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Research report

Motor-language coupling: Direct evidence from early Parkinson's disease and intracranial cortical recordings

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ABSTRACT

Language and action systems are functionally coupled in the brain as demonstrated by converging evidence using Functional magnetic resonance imaging (fMRI), electroencephalography (EEG), transcranial magnetic stimulation (TMS), and lesion studies. In particular, this coupling has been demonstrated using the action-sentence compatibility effect (ACE) in which motor activity and language interact. The ACE task requires participants to listen to sentences that described actions typically performed with an open hand (e.g., clapping), a closed hand (e.g., hammering), or without any hand action (neutral); and to press a large button with either an open hand position or closed hand position immediately upon comprehending each sentence. The ACE is defined as a longer reaction time (RT) in the action-sentence incompatible conditions than in the compatible conditions. Here we investigated direct motor-language coupling in two novel and uniquely

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ECoG
Intracranial N400
Intracranial MP

informative ways. First, we measured the behavioural ACE in patients with motor impairment (early Parkinson's disease – EPD), and second, in epileptic patients with direct electrocorticography (ECoG) recordings. In experiment 1, EPD participants with preserved general cognitive repertoire, showed a much diminished ACE relative to non-EPD volunteers. Moreover, a correlation between ACE performance and action-verb processing (kissing and dancing test – KDT) was observed. Direct cortical recordings (ECoG) in motor and language areas (experiment 2) demonstrated simultaneous bidirectional effects: motor preparation affected language processing (N400 at left inferior frontal gyrus and middle/superior temporal gyrus), and language processing affected activity in movement-related areas (motor potential at premotor and M1). Our findings show that the ACE paradigm requires ongoing integration of preserved motor and language coupling (abolished in EPD) and engages motor-temporal cortices in a bidirectional way. In addition, both experiments suggest the presence of a motor-language network which is not restricted to somatotopically defined brain areas. These results open new pathways in the fields of motor diseases, theoretical approaches to language understanding, and models of action-perception coupling.

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1. Introduction

Understanding the mutual coordination of motor and language systems is critical for different research programs. These systems are functionally coupled in the brain as demonstrated by converging evidence using Functional magnetic resonance imaging (fMRI), electroencephalography (EEG), transcranial magnetic stimulation (TMS), and lesion studies (Pulvermüller 2001; 2005; Pulvermüller and Fadiga, 2010). In addition, this coupling has been demonstrated behaviourally using the action-sentence compatibility effect (ACE) in which motor activity and language interact (Aravena et al., 2010; Glenberg, 2006; Glenberg et al., 2008a; Glenberg et al., 2008b; Glenberg and Kaschak, 2002; Kaschak and Borreggine, 2008; Masumoto et al., 2004). The ACE task required participants to listen to sentences and press a large button immediately upon comprehending each sentence. In one block, the button is pressed using an open hand (OH) response, and in one block, the button is pressed using a closed hand (CH) response. Importantly, participants keep their hands in the required pre-assigned shape throughout the block of trials. The OH sentences describe actions typically performed with an open hand (e.g., clapping), the CH sentences describe actions performed with a closed hand (e.g., hammering), and the neutral sentences (N) did not describe hand actions. The combination of response type and sentence 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 (N sentence with either response) trials. The ACE is defined as a longer reaction time (RT) in the incompatible conditions than in the compatible conditions. First, we measured the ACE in patients with motor impairment (early Parkinson's disease – EPD), and second in epileptic patients with direct electrocorticography (ECoG) recordings.

According to theories of a simultaneous action-perception cycle (Pulvermüller, 2001; 2005; Pulvermüller and Fadiga, 2010) and theories of language comprehension as simulation (Barsalou, 1999; Bergen et al., 2007; Gallese and Lakoff, 2005; Glenberg and Kaschak, 2002; Hesslow, 2002;

Jeannerod, 2001; Richardson et al., 2003; Zwaan et al., 2002) cortical motor lesions or impairments should affect language comprehension. In support of this prediction, neuroimaging findings (e.g., Aziz-Zadeh et al., 2006; Hauk et al., 2004; Tettamanti et al., 2005) have suggested that lexical stimuli (either single words or sentences) referring to different body parts (e.g., hand and mouth) somatotopically activate cortical regions. However, other studies have failed to find a strict somatotopic organization of action words. For instance, Postle et al. (2008) found no evidence of somatotopic organization for effector-related words using cytoarchitecturally and functionally defined maps of the primary and premotor cortex. Using Voxel-based Lesion-Symptom Mapping analyses in stroke patients, Arévalo et al. (2012) also found no evidence of a somatotopically-organized distribution of effector specific regions. These results put forward a partial overlap of actions and processing of action-related sentences. Arévalo et al. (2011) suggested that interaction between motor networks and the language network in humans may not be confined to a particular region in the premotor/motor cortex. Motor and language process would not be completely dependent of a cortical somatotopic organization. In experiment 1, we tested the relationship between action language and current motor activity in individuals with a subcortical motor impairment (EPD) and normal volunteers. In the EPD, only subcortical (non-somatotopic) motor regions are affected (early stages of the disease). Therefore, EPD, due to its non-specific non-somatotopic motor impairment, is ideal for testing the coupling between motor and language systems.

A growing body of research indicates that specific verb processing is impaired in Parkinson's disease, including verb production (Bertella et al., 2002; Boulenger et al., 2008; Crescentini et al., 2008; Peran et al., 2003); action-verb generation and conjugation (Longworth et al., 2005; Peran et al., 2009); sentence comprehension (Grossman et al., 1992; Grossman 1999; Lieberman et al., 1992; Ullman et al., 1997); action-verb identification (Boulenger et al., 2008); and specific verb processing during sentence comprehension (Whiting et al., 2005).

According to these findings, it has been suggested that the nigrostriatal circuit affected in Parkinson's disease (PD) is

involved in the modulation of action-verb processing in motor cortical areas. However, these studies have used experimental paradigms which do not relate motor performance to the meaning of the linguistic stimuli. To our knowledge, the current research is the first to study a motor-language integration paradigm to explore the ACE in a movement disorder such as EPD.

Based on previous evidence, we propose that processing of the ACE task should be affected by the non-specific (non-somatotopic) and subcortical motor system in EPD. Therefore, basal ganglia impairments as those seen in EPD group should affect the ACE, and patients with such impairments should not show compatibility effects. If instead, EPD patients display an ACE, this would suggest the ACE task is not dependent on motor system integrity.

Another complementary way to test the motor and semantic coupling consists of directly measuring the semantic and motor areas in the brain during ACE. The bidirectionality hypothesis in motor-language interaction claims that action-language comprehension and motor processes share neural resources that co-operate mutually; that is to say that motor processes influence the comprehension of the action sentence, and action-sentence comprehension influences the motor process (Aravena et al., 2010). The ECoG (Jerbi et al., 2009) provides fine-grained spatial and temporal brain information even with single case studies (Jacobs and Kahana, 2010), which allows the direct assessment of the motor-language bidirectional brain signatures. By recording ECoG we evaluated compatibility effects in brain areas related to motor (premotor and M1) processing as well as language (inferior frontal gyrus – IFG and left anterior temporal areas) processing. In a previous report with normal volunteers, ACE was recorded with scalp ERPs. Both the final verb onset and the motor response were used as temporal triggers for ERPs. An N400 was enhanced in the incompatible condition and the amplitude of motor potential (MP) showed a slight increase in compatible conditions (Aravena et al., 2010). The N400 component has shown larger amplitudes when the meaning of a stimulus is incongruent with its previous context (Kutas and Federmeier, 2011). Recent N400 studies have shown modulation of incongruent action sequences (e.g., Aravena et al., 2010; Ibáñez et al., 2010; 2011d; Kelly et al., 2010b; Kiefer et al., 2011; Proverbio et al., 2010; Sitnikova et al., 2003; van Elk et al., 2010). The MP (Deecke, 1987; Hatta et al., 2009; Smith and Staines, 2006) is negative around the response onset (–90 msec), indexing cortical activity at motor execution. Thus, this study (Aravena et al., 2010) suggests that semantic and motor areas are simultaneously coupled during ACE, but the poor spatial resolution of scalp ERPs limits the speculation about the brain regions engaged in ACE. By using ECoG, we directly investigated the brain areas involved in ACE. The bidirectionality hypothesis predicted that both N400 and MP compatibility modulation should be directly observed at semantic and motor areas, evidencing mutual influence of action and language processes.

In brief, we tested causal evidence of a bidirectional coupling in the motor-to-language and language-to-motor directions. In experiment 1, we hypothesized that EPD will have reduced ACE as compared to a control group (CG) of

normal volunteers matched by age, gender, handedness and educational level. ACE deficits in EPD should be observed with a relative preservation of other motor and cognitive domains (e.g., preserved motor response ability, basic executive functions preservation, and no cognitive deterioration). Moreover, possible reduced ACE in EPD participants should correlate with deficits in verbal processing. In experiment 2, the ECoG intracranial recordings should provide the intracranial sources of ACE. For instance, a fronto-temporal (motor and language) contribution to the ACE as showed by the spatiotemporal dynamics of semantic and motor brain signatures should be identified. Thus, we evaluated the direct interaction of motor-language coupling by showing ACE in motor diseases and bidirectional cortical motor-language interactions assessed with ECoG.

2. Materials and methods

2.1. Experiment 1: ACE in EPD and matched normal volunteers

2.1.1. Participants

In total, 17 early Parkinson's disease patients and 15 normal volunteers took part in this study. The two groups were matched for age, level of education, and proportion of males to females (a summary of sample characteristics is presented in Table 1). Normal volunteers were recruited using a database of healthy volunteers from the Institute of Cognitive Neurology.

EPD participants who met UK Parkinson's Disease Society Brain Bank criteria (Hughes et al., 1992) were evaluated using the Unified Parkinson's Disease Rating Scale (UPDRS) part III; and stages I and II of the Hoehn and Yahr scale (1967). Mean age for the patient population was 62.71 (± 7.34) years. Information on disease history and drug therapy was obtained by three neurologists (AC, GGA, OG) who specialize in PD. All selected patients had bilateral or unilateral disease onset in their dominant hand. Patients with different neurological signs or symptoms or radiological structural brain abnormalities compatible with diagnoses other than Parkinson's disease were excluded from this study. Patients and normal volunteers that scored under 24 on the Mini-Mental State Examination were also excluded from the study to ensure a relatively preserved cognitive profile. All patients were under pharmacological treatment either with levodopa or a dopamine agonist. Assessment was conducted during the "on" state of the medication. Since levodopa seems to improve verbal processing in a percentage of PD subjects (Mattis et al., 2011), any observed impairment of ACE or verbal processing cannot be explained by medication. Clinical and demographic data are included in Table 1. EPD is defined as disease duration of fewer than 5 years and a patient with Parkinson's disease who has not developed motor complications from levodopa (Lewis et al., 2005; Williams-Gray et al., 2008).

All participants read and signed a consent form in agreement with the Declaration of Helsinki before beginning the study, and the ethical committee of the Institution approved the research. Patients and normal volunteers received an extended evaluation including dementia measures, neuropsychological assessment of executive functions, and a verbal

Table 1 – Demographic and clinical data (EPD and CG).

	EPD	CG	F ANOVA value or Chi-square value (d.f.)	P value
n (male/female)	17(11/6)	15(10/5)		.69
Handedness (right/left)	(17/0)	(15/0)		
Age (Mean \pm SD)	62.71 \pm 7.34	61.33 \pm 8.96	$F_{(1,30)} = 1.37$.25
Level of education			$\chi^2_{(3)} = 1.09$.78
Primary education:	4	5		
Secondary education:	6	4		
Tertiary education completed:	2	3		
University education completed:	5	3		
Hoehn & Yahr	1.24 \pm .44	–		
Disease duration (years)	3.18 \pm 2.05	–		
UPDRS motor score	15.53 \pm 6.73	–		
Onset Disease (right/left)	(14/3)	–		
Levodopa Mg/day (range)	260 \pm 56.76 (n = 10; 150–350)	–		
Dopamine agonist Mg/day (range)				
Pramipexole	.63 \pm .53 (n = 2; .25–1.0)	–		
Piribedil	175 \pm 35.36 (n = 2; 150–200)	–		
Other antiparkinsonian drugs, Mg/day (range)		–		
Rasagiline	.88 \pm .25 (n = 4; .25–1.0)	–		

processing task (see “Neuropsychological assessment of EPD and normal volunteers” in Supplemental data available online).

