

Deficit in late-stage contingent negative variation provides evidence for disrupted movement preparation in patients with conversion paresis



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ARTICLE INFO

Article history:

Received 24 July 2014

Accepted 24 April 2015

Available online 4 May 2015

Keywords:

Conversion disorder

Functional paresis

Feigning

Motor preparation

Electromyography

Contingent negative variation

ABSTRACT

Conversion paresis is the presence of unexplained weakness without detectable neuropathology that is not feigned. To examine the ‘abnormal preparation’ and ‘disrupted execution’ hypotheses proposed to explain the movement deficits in conversion paresis, electroencephalographic, electromyographic and kinematic measures were recorded during motor preparation and execution. Six patients with unilateral upper limb conversion weakness, 24 participants feigning weakness and 12 control participants performed a 2-choice precued reaction time task. Precues provided advance information about the responding hand or finger. Patients and feigners demonstrated similar diminished force, longer movement time and extended duration of muscle activity in their symptomatic limb. Patients showed significantly suppressed contingent negative variation (CNV) amplitudes, but only when the symptomatic limb was precued. Despite the similarity in performance measures, this CNV suppression was not seen in feigners. Diminished CNV for symptomatic hand precues may reflect engagement of an inhibitory mechanism suppressing cortical activity related to preparatory processes.

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1. Introduction

Motor conversion disorder is characterised by impaired movement that cannot be explained by an organic neurological cause, inconsistent symptoms (e.g., the motor impairment diminishes with distraction) and reflexes and muscle tone that remain normal (American Psychiatric Association, 1994). It is distinguished from other “non-organic” movement disorders by a lack of conscious intention to deceive (Bass, 2001). Symptoms are thought to arise from underlying psychological stressors such as trauma or conflict,

but the neural mechanisms remain unknown (Scott & Anson, 2009; Vuilleumier, 2005).

The neurobiology underpinning conversion paresis and other conversion disorders remains mysterious. There are two particular aspects that need to be understood: first, what is the brain mechanism underlying the generation of abnormal activity in output of the motor control system that leads to, in the case of conversion paresis, weakened movement; and second, how is it that the patient is unconscious of the origin of their symptoms? In a recent paper, we provided evidence of disrupted early components in the sensory evoked potential in a simple reaction time (RT) task in a group of conversion paresis patients. Such changes in evoked potential amplitude did not occur in participants consciously feigning the same level of movement deficit (Blakemore, Hyland, Hammond-Tooke, & Anson, 2013). We proposed that these evoked potential changes may reflect processes associated with suppressing conscious awareness of self-agency.

In the present report, we address two proposed hypotheses that account for the generation of the abnormal motor command in

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motor conversion disorder in a choice reaction time task. The 'disrupted execution' hypothesis proposes that the intent to move and ability to generate motor programs is intact but 'lower' cortical areas, such as the motor cortex are inhibited so that the signal for motor execution from motor cortex is disrupted or delayed (Marshall, Halligan, Fink, Wade, & Frackowiak, 1997; Tiihonen, Kuikka, Viinamäki, Lehtonen, & Partanen, 1995). In contrast, the second hypothesis attributes impaired motor output to 'abnormal preparation' resulting from deficits in the genesis of a motor program during motor preparation (Spence, Crimlisk, Cope, Ron, & Grasby, 2000; Vuilleumier et al., 2001). The 'abnormal preparation' and 'disrupted execution' hypotheses have been derived from neuroimaging studies, based on whether activity was altered in motor preparatory or execution cortical regions. However, in most of these studies there was no requirement for overt movement, so determining whether the patients were actually in 'preparation' or 'attempted execution' phases is difficult. Preparation and execution are sequential events during movement performance, thus accurately resolving whether neural deficits affect preparation and/or execution requires investigation that is able to define the time-course of these components.

Evidence from previous behavioural studies has provided conflicting results regarding delays in preparing and/or executing movement in conversion paresis. Longer RTs without changes in movement duration were found in motor imagery tasks (Roelofs et al., 2001; Roelofs, van Galen, Keijsers, & Hoogduin, 2002), yet impairments in both RT and movement time have been reported in a simple RT task (Blakemore et al., 2013). One reason for these discrepant findings is that Roelofs et al. measured RT and movement time from verbal responses. Although verbal responses are commonly used in RT paradigms, they involve various complex processing stages for the initiation and production of speech (Levelt, 2001) typically resulting in less precise measures (with longer RT and larger standard deviations) than those taken from manual measuring instruments (e.g., Feyereisen, 1997). But even with more precise methods of RT measurement, such behavioural data alone cannot completely resolve the preparation versus execution debate because RT cannot be ascribed to one or the other process – RT as measured from imperative stimulus presentation to movement initiation includes processes of muscle activation that can be considered purely related to execution (Weiss, 1965).

To address this we have investigated motor preparation and execution, using electroencephalography (EEG) and a precued RT task (Rosenbaum, 1980), in a group of patients diagnosed with unilateral conversion paresis. Such patients are able to perform voluntary movement tasks with their symptomatic limb albeit weakly, unlike those with conversion paralysis in whom movement is abolished (as studied for example in de Lange, Roelofs, & Toni, 2007; Marshall et al., 1997; Schönfeldt-Lecuona, Connemann, Viviani, Spitzer, & Herwig, 2006; Tiihonen et al., 1995). We contrasted the patient data with healthy control participants, and a group of healthy volunteers feigning paresis.

In the present study we report data from choice RT conditions, in which the precue provided *partial* information about parameters defining the upcoming movement (hand or finger). This experimental manipulation allowed us to specifically address the 'preparation versus execution' debate that underlies explanations for impaired movement in conversion paresis. To further probe movement deficits in conversion paresis we examined concurrent changes in brain activity just prior to movement initiation (i.e., at the end of the preparatory period) by analysing the amplitude of the contingent negative variation. The CNV is a slow surface negativity that develops during the interval between the precue and imperative stimulus of RT tasks (Walter, Cooper, Aldridge, McCallum, & Winter, 1964), and is related to motor preparation. The use of CNV in psychiatry and neurology is well-established

(Tecce & Cattanach, 1987) and measurement of CNV amplitude is well suited to investigate deficits in voluntary movement in conversion disorder. Surprisingly, little empirical research has examined modulation of CNV in patients clinically diagnosed with conversion or somatoform disorders. In one study, Timsit-Berthier, Delaunoy, Koninckx, and Rousseau (1973) measured CNV amplitude in psychotic and neurotic patients and in a control group. The 'neurotic group' consisted of patients with symptoms of depression, phobias, obsessions and "mechanisms of conversion", though whether any of these patients were diagnosed with conversion disorder is unclear. Smaller CNV amplitudes were found in the neurotic patients than in the psychotic patients and controls, however explanations for the disrupted CNV development were lacking.

For the first time in studies of conversion disorder, we simultaneously recorded the CNV with the electromyogram (EMG) to fractionate RT into premotor (preparation) and motor (execution) phases of movement initiation. The results indicate temporally specific modulation of task performance and altered electrophysiological measures in patients compared to healthy controls and healthy controls instructed to feign paresis. Specifically, we report a novel finding that change in cortical preparatory activity was only observed when patients had prior knowledge about movement with their symptomatic limb.

2. Materials and methods

This study was approved by the Lower South Regional Ethics Committee (NAF-2005 v1). All participants provided informed consent.

2.1. Participants

Six patients (4 female; mean age 57 ± 7 years; mean symptom duration 18 ± 14 months) diagnosed with Conversion Disorder according to the criteria in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychiatric Association, 1994) were investigated. Patients were referred by a Consultant Physician in Neurology at the local hospital following full neurological exam including neuroimaging and offered the opportunity to participate if they met the following inclusion criteria: absence of intracranial abnormalities, pain-free unilateral upper limb paresis, and no evidence or history of neurological disease. Table 1 shows the clinical details for each patient. All but one of the patients had left hand paresis (i.e., affecting their non-preferred hand). Because differences in preferred versus non-preferred hand could link to differences in hemispheric functions and might confound CNV measures, data from the one patient with a right hand paresis were excluded from CNV analyses. All patients refrained from taking medication (listed in Table 1) 10 h prior to the experimental session.

For each patient, six sex- and aged-matched healthy volunteers were recruited (36 in total; mean age 54 ± 3 years, 24 female). Healthy volunteers were included if they had no diagnosis of a psychiatric disorder in the past 12 months, no upper limb pain or injuries, and no prior or current neurological disorder. The 36 healthy participants were randomly assigned to one of three groups ($n = 12$, 8 females in each): a control group, a 'Feign_{effort}' or a 'Feign_{resist}' group. These two feigning groups were included to investigate whether different instructions or strategies used to consciously generate weakness give rise to different neural and/or behavioural activity. Thus the feigning groups were differentiated on the basis of specific instructions given to mimic weakness. The Feign_{effort} group were instructed to imagine that their left arm, hand and fingers had become so weak, such as following a severe injury to the limb, that their muscles would be unable to exert a lot of force. The Feign_{resist} group participants were instructed to imagine that their left fingers were moving against a resistance that however hard they tried, they would find it difficult to depress the keys. Because there were no significant differences between the two feigning groups on any dependent measure, including CNV amplitude ($p > .05$), the results from the Feign_{effort} and Feign_{resist} groups were pooled to form one group, referred to as 'feigners' (grand mean CNV waveforms for each feigning group for responses made by the symptomatic and asymptomatic hands are illustrated in Figs. S1 and S2 respectively). For all subsequent analyses, the Group factor therefore compared three groups: patients, controls, and feigners. The difference in average age among the participant groups was not significant ($p = .33$). All participants had normal speech and hearing, normal or corrected-to-normal vision, and were right-handed, as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971), with a mean laterality quotient of 88% for the conversion paresis patients and 81% for the non-patient participants.

Supplementary material related to this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.biopsycho.2015.04.009>

Table 1
Characteristics of conversion disorder patients.

