Aberrant force processing in schizophrenia

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Abstract

Initially considered as mere side effects of antipsychotic medication, there is now evidence that motor and somatosensory disturbances precede the onset of the illness and can be found in drug-naïve patients. However, research on the topic is scarce. Here, we were interested in assessing the accuracy of the neural signal in detecting parametric variations of force linked to a voluntary motor act and a received tactile-sensation, either self- or externally-generated. Patients with a diagnosis of schizophrenia and healthy controls underwent functional magnetic resonance imaging while asked to press, or abstain from pressing, a lever in order to match a visual target force. Forces, exerted and received, varied on 10 levels from 0.5N to 5N in 0.5N increments. Healthy participants revealed a positive correlation between force and activity in contralateral primary somatosensory area (S1) when performing a movement as well as when receiving a tactile sensation, but only when this was externally, and not self-, generated. Patients showed evidence of altered force signalling in both motor and tactile conditions, as well as increased correlation with force when tactile sensation was self-generated. Findings are interpreted in line with accounts of predictive and sensory integration mechanisms and point towards alterations in the encoding of parametric forces in the motor and somatosensory domain in patients affected by schizophrenia.

Introduction

Motor and somatosensory disturbances have been consistently reported in the literature on schizophrenia. With regards to motor deficits, patients have shown to be slow when generating motor acts[1], to exhibit abnormal involuntary movements[2], altered coordination[3] and finger sequencing[4]. Other motor impairments include catatonia[5] and neurological soft signs (NSS[6]). With regards to somatosensory disturbances, evidence shows reduced sensory gating in the somatosensory domain[7] and pain sensitivity[8]. Patients are also thought to show lack of somatosensory attenuation, whereby self-, but not externally-, generated sensations are attenuated, putatively as a result of them being predicted[9-12]. In line with this, somatosensory brain response has shown to be increased when sensation is externally generated, as opposed to self-generated, in controls and not in patients[10]. In schizophrenia, lack of somatosensory attenuation has been associated with aberrant sense of agency and may lead to a misattribution of self-generated actions to external sources, thus contributing to the development of psychotic symptoms, such as auditory hallucinations and delusions of control[13].

There is now ample evidence showing that motor and somatosensory impairments are present in antipsychotic naïve schizophrenia patients[14-15], in individuals at risk of developing the illness[14, 16-17] and in patients' biological relatives[18-20], suggesting that these are not merely consequent on antipsychotic treatment. To this extent, recent models support the view that such symptoms constitute an important clinical dimension and may provide important insight into the biological and neurodevelopmental mechanisms underlying the disorder[21]. However, despite their clinical importance, research has yet to characterise the determinants of motor and somatosensory dysfunction in schizophrenia. In particular, very little is known regarding the level of accuracy of such systems in patients.

Accuracy of force processing, for example, is an important component in motor and somatosensory functional domains and it is likely that inappropriate tuning of motor and somatosensory brain areas to varying levels of force may account for some of the aforementioned deficits in schizophrenia. In particular, failure to appropriately encode generated motor force might give rise to problems associated with the correct execution and monitoring of movements[22]. Moreover, as the motor and somatosensory systems are largely intertwined, appropriate signalling of somatosensory feedback associated to motor acts is also likely to contribute to the same issues[23]. Lastly, altered somatosensory feedback of force, associated with received tactile sensations, might account for some of the sensory impairments detected in experimental settings, including reduced somatosensory attenuation, and at such may play an important role in psychosis. Nevertheless, accuracy of force processing in schizophrenia has received little investigation.

There is general agreement that motor and somatosensory areas increase activity with increasing force[24-26]. Here, we employed functional magnetic resonance imaging (fMRI) to research the neural mechanisms underlying force production and sensation with the hypothesis that schizophrenia patients would demonstrate aberrant signalling of force intensity in the motor and somatosensory network. In light of previous neuroimaging findings on healthy individuals[27-29, 25], analysis was focused on response in contralateral (to the hand engaged in task) primary motor cortex (M1), primary somatosensory cortex (S1) and supplemental motor area (SMA). Whereas force-related activation in M1 and S1 has been interpreted as reflecting the involvement of such areas in encoding general features of motor

and somatosensory stimuli, force-related activation in SMA has been predominantly associated with its specific role in motor planning and volitional control[29].