2.2. ACE paradigm

We evaluated the interaction between language and motor processes using an ACE paradigm. Participants listened to sentences that implied an action with the hand in a particular shape (open, $n = 52$, or closed, $n = 52$) as well as neutral sentences that did not imply an action with the hand ($n = 52$). Participants indicated as quickly as possible when they understood each sentence by pressing a button using a pre-assigned hand-shape (open or closed, see Fig. S1 in Supplemental data available online). All responses were performed with the dominant hand although both hands were positioned in the required shape (see Fig. S1 and “ACE paradigm description” in Supplemental data available online for more details on this paradigm). By controlling the posture of both hands at the required shape, we controlled possible bilateral hand interference, since posture modulates semantic processing (Badets and Pesenti 2010; Glenberg et al., 2008a; Lindeman et al., 2006; van Elk et al., 2008). To ensure that all participants understood the meaning of the sentences, they were asked to complete an offline questionnaire after finishing the ACE paradigm.

2.3. Data analysis

We used Repeated measures of Analysis of Variance (ANOVA) or χ^2 for neuropsychological assessment and for the ACE paradigm. In the ACE paradigm, mean RTs were calculated for each subject for each type of trial (compatible, incompatible and neutral) and each type of sentence (OH, CH and N). Single trials eliciting outlier’s values with RTs outside ± 3.5 SD were excluded from the analyses (11% in EPD and 9% in CG). The repeated measures ANOVAs categorized Group as a between-subject factor [Parkinson Group (EPD) and Control Group (CG)] and Compatibility (compatible, incompatible, and

neutral) as a within-subject factor. In order to test if EPD participants have preserved behavioural motor responses, we compared the RTs of stimulus content without any compatibility effect of hand positions. For instance, we compared the sentence content (open, closed and neutral) irrespective of the hand response position (i.e., by averaging the OH and CH responses for each of the three sentence content stimuli). Consequently, an additional factor, namely Sentence Type (N, OH and CH), was introduced. The N sentences are more predictable and frequently used in the language than OH and CH sentences, eliciting shorter RTs (Aravena et al., 2010). If the EPD evidence preserved sentence type modulation (N sentences being shorter than OH and CH sentences) as normal volunteer participants do, the ACE result in EPD cannot be explained as a general motor impairment or as a variable response. Tukey’s Honestly Significant Difference (HSD) method was used in the calculation of post-hoc contrasts. We further explored the individual differences in ACE. A global score of the ACE was defined by the difference in mean RT for the incompatible and compatible conditions. Those global scores were correlated with neuropsychological assessments and with tests of dementia in both groups using Spearman’s rank correlations, corrected for multiple comparisons with Tukey’s HSD test.

2.4. Experiment 2: ACE in ECoG

2.4.1. Participants

Participants were two right-handed males (patient 1: 31 years old, patient 2: 24 years old) suffering from drug resistant epilepsy, with no observed structural abnormality. They were both potential candidates for seizure surgery. The experimental protocol was reviewed and approved by the Institutional Ethics Committee of the Institute of Cognitive Neurology, which follows the guidelines of the Declaration of Helsinki. Written informed consent was obtained for both study participants. Intracranial recordings were performed

through subdural grid electrodes (with 10 mm inter-electrode distance). Patient 1 had a 64-electrode grid (eight rows and eight columns) covering all the left central and pericentral cortices (inferior frontal, temporal and parietal areas). The inferior limits were at the level of the inferior and middle temporal gyrus (MTG) from the temporal pole extending backwards to the posterior part of the inferior temporal sulcus close to the anterior occipital sulcus. Patient 2 had a 32-electrode grid (four rows and eight columns) covering the lateral surface including the anterior part of superior, medial and inferior frontal gyrus extending to the precentral sulcus. Both grids were situated over the left hemisphere. The selection of recording sites was made according to clinical criteria with no reference to the present study; nevertheless, recruited patients were selected for this study given the possibility of directly measuring motor and language areas using ECoG. Both patients scored over 26 on the Mini-Mental State Examination ensuring a relatively preserved cognitive profile. Both patients performed the ACE task 4 days after the implantation of the electrodes.

2.5. ACE paradigm

The ongoing intracranial signals were recorded while participants performed the ACE paradigm as reported in experiment 1.

2.6. ECoG recordings

A multi-channel EEG acquisition and monitoring system (Bioscience) was used to simultaneously record the intracerebral activity. Electrodes for ECoG were placed using rectangular grids, in left frontal and temporal areas. Following a previous report of this paradigm (Aravena et al., 2010), motor responses (eliciting a MP) and final verbs (eliciting a N400 component) were selected for further analysis. EEG data were segmented offline into 1 sec epochs spanning from 200 msec pre-stimulus to 800 msec post-stimulus for stimulus-locked segments (N400) and 1500 msec epochs from –500 msec to 800 msec for hand response-locked segments (MP). Non-biological artefacts were rejected by visual inspection as reported elsewhere (Hurtado et al., 2009; Ibáñez et al., 2010b, 2011a, 2011b, 2011c, 2011d, 2012; Petroni et al., 2011). For more details see “Epochs pre-processing” in Supplemental data available online. Following previous reports (Ossandón et al., 2011, 2012) a matching between a post-implantation computed tomography (CT) scan and a preimplantation 3-D magnetic resonance imaging (MRI) dataset allowed for direct visualization of the electrode contacts. We used a co-recording method of CT and MRI to obtain the spatial coordinates of each electrode (see “Channel localization using CT and MRI” in Supplementary data available online).

2.7. Data analysis

Intracranial ERP were analyzed during ACE in two steps. First, to select the electrode sites modulated by the ACE (compatible vs incompatible trials) at N400 and MP windows, we performed Monte Carlo permutation tests

(Manly, 1997), which have been used in other intracranial studies (Gaillard et al., 2006; Naccache et al., 2005), combined with bootstrapping. This simple method gives a straightforward solution for the multiple comparison problems and does not depend on multiple comparisons corrections or Gaussian distribution assumptions about the probability distribution of the data. The combined data from the compatible and incompatible trials underwent a random partition, and a t-test was calculated. This process was repeated 5000 times to construct the t-value distribution under the null hypothesis. The null hypothesis is rejected if an obtained t-value is greater than the most extreme 1% of the distribution (e.g., $p < .01$). Selected electrodes were grouped into regions of interest (ROIs) for further analysis using the Friedman Test. This test (non-parametric repeated measures comparison) was used for single-trial analysis (compatible, incompatible and neutral) of selected electrodes' ROIs. Unlike the parametric repeated measures ANOVA or paired t-test, this test makes no assumptions about the distribution of the data and has been used recently with intracranial ERPs (e.g., Vidal et al., 2010). The significant window obtained in the permutation analysis was selected for mean amplitude analysis (Friedman test): –75 to 35 msec for MP; 390–500 msec for motor N400 and 250–700 msec for temporal N400. Post hoc comparisons were performed with the HSD Tukey test.

3. Results

3.1. Experiment 1

3.1.1. ACE is impaired in neurodegenerative motor disease

We observed (Fig. 1A) a strong relationship between Group and Compatibility [$F(2,60) = 22.47, p < .0001$; See “ACE effects in EPD and CG” in Supplemental data available online]. Post hoc comparisons ($MS = 27,853, df = 37.34$) showed that in the CG, incompatible trials elicited longer RTs compared to compatible ($p < .001$) and neutral trials ($p < .001$); that is, there is an ACE. No differences between responses to compatible and neutral trials were observed in the CG ($p = .90$). Conversely, participants with EPD presented only differences in RTs in the neutral trials compared with compatible ($p < .005$) and incompatible trials ($p < .001$). No differences between compatible and incompatible trials were observed ($p = .99$); that is, there was no ACE. To confirm these effects, a separate ANOVA for each group was performed, confirming those results (see “EPD and CG ANOVAs for ACE” in Supplemental data available online).

To compare the performance from both groups while controlling for overall group differences in level of RT, we subtracted the mean RT in the neutral trials from both compatible and incompatible trials. After subtraction (Fig. 1B), group differences became larger [Group \times Compatibility Interaction, $F(1,30) = 89.14, p < .0001$]. In particular, in the CG, there was a large difference between compatible ($M = -24$ msec, $SD = 25.98$) and incompatible trials ($M = 209$ msec, $SD = 22.47, p < .001$), whereas in EPD participants, the means for compatible ($M = 94.69$ msec, $SD = 24.41$) and incompatible trials ($M = 104$ msec, $SD = 26.75, n.s.$) were quite similar.

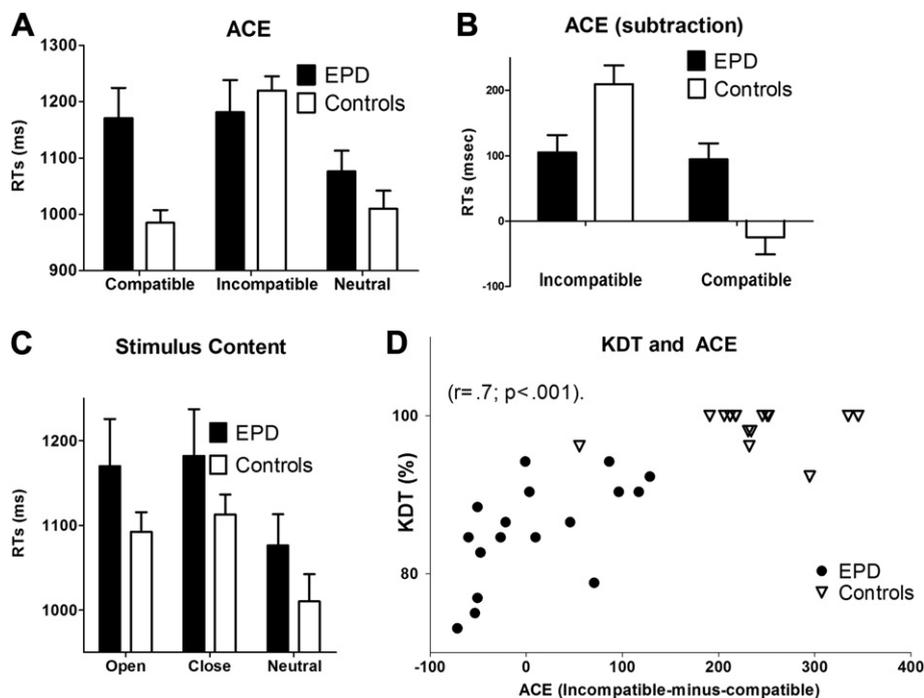


Fig. 1 – ACE in EPD. (A). Mean RTs from compatible, incompatible and neutral trials for EPD and CG participants. CG participants show a classic ACE (compatible facilitation and incompatible delay of RTs), whereas the ACE was absent for EPD participants. **(B).** ACE subtraction. Group comparison of ACE normalized by subtracting mean RT from the neutral trials from the mean RTs from the compatible and incompatible trials. **(C)** Preserved motor response discrimination for EPD participants. In both groups, OH and CH sentences produce longer RTs than neutral sentences due to a higher frequency and higher cloze probability of neutral sentences (Aravena et al., 2010). In panels A, B, and C, the bars depict the SD. **(D).** Verbal processing (KDT) is associated with the ACE. The ACE is computed as the subtraction between incompatible and compatible trials (the higher the time interval, the stronger the ACE). KDT scale denotes percentage of correct responses.

3.1.1.1. PRESERVED MOTOR RESPONSES TO LINGUISTIC VARIABLES IN EPD. Might the absence of an ACE in EPD participants be due to general motor impairment?

A comparison of N sentences to OH and CH sentences provides a test of this hypothesis. Because N sentences are composed of words having a higher frequency of occurrence in the language and a higher cloze probability than OH and CH sentences (Aravena et al., 2010), we expect N sentences to elicit faster responses (Dambacher et al., 2006; Fischler and Bloom, 1979; Kleiman, 1980; Kliegl et al., 2004; Kliegl et al., 2006). Indeed, both EPD and CG participants responded faster to N sentences than to OH and CH sentences (Fig. 1C; see “Stimulus content analysis” and Table S2, in Supplemental data available online). This result confirms that motor impairment in EPD participants was not so severe as to preclude effects of linguistic variables. Consequently, the ACE deficits in EPD cannot be explained by a general motor or language impairment.

