and motor-language coupling (Cardona et al., 2013; García et al., 2016a; García and Ibáñez, 2016), whereas the anterior cingulate cortex (Thothathiri et al., 2015) and hippocampal-prefrontal connections seem to play critical roles in syntactic processing (Opitz and Friederici, 2003). At the same time, neither are frontostriatal networks exclusively devoted to these language functions. Indeed, several of their constituting hubs have been implicated in fluency (Ardila et al., 2016), phonology (Tettamanti et al., 2005), and orthographic processing (Glezer et al., 2016). In sum, while these circuits and the three subdomains reviewed are critically linked, they do not stand in a one-to-one relationship.

Finally, and more generally, the DMGH implies that the lesion-model approach can partially circumvent some theoretical caveats in embodied cognition research. Since most neuroscientific evidence in the field is correlational, associations between neural substrates and high-order functions have been mainly postulated at an indirect level. Despite limitations of its own, the use of lesion models can reveal more direct links between specific cognitive domains and specific cerebral circuits, especially when complemented with neuroimaging data (García-Cordero et al., 2016; Melloni et al., 2016; Rorden and Karnath, 2004). In this sense, other extrapolations of the DMGH could be fruitfully incorporated into multiple research agendas within the embodied framework and neurolinguistics at large.

4.2. Challenges ahead

Admittedly, the three domains targeted above are not the only aspects of language compromised by frontostriatal atrophy. Indeed, PD and HD patients show impairments in phonological and semantic fluency (Ellfolk et al., 2014; Henry et al., 2004; Ho et al., 2002; Obeso et al., 2012; Rosser and Hodges, 1994), prosody (De Letter et al., 2007; Kan et al., 2002; Lloyd, 1999; Pell and Leonard, 2003; Skodda, 2011; Speedie et al., 1990), pragmatics (Holtgraves et al., 2013; McNamara and Durso, 2003; Saldert et al., 2014; Saldert et al., 2010), and discourse processing (Copland et al., 2001; Murray and Stout, 1999). However, except for fluency, these skills have not been systematically studied in either population. More importantly, none of them is *distinctively* compromised by frontostriatal damage. Indeed, deficits in such domains have been observed following occipital, parietal, and temporo-occipital damage in posterior cortical atrophy (Crutch et al., 2013), hippocampal abnormalities in amnesia (Kurczek et al., 2013), bilateral temporal atrophy in primary progressive aphasia (Adlam et al., 2006), anterior temporal lobe damage in semantic dementia, superior temporal lesions in Wernicke's aphasia (Thompson et al., 2015), and posterior middle and inferior temporal damage in semantic aphasia (Thompson et al., 2015).

To be firmly accepted as putative embodied functions of frontostriatal networks, action language, motor-language coupling, and syntax should not be significantly compromised in conditions which fully or largely spare such circuits. Available evidence suggests that this could be the case. For example, unlike subjects with frontal atrophy, semantic dementia patients (featuring antero-lateral temporal damage) are more impaired in object than action semantics (Bak and Hodges, 2003). Also, motor-language coupling deficits fail to emerge in motor disorders not triggered by frontostriatal lesions, such as neuromyelitis optica and acute transverse myelitis patients (Cardona et al., 2014). Likewise, syntactic abilities are typically preserved in conditions characterized by temporal degeneration, such as Alzheimer's disease and semantic dementia –for a review, see Ullman (2001). Yet, direct assessments of these domains in contrastive lesion models are scant. It would be critical for PD and HD samples to be compared with populations characterized by extra-striatal (e.g., temporal or parietal) damage to more stringently test the specificity of the proposed associations. Also, there is a paucity of evidence on whether the reported deficits (in particular, syntax) are related to the degree of motor impairment in each condition. Extant findings indicate that the level of motor compromise of individual PD patients can be robustly inferred on the basis of syntagmatic patterns in spontaneous discourse García et al. (2016b). However, more direct testing is required to ascertain the predictive power of these linguistic disorders for subject-level characterization. Also, future studies may tackle this relation in a more robust way by assessing whether specific aspects of motility in the patients (e.g., strength, acceleration, intensity, sequencing, and, coordination) can be predicted on the basis of their linguistic skills.