Participants	Gender	Age (years)	Symptom duration (months)	Sensory deficits ^a	Symptomatic hand	Psychiatric comorbidity ^b (DSM-IV)	Medication ^c
Patient 1	Female	53	24	+	Left	300.23	Paroxetine
Patient 2	Female	56	40	++	Left	None	Amitriptyline, fluoxetine, sodium valproate
Patient 3	Female	58	11	+++	Right	300.02, 296.23	Amitriptyline, carbamazepine, citalopram
Patient 4	Female	51	7	None	Left	300.29 N	None
Patient 5	Male	71	24	++	Left	None	Baclofen, nortriptyline, sodium valproate
Patient 6	Male	52	1	None	Left	None	Amitriptyline, clonazepam, sodium valproate, topiramate

^a Sensory deficits in the symptomatic limb: + small sensory deficits (some numbness on the symptomatic side); ++ moderate sensory deficits (some numbness on symptomatic side plus decreased sensation for light touch, vibration and temperature); +++ severe sensory deficits (some numbness, tingling on symptomatic side, decreased sensation for light touch, vibration and temperature plus presence of vertigo, dizziness).

^b Diagnoses present within 12 months prior to testing, as assessed by the Composite International Diagnostic Interview (CIDI-Auto v2.1) (World Health Organisation, 1997). DSM-IV categories: 300.23 social phobia; severe without psychotic features; 300.02 generalised anxiety disorder (primary diagnosis for Patient 3); 296.23 major depressive disorder, single episode; 300.29 N specific phobia, natural environment type.

^c Medication affecting the central nervous system.

2.2. Procedure and apparatus

All participants underwent the same experimental protocol in two sessions, on average four days apart. In session one, informed consent was obtained and participants completed a demographics and handedness questionnaire followed by a self-administered version of the Composite International Diagnostic Interview (CIDI-Auto v2.1; World Health Organisation, 1997). In session two, participants completed two experimental tasks (see Section 2.3 below).

The experimental apparatus was modified from previous tasks (Osman, Moore, & Ulrich, 1995; Possamai, Burle, Osman, & Hasbroucq, 2002; Wild-Wall, Sangals, Sommer, & Leuthold, 2003) and is shown in Fig. 1A. Participants were comfortably seated on an adjustable chair in a dimly lit room in front of a response panel. Both forearms and wrists were pronated and elbows flexed at approximately 90°. The index and middle fingers of each hand rested on top of the proximal end of the corresponding response key integrated in the response panel. The keys for each hand were arranged in parallel with an inverted v-space between hands as shown in Fig. 1A. The response panel was within the field of view, 60 cm in front of the participant. Blue light emitting diodes (LEDs) were embedded within each key to signal the precue and imperative stimulus, providing a highly compatible stimulus–response relationship. Each key could be pressed downward using finger flexion, with a maximum displacement of 8 mm at its proximal end. A force transducer located beneath the proximal end of each response key provided precise measures of changes in force from which reaction time and movement time were computed.

2.3. Tasks

All participants completed two tasks: an isometric maximum voluntary contraction (MVC) task and a choice RT task. Participants in the feigning groups were instructed to feign weakness with their left hand. In addition, feigners wore a bright orange sleeve over their left forearm, which served as a visual reminder to feign with the left limb throughout each task.

The MVC task was used to determine the maximum isometric flexion force that could be generated by the left and right middle and index fingers. Each finger was tested individually with the order of fingers randomised and counterbalanced across participants. The task involved depressing and holding (isometric contraction) the key at its end range of movement. A trial began with the onset of a tone when the key was fully depressed. Five, 5 s warm up trials were completed with 5 s rest between each. Participants began with a relatively low force and progressively increased their effort to a moderately hard effort by the fifth trial. Following 30 s rest, three test MVCs were performed (3 s each with a 30 s rest between each test trial), in which participants were instructed to press on the key as hard as possible. Throughout each test trial, the elbow and wrist remained in contact with the table. Participants were given verbal encouragement as well as visual feedback of the force profile on a computer monitor. The MVC for each trial was recorded as the maximum force applied within a 2 s duration. The MVC value recorded for each finger was the maximum obtained from the three test trials. In addition, feigners repeated the MVC tests with their left middle and left index finger *without* feigning to verify normal motor behaviour. These unaffected left hand MVC trials were completed at the end of the RT task.

For the choice RT task, participants were required to depress a single key as quickly and accurately as possible in response to an imperative visual stimulus. The imperative stimulus was preceded by a precue (Rosenbaum, 1980, 1983) that provided information about the hand (left or right) and finger (middle or index) to be used on a given trial (Fig. 1B). There were three 2-choice RT precue conditions, in which the precue was provided by the illumination of two keys that only partially specified the response. Specifically, in condition 1, the index and middle

finger keys of either the left or right hand were illuminated specifying the hand to be prepared, leaving the finger unspecified until the onset of the imperative stimulus (hand known, finger unknown – HKFU). In condition 2, either the index or middle fingers of each hand were specified by the precue, leaving the hand unspecified until stimulus onset (hand unknown, finger known – HUFK). In condition 3, either the left index and right middle, or left middle and right index finger were precued, leaving both hand and finger unspecified until stimulus onset (hand unknown, finger unknown – HUFU), a mutually conditional ambiguous 2-choice condition. Results from trials in a simple RT task, in which the precue signalled the hand and finger required for the response have been previously reported (Blakemore et al., 2013).

Participants completed one block of 20 familiarisation trials followed by 576 trials distributed across 8 blocks of 72 trials with a 2 min rest period between each block. The order of blocks was randomised for each participant to minimise any potential order effect. In each block there were an equal number of trials for each of the precue conditions and for each finger. Trials within a block were presented in a pseudo-random order. To minimise anticipatory responses, 11% of trials were catch trials (a trial in which the precue was not followed by a stimulus; equally distributed across conditions and finger). All participants were reminded of the task requirements during the interval between each block of trials. Patients were encouraged to continue trying to make each key press, even if they found it difficult to do so. Participants in the feigning groups received an additional (non-feigning) block of 72 trials (648 trials in total), which was completed at the end of the experimental session. This additional block contained only simple RT (HKFK condition) trials, in which participants were asked to move normally to verify normal motor ability of the left (feigning) hand.

The sequence of events for trials in each precue condition is illustrated in Fig. 1B. At the beginning of each trial, the index and middle fingers of the left and right hand rested on the proximal end of each key. The start of a trial was signalled by a warning signal (red LED) illuminated for 500 ms. After 1000 ms, a visual precue was presented for 500 ms, followed by a 1500 ms foreperiod (no keys lit), then the illumination of one of the precued keys – the imperative stimulus. The participant was required to respond by making a key press as quickly and as accurately as possible. After each response, the spring-loaded key automatically returned to its starting position. The inter-trial interval (ITI) was 2000 ms and began 1000 ms after the participant completed a movement response (the ITI therefore varied randomly dependent upon response duration). If no response occurred within 3000 ms of stimulus onset the trial terminated and the ITI began. The total time between the end of a movement response and the precue on the subsequent trial was therefore 4500 ms, allowing sufficient time for the EEG to return to baseline.

Force applied to each key was recorded continuously (1000 Hz) using a PowerLab/16sp and LabChart6 software (ADInstruments). Customised software (ManipGUI) generated the condition schedule for each block of 72 trials and transmitted the precue and stimulus timing information to the response panel via the blue LEDs embedded within the response keys. ManipGUI also recorded reaction time, movement time and error information for each trial.

2.4. Behavioural measures

Signals from the force transducers (resolution ± 0.005 N) for each trial were epoched into 5500 ms segments, beginning 2500 ms before the imperative stimulus. Data were then baseline corrected and filtered over the first 2600 ms of each epoch using a 4th-order low-pass digital Butterworth filter (cut-off frequency 100 Hz). Reaction time was calculated as the time between imperative stimulus onset and movement initiation (the time at which the force exerted on the key exceeded approximately 0.12 N [1 mm of displacement]). Movement time (ms) was calculated from the force trace as the time between RT and the end of key displacement

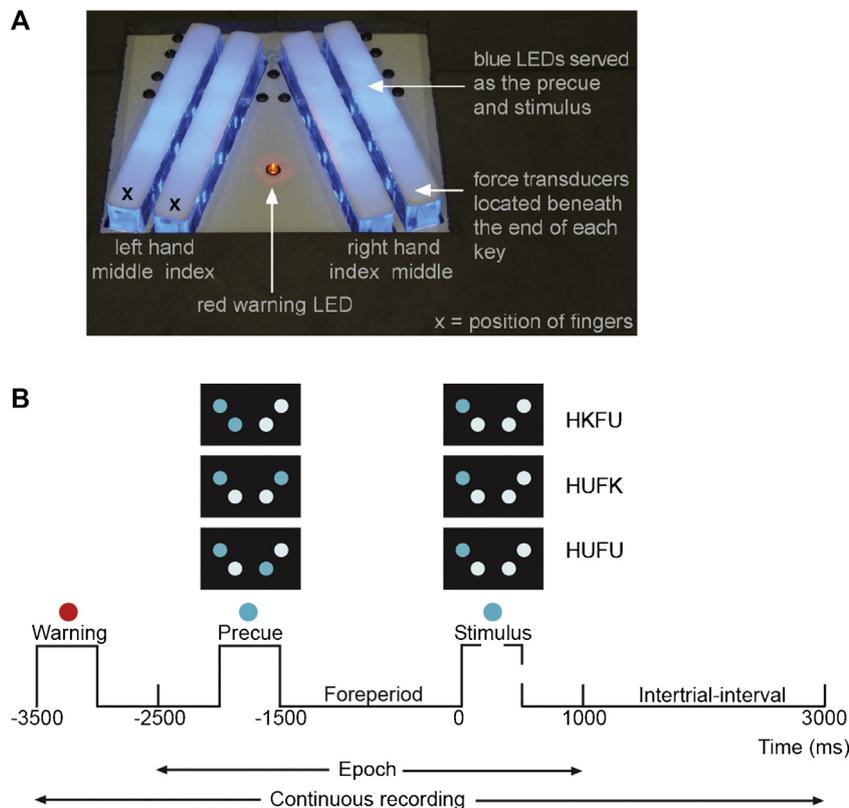


Fig. 1. Experimental setup and task. (A) Close-up perspective of the response panel consisting of a grey box (362 mm × 255 mm × 109 mm) containing a central red warning LED that served as a fixation point during each trial, and four response keys (20 mm × 143 mm × 40 mm) similar to the keys on a piano. (B) Temporal sequence of events in a single trial; an example of each precue condition. Circles in black rectangle represent response key positions; blue circles represent response keys illuminated for each precue condition. HKFU, hand known finger unknown; HUFK, hand unknown, finger known; HUFU, hand unknown, finger unknown.