The task employed here has been previously used in our lab for the investigation of basic sensory attenuation in patients[9-10]. We now exploit its features (described in Materials and Methods) to independently analyse the accuracy of the motor and somatosensory system in encoding parametric variations of force. Moreover, by comparing brain activation to tactile forces when these are self- as opposed to externally- generated, we could also investigate the effects of sensory attenuation on parametric force signal. Specifically, we predicted that a) healthy individuals would show a positive correlation with forces in contralateral M1 and SMA when performing a movement; b) commensurately in contralateral S1 when receiving a tactile sensation; c) but also in contralateral S1 when performing a movement as the result of the somatosensory feedback linked to the motor act; d) patients would show altered motor and sensory force signalling in all of the above; finally e) we predicted that healthy controls would show absent or reduced correlation between applied force and brain activation within contralateral S1 when the force could be predicted (i.e., was self-generated), as opposed to when the force could not be predicted (i.e., was externally generated), and that patients would fail to demonstrate this difference.

Materials and Methods

Participants

Volunteers were 21 patients with a diagnosis of schizophrenia (based on assessment using criteria from DSM-IV-TR[30]) being treated with stable antipsychotic medication, and 26 healthy individuals with no reported history of psychiatric illness assessed with the MINI International Neuropsychiatric Interview[31] (Table 1). Ethical approval was provided by South London and Maudsley Research and Ethics Committee. All participants provided informed written consent and were given a monetary inconvenience allowance for study participation. Participants met the following inclusion criteria: 1) capacity to consent; 2) age between 18-60 years; 3) sufficient command of the English language to understand task instructions and 4) right-handedness, as measured by the Edinburgh Handedness Inventory[32]. Participants were excluded if they had: 1) current drug or alcohol dependence; 2) brain disease or damage or if they 3) used psychotropic medication (except patients). Diagnosis of schizophrenia was

confirmed by an experienced clinician and severity of symptoms was assessed with the Positive and Negative Symptoms Scale (PANSS[33]).

Data acquisition

Blood oxygenation level-dependent (BOLD) functional images were acquired on a GE 3 Tesla system (Signa Excite; General Electric) with an 8-channel head coil using an echo planar imaging sequence with the following parameters: repetition time, 2600 milliseconds; echo time, 30 milliseconds; and flip angle, 90°. In each of the three runs, 330 volumes that comprised 40 descending, sequentially ordered 2-mm axial slices (with 1-mm gap between slices) and an in-plane resolution of 3 × 3 mm were acquired.

Task paradigm

Participants performed a sensorimotor task with the use of the experimental apparatus depicted in Figure 1[9-10] which enabled forces to be measured through the use of two pressure sensors mounted one above the other. The upper sensor was fixed in space, and the lower sensor was mounted on the end of a lever attached to a small torque motor. This apparatus permitted a press (by the right index finger) on the upper sensor to either be transmitted to the left index finger or not. Moreover, the tactile stimulus on the left finger could also be presented in the absence of any corresponding right finger press. Thus, four experimental conditions were presented: movement with self-produced tactile sensation (M1S1), externally produced tactile sensation with no movement (M0S1), self-produced movement without tactile sensation (M1S0) and a no movement and no tactile sensation rest (M0S0). Forces exerted and received varied on 10 levels from 0.5N to 5N in 0.5N increments. Thus, this set up allowed investigating brain activation associated to parametric force when both performing a motor act and receiving a tactile sensation, the latter being either self- or externally-generated. Note that in M1S1, the intensity of the self-generated force was transferred to the left finger and was thus predictable, whereas in M0S1, the force was generated by the apparatus and thus its intensity could not be predicted by subjects.