Likewise, direct neural markers of these embodied links have only been sparsely produced. Although various cognitive functions have been systematically examined through imaging techniques in PD and HD (Postuma and Berg, 2016; Ross et al., 2014), only a handful of studies have examined the neurological correlates of action language (Abrevaya et al., 2017; Péran et al., 2009), motor-language coupling (Melloni et al., 2015), and syntax (Friederici et al., 2003a) in PD, and even fewer have done so in HD (e.g., Teichmann et al., 2008). The DMGH requires further assessment by combining neuroscientific methods with specific lesion models (Rorden and Karnath, 2004) adapted for research in neurodegeneration. In particular, significant

theoretical refinements could be attained by examining neurocognitive correlates of these three target functions in *contrastive* patient samples, as shown by recent studies on other domains, such as interoception (García-Cordero et al., 2016) and social negotiation (Melloni et al., 2016).

Further research is also needed to fully embrace the claim that the impairments reviewed above are *sui generis* in nature. Although a considerable amount of evidence aligns with such a claim (e.g., Bocanegra et al., 2017; Bocanegra et al., 2015; Cardona et al., 2013; García et al., 2017a; García et al., 2017c; Ibanez et al., 2013), the evidence is not entirely consistent. This weakens their relevance as potential behavioral markers of PD and HD. To foster progress in this direction, three methodological strategies present in the literature could be more systematically applied. First, results from domain-general (e.g., executive functions) tasks could be entered as covariables or regressors in the analyses of linguistic performance. Second, patient samples could be divided in terms of their cognitive state (e.g., subjects with and without MCI). Third, tasks tapping any of the three embodied functions could be adapted to feature conditions which differ in their extralinguistic (e.g., working memory) demands. Such methodological maneuvers could help specify the primary or secondary nature of the anatomo-clinical associations targeted in this work.

It is also worth noting that, despite our emphasis on the commonalities between PD and HD, these diseases are far from identical. Clinically, PD is characterized by tremors, slowness of movement, increased muscular tone, a paucity of spontaneous movements. Conversely, HD patients present excessive, uncontrollable, and relatively rapid movements. Moreover, frontostriatal atrophy initially targets different basal ganglia structures in each condition (the substantia nigra in PD, the neostriatum in HD). In addition, extra-striatal degeneration advances differentially in each case: in PD, it affects the hippocampus (Camicioli et al., 2003), the cerebellum, the left precuneus, and the bilateral temporal lobes (Camicioli et al., 2009), whereas in HD it extends to the bilateral insula, the dorsal midbrain, the intra-parietal sulci (Peinemann et al., 2005; Thieben et al., 2002), the orbitofrontal cortex (Henley et al., 2009; Ille et al., 2011), the amygdala (Kipps et al., 2007), and the cingulate cortex (Hobbs et al., 2011). Furthermore, cognitive impairments follow different trajectories in each condition. PD patients may or may not present MCI since early stages (Aarsland et al., 2010; Caviness et al., 2007; Litvan et al., 2011; Muslimović et al., 2005). The evidence suggests that the cognitive profile of PD-MCI is predominantly non-amnesic and characterized mainly by executive dysfunction (Aarsland et al., 2010; Caviness et al., 2007; Janvin et al., 2006; Yu et al., 2012). Conversely, symptomatic and pre-symptomatic HD patients typically feature greater cognitive dysfunctions and tend to develop dementia. For example, they may feature facial emotion recognition impairments correlated with regional loss of brain tissue, altered brain activation, and changes in brain connectivity (Kordsachia et al., 2016), alongside mood changes such as apathy, depression, and irritability (Thompson et al., 2002). These discrepancies suggest that, despite the numerous similarities, differential cognitive alterations may emerge in each disease.

Yet, as seen throughout the review, research on motor grounding domains is considerably scarcer in HD than in PD. Although this weakens the transnosological relevance of our conclusions, the few studies on HD align well with the more copious evidence from PD supporting the DMGH. However, it would be essential for future studies to systematically assess the three language domains in HD and, if possible, directly comparing samples from both populations.