(8 mm). There was no difference among the four response keys in the amount of force required to displace the key 1 mm or 8 mm ($p > .1$).

Movement errors included *anticipation* (key displacement greater than 1 mm before or within 100 ms following the imperative stimulus), *incorrect key*, *miss* (no displacement of a key detected during a trial), and *incomplete* (movement initiated but the response not completed). The percentage of movement errors was calculated for each condition and response key, then pooled over the three 2-choice RT conditions for statistical analyses, following an arcsine transformation (Zar, 1999). In addition to operationally defined movement errors, clinical populations often show a greater number of spurious reaction times than healthy groups. A standardised outlier rejection procedure was applied to all participants. Trials were omitted from movement time, EMG and EEG analyses if deemed a movement error or if reaction time or movement time was greater than three standard deviations above their mean, in each condition and for each response key. Analyses of movement time were therefore conducted on a total of 4372 correct trials for controls, 1972 correct trials for patients, and 8712 correct trials for feigners (two groups pooled). The range of trials for analyses for each participant within each condition were 103–126 trials for controls, 84–125 trials for patients and 92–128 trials for feigners.

2.5. Electrophysiological measures

Surface EMG was recorded from flexor digitorum superficialis (FDS) of both forearms (Perotto, 2005). Pairs of AgAgCl disposable surface electrodes (Medicostet N-00-s) were positioned 3.5 cm apart over the motor point of each muscle along its longitudinal axis. A reference electrode was positioned on the lateral aspect of the olecranon process of the right arm. EMG signals were amplified (gain 2000; Grass P511 K Preamplifiers) and filtered (10–300 Hz) prior to acquisition at 1000 Hz using LabChart6 software (ADInstruments).

For analysis, EMG recordings were divided into epochs of 3500 ms duration, beginning 500 ms before precue onset, baseline corrected and rectified. Premotor time (PMT) and motor time were measured from the EMG recording of the left and right FDS. PMT, a measure indexing central processing delays, was the duration between imperative stimulus onset and abrupt (greater than two standard deviations above the mean of baseline EMG) change in the amplitude of the rectified EMG signal. PMT was calculated by visual inspection of each EMG signal for every correct trial (Matlab 2009a; Mathworks Inc.). Motor time, the peripheral component of RT, was the duration of muscular contraction prior to the onset of movement. Motor time was calculated by subtracting the premotor time from the reaction time for

each trial. If a clear EMG burst onset could not be detected, the trial was excluded from the EMG analyses. Therefore, the final numbers of trials available for premotor and motor time analyses were 4352 for controls, 1854 for patients and 7689 for feigners. The range of trials for analyses for each participant within each condition were 102–126 trials for controls, 79–121 trials for patients and 70–126 trials for feigners.

Surface electroencephalography (EEG) was acquired with AgAgCl electrodes using a sintered Quikcap (C190) and a 32-channel Neuroscan Synamps system (model 5083) with Scan 4.3 software (Neurosoft Inc., Compumedics). In the present study, we were interested in change in CNV amplitude from central and frontal electrode locations, because frontocentral cortical regions have shown marked changes in regional cerebral blood flow in neuroimaging studies of voluntary movement deficits in conversion disorder. EEG data were recorded bilaterally from frontal (F3, F4) and central (C3' and C4') electrodes according to the 10–20 system (Jasper, 1958) referenced to linked mastoids, and a ground electrode was located at AFz. C3' and C4' (4 cm to the left and to the right respectively of Cz) were used to optimise the location of the hand areas of the primary motor cortices (Leuthold, Sommer, & Ulrich, 1996). Eye position (electrooculography – EOG) was recorded using two pairs of electrodes in horizontal and vertical directions. Surface EEG and EOG signals were bandpass filtered DC to 200 Hz, amplified (gain 500), sampled at 1000 Hz, recorded continuously and synchronously with EMG and force data. All electrode impedances were below 5 k Ω .

Prior to EEG analysis, EEG signals were low-pass filtered off-line (Butterworth zero phase filter, cut-off frequency 30 Hz, slope of 48 dB/octave) and a DC detrend applied using a global correction method (Hennighausen, Heil, & Rösler, 1993). Eyeblink and eye movement artefact within the continuous data were corrected (Gratton, Coles, & Donchin, 1983). The data were then divided into epochs of 3500 ms duration, beginning 500 ms before precue onset, and normalised to a baseline calculated from the 500 ms immediately before precue onset. Trials with excessive noise and artefacts were removed, yielding 2012 trials for controls, 654 trials for patients and 3646 trials for feigners. Note that the number of trials included in the EMG and CNV analyses differ. This is due to differences in the trial exclusion criteria for the two electrophysiological techniques (difficulty in determining a clear EMG burst or artefact contamination in the EEG), yielding variations in the number of artefact-free or 'clean' trials that could be included in each analysis.

EEG signals were averaged for each precue condition for each participant. The mean number of epochs per participant that contributed to each CNV amplitude average was 28 epochs for controls, 22 epochs for patients and 25 epochs for feigners.

The minimum number of epochs contributing to a CNV amplitude average was 12. To ensure that trial rejection for CNV analysis did not by chance result in a particular group of remaining trials that differed in performance parameters from the entire data set, we compared the present PMT results to the results of a subset of PMT data that included only those trials contributing to the CNV averages, and found no difference ($p < .05$). Furthermore, there was no difference in CNV amplitude between index and middle finger responses ($p > .05$). Mean CNV amplitude was computed separately for left and right hand responses in each precue condition, for the 100 ms immediately prior to stimulus onset (–99 ms to 0 ms) for each electrode. Patient 3 (with a right hand paresis) was excluded from CNV analyses. Thus all analyses of CNV amplitudes for left hand responses correspond to movements made by the non-preferred hand, and in patients and feigners, also the symptomatic hand, while all CNV amplitudes associated with right hand responses correspond to movements made by the preferred (and/or asymptomatic) hand.

2.6. Statistical analyses

Data were analysed using linear mixed models (LMM; PASW Statistics 18, SPSS Inc.). LMM allows for an appropriate variance–covariance data structure to be modelled and models between-subject and within-subject variance when a random factor is included (Norušis, 2010). LMM does not need to assume independence or equal variances and it uses the restricted maximum likelihood estimation method, providing parameter estimates better suited for unbalanced designs. LMM allows for inferences to be applied beyond the participant sample and decreases the occurrence of false positives in small sample sizes (Mumford & Poldrack, 2007; Norušis, 2010).

MVC data were analysed using a two-factor LMM to examine the effects of Group (patients, feigners, controls) and Hand (symptomatic/left hand, asymptomatic/right hand). Percentage of movement error was analysed using a two-factor repeated measures LMM to examine the effect of Group and Hand. To examine the possible effect of prior knowledge of 'Hand' and 'Finger' (precued information – HKFU, HUFK, HUFU conditions) on PMT, motor time, movement time, and CNV amplitude, 'Condition' was also included as a factor in these analyses. Initial statistical analyses indicated that the pattern of result for RT and PMT was identical. Given this outcome and that the PMT results more precisely indicate changes in preparation time (i.e., time before change in muscle activation), RT results will not be discussed further. Furthermore, because the differences in PMT and CNV amplitude between index and middle finger within each hand were not significant ($p > .05$) data for each dependent measure were pooled across fingers within hand. Therefore, premotor time, motor time and movement time were each analysed using a three-factor repeated measures LMM to examine the effect of Hand (2 levels), Group (3 levels) and Condition (3 levels). Note that the results for MVC, premotor time, motor time and movement time were not modified by exclusion of the patient with right hand paresis. CNV amplitude for each hand was analysed using a four-factor repeated measures LMM to examine the effect of Group (3 levels), Condition (3 levels), Hemisphere (2 levels; left, right hemisphere) and Region (2 levels; central, frontal electrodes). Additional multiple regression analyses were also conducted to explore potential effects of age and symptom duration on each dependent measure. No significant relationships were found ($r < 0.3$, $p > .05$).

For all LMM analyses, 'Participant' was included as random factor, and the unstructured and compound symmetry heterogeneity variance–covariance matrices were used to model the residuals for the between-group and within-group analyses respectively, because the Hurvich and Tsai's Criterion showed these models to be the most appropriate when modelling the residual matrices (Norušis, 2010). For all analyses, normality of the residuals was assessed and found to be satisfactory. The bonferroni correction was used for all multiple pairwise comparisons. Effect sizes (η^2) were calculated (Cohen, 1988), where $\eta^2 = .01$ is considered a small effect size; $\eta^2 = .06$ a moderate effect size; $\eta^2 = .14$ a large effect size. Effect sizes are reported when $\eta^2 > .06$ for pairwise comparisons. Alpha was set at .05.