3.1.1.2. ACE IS ASSOCIATED WITH PROCESSING OF VERBS, IMPLYING HAND ACTIONS IN THE ABSENCE OF OTHER COGNITIVE DEFICITS IN EPD. No differences were observed between the groups regarding cognitive impairments or dementia (see Table S1 in Supplementary data). In addition, most of the neuropsychological assessments evaluating executive functions, memory, and

working memory yielded no differences between groups. Only in one of three measures of working memory were the EPD participants impaired compared to CG participants (see Table S1, and “Clinical and Neuropsychological assessment” in Supplemental data online).

In addition, we examined performance in verbal processing. The kissing and dancing test (KDT; Bak and Hodges 2003) is designed to detect verb-processing impairments (see “Neuropsychological assessment of EPD and normal volunteers” in Supplemental data online). The KDT deficits have already been reported in other movement disorders such as progressive supranuclear palsy (Bak et al., 2006) (see “EPD deficits of KDT” in Supplemental data online). To explore the relationship between the specific cognitive profile and the ACE, we performed a multivariate analysis between those measures. No significant correlations between scores of dementia and ACE were observed. In contrast, the KDT accuracy was highly associated with the ACE (more KDT accuracy, more ACE: $r = .7; p < .001$; Fig. 1D). In addition, we reanalyzed the KDT error trials and ACE association by dividing the KDT into scenarios that included hand actions and those that did not (see “Neuropsychological assessment of EPD and normal volunteers” in Supplemental data online). We found, only in EPD participants, a negative correlation between hand-KDT error trials and the ACE (more KDT errors, less ACE: -0.5 ,

$p = .02$); but the correlation with ACE was not significant for the KDT error trials that did not include hand trials (for all reported correlations, see “ACE correlations” in Supplemental data available online).

In brief, we found that EPD participants show specific deficits on ACE and verbal processing with a well-preserved cognitive profile.

3.2. Experiment 2

3.2.1. Direct ECoG recordings of ACE

We tested the motor-language coupling by measuring the direct cortical activity (ECoG) in both movement-related and language-related areas. This approach allows us to describe the brain dynamics of motor and language interactions. We aligned EEG traces both with the onset of the final verb (to measure the N400) and with the motor response onset (to measure the MP) for left fronto-temporal (language) as well as left frontal (premotor/motor) areas (see Table 2 for spatial coordinates of selected electrodes, and “Electrode selection for ACE-ECoG” in Supplemental data available online). To identify the spatial coordinates of grid electrodes, we combined CT and MRI using a semi-automatic method (see Fig. 2A–E, and “Channel localization using CT and MRI” in Supplemental data available online). To select the electrode sites modulated by the ACE (compatible vs incompatible trials) at the N400 and MP windows, we performed a permutation and bootstrapping test on all electrodes sites to find those that showed a significant difference between compatible and incompatible trials. The selected electrodes were grouped in ROIs for further analysis using a Friedman’s Test.

3.2.1.1. ACE AT THE VERB (N400).

3.2.1.1.1. MOTOR AREAS (M-N400). The permutation test of the ECoG ERPs at the frontal grid in patient 2 showed significant effects of compatible versus incompatible trials in the

M-N400 window (390–500 msec) in a cluster of neighbouring electrodes (8, 15, 16 and 24, see Table 2). Those electrodes were placed in motor and premotor areas, contralateral to the hand used for responding. Electrode 8 was situated in M1 (pre-central gyrus), electrodes 16 and 15 were in the premotor cortex (PM ventral), and electrode 24 was localized in the dorsal section of the PM area (Picard and Strick, 2001). For all of them, the incongruent trials elicited more negative amplitude in the signal than in the congruent trials (See Fig. 3B and C, second column, Fig. S2 for all electrodes comparisons). The selected ROIs at motor areas in frontal sites (Fig. 3A, second column,) yielded an effect of compatibility [Friedman-ANOVA, $\chi^2(2,46) = 14.39$ $p < .001$]. The incompatible trials ($M = -81.02$ μV , $SD = 117.25$) presented more negative values compared with the compatible ($M = 29.23$ μV , $SD = 124.59$) and neutral ($M = 9.09$ μV , $SD = 64.84$) trials. Post hoc comparisons (HSD test, $MS = 12,264$, $df = 90$) showed statistical differences between compatible and incompatible categories ($p < .001$), as well as between neutral and incompatible categories ($p < .001$). No differences between neutral and compatible categories were observed ($p = .65$). The second column in Fig. 4B shows the intracerebral event-related potentials (iERPs), and Fig. 4C shows the mean amplitude for each type of trial.

3.2.1.1.2. LANGUAGE AREAS (L-N400). In language-related areas, several electrodes showed a significant ACE effect in the 250–700 msec time window (patient 1). Six neighbouring electrodes (13, 21, 22, 23, 30 and 31; see Table 2) showed an ACE (see Fig. 3B and C, third column, Fig. S2 and “Electrode selection for ACE-ECoG” in Supplemental data available online). Electrodes were localized in temporal sites (electrodes 21, 22 and 23 in superior temporal gyrus – STG; and electrode 13 in MTG) as well as Broca’s area (IFG, electrode 31 in pars opercularis and electrode 30 in pars triangularis). For all of them, the incongruent condition elicited a more negative response than the congruent one. The L-N400 ROI yielded a compatibility effect [$\chi^2(2,47) = 20.47$ $p < .001$] evidencing an enhanced N400 amplitude in the incompatible ($M = -102.96$ μV , $SD = 85.34$) compared to the compatible trials ($M = -9.32$ μV , $SD = 51.28$) and the neutral ($M = -4.14$ μV , $SD = 76.70$) trials. Post hoc comparisons (HSD test, $MS = 1422$, $df = 92$) showed statistical differences between compatible and incompatible trials ($p < .001$), as well as between neutral and incompatible trials ($p < .001$), but no differences between neutral and compatible trials ($p = .97$).

The overall results of N400-like amplitude suggest that the ACE is modulated by incompatible stimuli compared to compatible and neutral stimuli at motor and language-related sites (see Fig. 4A–C, third column). The L-N400 effect was observed earlier and in a more extended window (250–700 msec) than the M-N400 at motor sites (390–500 msec).

3.2.1.2. ACE AT THE MOTOR RESPONSE (MP).

3.2.1.2.1. MOTOR AREAS. In the motor response window (from –75 to 35 msec) several electrodes showed a significant ACE (patient 2, see Fig. S2). As in the case of M-N400 (see “Electrode selection for ACE-ECoG” in Supplementary

Table 2 – Localization of selected electrodes using MRI/CT co-recordings.

Electrode	Cortical area	Brodmann areas
Frontal grid (patient 2)		
7	Inferior motor cortex	4
8	Inferior motor cortex	4
14	Ventral premotor cortex	6
15	Ventral premotor cortex	6
16	Ventral premotor cortex	6
22	Ventral premotor cortex	9
23	Ventral premotor cortex	6
24	Dorsal premotor cortex	6
30	MFG	9
31	MFG	9
Fronto-temporal grid (patient 1)		
13	MTG	21
21	STG	22
22	STG	21
23	STG	38
30	IFG opercularis	6
31	IFG triangularis	45

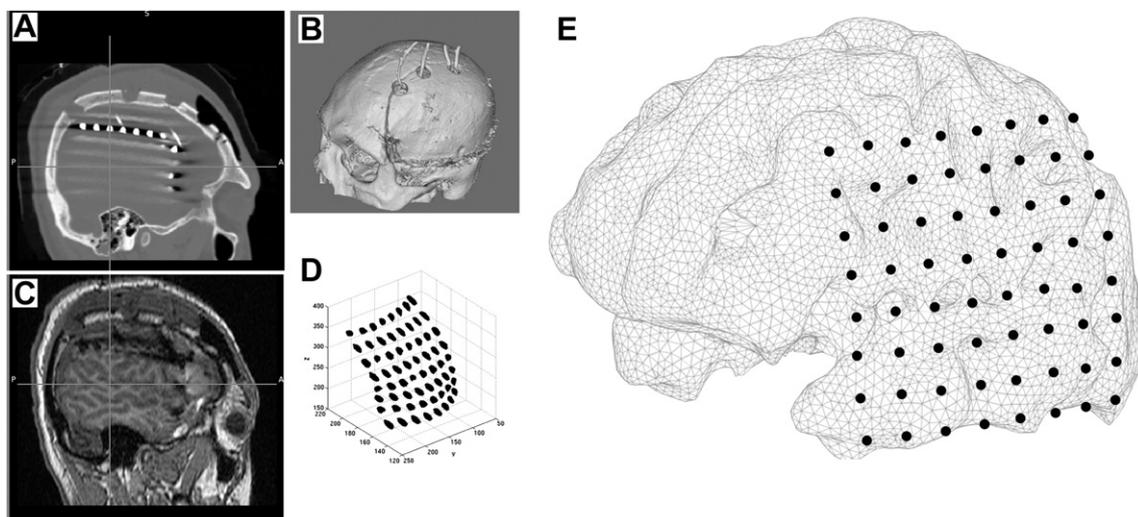


Fig. 2 – Measuring the spatial coordinates of grids using CT and MRI. First, CT and MRI volumetric images were affine registered in SMP8 toolbox. After that, CT was masked with an in-skull mask (obtained from MRI segmentation) and then thresholded to conserve relevant voxels of metallic elements. Voxels corresponding to wires were manually excluded. Next, each electrode in the CT included several voxel coordinates (VC) that were grouped using the k clustering technique. Finally, mean location of each cluster was assigned to the corresponding channel. (A). Volumetric X-ray CT showing the subdural implanted grid. The voxels size is $.36 \times .5 \times .36$ mm. (B) 3D reconstruction of CT. Note the skull incision where the grid electrode was implanted. (C) MRI of the patient showing the grid. The voxels size is $.93 \times .93 \times .5$ mm. (D) VC exceeding a signal threshold. (E) Coordinates where the electrodes were situated over a brain surface reconstruction. These figures show images of patient 1. For more details see “Channel localization using CT and MRI” in Supplemental data available online.

data available online), we obtained the electrodes with the most significant permutation effects (See Fig. 3A–C) resulting in a cluster containing electrodes 7, 14, 15, 16, 22, 23, 24, 30 and 31 (see Table 2 for spatial coordinates). Electrode 7 was situated in M1 (precentral gyrus), electrodes 14, 15, 16, 22, and 23, were in the premotor cortex (ventral PM), and electrode 24 sat in the dorsal section of the PM area. Electrodes 30 and 31 were also localized in PM (prefrontal cortex, middle frontal gyrus – MFG). Using a Friedman-ANOVA, the MP ROI yielded an effect of compatibility [$F(2,41) = 48.43; p < .001$]. In contrast to the N400-like components, post hoc effects (HSD test, $MS = 1582$, $df = 80$) indicated a greater negative amplitude for the compatible trials ($M = -167.21 \mu V$, $SD = 100.48$) compared to the incompatible trials ($M = -27.18 \mu V$, $SD = 143.61; p < .001$) and neutral trials ($M = 114.51 \mu V$, $SD = 139.53; p < .001$). Finally, a comparison of neutral and incompatible trials also yielded a significant difference ($p < .001$; see Fig. 4A–C, first column).

3.2.1.2.2. LANGUAGE AREAS (PATIENT 1). No significant effects were observed.

4. Discussion

This report provides direct evidence for simultaneous influence of motor activity in language processing and language modulation in motor processing. Motor impairment in EPD participants abolished the ACE, thereby suggesting that the

ACE reveals the ongoing integration of preserved motor and language coupling (experiment 1). In experiment 2, direct cortical recordings of the ACE showed that current action affects sentence processing in temporal and motor areas (L-N400 and M-N400, respectively), and simultaneously, sentences affect motor cortical processing (MP). Thus, we have demonstrated a bidirectional influence of motor and language networks.