The experimental session comprised three 13-minute runs, containing a total of 468 trials split in alternating blocks of 13 trials each. Each block included 10 experimental trials from one sole condition and 3 null trials, yielding a total of 90 experimental trials and 27 null trials per condition. Within each run, 3 blocks of each condition were presented in random order. Force levels within each block were fully randomised, so that even if subjects knew they

would receive a non-self generated tactile sensation on the left finger in M0S1, they were not able to predict its force. At the start of each block, participants were shown an instruction screen 'press' or 'don't press' (depending on condition) for 3s - no instruction was given regarding tactile sensation. Each trial was 4s long (1s target + 3s response) and inter-trial interval was 1s. Same timings applied to no movement trials in that the lever pressed subjects' left finger after 1s target display. In line with previous studies[9-10], the average force associated with movement and tactile sensation during the last two seconds of the trial was calculated for each subject and used to run behavioural and neural analyses. We chose to exclude the first second of response to ensure a more accurate measure of peak forces generated and received.

Before scanning, all participants received full instructions regarding task features and underwent a training phase using the same experimental apparatus described above, comprehensive of all four experimental conditions. In line with previous studies from our lab[9-10], participants learnt a correspondence between target on the screen and force applied. However, they didn't have to hold this information in memory, but could rather visually follow the cursor moving towards the target while pressing. To avoid pressing on the lower sensor, subjects' left finger was taped to the apparatus. To facilitate the required sustained attention, sessions were split by a short relaxation period during which the participants remained in the scanner.

Functional data analysis

The fMRI data were processed using SPM8 (Statistical Parametric Mapping, Wellcome Department of Imaging Neuroscience, University of London). Data were realigned to the first image, normalized to a standard template of the Montreal Neurological Institute brain, and smoothed using an 8-mm full-width at half-maximum Gaussian kernel. BOLD response was modelled with a canonical hemodynamic response function and a general linear model (GLM) including four stick function regressors associated with trial onset, one for each condition, and four stick function regressors associated with the last two seconds of the trial, one for each condition. To investigate the relationship between force and BOLD activity on a single-trial basis, condition-specific average forces during the last two seconds of the trials following right-index finger movement and left-index finger sensation were calculated for each individual and included as first-order parametric modulators of BOLD activity for relevant conditions. Effects of head motion were minimized by the inclusion of 6 realignment

parameter vectors as regressors of no interest. To further investigate group differences in head motion, we performed group comparisons on the computed mean of the absolute values of the motion correction parameters for translation (X, Y, Z) and rotation (pitch Z, roll Y, yaw Z) across all runs[34] (see Supplemental Materials).

First-level contrast images associated to parametric modulators were entered into a second-level random-effects model. Across subjects, the parameters associated to the parametric modulators were used for one-sample (within groups) and independent-samples (between groups) t-tests. To account for the putative influence of gender and task accuracy on our results, we included two covariates in our second-level model, reflecting gender and subjects' accuracy on the motor task. Accuracy of generated forces was estimated by conducting a linear regression between expected and actual forces, separately for each condition and subject. Estimated betas (indicating subjects' accuracy in generating forces according to target) were then used as covariates in all our second level analyses. To investigate whether patients' medication could account for the observed group differences, we correlated chlorpromazine equivalent medication dosage with patients' fMRI BOLD activation in the peak significant for the between group contrasts (see Supplemental Materials). Further analyses were run to investigate the association between severity of symptoms and alterations of force signalling in the illness. In line with this, contrast images associated with parametric modulators were further included in a regression model and correlated with PANSS scores for the positive and negative scales as a covariate of interest for force related conditions.

A region of interest (ROI) approach was adopted to investigate task effects in M1, S1 and SMA. A priori ROIs in M1, S1 and SMA were created at the group level, with a 5mm-radius sphere centred on the foci of standard peak activations for right and left finger movement[29, 35]. The Human Motor Area Template (HMAT[36]) was used as masking to ensure proper location of observed activations in M1, S1 or SMA. For hypothesis testing, the peak voxel statistics were small volume corrected for our a-priori ROIs, with a $p < 0.05$ Family Wise Error (FWE) significance criterion. Note that different contrasts may highlight different peak activation voxels, even if the same ROI is used for both these contrasts. For completeness, we also ran an exploratory whole brain analysis where statistics were corrected for the whole brain ($p < 0.05$ FWE).