3. Results

3.1. Behaviour and electromyography

3.1.1. In patients, motor conversion disorder diminished force output in the symptomatic and asymptomatic hands

Mean MVC force for each group is presented in Table 2. As expected, both patients ($p = .011$, $\eta^2 = .49$) and feigners ($p = .001$, $\eta^2 = .61$) produced less force with their symptomatic hand than with their asymptomatic hand, while there was no between-hand difference in force produced for controls. A significant Group \times Hand interaction ($F_{(2,78)} = 9.1$, $p = .001$) occurred due to the lack of a between-hand difference in controls and a significant symptomatic hand effect in patients and feigners. Under non-feigning conditions (data not shown) feigners exhibited no significant difference in the maximum force between the

Table 2
Maximum voluntary contraction force.

	Maximum force (N) ^a	
	Symptomatic (left) hand	Asymptomatic (right) hand
Patients	6.6 \pm 5.3	18.4 \pm 7.7
Feigners	11.3 \pm 11.0	42.4 \pm 14.0
Controls	40.5 \pm 12.0	48.3 \pm 12.0

^a Values are given as mean (\pm SD) for the left and right hand of controls ($n = 12$), and for the symptomatic and asymptomatic hand of conversion patients ($n = 6$) and feigners ($n = 24$).

asymptomatic (right) hand and the 'symptomatic' (left) hand performing normally. Between-group comparisons revealed that patients and feigners produced less force with their symptomatic hand compared to controls ($p = .001$, $\eta^2 > .67$). These data are consistent with the diagnosis of paresis in patients and the capability of healthy volunteers implementing a feigning instruction to voluntarily impair performance. Additionally, patients also produced significantly smaller MVC force with their asymptomatic hand compared to the right hand of both controls and feigners ($p = .001$, $\eta^2 > .47$), even though they reported no weakness in this hand.

3.1.2. Conversion patients demonstrated poorer performance accuracy than controls and feigners

Overall, error rates in the RT task were small ($< 10\%$). Taking all error types together, there was a significant main effect of Group ($F_{(2,39)} = 4.4$, $p = .019$). Patients (149 errors of 2208 trials; 6.7 \pm 5.7%) made significantly more errors than feigners (232 errors of 9216 trials; 2.5 \pm 6.6%; $p = 0.016$, $\eta^2 = .10$) indicating that a speed accuracy trade-off strategy was unlikely, but this contrast did not reach significance for controls (121 errors of 4608 trials; 2.6 \pm 2.6%, $p > .05$, $\eta^2 = .24$). There was no significant between-hand differences in accuracy for any of the groups although a trend occurred towards higher error rates for movements made by the patients and feigners symptomatic hand (9.5 \pm 6.4% and 3.3 \pm 9.3% respectively) compared to their asymptomatic hand (patients, 3.8 \pm 3.3%, $\eta^2 = .27$; feigners, 1.7 \pm 1.2%).

3.1.3. Premotor time was longer in conversion patients and for individuals feigning paresis

Results for premotor time (the central component of RT indexing central processing delays) are illustrated in Fig. 2A (individual data for participants in each group for the HKFU condition are illustrated in Fig. S3A). To unpack the significant Group \times Hand \times Condition interaction ($F_{(4,39)} = 4.1$, $p = .008$), we examined: (i) the effect of Hand within each group (pooled across conditions), (ii) the effect of Group for each hand (pooled across conditions), and (iii) the effect of Condition within each group, for the symptomatic and asymptomatic hands.

Supplementary material related to this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.biopsycho.2015.04.009>

First, the within Group analysis revealed a significant between-hand difference in PMT for patients and feigners; premotor time was longer in the symptomatic hand than in the asymptomatic hand ($p = .031$, $\eta^2 = .14$; $p = .000$, $\eta^2 = .21$). Second, across Group analysis confirmed that PMT for the symptomatic hand was significantly longer in the patients ($p = .002$, $\eta^2 = .42$) and feigners ($p = .001$, $\eta^2 = .21$) compared to controls. For the asymptomatic hand PMT was significantly longer in patients than feigners ($p = .001$, $\eta^2 = .17$) and controls ($p = .001$, $\eta^2 = .46$), and in feigners compared to controls ($p = .005$, $\eta^2 = .12$). Together, these data indicate that the conversion patients and the participants feigning paresis performed in a similar manner reflecting a disruption of central processing, delaying

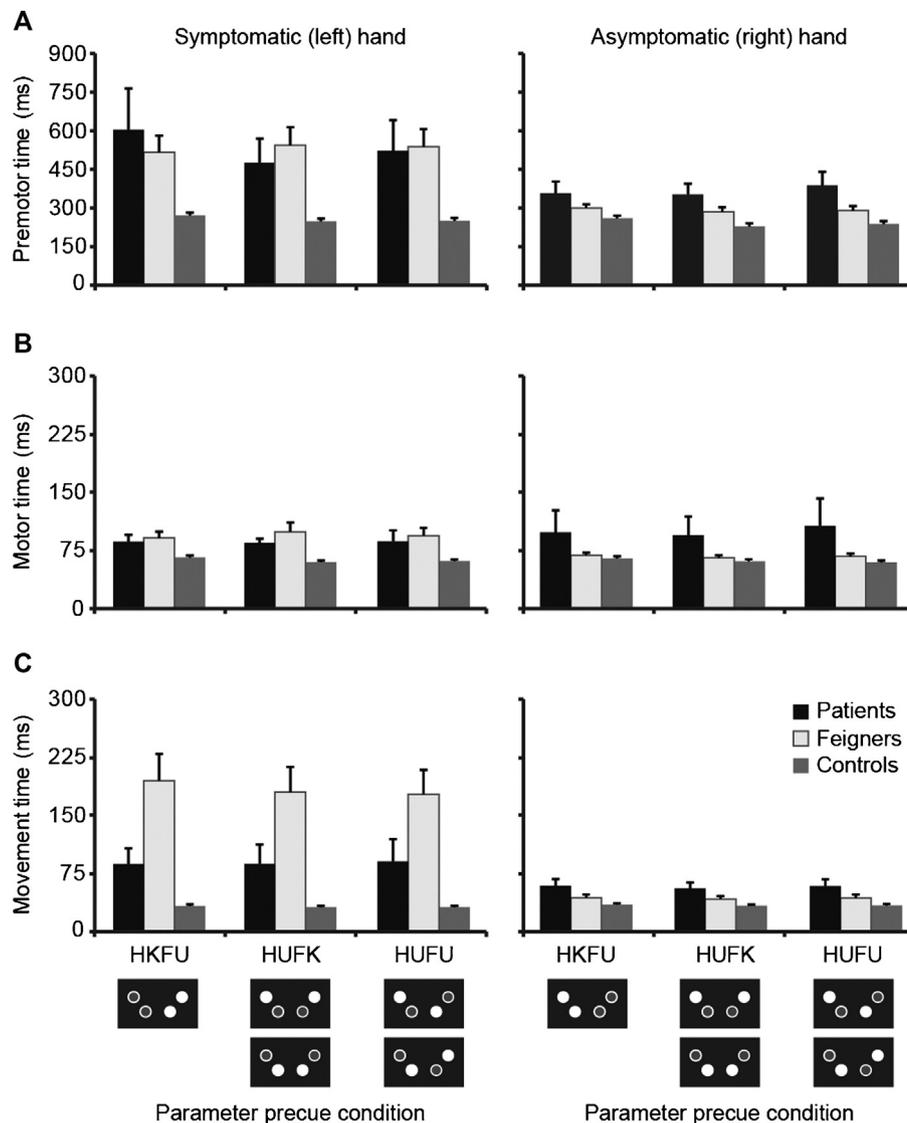


Fig. 2. (A) Mean premotor time (ms); (B) mean motor time (ms); and (C) mean movement time (ms) (+SEM) for the symptomatic (left) hand (left column), and asymptomatic (right) hand (right column) for patients ($n = 6$; black bars), feigners ($n = 24$; light grey bars) and controls ($n = 12$; dark grey bars) for each 2-choice precue condition: HKFU, hand known, finger unknown; HUFK, hand unknown, finger known; HUFU, hand unknown, finger unknown. Dark circles in black rectangles represent response keys illuminated for each precue condition. EMG data from flexor digitorum superficialis muscle.

the onset of muscle activity and the subsequent initiation of movement. Of note, longer PMTs were also evident in the ‘non-feigning’ (asymptomatic) limb of feigners, and in the ‘asymptomatic’ limb of patients, thus there was a generalised effect of motor conversion disorder and feigning on preparation of the asymptomatic limb. Finally, within-group analysis of the effect of Condition for each hand separately found no significant effect of uncertainty for patients or feigners. In contrast, there was a significant effect of Condition in the control group ($F_{(3,45)} = 33.6, p = .001$). PMT was longer in HKFU compared with HUFK and HUFU ($p < .001$).¹

¹ Although it is commonly observed that advanced specification of hand speeds RT compared to conditions in which hand is not specified (Anson, Hyland, Kötter, & Wickens, 2000; Possamai et al., 2002; Rosenbaum, 1980), this result for the control group is consistent with findings from previous studies in which the parameter ‘finger’ (within hand) is included in the paradigm (Kornblum, 1965; Rosenbaum & Kornblum, 1982). Thus when examining precue conditions involving the specification of hand and/or finger, this finding indicates that RT is faster when fingers are anatomically independent (e.g., in HUFK and HUFU) than when fingers are within the same hand (e.g., HKFU).

3.1.4. Conversion patients’ muscles took longer to generate force to initiate movement

Results for motor time (the peripheral component of RT) are summarised in Fig. 2B. There was a significant Group \times Hand interaction ($F_{(2,39)} = 3.6, p = .037$). Post hoc analyses of between-hand differences revealed that feigning resulted in slower muscle activation in the symptomatic limb compared to the asymptomatic limb ($p = .001, \eta^2 = .13$). Regarding differences in motor time among the groups, Fig. 2B shows that in general, muscle activation in patients was slower than in controls. Post hoc tests confirmed that motor time for the patients’ asymptomatic limb was significantly longer than both feigners and controls ($p < .001, \eta^2 > .19$). For the symptomatic limb, motor time was longer in feigners than controls ($p = .001, \eta^2 = .14$), with a trend for motor time of patients to be longer than controls signalled by a large effect size ($\eta^2 = .42$). While motor time was affected in both patients and feigners, conversion disorder had a rather global effect on motor time for both hands in patients, whereas in feigners the effect was localised to the symptomatic hand. Finally, there was no independent effect of Condition on motor time within each Group or Hand. Muscle

activation time when hand was precued (HKFU) was not different to the condition in which hand was not precued (HUFK, HUFU) prior to stimulus onset.