This study provides support for theories of a simultaneous action-perception cycle (Pulvermüller, 2001, 2005; Pulvermüller and Fadiga, 2010) and theories of language comprehension as simulation (Barsalou 1999; Bergen et al., 2007; Gallese and Lakoff, 2005; Glenberg and Kaschak, 2002; Hesslow, 2002; Jeannerod, 2001; Richardson et al., 2003; Zwaan et al., 2002). These theories propose that during action (or language) perception, the brain activates the same sensory-motor systems that are engaged during movement, providing a continuous loop between perception and action. Simulation theory claims that the internal enactment of language engages specific areas of the motor cortex that control the simulated effectors of the action (Boulenger et al., 2006; Buccino et al., 2005; Ehrsson et al., 2003; Goldberg et al., 2006; Hauk et al., 2004; Lotze et al., 1999; Richardson et al., 2003; Tettamanti et al., 2005). Studies on action words have shown activation of brain areas related to motor planning and execution (Aziz-Zadeh et al., 2006; Boulenger et al., 2006; Buccino et al., 2004; Pulvermüller et al., 2005; Tettamanti et al., 2005). In a similar vein, research on gestures has evidenced a direct link between language processing and body

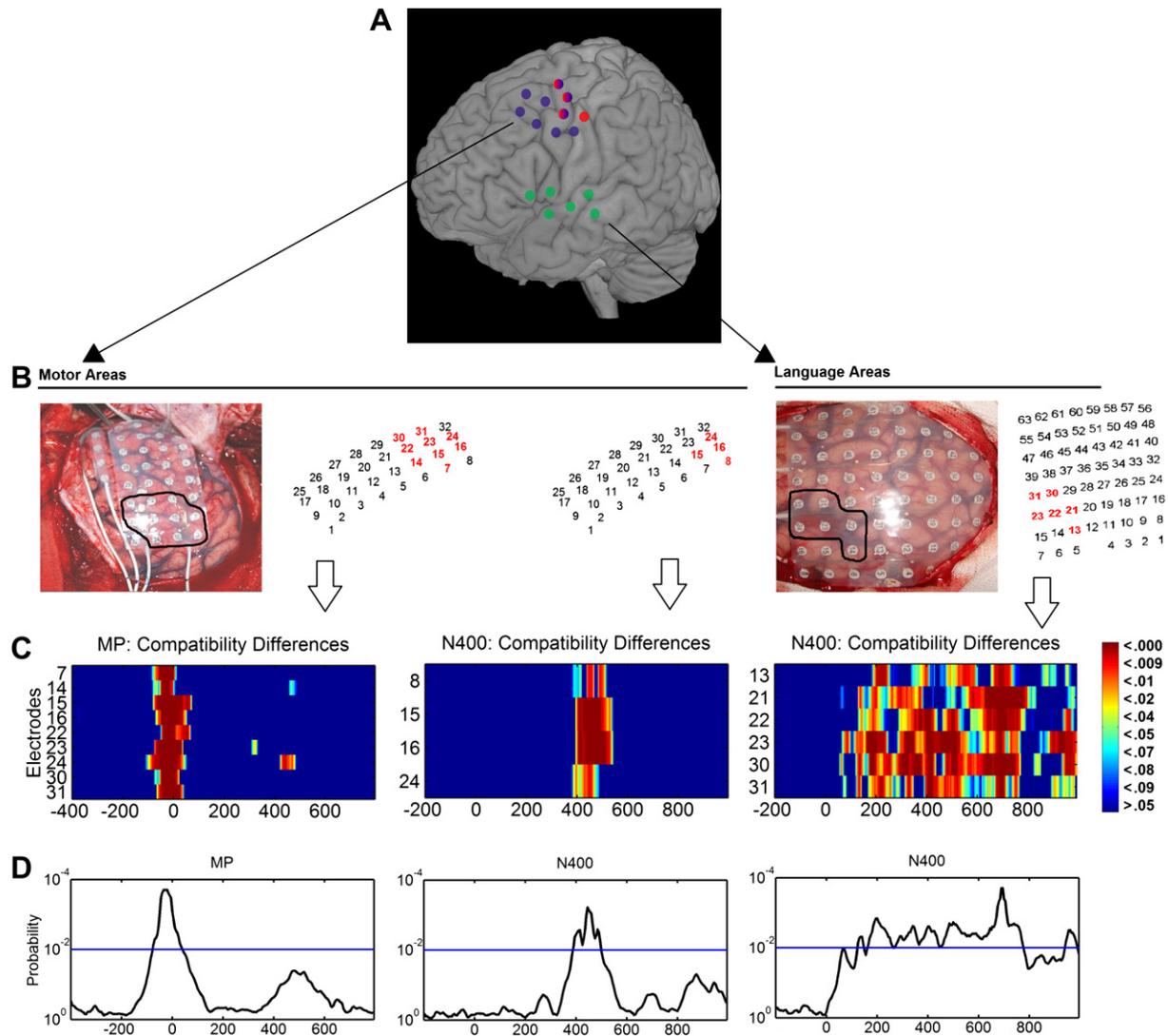


Fig. 3 – ECoG of ACE. (A). Motor and language areas producing an ACE. Normalized position of the electrodes showing a significant ACE (compatibility effect) superimposed in a render 3D map of the canonical CH2bet from MRICron software. The figure depicts the position of electrodes evincing an ACE from both patients' grids in a common space showing the activation of IFG, STG and MTG (language-related areas) and the MFG, PM and M1 (motor-related areas). Electrode colour is indicative of iERP modulation: MP (Blue); M-N400 (Red); L-N400 (Green). **(B)** Pictures of subdural grids and electrode arrays. Codes (number) of electrodes in left picture are not the same as the grid codes (+1) since it includes the electrode for triggers (number 5 in the picture). In the three schematic grids, numbers in red are indicative of significant compatibility effects observed at those sites for MP, M-N400 and L-N400 (from left to right). **(C)** Time-probability charts showing the significant effects at MP in premotor/motor (M1, ventral and dorsal PM) areas and N400 windows (M-N400 localized in premotor/motor areas including M1 and ventral-dorsal PM area; and a L-N400 localized in STG, MTG and IFG). **(D)** Point-by-point p -value waveform of the compatibility effect for MP, M-N400, and L-N400. The blue lines highlight the $p < .01$ threshold. Note that in panels C and D, a value of zero on the abscissa indicates the time of the response for MP, whereas a value of zero indicates the time at which the verb was presented for M-N400 and L-N400. Note that motor areas (first and second columns) correspond to Patient 2; and language areas (third column) are from the electrodes on Patient 1.

actions (Beilock and Goldin-Meadow, 2010; Broaders and Goldin-Meadow, 2010; Corballis, 2003; Frey, 2008; Goldin-Meadow 1999; Habets et al., 2011; Hubbard et al., 2009; Ibáñez et al., 2010; 2011d; Iverson and Goldin-Meadow 1998; Kelly et al., 2010b; Obermeier et al., 2011; Ozyurek et al., 2007; Pazzaglia et al., 2008; Straube et al., 2009; Willems et al., 2007). Meaning and comprehension (in language, gestures, or

actions) appear to be general processes of cognition related to motor process (Cornejo et al., 2009; Cosmelli and Ibáñez, 2008; Davison, 2001; Diamond et al., 2008; Groeben and Scheele 2000; Ibáñez et al., 2010; Ibáñez and Cosmelli, 2008; Jeannerod, 2001; Kelly et al., 2002, 2004, 2007, 2010b; Koelsch, 2009; Wu and Coulson, 2005) and deeply grounded in the relational nature of the body to the world.

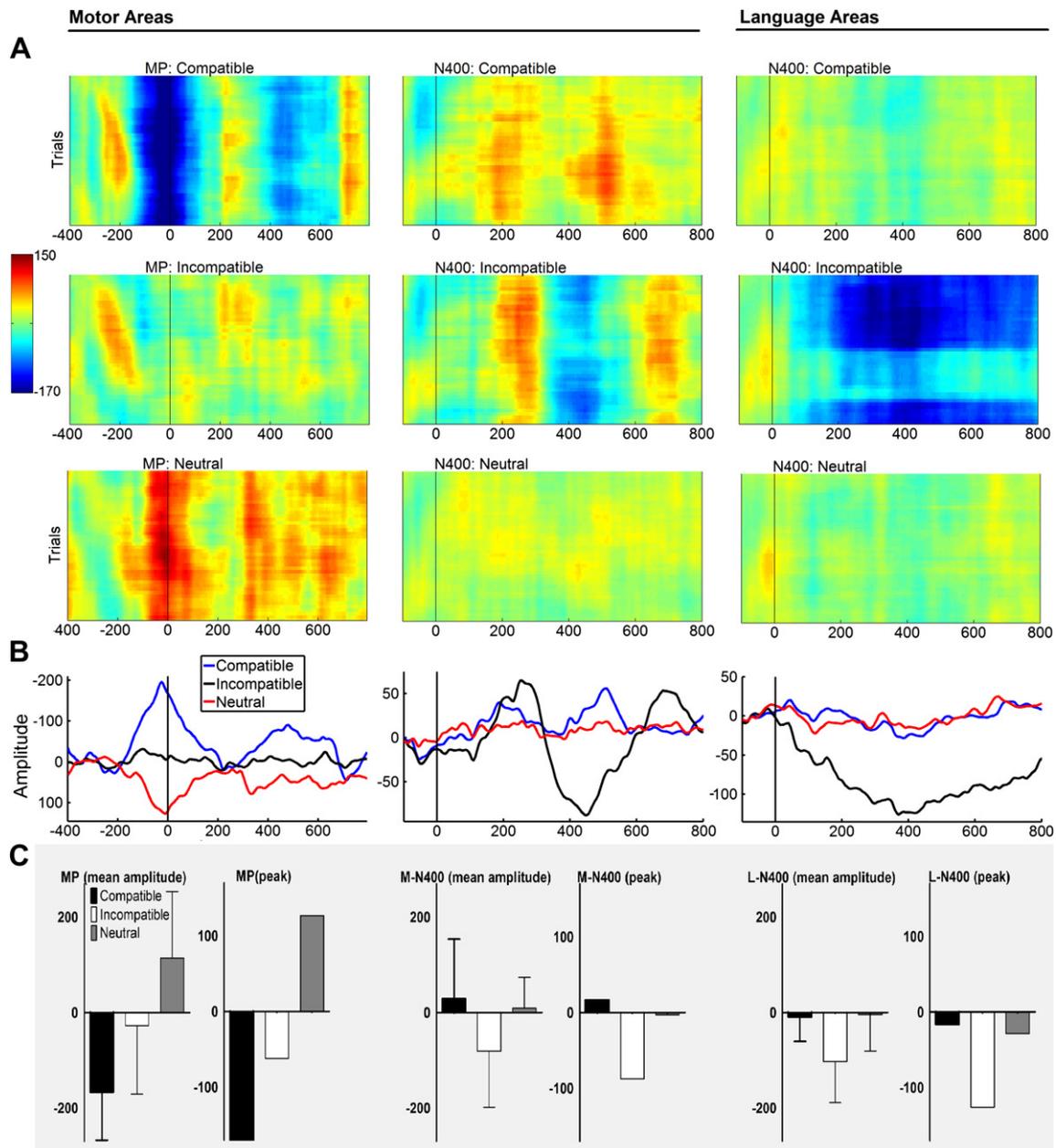


Fig. 4 – Single-trial neural activity and iERPs (MP and N400) at premotor/motor and language ROIs. (A) Single-trial power activity for compatible, incompatible and neutral trials at MP, M-N400 and L-N400 windows. (B) iERP waveforms for the same conditions and windows. (C) Mean amplitude and peak of MP (–75 to 35 msec), M-N400 (390–500 msec) and L-N400 (250–700 msec). Note that in panels A and B, a value of zero on the abscissa indicates the time of the response for MP, whereas a value of zero indicates the time at which the verb was presented for M-N400 and L-N400. Motor areas (first and second columns) correspond to Patient 2; and language areas (third column) are from electrodes on Patient 1.

4.1. Experiment 1: motor-language interaction in EPD

The ACE in normal volunteers confirmed the previously reported compatibility effects (Aravena et al., 2010; Borghi et al., 2004; Borreggine and Kaschak, 2006; De Vega, 2010; Fischler and Bloom, 1979; Glenberg et al., 2008a; Glenberg and Kaschak, 2002; Havas et al., 2007; Kaschak et al., 2005; Tseng and Bergen, 2005; Wheeler and Bergen, 2010; Zwaan and

Taylor, 2006). Results with EPD participants suggest a direct involvement of the motor system in language processing. This result is consistent with reports of verbal processing deficits in Parkinson's disease (Bertella et al., 2002; Boulenger et al., 2008; Crescentini et al., 2008; Peran et al., 2003; Peran et al., 2009). However, no previous report of action-sentence integration has been assessed in EPD participants or any other motor disease.