Although direct comparisons of language skills between PD and HD are scant, available evidence points to differential patterns. For example, despite similar performance in cognitive and motor speech tests, HD patients were observed to produce syntactically simpler utterances than PD patients during spontaneous discourse (Murray, 2000) –but see (Murray and Lenz, 2001). Also, it would seem that damage to the specific motor hubs targeted by the preclinical physiopathology of each disease could differentially compromise specific syntactic skills. For example, as stated before, specific atrophy of mesencephalic and telencephalic portions of the basal ganglia in preclinical PD and HD, respectively, can entail selective deficits in grammatical processes of different complexity (e.g., functional-role assignment and establishment of long-distance dependencies). In short, the specific physiopathological processes of PD and HD may involve differential deficits, or at least trigger similar deficits at different moments in the course of each disease, although further research is needed to assess this possibility.

In this sense, not all subportions of this motor network seem to be equally involved in the three domains considered. First, as seen above, evidence from preclinical samples suggests a partial dissociation between nigral and neostriatal components to different syntactic functions, suggesting that specific syntactic deficits could be distinctively related to very early disturbances leading to either PD or HD. Moreover, specializations of different cortico-striatal pathways also seem present for action semantics. For instance, evidence from asymptomatic HD relatives indicates that relatively focal atypicalities of the neostriatum can selectively compromise action (as opposed to object) semantics (García et al., 2017b), but no such deficit is observed when alterations mainly affect the substantia nigra, as is the case in preclinical PD (García et al., 2017c). In sum, these partial dissociative patterns indicate that different motor hubs comprised by frontostriatal circuits may be specialized for specific syntactic and semantic subdomains.

Finally, it is worth reemphasizing that a number of studies revealed disruptions of motor grounding in early and even preclinical stages of both diseases. However, the clinical notion of “early stage” subsumes different extents of physiopathology. Similarly, preclinical stages present high variability, as they involve patterns of progressive neurodegeneration which may last up to 15 years (Braak et al., 2003). In this sense, a major caveat of the literature is that available studies do not consistently report the patients’ disease stage or their extralinguistic cognitive profile, let alone the lack of longitudinal studies. More systematic recording of the patients’ disease stages and continuous monitoring of their cognitive profiles would thus be critical to ascertain the translational potential of the DMGH. Notwithstanding, available findings already pave the way for clinical applications, as discussed below.

4.3. Potential clinical applications

In recent decades, not only have high-order deficits in PD and HD become well established, but they have also entered the field's clinical agenda (Ross and Tabrizi, 2011; Svenningsson et al., 2012). Here, in the context of the DMGH, we have underscored the systematicity of three forms of linguistic impairment in early and even preclinical stages of both diseases. Consequently, relevant language embodiment tasks may offer useful insights into the integrity of the patients’ frontostriatal networks even before full-blown clinical manifestation (García and Ibáñez, 2014; García and Ibáñez, 2016).

Such tasks could complement standard assessment tools to characterize cognitive deficits in early stages and, more promisingly, to detect subtle frontostriatal abnormalities in asymptomatic carriers of associated mutations. The sensitivity of the motor grounding impairments reviewed above is highlighted by two observations. First, they have been repeatedly documented in patients without dementia or MCI, suggesting that they could be primary in nature (i.e., not epiphenomenal to widespread cognitive dysfunction). Second, at least some of them are independent of executive deficits, which highlights their relevance to detect neurofunctional alterations even if traditional executive screening procedures yield null results –see, for example, García et al. (2016b).

Moreover, some of the studies reviewed are pregnant with possibilities for translational innovations. First, during action-verb processing, PD patients seem to recruit a non-motor pathway in a manner proportional to their level of basal ganglia atrophy (Abrevaya et al., 2017).

These results may inspire breakthroughs for non-invasive brain stimulation protocols. Unlike what happens in healthy subjects, stimulation of motor hubs in PD does not facilitate processing of specific types of action verbs (Tomasino et al., 2014). While several explanations seem plausible (e.g., damage-induced desensitization of the motor system to stimulation, compensatory side effects, or other neuroadaptation phenomena), such null results might also reflect the partial functional irrelevance of motor structures for action-verb processing in patients and, more generally, they could imply that other high-order functions are being processed via non-putative circuitry. Future stimulation studies could assess this conjecture by targeting non-canonical regions to enhance processing of specific cognitive functions. In this sense, action verbs would be good starting candidates.