Results

In the healthy controls, we observed a positive correlation between exerted force and brain activity in left S1 in both conditions with movement, namely M1S1 (-34, -26, 54; Z = 3.08; p = 0.018 SVC) and M1S0 (-32, -24, 54; Z = 3.49; p = 0.008 SVC). Note that this effect emerged in left S1, contralateral to the finger used to produce the movement and hence putatively reflects the somatosensory feedback to the same finger. No difference was found for the contrast M1S1 vs. M1S0 in left S1. Contrary to expectations, no positive correlation was detected between exerted force and brain activity in other ROIs for these conditions. Schizophrenia patients also exhibited a positive correlation between exerted force during movement and brain activity in left S1 in both M1S1 (-38, -22, 56; Z = 3.55; p = 0.004 SVC) and M1S0 (-40, -20, 54; Z = 3.09; p = 0.015 SVC). No difference was found for the contrast M1S1 vs. M1S0 in left S1. Between groups contrasts revealed a trend towards increased correlation between exerted forces and left S1 activity in patients compared to healthy controls in M1S1 (Fig 2A: -38, -22, 56; Z = 2.57; p = 0.052, SVC) and M1S0 (Fig 2B: -34, -20, 48; Z = 2.59; p = 0.067, SVC). No group showed force related activation in the side ipsilateral to the hand performing the movement in M1S0 in any of our ROIs. Taken together, these findings suggest that in both groups S1 encodes parametric variation of force associated with the somatosensory feedback from the finger performing the motor act, and that in patients such encoding is increased.

In the right S1 (i.e., associated to the left finger receiving the tactile sensation), healthy controls exhibited a positive correlation between the intensity of tactile sensation and activation during M0S1 (32, -24, 50; Z = 3.75; p = 0.003 SVC). On the contrary, patients failed to show such effect. Healthy controls exhibited no correlation between force on the left finger and activity in right S1 when this was obtained by a self-generated movement (M1S1). Patients exhibited some activation for M1S1, but this did not survive SVC (38, -28, 56; Z = 1.95; p = 0.15, SVC). In line with accounts of sensory attenuation, controls showed increased correlation when the sensation was externally, as opposed to self-, produced (Fig 3A: 34, -26, 50; Z = 3.19; p = 0.014 SVC). On the contrary, patients failed to exhibit such pattern of results, resulting in reduced difference for the contrast M0S1 > M1S1 compared to healthy controls (36, -24, 54; Z = 3.48; p = 0.005). Moreover, we found that patients showed an opposite pattern of activation, whereby correlation with parametric force was higher when the

latter was self-generated (i.e., M1S1 > M0S1; Fig 3B: 38, -24, 56; Z = 2.61; p = 0.048). This seemed to be driven by reduced correlation with force in M0S1 compared to healthy controls (Fig 3C: 36, -24, 52; Z = 3.51; p = 0.005 SVC). Neither group showed significant correlations between received force intensity and brain activity in other ROIs. No group showed force related activation in the side ipsilateral to the hand receiving the tactile sensation in M0S1 in any of our ROIs. Taken together, these findings suggest that in healthy individuals, S1 tunes to parametric forces associated to tactile sensation only when these are externally generated and thus unpredicted. On the contrary, patients fail to show such somatosensory attenuation and instead exhibit more accurate encoding of parametric tactile forces when these are predictable.