Our results confirmed that the semantic processing that produces an ACE requires a preserved motor repertoire. Reduced ACE in EPD participants was directly associated with verbal processing deficits and was unrelated to other cognitive domains. Parkinson's disease is caused by an impairment of the basal ganglia that affects the nigrostriatal dopaminergic pathway (Liu et al., 2006; Rodriguez-Oroz et al., 2009; Rosin et al., 1997; Wilson, 1925). Originally EPD was defined as a purely motor deficit because the basal ganglia were not associated with other cognitive domains. Nevertheless, current research highlights cognitive deficits in Parkinson's disease, specifically, impairment in working memory and executive functions due to striato-frontal circuit malfunction (Lieberman et al., 1992). Moreover, recent literature (Booth et al., 2007; Kotz et al., 2009) assigns an important role to subcortical neural systems and especially the basal ganglia (Houk, 2005) in linguistic processing, caused by the direct connections of putamen with the motor, premotor and prefrontal cortices (Lehericy et al., 2004) (see "Basal ganglia and language" in Supplemental data available online). It is possible that auditory-motor interaction at the basal ganglia (Grahn, 2009; Grahn and Rowe, 2009) is impaired in Parkinson's disease (Grahn and Brett, 2009), affecting the coupling between motor and semantic actions. Interestingly, our results suggest a coupling between action language and motor activity, as predicted by the action-perception cycle and simulation theories. But unlike most radical claims of those approaches, we have shown that language-action coupling is affected by neither cortical nor specific nor somatotopic motor activity, but by a basal ganglia deficit. As suggested by Arévalo et al. (2012), rather than following the strict interpretation of homuncular somatotopy for embodied semantics, their findings and our results suggest the presence of a motor-language network which is not restricted to somatotopically defined cortical areas (see also Arévalo et al., 2007). The damage to certain subcortical regions of this extended language-motor network will not completely block patients' ability to process motor-associated concepts, but may result in subtle verbal processing impairment (RTs unaffected by ACE).

Our report provides a new potential cognitive marker of EPD, related to action-sentence integration. This marker can complement the early diagnosis of Parkinson's disease and can be potentially investigated in other motor diseases such as progressive supranuclear palsy, corticobasal degeneration, spinobulbar muscular atrophy, Charcot-Marie-Tooth disease, or amyotrophic lateral sclerosis, among others. Of course, while this might prove to be accurate in the future, these findings need to be replicated and extended to other patients groups before they can be considered as a new biomarker for PD.

4.2. Experiment 2: direct evidence of intertwined motor and language cortical processing

Present results show that the N400 (time-locked to the target final verb) and the MP (time-locked to the onset of motor response) were modulated in a bidirectional way: (a) in the language-to-motor direction, based on the evidence that motor areas (MP) are directly influenced by language context; and (b), in the motor-to-language direction, based on the

evidence that anterior temporal and frontal areas (N400) are directly modulated by motor plans (hand position). In essence, language and action, both co-operators of the coupling, impact each other (see the bidirectionality hypothesis below).

4.2.1. Motor effects on language cortical processing

The N400 component is elicited when the meaning of a stimulus is incongruent with its previous context. Although this component was initially studied using linguistic stimuli, recent studies have extended the previous results to richer action sequences, such as action pictures, action videos, gestures, and motor events (Aravena et al., 2010; Ibáñez et al., 2010, 2011; Kelly et al., 2010a; Kiefer et al., 2011; Proverbio et al., 2010; Sitnikova et al., 2003; van Elk et al., 2010). These N400 studies point to a distributed and multimodal system that is simultaneously open to verbal and non-verbal meanings (Kutas and Federmeier, 2011). Consistent with this evidence, we found the N400 modulation of incongruent action-sentence pairs in anterior temporal areas, Broca's area, and frontal (premotor/motor) sites.

Although the spatial resolution provided by ERP does not allow precise localization, evidence from lesion studies, magnetoencephalography (MEG), and ERP source recordings converge with our data to implicate left temporal areas (the STG/MTG, the anterior-medial temporal lobe, the parahippocampal cortex and the anterior fusiform gyrus) as candidate sources of the N400 (Van Petten and Luka, 2006). Classic N400 effects assessed with depth recordings point to the anterior temporal lobe (Grunwald and Kurthen, 2006; McCarthy et al., 1995; Nobre and McCarthy 1995; Trautner et al., 2004) and medial temporal lobe (Fell et al., 2008) as the main sources of semantic processing. This is the first ECoG study of the N400 involving actions, confirming the role of left temporal cortex (STG and MTG) in semantic integration. In addition, we found N400 activation in Broca's region (IFG), thus supporting the role of this area in N400 modulation (Hagoort et al., 1996; Swaab et al., 1998; ter Keurs et al., 2002). Furthermore, we found a delayed M-N400 effect in motor areas (M1 and ventral-dorsal PM area) when compared to L-N400, suggesting a direct motor involvement in language processing (Halgren et al., 1994; van Elk et al., 2010). Finally, during clinical assessments of electrode placement, direct electrical stimulation on temporal areas (electrodes 13, 21, 22), Broca's (electrodes 30, 31), and motor areas (electrodes 7 and 8) produced language comprehension deficits, language production impairments, and motor activity, respectively.

Finally, modulation of an early L-N400 (beginning at 250 msec) and a late M-N400 (beginning at 390 msec) in response to compatible and incompatible trials suggests a perception (or language-action) cycle in which language and motor processes overlap and mutually influence one another. We remind the reader that participants kept both of their hands in the required shape throughout each block of trials, as posture has been shown to modulate semantic processing (Badets and Pesenti 2010; Glenberg et al., 2008b; Lindeman et al., 2006; van Elk et al., 2008). In addition, N400 effects of anticipation have already been reported [spoken words: (van den Brink et al., 2001, see also Guerra et al., 2009; Ibáñez et al., 2006); video clips: (Cornejo et al., 2009; Ibáñez et al., 2010; Sitnikova et al., 2003)].

4.2.2. Language effects on motor cortical processing

The MP (Hatta et al., 2009) or late motor-related potential (late MRP; Deecke 1987; Smith and Staines 2006), is a negativity beginning shortly before the response onset (–90 msec), possibly indexing pyramidal neuron activity in the premotor cortex (PM) and in the primary motor cortex (M1) at motor execution. Intracranial recordings of the MP are observed at contralateral premotor/motor representations (Szurhaj and Derambure, 2006; Toro et al., 1994) and are considered to be a measure of motor cortex excitability (Karl et al., 2004). MP amplitude modulation has been associated with the rate of force, precision of movement, speed (Aravena et al., 2010; Hatta et al., 2009; Slobounov et al., 2002), and also with short-term training effects (Smith and Staines, 2006).

We observed larger amplitudes of MP in the compatible condition (confirming previous results: Aravena et al., 2010). The MP reported here was localized in the premotor and motor areas. It is important to note that the observed effects include the contralateral motor representation area, and (during clinical assessments of electrode placement) direct stimulation of these electrodes (especially 7 and 8) elicited motor activity in the patient's contralateral hand. Our results allow us to speculate that language priming facilitates compatible motor programming.

The overall results are consistent with previous findings of motor facilitation produced by action verbs (Aziz-Zadeh et al., 2006; Boulenger et al., 2006, 2009; Gentilucci and Gangitano 1998; Glenberg and Kaschak, 2002; Glover et al., 2004; Hauk et al., 2004; Hauk and Pulvermüller 2004; Oliveri et al., 2004; Pulvermüller 2005; Pulvermüller et al., 2005; Tettamanti et al., 2005; Wheeler and Bergen 2010). Similarly, reports based on ERP (Shtyrov et al., 2004) and MEG (Pulvermüller and Shtyrov, 2006) have confirmed that action words elicit early motor programs, and Glenberg et al. (2008b) found that greater activity modulation occurs in the hand muscles when reading sentences that describe the transfer of objects with the hand. Nevertheless, no previous study has provided direct cortical measures of action-sentence MP modulation in the context of a bidirectional effect.

On the other hand, our ECoG results (convergent with EPD results) do not provide a specific somatotopic association of language content and related motor hand sites, but rather, quite the opposite. We found a broad activation of premotor and motor areas sensitive to ACE. This result is consistent with recent studies demonstrating a lack of somatotopic motor organization for action semantics (Arévalo et al., 2012; Postle et al., 2008).

5. Conclusion

The bidirectionality hypothesis claims that both action-language comprehension and motor processes share neural resources that co-operate mutually; that is to say that motor processes influences the comprehension of action sentences, and action-sentence comprehension influences motor processes (Aravena et al., 2010). This hypothesis is consistent with recent models of contextual integration in action meaning (Amoruso et al., 2011) and social cognition (Ibáñez and Manes, in press).

Some motor-language models propose that the motor system plays a key role in language processing (e.g., Rizzolatti and Craighero, 2004). Those approaches have been recently criticized (Louwerse and Jeuniaux, 2008; Mahon and Caramazza, 2008; Toni et al., 2008; Willems and Hagoort, 2007), specifically, regarding the claims of sensory-motor resonance as a causal mechanism for bringing language comprehension and human communication within the realm of the motor system. Those criticisms are sometimes focused on the mirror neuron system (Barrett et al., 2005; Jacob and Jeannerod, 2005; Mahon and Caramazza, 2008; Toni et al., 2008; Willems and Hagoort, 2007). However, a framework supporting a motor-language coupling cannot only be based in an exclusively mirror neuron mechanism (Hickok, 2009; Mahon and Caramazza, 2005; Negri et al., 2007; Willems and Hagoort, 2007). These frameworks consider the interaction of semantic knowledge and motor process (Toni et al., 2008), beyond the mirror neuron as a unique neural mechanism for language (Arbib, 2010; Heyes 2010; Molenberghs et al., 2009).

Neuropsychological research has been another source of criticism. For instance, language is not always impaired with disruption to motor regions and vice versa (Arbib, 2006; Heilman and Rothi, 2003; Papagno et al., 1993), but such evidence is controversial (Hickok and Poeppel, 2000). In contrast, there is cumulative evidence that motor impairment affects verb processing: progressive supranuclear palsy is associated with selective impairment in verb processing (Bak et al., 2001; Bak et al., 2006), fronto-temporal dementia shows a similar pattern (d'Honinckhun and Pillon, 2008; Rhee et al., 2001), Parkinson's disease patients have deficits producing verbs (Boulenger et al., 2008; Peran et al., 2009) and verb-processing deficits have been reported in Amyotrophic Lateral Sclerosis (Neary et al., 2000).

This wide range of effects can be understood in terms of a dynamic coupling between non-somatotopic motor cortex and language systems, and that coupling is sensitive to dynamic changes triggered by experience (Elman and Bates, 1997; Haslinger et al., 2005; Ostry et al., 2010). As an example, recovered aphasia patients have evidenced compensatory plasticity (Cappa et al., 1997; Cappa and Vallar, 1992). Any cognitive process requires dynamic large-scale neural network integration (Aravena et al., 2010; Fuster, 2003; Mesulam, 1990; Mesulam, 1998; Nachev et al., 2008; Toni et al., 2008). The bidirectionality hypothesis can accommodate apparent contradictory findings from the motor-language realm because it does not assume a strong dependency of motor involvement for language processing but a brain dynamic coordination with other (non-motor) regions of semantic processing. Our results are consistent with the bidirectionality hypothesis, proposing an interplay between multiple domains.

Understanding the motor-language mutual coordination is critical for different research programs. This is the first report showing direct evidence of a bidirectional coupling in the motor-to-language and language-to-motor directions. We provide evidence of a motor influence in language comprehension by the impaired ACE in EPD participants. Furthermore, the ECoG measures of frontal (motor) and fronto-temporal (language) activity demonstrated the bidirectional interactions between language and motor processes. Our results

suggest that language-motor coupling does not have a strong somatotopic organization, and it extends to subcortical motor networks as well as to the motor and premotor cortices. Our results open new pathways of research in the fields of motor diseases, theoretical approaches to language understanding, and models of action-perception coupling.

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Conflict of interest

None to declare.

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Supplementary material

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.cortex.2012.02.014](https://doi.org/10.1016/j.cortex.2012.02.014).