Second, using automated text analysis tools, García et al. (2016b) found that reduced reliance on action semantics in PD could be tapped via naturalistic speech production tasks. This novel paradigm circumvents the limitations of standard atomistic paradigms, which typically exhaust patients by having them concentrate on long lists of disconnected stimuli presented in random or arbitrary succession. As shown in previous studies with other samples (Bedi et al., 2014), such an approach bypasses the biases and bottlenecks of human-based text analysis and allows researchers to automatically classify individuals as belonging to a certain patient group. Moreover, García et al. (2016b) also found that syntactic and syntagmatic abnormalities during natural speech in PD allowed classifying individual patients with 75% accuracy, and inferring their level of motor impairment with 76% accuracy. Prospectively, if available results are replicated, spontaneous speech production tasks could be applied remotely and repeatedly to complement traditional clinical and neuropsychological assessments, offering a chance to naturally monitor the progression of cognitive deficits or even the impact of clinical interventions. In particular, as this approach entails a dramatic reduction of human labor in the administration, scoring, tabulation, and analysis of data, it could offer unprecedented opportunities for massive application across geographical boundaries.

Third, both neurodegenerative disorders reviewed here are associated with well-known genetic alterations. Specifically, many forms of PD have genetic determinants such as mutations in the PARK2 and LRRK2 genes (Spatola and Wider, 2014), and HD is an autosomal dominant disorder resulting from mutations in the huntingtin gene (Walker, 2013). While functional scales and traditional tests may be blind to the subtle consequences of preclinical frontostriatal damage, the three language domains reviewed can become significantly impaired in asymptomatic carriers of associated mutations. Insofar as timely intervention is a key prerequisite for clinicians to mitigate the impact of disease, linguistic tasks affording sensitive prodromal markers could become critical complements to more traditional assessments.

Finally, despite our focus on PD and HD, tasks tapping these three linguistic domains could also reveal fine-grained cognitive deficits in other movement disorders. Indeed, several reports have documented selective action-verb, motor-language coupling, and/or syntactic impairments in progressive supranuclear palsy (Bak et al., 2006), amyotrophic lateral sclerosis (Ash et al., 2015; Neary et al., 2000; Papeo et al., 2015; Yoshizawa et al., 2014), and cerebral palsy (Geytenbeek et al., 2015). Moreover, the DMGH could be extended beyond models of motor network damage. For example, specific language motor grounding mechanisms have been identified in regions specialized for emotional processing (Naccache et al., 2005), olfaction (González et al., 2006), and chromatic perception (Simmons et al., 2007). Tasks aimed to assess verbal processing of those experiential domains (e.g., targeting processing of emotional, olfactory, or color words) might offer sensitive clues about the functional integrity of their putative regions across specific patient populations.

5. Conclusion

Embodied cognition research offers new views into the organization of linguistic subsystems in the brain, showing their critical links with specific sensorimotor networks. In particular, the DMGH may represent a useful heuristic tool in the quest of cognitive biomarkers for neurodegenerative motor diseases. While an embodied conceptualization is neither sufficient nor necessary to such an end, it may certainly contribute to this mission by promoting testable fine-grained hypotheses on potentially specific markers. As seen in this review, this conceptual approach could open new windows for theoretical and translational breakthroughs. The functional affinities between the motor specialization of frontostriatal networks and three specific motor grounding domains (action language, motor-language coupling, and syntax) call for extensions and refinements of extant language models. Moreover, they offer promising alternatives to characterize early deficits in movement disorders and even promote their preclinical detection. In this sense, the DMGH may afford a fruitful overarching framework for future basic and applied research in neurolinguistics and cognitive neuroscience at large.

Conflict of interest

None to declare.

Acknowledgments

This work was partially supported by grants from CONICET, CONICYT/FONDECYT Regular (1170010), FONCyT-PICT 2012-0412, FONCyT-PICT 2012-1309, FONDAP 15150012, and the INECO Foundation.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.neubiorev.2017.07.011.

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