3.1.5. Paresis, whether clinical or feigned, slowed movement time

A significant Group \times Hand interaction for movement time ($F_{(2,39)}=6.5$, $p=.004$; Fig. 2C) was attributed to the different between-hand pattern of results within each group. The symptomatic hand of patients ($p=.039$, $\eta^2=.12$) and feigners ($p=.001$, $\eta^2=.28$) moved more slowly than the asymptomatic hand, whereas movement time for both hands in the control group was essentially the same. Fig. 2C also illustrates that in general, patients and feigners took longer to press the key than controls. Post hoc analyses to further investigate the effect of Group showed that for the symptomatic hand, movement time of feigners was significantly longer than patients ($p=.011$, $\eta^2=.10$) and controls ($p=.001$, $\eta^2=.26$). A large effect size ($\eta^2=.46$) supported the observation of longer movement time in patients than controls. For the asymptomatic hand, movements were significantly slower for patients compared to feigners ($p=.002$, $\eta^2=.14$) and controls ($p=.001$, $\eta^2=.52$). Feigners were slower than controls ($p=.021$, $\eta^2=.08$). As observed for motor time, there was no effect of Condition, indicating that the nature of uncertainty prior to the imperative stimulus had no effect on processes occurring subsequent to EMG initiation.

3.2. Electroencephalography

3.2.1. In patients, CNV amplitudes indexing motor preparation were smaller when the symptomatic (left) hand was precued

The grand mean CNV waveforms for each group are illustrated in Fig. 3 and the change in CNV amplitude, measured as an average of the 100 ms just before stimulus onset, is shown in Fig. 4 (individual data for participants in each group for the HKFU condition are illustrated in Fig. S3B [left column]). A significant four-way Group \times Condition \times Hemisphere \times Region was found ($F_{(4,38)}=3.5$, $p=.017$). To further examine this interaction we first sought for

differences among groups for each electrode region. As we also found significant Group \times Condition \times Hemisphere interactions for each region (central: $F_{(4,38)}=5.7$, $p=.001$ and frontal: $F_{(4,38)}=4.1$, $p=.025$), we analysed the effect of Group and Hemisphere for each condition and each region separately. In the HKFU condition, in which the precue provided patients and feigners explicit information about whether the trial would require movement of their symptomatic limb, we found significant Group \times Hemisphere interactions (central: $F_{(2,38)}=7.9$, $p=.001$ and frontal: $F_{(2,38)}=3.3$, $p=.046$) with a marked effect of group for CNV amplitudes over central electrodes (C3': $F_{(2,38)}=3.8$, $p=.031$ and C4': $F_{(2,38)}=7.7$, $p=.002$). Visual inspections of the CNV waveforms in the HKFU condition (Fig. 3A) show a clear suppression of CNV amplitudes over the primary motor cortices, indicating a between-group difference. Indeed, post hoc tests of the interaction confirmed that in HKFU, patients showed significantly smaller C3' amplitudes compared to controls ($p=.031$, $\eta^2=.34$; Fig. 4A) and smaller C4' amplitudes compared to controls and to feigners ($p<.01$, $\eta^2>.37$; Fig. 4B). Importantly, this effect was absent in the conditions in which hand could not be prepared in advance (Fig. 3B and C). That is, we found no significant between-group effects on CNV amplitude for the hand unknown conditions (HUFK, HUFU; Fig. 4A and B). Similarly, at frontal electrodes, CNV amplitude over the left frontal hemisphere of patients (F3) was significantly smaller in HFKU compared to controls ($F_{(2,38)}=3.5$, $p=.043$, $\eta^2=.30$; Fig. 4C), with a trend (effect size, $\eta^2=.24$) indicating patient CNV amplitudes were substantially smaller than feigners ($p=.073$).

To specifically address the question whether the type of information had an effect on CNV amplitude within groups, we performed a second analysis to further unpack the interaction with Condition and Hemisphere as factors, for each group and region separately. In patients it is apparent that CNV amplitudes were smaller when their symptomatic hand was specified in the precue (HKFU) compared to when hand was unknown (HUFK, HUFU). There were medium to large effect sizes when contrasting CNV amplitude in HKFU to the other two conditions at both central and

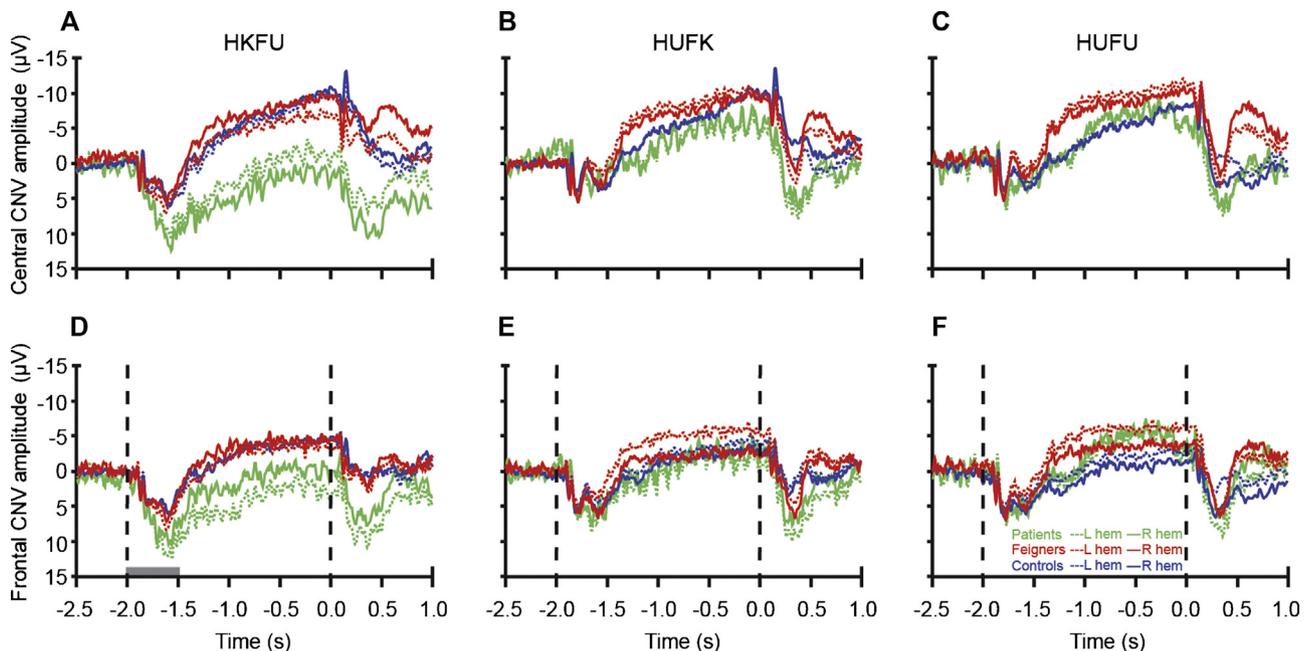


Fig. 3. Grand mean EEG traces for symptomatic (left) hand responses. CNV waveforms plotted as amplitude (μV) over time (s) for each precue condition, (A) HKFU (hand known, finger unknown); (B) HUFK (hand unknown, finger known); and (C) HUFU (hand unknown, finger unknown). Upper row shows recordings from central (C3', C4') electrodes; lower row from frontal (F3, F4) electrodes. Green traces show patient data ($n=5$), red traces for feigners ($n=24$), and blue traces for controls ($n=12$). Dashed lines show data for the left hemisphere (L hem; ipsilateral to the moving hand); solids traces for the right hemisphere (R hem; contralateral to the moving hand). Dashed vertical lines at $t=-2.0$ s and $t=0$ ms represent the onset of the precue and imperative stimulus respectively; grey horizontal bar shows precue duration. Negative is plotted upwards. (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this article.)