REFERENCES

- Amoruso L, Couto B, and Ibáñez A. Beyond Extrastriate Body Area (EBA) and Fusiform Body Area (FBA): Context integration in the meaning of actions. *Frontiers in Human Neuroscience*, 5: 124, 2011.
- Aravena P, Hurtado E, Riveros R, Cardona JF, Manes F, and Ibáñez A. Applauding with closed hands: Neural signature of action-sentence compatibility effects. *PLoS ONE*, 5(7): e11751, 2010.
- Arbib MA. A sentence is to speech as what is to action? *Cortex*, 42(4): 507–514, 2006.
- Arbib MA. Mirror system activity for action and language is embedded in the integration of dorsal and ventral pathways. *Brain and Language*, 112(1): 12–24, 2010.
- Arévalo AL, Baldo JV, and Dronkers NF. What do brain lesions tell us about theories of embodied semantics and the human mirror neuron system? *Cortex*, 48(2): 242–254, 2012.
- Arévalo AL, Lu CC, Huang LB, Bates EA, and Dronkers NF. Action and object processing in brain-injured speakers of Chinese. *Neuropsychology*, 25(6): 792–805, 2011.
- Arévalo A, Perani D, Cappa S, Butler A, Bates E, and Dronkers N. Action and object processing in aphasia: From nouns and verbs to the effect of manipulability. *Brain and Language*, 100(1): 79–94, 2007.
- Aziz-Zadeh L, Wilson SM, Rizzolatti G, and Iacoboni M. Congruent embodied representations for visually presented actions and linguistic phrases describing actions. *Current Biology*, 16(18): 1818–1823, 2006.
- Badets A and Pesenti M. Creating number semantics through finger movement perception. *Cognition*, 115(1): 46–53, 2010.
- Bak TH and Hodges JR. Kissing and dancing – a test to distinguish the lexical and conceptual contributions to noun/verb and action/object dissociation. Preliminary results in patients with frontotemporal dementia. *Journal of Neurolinguistics*, 16(2): 169–181, 2003.
- Bak TH, O'Donovan DG, Xuereb JH, Boniface S, and Hodges JR. Selective impairment of verb processing associated with pathological changes in Brodmann areas 44 and 45 in the motor neurone disease-dementia-aphasia syndrome. *Brain*, 124(Pt 1): 103–120, 2001.
- Bak TH, Yancopoulos D, Nestor PJ, Xuereb JH, Spillantini MG, Pulvermüller F, et al. Clinical, imaging and pathological correlates of a hereditary deficit in verb and action processing. *Brain*, 129(Pt 2): 321–332, 2006.
- Barrett AM, Foudas AL, and Heilman KL. Speech and gesture are mediated by independent systems. *Behavioral and Brain Sciences*, 28(2): 125–126, 2005.
- Barsalou LW. Perceptual symbol systems. *Behavioral and Brain Sciences*, 22(4): 577–609, 1999.
- Beilock SL and Goldin-Meadow S. Gesture changes thought by grounding it in action. *Psychological Science*, 21(11): 1605–1610, 2010.
- Bergen B, Lindsay S, Matlock S, and Narayanan S. Spatial and linguistic aspects of visual imagery in sentence comprehension. *Cognitive Science*, 31(5): 733–764, 2007.
- Bertella L, Albani G, Greco E, Priano L, Mauro A, Marchi S, et al. Noun verb dissociation in Parkinson's disease. *Brain and Cognition*, 48(2–3): 277–280, 2002.
- Booth JR, Wood L, Lu D, Houk JC, and Bitan T. The role of the basal ganglia and cerebellum in language processing. *Brain Research*, 1133(1): 136–144, 2007.
- Borghi AM, Glenberg AM, and Kaschak MP. Putting words in perspective. *Memory and Cognition*, 32(6): 863–873, 2004.
- Borreggine KL and Kaschak MP. The action-sentence compatibility effect: It's all in the timing. *Cognitive Science*, 30(6): 1097–1112, 2006.
- Boulenger V, Hauk O, and Pulvermüller F. Grasping ideas with the motor system: Semantic somatotopy in idiom comprehension. *Cerebral Cortex*, 19(8): 1905–1914, 2009.
- Boulenger V, Mechtouff L, Thobois S, Broussolle E, Jeannerod M, and Nazir TA. Word processing in Parkinson's disease is impaired for action verbs but not for concrete nouns. *Neuropsychologia*, 46(2): 743–756, 2008.
- Boulenger V, Roy AC, Paulignan Y, Deprez V, Jeannerod M, and Nazir TA. Cross-talk between language processes and overt motor behavior in the first 200 msec of processing. *Journal of Cognitive Neuroscience*, 18(10): 1607–1615, 2006.
- Broaders SC and Goldin-Meadow S. Truth is at hand: How gesture adds information during investigative interviews. *Psychological Science*, 21(5): 623–628, 2010.
- Buccino G, Lui F, Canessa N, Patteri I, Lagravinese G, Benuzzi F, et al. Neural circuits involved in the recognition of actions performed by non-specifics: An fMRI study. *Journal of Cognitive Neuroscience*, 16(1): 114–126, 2004.
- Buccino G, Riggio L, Melli G, Binkofski F, Gallese V, and Rizzolatti G. Listening to action-related sentences modulates the activity of the motor system: A combined TMS and behavioral study. *Brain Research. Cognitive Brain Research*, 24(3): 355–363, 2005.
- Cappa SF, Perani D, Grassi F, Bressi S, Alberoni M, Franceschi M, et al. A PET follow-up study of recovery after stroke in acute aphasics. *Brain and Language*, 56(1): 55–67, 1997.

- Cappa SF and Vallar G. The role of the left and right hemispheres in recovery from aphasia. *Aphasiology*, 6(4): 359–372, 1992.
- Cosmelli D and Ibáñez A. Human cognition in context: On the biologic, cognitive and social reconsideration of meaning as making sense of action. *Integrative Psychological and Behavioral Science*, 42(2): 233–244, 2008.
- Corballis MC. From mouth to hand: Gesture, speech, and the evolution of right-handedness. *Behavioral and Brain Sciences*, 26(2): 199–208, 2003.
- Cornejo C, Simonetti F, Ibáñez A, Aldunate N, Ceric F, Lopez V, et al. Gesture and metaphor comprehension: Electrophysiological evidence of cross-modal coordination by audiovisual stimulation. *Brain and Cognition*, 70(1): 42–52, 2009.
- Crescentini C, Mondolo F, Biasutti E, and Shallice T. Supervisory and routine processes in noun and verb generation in nondemented patients with Parkinson's disease. *Neuropsychologia*, 46(2): 434–447, 2008.
- d'Honinchtun P and Pillon A. Verb comprehension and naming in frontotemporal degeneration: The role of the static depiction of actions. *Cortex*, 44(7): 834–847, 2008.
- Dambacher M, Kliegl R, Hofmann M, and Jacobs AM. Frequency and predictability effects on event-related potentials during reading. *Brain Research*, 1084(1): 89–103, 2006.
- Davison D. *Subjective, Intersubjective, Objective*. Oxford, England: Oxford University Press, 2001.
- De Vega M. Levels of embodied meaning: From pointing to counterfactuals. In Glenberg AM, de Vega M, and Graesser A (Eds), *The Garachico Workshop of Symbols and Embodied*. Oxford, England: Oxford University Press, 2010.
- Deecke L. Bereitschaftspotential as an indicator of movement preparation in supplementary motor area and motor cortex. *Ciba Foundation Symposium*, 132: 231–250, 1987.
- Diamond ME, Von Heimendahl M, Knutsen PM, Kleinfeld D, and Ahissar E. 'Where' and 'what' in the whisker sensorimotor system. *Nature Reviews Neuroscience*, 9(8): 601–612, 2008.
- Ehrsson HH, Geyer S, and Naito E. Imagery of voluntary movement of fingers, toes, and tongue activates corresponding body-part-specific motor representations. *Journal of Neurophysiology*, 90(5): 3304–3316, 2003.
- Elman J and Bates E. Acquiring language: Response. *Science (Letters)*, 276: 1180, 1997.
- Fell J, Ludowig E, Rosburg T, Axmacher N, and Elger CE. Phase-locking within human mediotemporal lobe predicts memory formation. *NeuroImage*, 43(2): 410–419, 2008.
- Fischler I and Bloom PA. Automatic and attentional processes in the effects of sentence contexts on word recognition. *Journal of Verbal Learning and Verbal Behavior*, 18: 1–20, 1979.
- Frey SH. Tool use, communicative gesture and cerebral asymmetries in the modern human brain. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 363(1499): 1951–1957, 2008.
- Fuster JM. *Cortex and Mind*. New York: Oxford University Press, 2003.
- Gaillard R, Naccache L, Pinel P, Clemenceau S, Volle E, Hasboun D, et al. Direct intracranial, fMRI, and lesion evidence for the causal role of left inferotemporal cortex in reading. *Neuron*, 50(2): 191–204, 2006.
- Gallese V and Lakoff G. The Brain's concepts: The role of the sensory-motor system in conceptual knowledge. *Cognitive Neuropsychology*, 22(3): 455–479, 2005.
- Gentilucci M and Gangitano M. Influence of automatic word reading on motor control. *European Journal of Neuroscience*, 10: 752–756, 1998.
- Guerra S, Ibáñez A, Martin M, Bobes MA, Reyes A, Mendoza R, et al. N400 deficits from semantic matching of pictures in probands and first-degree relatives from multiplex schizophrenia families. *Brain and Cognition*, 70(2): 221–230, 2009.
- Glenberg AM. Naturalizing cognition: The integration of cognitive science and biology. *Current Biology*, 16(18): R802–R804, 2006.
- Glenberg AM and Kaschak MP. Grounding language in action. *Psychonomic Bulletin & Review*, 9(3): 558–565, 2002.
- Glenberg AM, Sato M, and Cattaneo L. Use-induced motor plasticity affects the processing of abstract and concrete language. *Current Biology*, 18(7): R290–R291, 2008a.
- Glenberg AM, Sato M, Cattaneo L, Riggio L, Palumbo D, and Buccino G. Processing abstract language modulates motor system activity. *Quarterly Journal of Experimental Psychology (Colchester)*, 61(6): 905–919, 2008b.
- Glover S, Rosenbaum DA, Graham J, and Dixon P. Grasping the meaning of words. *Experimental Brain Research*, 154(1): 103–108, 2004.
- Goldberg RF, Perfetti CA, and Schneider W. Perceptual knowledge retrieval activates sensory brain regions. *The Journal of Neuroscience*, 26(18): 4917–4921, 2006.
- Goldin-Meadow S. The role of gesture in communication and thinking. *Trends in Cognitive Sciences*, 3(11): 419–429, 1999.
- Grahn JA. The role of the basal ganglia in beat perception: Neuroimaging and neuropsychological investigations. *Annals of the New York Academy of Sciences*, 1169: 35–45, 2009.
- Grahn JA and Brett M. Impairment of beat-based rhythm discrimination in Parkinson's disease. *Cortex*, 45(1): 54–61, 2009.
- Grahn JA and Rowe JB. Feeling the beat: Premotor and striatal interactions in musicians and nonmusicians during beat perception. *The Journal of Neuroscience*, 29(23): 7540–7548, 2009.
- Groeben N and Scheele B. Dialog-Konsens-Methodik im Forschungsprogramm Subjektive Theorien. *Forum Qualitative Sozialforschung*, 2: 10, 2000.
- Grossman M. Sentence processing in Parkinson's disease. *Brain and Cognition*, 40(2): 387–413, 1999.
- Grossman M, Carvell S, Stern MB, Gollomp S, and Hurtig HI. Sentence comprehension in Parkinson's disease: The role of attention and memory. *Brain and Language*, 42(4): 347–384, 1992.
- Grunwald T and Kurthen M. Novelty detection and encoding for declarative memory within the human hippocampus. *Clinical EEG and Neuroscience*, 37(4): 309–314, 2006.
- Habets B, Kita S, Shao Z, Ozyurek A, and Hagoort P. The role of synchrony and ambiguity in speech-gesture integration during comprehension. *Journal of Cognitive Neuroscience*, 23(8): 1845–1854, 2011.
- Hagoort P, Brown CM, and Swaab TY. Lexical-semantic event-related potential effects in patients with left hemisphere lesions and aphasia, and patients with right hemisphere lesions without aphasia. *Brain*, 119(Pt 2): 627–649, 1996.
- Halgren E, Baudena P, Heit G, Clarke JM, Marinkovic K, Chauvel P, et al. Spatio-temporal stages in face and word processing. 2. Depth-recorded potentials in the human frontal and Rolandic cortices. *Journal of Physiology – Paris*, 88(1): 51–80, 1994.
- Haslinger B, Erhard P, Altenmüller E, Schroeder U, Boecker H, and Ceballos-Baumann AO. Transmodal sensorimotor networks during action observation in professional pianists. *Journal of Cognitive Neuroscience*, 17(2): 282–293, 2005.
- Hatta A, Nishihira Y, Higashiura T, Kim SR, and Kaneda T. Long-term motor practice induces practice-dependent modulation of movement-related cortical potentials (MRCP) preceding a self-paced non-dominant handgrip movement in kendo players. *Neuroscience Letters*, 459(3): 105–108, 2009.
- Hauk O, Johnsrude I, and Pulvermüller F. Somatotopic representation of action words in human motor and premotor cortex. *Neuron*, 41(2): 301–307, 2004.
- Hauk O and Pulvermüller F. Neurophysiological distinction of action words in the fronto-central cortex. *Human Brain Mapping*, 21(3): 191–201, 2004.