We found no difference in motion parameters across groups (see Supplemental Materials), suggesting that residual differences in motion did not contribute to results above. Also, we found no group differences in baseline condition M0S0, for any of our a-priori ROIs. Furthermore, patients exhibited no correlation between chlorpromazine equivalent dosage and peak activation of between groups contrast estimates (see Supplemental Materials), suggesting that antipsychotic medication could not account for observed group differences. We found no correlation between PANSS scores on either the negative or positive subscales and brain activity when investigating the whole brain (FWE correction). However, we did find positive correlations with negative symptoms when investigating activation within our ROIs – these results are reported as exploratory findings in the Supplemental Materials.

Whole-brain analysis revealed significant correlation between exerted force and brain activity in left S1 for the M1S1 condition in healthy controls (-38, -30, 66; Z = 5.08; p = 0.023, FWE). No significant whole-brain activations were found for other brain regions, conditions or symptoms in schizophrenia patients after correcting for multiple comparisons. We therefore report results from a whole-brain analysis with $p < 0.001$ uncorrected in the Supplementary Materials.

Discussion

Motor and somatosensory disturbances are well established in schizophrenia. Initially considered as mere side effects of antipsychotic medication, there is now evidence suggesting

that such disturbances precede the onset of the illness and can be found in drug-naïve patients or first-degree relatives. In line with this, a few studies attempted to investigate the neural mechanisms underlying such disturbances. However, research of this kind is relatively scarce, specifically there is little data regarding the accuracy of the motor and somatosensory system in patients. Here, we were interested in researching the accuracy of the neural signal in detecting parametric variations of force intensity linked to a voluntary motor act or a received tactile-sensation. Moreover, given the hypothesised importance of motor action prediction for sense of agency disturbance in the illness, we were also interested in investigating how the accuracy of the parametric force signal would change as a function of its predictability (i.e., forces being either self- or externally-generated). Note that whereas the influence of predictive mechanisms on somatosensory attenuation has been investigated in relation to general sensory processing[9-10], this has never been investigated in relation to specific features of sensory processing such as parametric force encoding.

Force processing is known to employ key structures of the motor and somatosensory system. In particular, research on healthy individuals has shown a positive correlation between exerted force during a movement and brain activity in contralateral sensorimotor areas[24-25, 37]. Likewise, positive correlations between force intensity and contralateral somatosensory areas have also been found in relation to received tactile-sensations[38-40]. However, how such force processing differs when the tactile-sensation is self, as opposed to externally, generated is unknown. Here, we aimed to investigate force processing in schizophrenia in regards to all the above mentioned aspects. Based on the literature on healthy individuals, we confined our analysis to M1, S1 and SMA.

In healthy controls, we found a positive correlation between exerted force during movement conditions and activation in S1 contralateral to the finger used for movement production. This fits with what has previously been observed in the literature consistent with a somatosensory feedback linked to performing a movement[24-25, 37]. Surprisingly, controls failed to exhibit positive correlation between force and brain activity in motor areas such as M1 and SMA. Lack of activation in SMA may be related to the fact that movements in motor conditions (i.e., M1S1 and M1S0) were here triggered by an external cue (i.e., the appearance of the target on the screen) and were not the product of self-paced voluntary intentions. The role of SMA in differentiating between self-paced and externally-triggered movements has recently received increasing empirical support, confirming the crucial role of SMA in transforming intentions to move into planned and executable voluntary actions[41]. Interpretation of lack of

activation in M1 is harder, as the latter has shown to correlate with force on several occasions[24-25, 27]. It is possible that such discrepancy is attributable to the nature of the task employed here, which required participants to both press and hold down a lever to a certain intensity level. In support of this interpretation, recent studies comparing static and dynamic force movements found that activation with parametric forces was higher when the latter were dynamic compared to static[42]. It is thus likely that press and hold movements more heavily rely on somatosensory feedback than those used to investigate force processing in other studies (e.g., precision grip force, opposition force, etc.), hence resulting in lack of force-related M1 activation in our study.