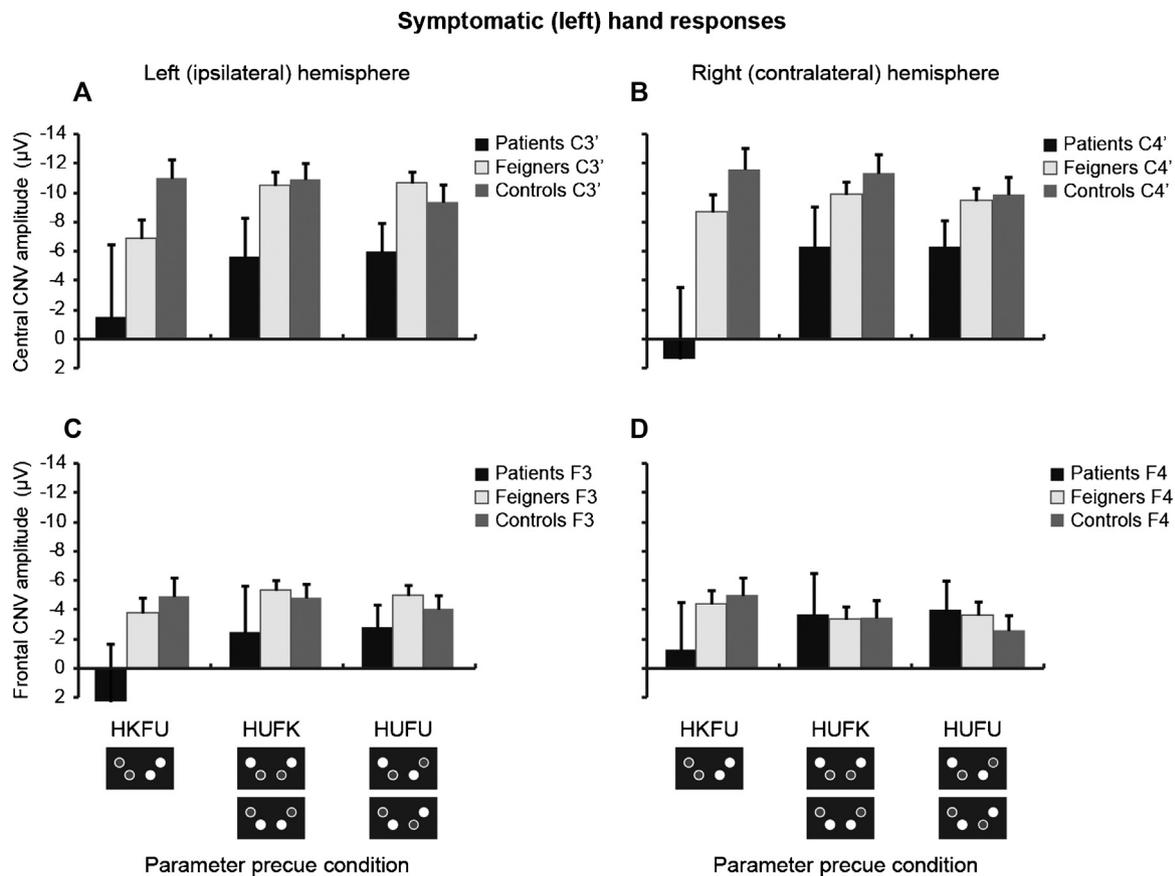


Fig. 4. Contingent negative variation amplitude (μV) (+SEM) for symptomatic (left) hand responses in each precue condition from (A) left hemisphere central electrodes (C3'); (B) right hemisphere central electrodes (C4'); (C) left hemisphere frontal electrodes (F3); and (D) right hemisphere frontal electrodes (F4). Data shown for patients ($n=5$; black bars), feigners ($n=24$; light grey bars) and controls ($n=12$; dark grey bars). Patient 3 who had right-hand paresis was omitted from these analyses. Amplitudes are an average of 100 ms immediately prior to stimulus onset (-99 ms to 0 ms). Negative is plotted up. HKFU, hand known, finger unknown; HUFK, hand unknown, finger known; HUFU, hand unknown, finger unknown. Dark circles in black rectangles represent response keys illuminated for each precue condition.

frontal electrodes (central: HUFK, $\eta^2 > .07$, HUFU, $\eta^2 > .08$; frontal: HUFK, $\eta^2 > .10$, HUFU, $\eta^2 > .04$), however the large variability in the patient data mitigated against significance being achieved. Feigners also demonstrated smaller central CNV amplitudes when the feigning limb was specified in advance compared with HUFK and HUFU ($F_{(2,90)} = 4.3$, $p < .05$; Fig. 4A and B).

A significant effect of Hemisphere was also found but only for frontal electrodes. Patients demonstrated consistently larger contralateral CNV amplitudes over the right frontal hemisphere (F4) compared with the left hemisphere ($F_{(1,18)} = 4.9$, $p = .04$; Fig. 4C and D) irrespective of whether their symptomatic hand was precued or not. In contrast, controls and feigners showed larger CNV amplitudes over the left compared to the right frontal cortex, for the hand unknown precues. No other significant effects of hemisphere or two-way interactions were found. An additional analysis examining the difference in CNV amplitude between the contralateral and ipsilateral hemispheres (i.e., C4'–C3'; F4–F3) among groups confirmed that the lateralisation of preparatory activity at frontal electrodes ($F_{(2,38)} = 4.0$, $p = .027$) was greater in patients compared to controls and feigners ($p < .05$).

3.2.2. No difference in CNV amplitude was found among groups when the asymptomatic (right) hand was specified in advance

Analyses of behaviour and change in muscle activity revealed a significant difference among the 'asymptomatic' hand of patients, feigners and controls (Fig. 2). In order to examine whether these differences were also present at the cortical level, we analysed CNV amplitudes just prior to stimulus onset for responses of the

asymptomatic (right) hand for each group. The grand mean CNV waveforms and CNV amplitudes are shown in Figs. 5 and 6 respectively (individual data for participants in each group for the HKFU condition are illustrated in Fig. S3B [right column]).

Strikingly different effects were found for the asymptomatic (right) hand. For patients, the pattern of CNV amplitudes for their asymptomatic hand was similar to those of the feigners and controls as shown in Fig. 6. No significant four- or three-way interactions were found. However, there was a significant Group \times Condition interaction ($F_{(4,38)} = 3.8$, $p = .011$) and a significant Condition \times Hemisphere interaction ($F_{(2,38)} = 8.8$, $p = .001$). Additionally, a main effect of electrode region was found ($F_{(1,38)} = 106.6$, $p = .001$), whereby CNV amplitudes were greater over central compared to frontal electrodes. The Group \times Hemisphere interaction was not significant. Thus no lateralisation effects across groups for either electrode region were found. This null result was confirmed by an additional analysis examining the difference in CNV amplitude between the contralateral and ipsilateral hemispheres (i.e., C3'–C4'; F3–F4) among groups.

Regarding the Group by Condition interaction, between-group analyses conducted for each condition separately confirmed that in the HKFU condition, there was no significant difference in CNV amplitude among groups (Fig. 6). Similarly, there was no effect of Group for CNV amplitudes in the hand unknown conditions (HUFK, HUFU). Next, analyses to examine the Condition by Hemisphere interaction revealed that in HKFU CNV amplitudes were larger overall over the left hemisphere compared to the right hemisphere

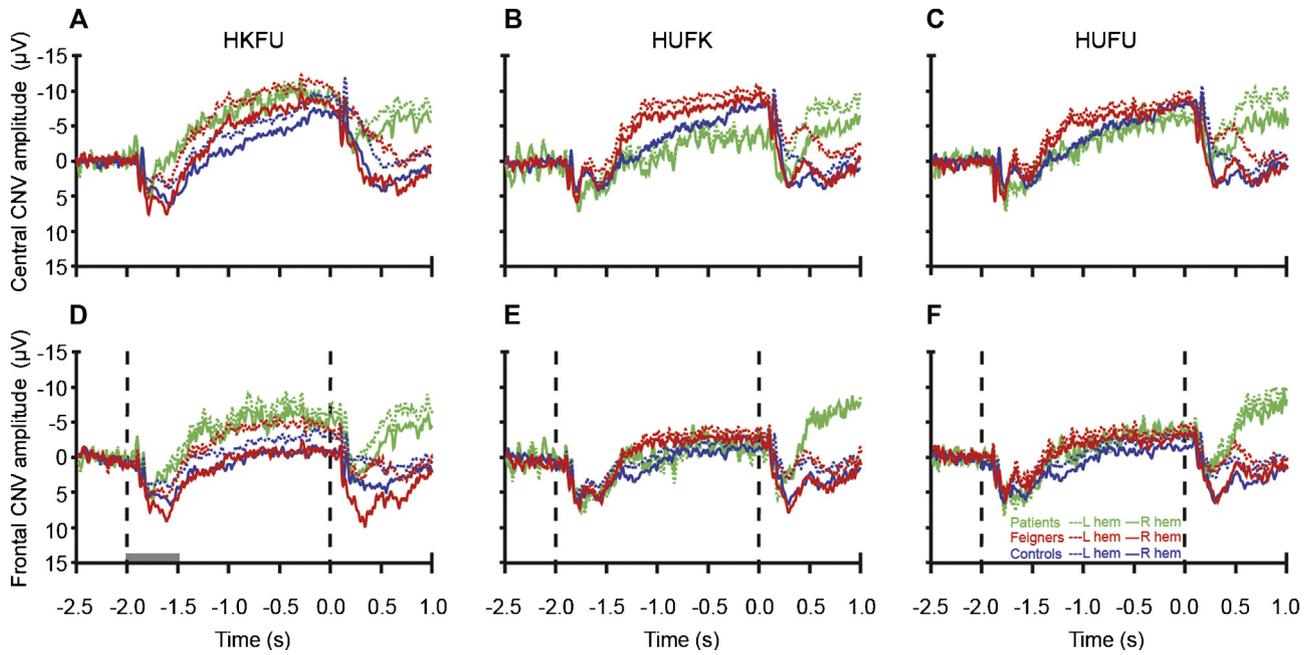


Fig. 5. Grand mean EEG traces for asymptomatic (right) hand responses. CNV waveforms plotted as amplitude (μV) over time (s) for each precue condition: (A) HKFU (hand known, finger unknown); (B) HUFK (hand unknown, finger known); and (C) HUFU (hand unknown, finger unknown). Upper row shows recordings from central ($\text{C3}'$, $\text{C4}'$) electrodes; lower row from frontal (F3 , F4) electrodes. Green traces show patient data ($n=5$), red traces for feigners ($n=24$), and blue traces for controls ($n=12$). Dashed lines show data for the left hemisphere (L hem; contralateral to the moving hand); solids traces for the right hemisphere (R hem; ipsilateral to the moving hand). Dashed vertical lines at $t = -2.0\text{ s}$ and $t = 0\text{ ms}$ represent the onset of the precue and imperative stimulus respectively; grey horizontal bar shows precue duration. Negative is plotted upwards. (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this article.)