- Havas DA, Glenberg AM, and Rinck M. Emotion simulation during language comprehension. *Psychonomic Bulletin & Review*, 14(3): 436–441, 2007.
- Heilman KM and Rothi LG. Apraxia. In Heilman KM and Valenstein E (Eds), *Clinical Neuropsychology*. New York: Oxford University Press, 2003: 215–235.
- Hesslow G. Conscious thought as simulation of behaviour and perception. *Trends in Cognitive Sciences*, 6(6): 242–247, 2002.
- Heyes C. Mesmerising mirror neurons. *NeuroImage*, 51(2): 789–791, 2010.
- Hickok G. Eight problems for the mirror neuron theory of action understanding in monkeys and humans. *Journal of Cognitive Neuroscience*, 21(7): 1229–1243, 2009.
- Hickok G and Poeppel D. Towards a functional neuroanatomy of speech perception. *Trends in Cognitive Sciences*, 4: 131–138, 2000.
- Hoehn MM and Yahr MD. Parkinsonism: Onset, progression and mortality. *Neurology*, 17(5): 427–442, 1967.
- Houk JC. Agents of the mind. *Biological Cybernetics*, 92(6): 427–437, 2005.
- Hubbard AL, Wilson SM, Callan DE, and Dapretto M. Giving speech a hand: Gesture modulates activity in auditory cortex during speech perception. *Human Brain Mapping*, 30(3): 1028–1037, 2009.
- Hughes AJ, Daniel SE, Kilford L, and Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: A clinicopathological study of 100 cases. *Journal of Neurology, Neurosurgery and Psychiatry*, 55(3): 181–184, 1992.
- Hurtado E, Haye A, Gonzalez R, Manes F, and Ibáñez A. Contextual blending of ingroup/outgroup face stimuli and word valence: LPP modulation and convergence of measures. *BMC Neuroscience*, 10: 69, 2009.
- Ibáñez A, Lopez V, and Cornejo C. ERPs and contextual semantic discrimination: Degrees of congruence in wakefulness and sleep. *Brain and Language*, 98(3): 264–275, 2006.
- Ibáñez A and Cosmelli D. Moving beyond computational cognitivism: Understanding intentionality, intersubjectivity and ecology of mind. *Integrative Psychological and Behavioral Science*, 42(2): 129–136, 2008.
- Ibáñez A, Manes F, Escobar J, Trujillo N, Andreucci P, and Hurtado E. Gesture influences the processing of figurative language in non-native speakers: ERP evidence. *Neuroscience Letters*, 471(1): 48–52, 2010.
- Ibáñez A, Gleichgerrcht E, Hurtado E, González R, Haye A, and Manes F. Early neural markers of implicit attitudes: N170 modulated by intergroup and evaluative contexts in IAT. *Frontiers in Human Neuroscience*, 4: 188, 2010b.
- Ibáñez A, Hurtado E, Lobos A, Escobar J, Trujillo N, Baez S, et al. Subliminal presentation of other faces (but not own face) primes behavioral and evoked cortical processing of empathy for pain. *Brain Research*, 1398: 72–85, 2011a.
- Ibáñez A, Hurtado E, Riveros R, Urquina H, Cardona JF, Petroni A, et al. Facial and semantic emotional interference: A pilot study on the behavioral and cortical responses to the dual valence association task. *Behavior and Brain Functions*, 7: 8, 2011b.
- Ibáñez A, Petroni A, Urquina H, Torrente F, Torralva T, Hurtado E, et al. Cortical deficits of emotional face processing in adults with ADHD: Its relation to social cognition and executive function. *Social Neuroscience*, 6(5–6): 464–481, 2011c.
- Ibáñez A, Toro P, Cornejo C, Urquina H, Manes F, Weisbrod M, et al. High contextual sensitivity of metaphorical expressions and gesture blending: A video event-related potential design. *Psychiatry Research*, 191(1): 68–75, 2011d.
- Ibáñez A, Riveros R, Hurtado E, Gleichgerrcht E, Urquina H, Herrera E, et al. The face and its emotion: Right N170 deficits in structural processing and early emotional discrimination in schizophrenic patients and relatives. *Psychiatry Research*, 195(1–2): 18–26, 2012.
- Ibáñez A and Manes F. Contextual social cognition and the behavioral variant of frontotemporal dementia. *Neurology*, in press.
- Iverson JM and Goldin-Meadow S. Why people gesture when they speak. *Nature*, 396(6708): 228, 1998.
- Jacob P and Jeannerod M. The motor theory of social cognition: A critique. *Trends in Cognitive Sciences*, 9(1): 21–25, 2005.
- Jacobs J and Kahana MJ. Direct brain recordings fuel advances in cognitive electrophysiology. *Trends in Cognitive Sciences*, 14(4): 162–171, 2010.
- Jeannerod M. Neural simulation of action: A unifying mechanism for motor cognition. *NeuroImage*, 14(1 Pt 2): S103–S109, 2001.
- Jerbi K, Ossandón T, Hamamé CM, Senova S, Dalal SS, Jung J, et al. Task-related gamma-band dynamics from an intracerebral perspective: Review and implications for surface EEG and MEG. *Human Brain Mapping*, 30(6): 1758–1771, 2009.
- Karl A, Muhlcnickel W, Kurth R, and Flor H. Neuroelectric source imaging of steady-state movement-related cortical potentials in human upper extremity amputees with and without phantom limb pain. *Pain*, 110(1–2): 90–102, 2004.
- Kaschak MP and Borreggine KL. Temporal dynamics of the action-sentence compatibility effect. *Quarterly Journal of Experimental Psychology (Colchester)*, 61(6): 883–895, 2008.
- Kaschak MP, Madden CJ, Therriault DJ, Yaxley RH, Aveyard M, Blanchard AA, et al. Perception of motion affects language processing. *Cognition*, 94(3): B79–B89, 2005.
- Kelly SD, Creigh P, and Bartolotti J. Integrating speech and iconic gestures in a Stroop-like task: Evidence for automatic processing. *Journal of Cognitive Neuroscience*, 22(4): 683–694, 2010a.
- Kelly SD, Iverson JM, Terranova J, Niego J, Hopkins M, and Goldsmith L. Putting language back in the body: Speech and gesture on three time frames. *Developmental Neuropsychology*, 22(1): 323–349, 2002.
- Kelly SD, Kravitz C, and Hopkins M. Neural correlates of bimodal speech and gesture comprehension. *Brain and Language*, 89(1): 253–260, 2004.
- Kelly SD, Ozyurek A, and Maris E. Two sides of the same coin: Speech and gesture mutually interact to enhance comprehension. *Psychological Science*, 21(2): 260–267, 2010b.
- Kelly SD, Ward S, Creigh P, and Bartolotti J. An intentional stance modulates the integration of gesture and speech during comprehension. *Brain and Language*, 101(3): 222–233, 2007.
- Kiefer M, Sim EJ, Helbig H, and Graf M. Tracking the time course of action priming on object recognition: Evidence for fast and slow influences of action on perception. *Journal of Cognitive Neuroscience*, 23(8): 1864–1874, 2011.
- Kleiman GM. Sentence frame contexts and lexical decisions: Sentence-acceptability and word-relatedness effects. *Memory and Cognition*, 8(4): 336–344, 1980.
- Kliegl R, Grabner E, Rolfs M, and Engbert R. Length, frequency, and predictability effects of words on eye movements in reading. *European Journal of Cognitive Psychology*, 16: 262–284, 2004.
- Kliegl R, Nuthmann A, and Engbert R. Tracking the mind during reading: The influence of past, present, and future words on fixation durations. *Journal of Experimental Psychology: General*, 135(1): 12–35, 2006.
- Koelsch S. Music-syntactic processing and auditory memory: Similarities and differences between ERAN and MMN. *Psychophysiology*, 46(1): 179–190, 2009.
- Kotz SA, Schwartz M, and Schmidt-Kassow M. Non-motor basal ganglia functions: A review and proposal for a model of sensory predictability in auditory language perception. *Cortex*, 45(8): 982–990, 2009.