Asymptomatic (right) hand responses

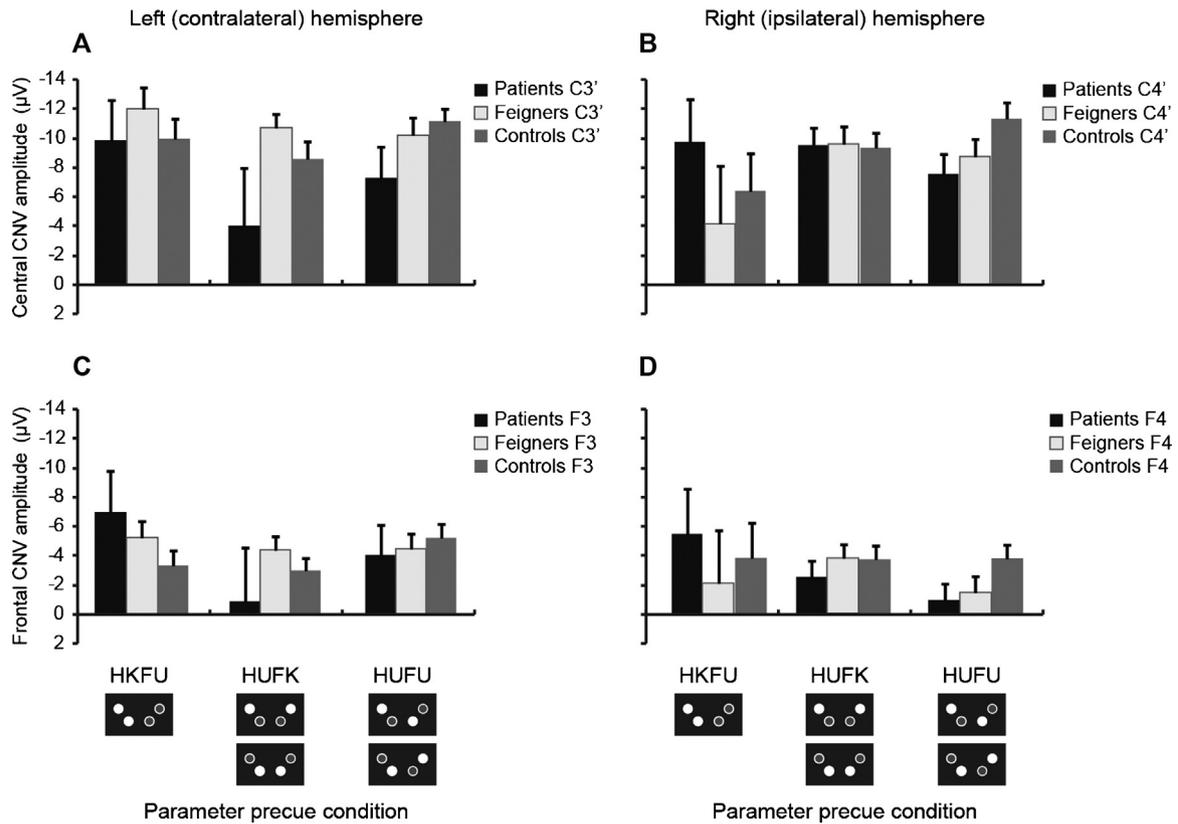


Fig. 6. Contingent negative variation amplitude (μV) (+SEM) for asymptomatic (right) hand responses in each precue condition from (A) left hemisphere central electrodes ($\text{C3}'$); (B) right hemisphere central electrodes ($\text{C4}'$); (C) left hemisphere frontal electrodes (F3); and (D) right hemisphere frontal electrodes (F4). Data shown for patients ($n=5$; black bars), feigners ($n=24$; light grey bars) and controls ($n=12$; dark grey bars). Patient 3 who had right-hand paresis was omitted from these analyses. Amplitudes are an average of 100 ms immediately prior to stimulus onset (-99 ms to 0 ms). Negative is plotted up. HKFU, hand known, finger unknown; HUFK, hand unknown, finger known; HUFU, hand unknown, finger unknown. Dark circles in black rectangles represent response keys illuminated for each precue condition.

($p = .005$). This result confirms the typical pattern of lateralisation when hand is known in advance. As expected, there were no differences between left and right hemisphere CNV amplitudes when hand was unknown before stimulus onset.

3.2.3. CNV amplitudes were significantly reduced for the patients' symptomatic hand compared to their asymptomatic hand

Comparison of the CNV traces for hand precues (Figs. 3A, D and 5A, D) and the associated CNV mean values (Figs. 4 and 6) show that overall, CNV amplitudes for the symptomatic hand were smaller than those for the asymptomatic hand. To directly examine between-hand CNV amplitude differences in the HKFU condition in patients, we performed an additional planned comparison analysis. For this comparison, data over the left and right hemisphere electrodes were averaged to avoid confounding by 'Hemisphere'. Thus, although this analysis masks any CNV differences within hemisphere, it permits examination of whether symptomatic hand precues had a *general suppressive effect* on CNV amplitude (specific lateralisation effects of motor preparation processes have been addressed in Sections 3.2.1 and 3.2.2). Results for patients revealed significantly smaller CNV amplitudes for the symptomatic hand compared to the asymptomatic hand at central and frontal sites (central: $F_{(1,18)} = 6.5$, $p = .02$, $\eta^2 = .27$; frontal: $F_{(1,18)} = 4.5$, $p = .048$, $\eta^2 = .21$) consistent with a global reduction of preparatory activity for the symptomatic hand.

4. Discussion

In motor conversion disorder the ability to perform voluntary movement is compromised. Two contrasting hypotheses have been proposed to account for these deficits: 'abnormal preparation' (Spence et al., 2000; Vuilleumier et al., 2001) and 'disrupted execution' (Marshall et al., 1997; Tiihonen et al., 1995). In our previous paper we reported results from simple RT trials in which the precue provided complete advanced information about the hand and finger required to perform the movement (Blakemore et al., 2013). Analyses focused on sensory-evoked potentials elicited by the visual precue (at the beginning of the preparatory period). We demonstrated diminished N1 amplitude and enhanced P3 amplitude in conversion patients when the precue signalled the symptomatic hand. In the present paper we combined EMG recordings to fractionate RT into premotor and motor components, with an EEG measure (CNV) that is directly associated with motor preparation. This enabled us to further tease out whether processes prior to and/or during performance are affected in conversion paresis.

Here we report findings in more complex 2-choice RT conditions where the precue provided partial information about the upcoming movement. Analysis of EEG data immediately prior to stimulus onset (at the end of the preparatory interval) showed that conversion paresis is also associated with significantly suppressed CNV amplitude compared to control participants. Significantly, the novel finding is that these deficits in CNV amplitude were found uniquely when patients have prior knowledge about moving their symptomatic limb, consistent with impaired preparatory processes. Such deficits in preparation were not observed when hand was not precued (HU conditions), even if the symptomatic limb performed the movement. These data strongly indicate that abnormalities of preparation are involved in conversion paresis. Deficits in activity of 'execution' related circuits, for example, the generation of final output signals at the cortical level to the spinal cord, would thus be necessarily disrupted. Such disruption could be due to the deficient preparatory activity as well as to any additional direct suppression of such circuits as proposed by Tiihonen et al. (1995) and Marshall et al. (1997). Modulation of the activity of these execution-related pathways can in turn be measured to

index deficits in execution processes. Accordingly, we also observed longer movement durations, poorer performance accuracy and reduced force production, consistent with their paresis symptoms. Thus, rather than uniquely supporting one of these hypotheses, our data support the notion that both preparatory and execution phases of voluntary movement control are affected in individuals with motor conversion disorder.

The executive command controlling motor activity is generated in the motor cortex and transmitted via the spinal cord and peripheral nerves to muscles where muscular contraction results in movement initiation. Deficits in execution can therefore occur as a result of dysfunction at any of these levels. We found that the duration of muscular activation prior to movement onset (motor time) was prolonged in patients compared to controls. Thus one locus of impairment in execution in conversion paresis occurs before movement has been initiated. One possible cause of these effects could be pathology of force development of the muscle itself, either primary or secondary to disuse. However this is unlikely, as no atrophy was evident on clinical examination. Rather, longer motor times and decreased force production in patients more likely indicates decreased rate of motor unit recruitment (Possamai et al., 2002), which in turn reflects deficiency in activation of spinal motor neurons by descending control signals. In agreement, we also found that the onset of muscle activation (PMT) was longer in patients, indicating a delay in the activation of spinal motor neurons by the descending pathways (assuming no pathology of peripheral nerves or synapses). Together, these changes reflect dysfunction of execution processes generated in the motor cortex. This notion is consistent with neuroimaging findings, in which impairments in movement execution in conversion patients have been ascribed to inhibitory processes imposed upon the motor cortex (Marshall et al., 1997; Tiihonen et al., 1995).

Performance measures alone however cannot resolve the preparation versus execution debate. This is because deficits in motor cortex output could either be secondary to an imposed inhibitory process at the output stage, or as we will argue, secondary to an upstream primary deficit in preparatory processes that lead to insufficient or delayed activation of output pathways. Such upstream processes can be more clearly addressed using precued RT tasks. In such tasks, the period from the precue to imperative signal provides time for response preparation, as evidenced by shortened RT when such information is completely provided compared to when it is not (Anson et al., 2000; Rosenbaum, 1980; Wild-Wall et al., 2003), and is distinct from the movement execution phase. Neural processes during the foreperiod are thus unambiguously associated with movement planning and preparation. We assessed these processes using measurement of the CNV amplitude.

The CNV results in this study showed a significant reduction in amplitude in conversion patients compared to controls and feigners. Reduced CNV amplitudes in psychiatric populations have been previously reported, for example in depressed and neurotic patients (Giedke & Bolz, 1980; Hansenne & Anseau, 2001; Timsit-Berthier et al., 1973) and in individuals with high levels of anxiety or stress (Knott & Irwin, 1973; Low & Swift, 1971; McCallum & Walter, 1968a, 1968b). It is therefore possible that our results were confounded by the presence of comorbid psychiatric disorder, which is common in patients with conversion symptoms (Binzer, Andersen, & Kullgren, 1997; Crimlisk et al., 1998). Furthermore, effects of medication for conversion symptoms and/or psychiatric disorder could have also influenced our CNV results. Although patients were tested 'off' medication, this was not a true wash-out but was defined as having not taken any medication for at least 10 h before the experimental session. It is unlikely however that psychiatric comorbidity or medication significantly affected CNV amplitude because reduced CNV amplitudes were only found when

patients knew in advance they had to prepare a movement with their symptomatic hand. There was no difference in CNV amplitude among groups when the symptomatic hand was unknown during the preparation period. Medication and psychiatric comorbidity are therefore unlikely to selectively impair motor preparation of one limb. The present data therefore provide further support for the hypothesis that there is ‘abnormal motor preparation’ associated with conversion paresis (Spence et al., 2000; Vuilleumier et al., 2001). Previous neuroimaging experiments found altered activity in dorsolateral prefrontal cortex (Spence et al., 2000) and motor circuits through the basal ganglia (Vuilleumier et al., 2001), and dysfunction of motor programming processes was inferred from the presumed functions of these regions. In the current study, the temporal resolution of CNV measures enabled us to locate these changes in frontal and central regions explicitly within the preparatory period.

Our CNV results disagree however, with those of Cojan, Waber, Carruzzo, and Vuilleumier (2009) who used a precued go-nogo task that also probed motor preparation to investigate the neural correlates of conversion paralysis. They found normal activation of right motor cortex during response preparation in a patient with left hand paralysis despite impairments in movement execution. In this study between-group comparisons were not conducted so it is difficult to determine the extent to which change in M1 activation differed between the patient and the control group. Additionally, Cojan et al. only tested one patient who did not exhibit any overt movement with the symptomatic hand so concomitant impairments in behavioural measures indexing motor preparation were not obtained. It is possible their results do not generalise to our group of patients who were able to successfully perform a similar index finger button-press response (with only 6.6% of trials deemed errors). Importantly, the patients in the current study demonstrated changes in brain function that were limb-specific and context-dependent. That is, our results do not simply reflect generic deficits in cortical preparatory activity. When patients had no advanced knowledge about moving their symptomatic limb (HUFK or HUFU) or when responses of the asymptomatic hand were precued, we found no difference in CNV amplitude between patients and controls. Thus the novel CNV findings in this experiment include that when hand was unknown the ability to sufficiently prepare an overt motor response during the foreperiod remained intact and that deficits in CNV amplitude were only observed when patients had prior knowledge about moving their symptomatic limb.

Diminished CNV amplitude when the patients’ symptomatic hand was precued could reflect several different mechanisms. One possibility is that it reflects “preparation to move weakly”. This is unlikely because patients and feigners showed similar behavioural deficits but the diminished CNV amplitude was only seen in patients. Other possibilities unique to patients include dysfunction of early sensory processing, or later processes involved in CNV generation. A sensory processing impairment would leave patients unable to use the advance information effectively to prepare a motor response, thus disrupting activity of circuits related to execution giving rise to measures of impaired performance and weakness. There is evidence that conversion patients show a generalised reduction in sensory processing (Blakemore et al., 2013) and that extracting and categorising behaviourally relevant stimulus information is disturbed in conversion disorder (Fukuda et al., 1996; Lorenz, Kunze, & Bromm, 1998; Towle, Sutcliffe, & Sokol, 1985). The changes in CNV could also reflect engagement of an inhibitory system that actively suppresses activity of brain circuits associated with preparatory processes. ‘Excessive inhibition’ mechanisms have been invoked to explain suppressed motor cortex activity that has been used as the basis of the ‘disrupted execution’ hypothesis for conversion disorder (Marshall et al., 1997; Tiihonen

et al., 1995). However, such inhibitory modulation, that could come for instance from prefrontal cortical areas, need not necessarily imply suppression of motor execution – it could equally apply to processes necessary for motor preparation.

The concept of frontal inhibition on the motor cortex is not new. In the early 20th century, Pavlov (1941) proposed that overexcitation of subcortical areas may result in cortical inhibition, possibly from the frontal cortex, which may in turn modulate the sensorimotor system thus giving rise to symptoms of paralysis, blindness or anaesthesia. Furthermore, increased activation in the prefrontal cortex was demonstrated by Marshall et al. (1997) when a conversion patient attempted to move the affected limb. What is interesting is that in both studies by Tiihonen et al. (1995) and Marshall et al. (1997), the increase in prefrontal activity was found specifically in the right hemisphere. Consistent with this, we found larger CNV amplitudes over the right frontal hemisphere only in patients for movements during the precue period when the precue indicated that movement of the symptomatic hand would be required. Feigners and controls showed larger CNV amplitudes over the left frontal hemisphere in the hand known and hand unknown conditions, consistent with the notion that the left hemisphere has a general role in movement preparation independent of the specific limb to be moved (Serrien, Ivry, & Swinnen, 2006; Swinnen, 2002). Conversely, previous studies have shown the right anterior prefrontal cortex to be involved in processes of response inhibition that prevent or cancel an intended movement (Aron, Robbins, & Poldrack, 2004; Aron, 2007). Although processes of response inhibition cannot be directly tested with the current paradigm, our findings of increased right frontal activity and suppressed activity over motor cortex in patients is consistent with existing literature indicating involvement of an inhibitory frontocortical mechanism in conversion disorder. Such inappropriate right prefrontal activation may thus reflect activation of an (unconscious) inhibitory system that could suppress motor preparation occurring in more caudal motor areas. This would leave motor cortical cell assemblies (Wickens, Hyland, & Anson, 1994) coding the motor program poorly formed or dysfunctional, leading to weakness and RT deficits in conversion paresis.

An interesting and important practical question is the extent to which data from patients clinically diagnosed with conversion disorder in the present study were similar to the feigning participants. The distinction between conversion disorder and malingering is important socially and legally, and can be difficult to tease out in clinical settings, particularly where fiscal or other motivations exist (Nicholson, Stone, & Kanaan, 2011). Feigners explicitly attempt to generate weakness through conscious intent, and in our study showed very similar behavioural deficits to the patients, who by definition are unconscious of whatever processes generate their weakness. Thus with instruction, healthy volunteers can intentionally disrupt motor performance in a manner similar to conversion paresis. These similarities highlight the challenging nature of differential diagnosis. In feigners, the same proposed mechanisms underlying increased premotor and motor time could apply as for patients, including altered motor programs by specifying a decreased rate of change of force (Ashe, 1997; Possamai et al., 2002). Longer movement durations would also allow feigning participants to take advantage of sensory and proprioceptive information via feedback mechanisms, which could be utilised to “correct” the force exerted in order to adhere to the task instructions of feigning impairment.

Of particular interest in terms of teasing out the clinical syndrome from intentional weakness is that in our study, we also note clear differences between conversion and feigned paresis. We found the CNV data segregated the patients from the feigners completely, with only patients showing a deficit in CNV amplitude; yet the CNV data of feigners were not different from controls even

though the movement parameters between these groups were different. The results for feigners are consistent with the action of a late inhibitory process superimposed on normally developed preparation. But given that feigners could be actively preparing not to move during the foreperiod, another possibility is that processes related to greater task involvement such as enhanced attentiveness and vigilance in feigners to ensure correct responding, preserved the development of the CNV (Tecce & Cattanach, 1987) thus producing a signal that cannot be distinguished from ordinary planning. Greater attention to the task in feigners may also explain increased PMT in the feigners' asymptomatic limb whereby the requirement to correctly respond with each limb according to the movement instructions, lengthened central processing time overall. However, it was only in patients and not feigners that we found measurable deficits in execution (maximum force, motor time, movement time) for the asymptomatic limb. Although patients made no clinical complaints in this limb, this novel observation of an 'overflow' effect points towards a general disturbance in execution of the intentional motor system in conversion paresis (Roelofs et al., 2001, 2002).

From a clinical perspective, our results indicate that examining movement performance in the asymptomatic limb of patients with unilateral conversion paresis is important to elucidate the extent of voluntary movement impairment. The striking difference in CNV amplitude among groups raises the question as to whether such a measure may have clinical utility to aid in distinguishing between conversion and feigned paresis. Although we did not record changes in brain activity from a large scalp array, recording from a limited number of electrodes is more akin to EEG use in clinical settings. Indeed, the Bereitschaftspotential, a slow negative wave preceding self-paced voluntary movements, has shown to have clinical value in assessing psychogenic movement disorders at the individual level (Colebatch, 2007; Shibasaki & Hallett, 2006; Terada et al., 1995). Thus analysis of CNV in precued RT tasks may provide useful ancillary information in the assessment of unilateral paresis with no detectable organic cause. Further work is needed however to examine the robustness of individual differences in CNV amplitude. More generally, our findings emphasise the significance of including a control group in empirical research to enable valid conclusions to be drawn about motor preparation and execution deficits. Comparisons with healthy participants have been frequently absent (for example, de Lange et al., 2007; de Lange, Roelofs, & Toni, 2008; de Lange, Toni, & Roelofs, 2010; Marshall et al., 1997; Roelofs, de Buijn, & van Galen, 2006; Tiisonen et al., 1995; Vuilleumier et al., 2001).

In conclusion, conversion disorder is a complex disorder that likely has multi-faceted neural underpinnings affecting processes during motor preparation and execution. We showed at the behavioural level in a 2-choice RT task that for responses with the symptomatic limb conversion paresis appears difficult to dissociate from feigned paresis. However we found significantly reduced CNV amplitudes when patients had prior knowledge they would be required to move their symptomatic limb (hand precues). This direct change in brain function associated with motor preparation was observed in patients but not feigners, demonstrating discrete differences in cortical preparatory activity that points towards distinct neural processes underlying unconsciously generated and consciously generated volitional movement.

Acknowledgements

The authors wish to acknowledge Professor Elizabeth Franz (Department of Psychology, University of Otago) and Dr Jon Shemmell (School of Physical Education, Sport and Exercise Sciences, University of Otago) for their early discussion and comments, and

Nigel Barrett, Gavin Kennedy and Glenn Braid (School of Physical Education, Sport and Exercise Sciences, University of Otago) for technical, electronic and programming support.

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