- Kutas M and Federmeier KD. Thirty years and counting: Finding meaning in the N400 component of the event-related brain potential (ERP). *Annual Review of Psychology*, 62: 621–647, 2011.
- Lehericy S, Ducros M, Van de Moortele PF, Francois C, Thivard L, Poupon C, et al. Diffusion tensor fiber tracking shows distinct corticostriatal circuits in humans. *Annals of Neurology*, 55(4): 522–529, 2004.
- Lewis SJ, Foltynie T, Blackwell AD, Robbins TW, Owen AM, and Barker RA. Heterogeneity of Parkinson's disease in the early clinical stages using a data driven approach. *Journal of Neurology, Neurosurgery and Psychiatry*, 76(3): 343–348, 2005.
- Lieberman P, Kako E, Friedman J, Tajchman G, Feldman LS, and Jimenez EB. Speech production, syntax comprehension, and cognitive deficits in Parkinson's disease. *Brain and Language*, 43(2): 169–189, 1992.
- Lindeman W, Yanagida Y, Norma H, and Hosaka K. Wearable vibrotactile systems for virtual contact and information display. *Virtual Reality*, 9(2–3): 203–213, 2006.
- Liu W, McIntire K, Kim SH, Zhang J, Dascalos S, Lyons KE, et al. Bilateral subthalamic stimulation improves gait initiation in patients with Parkinson's disease. *Gait and Posture*, 23(4): 492–498, 2006.
- Longworth CE, Keenan SE, Barker RA, Marslen-Wilson WD, and Tyler LK. The basal ganglia and rule-governed language use: Evidence from vascular and degenerative conditions. *Brain*, 128(Pt 3): 584–596, 2005.
- Lotze M, Montoya P, Erb M, Hulsmann E, Flor H, Klose U, et al. Activation of cortical and cerebellar motor areas during executed and imagined hand movements: An fMRI study. *Journal of Cognitive Neuroscience*, 11(5): 491–501, 1999.
- Louwerse MM and Jeuniaux P. How fundamental is embodiment to language comprehension? Constraints on embodied cognition. In: Proceedings of the 30th Annual Conference of the Cognitive Science Society: 1313–318, 2008.
- Mahon BZ and Caramazza A. The orchestration of the sensory-motor systems: Clues from neuropsychology. *Cognitive Neuropsychology*, 22(3): 480–494, 2005.
- Mahon BZ and Caramazza A. A critical look at the embodied cognition hypothesis and a new proposal for grounding conceptual content. *Journal of Physiology – Paris*, 102(1–3): 59–70, 2008.
- Manly BFJ. *Randomization, Bootstrap and Montecarlo Methods in Biology*. London, 1997.
- Masumoto K, Takai T, Tsuneto S, and Kashiwagi T. Influence of motoric encoding on forgetting function of memory for action sentences in patients with Alzheimer's disease. *Perceptual and Motor Skills*, 98(1): 299–306, 2004.
- Mattis PJ, Tang CC, Ma Y, Dhawan V, and Eidelberg D. Network correlates of the cognitive response to levodopa in Parkinson disease. *Neurology*, 77(9): 858–865, 2011.
- McCarthy G, Nobre AC, Bentin S, and Spencer DD. Language-related field potentials in the anterior-medial temporal lobe: I. Intracranial distribution and neural generators. *The Journal of Neuroscience*, 15(2): 1080–1089, 1995.
- Mesulam MM. Large-scale neurocognitive networks and distributed processing for attention, language, and memory. *Annals of Neurology*, 28(5): 597–613, 1990.
- Mesulam MM. From sensation to cognition. *Brain*, 121(Pt 6): 1013–1052, 1998.
- Molenberghs P, Cunnington R, and Mattingley JB. Is the mirror neuron system involved in imitation? A short review and meta-analysis. *Neuroscience and Biobehavioral Reviews*, 33(7): 975–980, 2009.
- Naccache L, Gaillard R, Adam C, Hasboun D, Clemenceau S, Baulac M, et al. A direct intracranial record of emotions evoked by subliminal words. *Proceedings of the National Academic of Science of the United States of America*, 102(21): 7713–7717, 2005.
- Nachev P, Kennard C, and Husain M. Functional role of the supplementary and pre-supplementary motor areas. *Nature Reviews Neuroscience*, 9(11): 856–869, 2008.
- Nearly D, Snowden JS, and Mann DM. Cognitive change in motor neurone disease/amyotrophic lateral sclerosis (MND/ALS). *Journal of the Neurological Sciences*, 180(1–2): 15–20, 2000.
- Negri GA, Rumiati RI, Zadini A, Ukmair M, Mahon BZ, and Caramazza A. What is the role of motor simulation in action and object recognition? Evidence from apraxia. *Cognitive Neuropsychology*, 24(8): 795–816, 2007.
- Nobre AC and McCarthy G. Language-related field potentials in the anterior-medial temporal lobe: II. Effects of word type and semantic priming. *The Journal of Neuroscience*, 15(2): 1090–1098, 1995.
- Obermeier C, Holle H, and Gunter TC. What iconic gesture fragments reveal about gesture-speech integration: When synchrony is lost, memory can help. *Journal of Cognitive Neuroscience*, 23(7): 1648–1663, 2011.
- Oliveri M, Finocchiaro C, Shapiro K, Gangitano M, Caramazza A, and Pascual-Leone A. All talk and no action: A transcranial magnetic stimulation study of motor cortex activation during action word production. *Journal of Cognitive Neuroscience*, 16(3): 374–381, 2004.
- Ossandón T, Jerbi K, Vidal JR, Bayle DJ, Henaff MA, Jung J, et al. Transient suppression of broadband gamma power in the default-mode network is correlated with task complexity and subject performance. *The Journal of Neuroscience*, 31(41): 14521–14530, 2011.
- Ossandón T, Vidal J, Ciumas C, Jerbi K, Hamamé C, Dalal S, et al. Efficient 'Pop-Out' visual search elicits sustained broadband gamma activity in the dorsal attention network. *The Journal of Neuroscience*, 32(10): 3414–3421, 2012.
- Ostry DJ, Darainy M, Mattar AA, Wong J, and Gribble PL. Somatosensory plasticity and motor learning. *The Journal of Neuroscience*, 30(15): 5384–5393, 2010.
- Ozyurek A, Willems RM, Kita S, and Hagoort P. On-line integration of semantic information from speech and gesture: Insights from event-related brain potentials. *Journal of Cognitive Neuroscience*, 19(4): 605–616, 2007.
- Papagno C, Della SS, and Basso A. Ideomotor apraxia without aphasia and aphasia without apraxia: The anatomical support for a double dissociation. *Journal of Neurology, Neurosurgery and Psychiatry*, 56(3): 286–289, 1993.
- Pazzaglia M, Smania N, Corato E, and Aglioti SM. Neural underpinnings of gesture discrimination in patients with limb apraxia. *The Journal of Neuroscience*, 28(12): 3030–3041, 2008.
- Peran P, Cardebat D, Cherubini A, Piras F, Luccichenti G, Peppe A, et al. Object naming and action-verb generation in Parkinson's disease: A fMRI study. *Cortex*, 45(8): 960–971, 2009.
- Peran P, Rascol O, Demonet JF, Celsis P, Nespoulous JL, Dubois B, et al. Deficit of verb generation in nondemented patients with Parkinson's disease. *Movement Disorders*, 18(2): 150–156, 2003.
- Petroni A, Canales-Johnson A, Urquina H, Guex R, Hurtado E, Blenkmann A, et al. The cortical processing of facial emotional expression is associated with social cognition skills and executive functioning: A preliminary study. *Neuroscience Letters*, 505(1): 41–46, 2011.
- Picard N and Strick PL. Imaging the premotor areas. *Current Opinion in Neurobiology*, 11(6): 663–672, 2001.
- Postle N, McMahon KL, Ashton R, Meredith M, and de Zubicaray GI. Action word meaning representations in cytoarchitecturally defined primary and premotor cortices. *NeuroImage*, 43(3): 634–644, 2008.
- Proverbio AM, Riva F, and Zani A. When neurons do not mirror the agent's intentions: Sex differences in neural coding of goal-directed actions. *Neuropsychologia*, 48(5): 1454–1463, 2010.
- Pulvermüller F. Brain reflections of words and their meaning. *Trends in Cognitive Sciences*, 5(12): 517–524, 2001.

- Pulvermüller F. Brain mechanisms linking language and action. *Nature Reviews Neuroscience*, 6(7): 576–582, 2005.
- Pulvermüller F and Fadiga L. Active perception: Sensorimotor circuits as a cortical basis for language. *Nature Reviews Neuroscience*, 11(5): 351–360, 2010.
- Pulvermüller F, Hauk O, Nikulin VV, and Ilmoniemi RJ. Functional links between motor and language systems. *European Journal of Neuroscience*, 21(3): 793–797, 2005.
- Pulvermüller F and Shtyrov Y. Language outside the focus of attention: The mismatch negativity as a tool for studying higher cognitive processes. *Progress in Neurobiology*, 79(1): 49–71, 2006.
- Rhee J, Antiquena P, and Grossman M. Verb comprehension in frontotemporal degeneration: The role of grammatical, semantic and executive components. *Neurocase*, 7(2): 173–184, 2001.
- Richardson D, Spivey M, Barsalou L, and McRae K. Spatial representations activated during real-time comprehension of verbs. *Cognitive Science*, 31(5): 733–764, 2003.
- Rizzolatti G and Craighero L. The mirror-neuron system. *Annual Review of Neuroscience*, 27: 169–192, 2004.
- Rodriguez-Oroz MC, Jahanshahi M, Krack P, Litvan I, Macias R, Bezdard E, et al. Initial clinical manifestations of Parkinson's disease: Features and pathophysiological mechanisms. *Lancet Neurology*, 8(12): 1128–1139, 2009.
- Rosin R, Topka H, and Dichgans J. Gait initiation in Parkinson's disease. *Movement Disorders*, 12(5): 682–690, 1997.
- Shtyrov Y, Hauk O, and Pulvermüller F. Distributed neuronal networks for encoding category-specific semantic information: The mismatch negativity to action words. *European Journal of Neuroscience*, 19(4): 1083–1092, 2004.
- Sitnikova T, Kuperberg G, and Holcomb PJ. Semantic integration in videos of real-world events: An electrophysiological investigation. *Psychophysiology*, 40(1): 160–164, 2003.
- Slobounov S, Johnston J, Chiang H, and Ray WJ. Motor-related cortical potentials accompanying enslaving effect in single versus combination of fingers force production tasks. *Clinical Neurophysiology*, 113(9): 1444–1453, 2002.
- Smith AL and Staines WR. Cortical adaptations and motor performance improvements associated with short-term bimanual training. *Brain Research*, 1071(1): 165–174, 2006.
- Straube B, Green A, Weis S, Chatterjee A, and Kircher T. Memory effects of speech and gesture binding: Cortical and hippocampal activation in relation to subsequent memory performance. *Journal of Cognitive Neuroscience*, 21(4): 821–836, 2009.
- Swaab TY, Brown C, and Hagoort P. Understanding ambiguous words in sentence contexts: Electrophysiological evidence for delayed contextual selection in Broca's aphasia. *Neuropsychologia*, 36(8): 737–761, 1998.
- Szurhaj W and Derambure P. Intracerebral study of gamma oscillations in the human sensorimotor cortex. *Progress in Brain Research*, 159: 297–310, 2006.
- ter Keurs M, Brown CM, and Hagoort P. Lexical processing of vocabulary class in patients with Broca's aphasia: An event-related brain potential study on agrammatic comprehension. *Neuropsychologia*, 40(9): 1547–1561, 2002.
- Tettamanti M, Buccino G, Saccuman MC, Gallese V, Danna M, Scifo P, et al. Listening to action-related sentences activates fronto-parietal motor circuits. *Journal of Cognitive Neuroscience*, 17(2): 273–281, 2005.
- Toni I, de Lange FP, Noordzij ML, and Hagoort P. Language beyond action. *Journal of Physiology – Paris*, 102(1–3): 71–79, 2008.
- Toro C, Deuschl G, Thatcher R, Sato S, Kufta C, and Hallett M. Event-related desynchronization and movement-related cortical potentials on the ECoG and EEG. *Electroencephalography and Clinical Neurophysiology*, 93(5): 380–389, 1994.
- Trautner P, Dietl T, Staedtgen M, Mecklinger A, Grunwald T, Elger CE, et al. Recognition of famous faces in the medial temporal lobe: An invasive ERP study. *Neurology*, 63(7): 1203–1208, 2004.
- Tseng M and Bergen B. Lexical processing drives motor simulation. In: *Proceedings of the Twenty-Seventh Annual Conference of the Cognitive Science Society*.
- Ullman MT, Corkin S, Coppola M, Hickok G, Growdon JH, Koroshetz WJ, et al. A neural dissociation within language: Evidence that the mental dictionary is part of declarative memory, and that grammatical rules are processed by the procedural system. *Journal of Cognitive Neuroscience*, 9(2): 266–276, 1997.
- van den Brink D, Brown CM, and Hagoort P. Electrophysiological evidence for early contextual influences during spoken-word recognition: N200 versus N400 effects. *Journal of Cognitive Neuroscience*, 13(7): 967–985, 2001.
- van Elk M, van Schie HT, and Bekkering H. Semantics in action: An electrophysiological study on the use of semantic knowledge for action. *Journal of Physiology – Paris*, 102(1–3): 95–100, 2008.
- van Elk M, van Schie HT, Zwaan RA, and Bekkering H. The functional role of motor activation in language processing: Motor cortical oscillations support lexical-semantic retrieval. *NeuroImage*, 50(2): 665–677, 2010.
- Van Petten C and Luka BJ. Neural localization of semantic context effects in electromagnetic and hemodynamic studies. *Brain and Language*, 97(3): 279–293, 2006.
- Vidal JR, Ossandon T, Jerbi K, Dalal SS, Minotti L, Ryvlin P, et al. Category-specific visual responses: An intracranial study comparing gamma, beta, alpha, and ERP response selectivity. *Frontiers in Human Neuroscience*, 4: 195, 2010.
- Wheeler K and Bergen B. Meaning in the palm of your hand. In Rice S and Newman J (Eds), *Empirical and Experimental Methods in Conceptual Structure, Discourse, and Language*. Stanford: 2010.
- Whiting E, Copland D, and Angwin A. Verb and context processing in Parkinson's disease. *Journal of Neurolinguistics*, 18(3): 259–276, 2005.
- Willems RM and Hagoort P. Neural evidence for the interplay between language, gesture, and action: A review. *Brain and Language*, 101(3): 278–289, 2007.
- Willems RM, Ozyurek A, and Hagoort P. When language meets action: The neural integration of gesture and speech. *Cerebral Cortex*, 17(10): 2322–2333, 2007.
- Williams-Gray CH, Hampshire A, Barker RA, and Owen AM. Attentional control in Parkinson's disease is dependent on COMT val 158 met genotype. *Brain*, 131(Pt 2): 397–408, 2008.
- Wilson SAK. Disorders of motility and tone. *Lancet*, 206: 1–10, 1925.
- Wu YC and Coulson S. Meaningful gestures: Electrophysiological indices of iconic gesture comprehension. *Psychophysiology*, 42(6): 654–667, 2005.
- Zwaan RA, Stanfield RA, and Yaxley RH. Language comprehenders mentally represent the shapes of objects. *Psychological Science*, 13(2): 168–171, 2002.
- Zwaan RA and Taylor LJ. Seeing, acting, understanding: Motor resonance in language comprehension. *Journal of Experimental Psychology: General*, 135(1): 1–11, 2006.