Patients exhibited increased correlation between forces and brain activity in S1 (contralateral to the movement) when actively pressing the lever (i.e., M1S1 and M1S0). One potential interpretation for this finding links to sensory attenuation disturbances. As the sensation is associated to a self-generated motor act, accurate force processing can be attenuated in healthy individuals. Increased correlation between somatosensory activation and force in patients compared to healthy individuals might reflect lack of such attenuating mechanism. However, such interpretation remains speculative, as the current paradigm does not allow testing sensory attenuation linked to the finger performing the movement.

With regards to processing of applied tactile force, healthy controls exhibited a positive correlation between the intensity of the sensation on the left finger and activation in contralateral S1 when the sensation was externally generated, but not when this was self-produced. This finding resonates with observations that tactile-sensations are attenuated when self-generated, and thus predicted, as opposed to when they are externally generated and thus unpredicted[9-10]. Likewise, one might expect that accurate encoding of forces is only really necessary when the sensation is not predicted. As a result of this, somatosensory areas would not tune to parametric variations of forces when these are self-generated. Note that this would not be the case, in healthy controls, for somatosensory activation associated to body parts involved in generating movements, as discussed above, as this would still be relevant for the accurate performance of the task.

Contrary to controls, schizophrenia patients showed no correlation between force and activation in S1 when receiving an externally generated tactile-sensation (M0S1). This resulted in patients failing to show increased S1 activation when receiving an externally generated tactile sensation (M0S1) compared to a self-generated one (M1S1). Remarkably, in

patients the sensory signal encoding parametric tactile force was higher when the force could be predicted (M1S1) as opposed to when it was unpredicted (M0S1). A possible explanation of this result relies on sensory integration accounts, which emphasise the interplay between predictive and postdictive mechanisms in the experience of agency[43]. In particular, individuals with schizophrenia have been shown to rely more on visual postdictive feedback associated to motor actions[44]. In our study, an increased weight attributed to visual postdictive feedback may lead patients to be less accurate in conditions when such visual feedback is unrelated with the level of tactile stimulation. This lack of relationship characterizes M0S1 alone (and not M1S1, M1S0, M0S1) where, by design, tactile forces generated by the apparatus did not correspond to visual information on the screen. The hypothesis that patients' somatosensory encoding relies largely on visual feedback might entail a decreased influence of motor predictions and in turn a decreased attenuation[43]. This connects to data reported above showing an increased accuracy for both M1S1 and M1S0 in left S1 (associated to the pressing finger) in patients compared to controls. Future studies should aim to test whether an increased weight on postdictive visual feedback is directly associated with a decreased weight on tactile predictions (derived from motor commands) which in turn may be responsible for decreased attenuation of tactile inputs in schizophrenia. More insight on the matter may be gained by investigating the anticipatory mechanisms involved in motor execution and receipt of tactile sensation. It is indeed possible that groups differ in the way they prepare for the task, also influencing the weight attributed to the various predictive and postidictive components involved.

This study presents a number of limitations. First, all patients were on stable antipsychotic treatment at the time of the experiment, possibly affecting our results. The effects of antipsychotic medication on the motor system are unclear, with studies reporting improvement, deterioration or no change on motor disturbance as a result of treatment[45]. However, we here found no association between medication dosage and brain activity in patients suggesting that our results were not due to antipsychotic medication. Second, we did not collect information on constancy of response across time, which may have had an impact on task performance. Third, this study failed to stratify patients on the basis of their specific motor profile. Indeed, recent studies suggest that specific motor disturbances may be associated with specific patterns of brain dysfunction[21]. Particularly relevant for the current task are models of motor slowing, which propose that the latter may be associated with defective interaction of cortical and subcortical areas of the motor loop accompanied by

compensatory mechanisms from the premotor cortex[46]. It is hard to reconcile these models with our findings, as we failed to find activity in premotor areas and did not collect information regarding motor slowing. In order to investigate whether motor slowing affects encoding of parametric forces, future studies should stratify patients on the basis of their motor profile while also using a force task that better taps on SMA and pre-SMA functioning. Lastly, we failed to show a correlation between positive symptoms and predictive dysfunctions in patients. One possible reason links to our sample, which did not provide sufficient sensitivity on the delusional scale, most often associated to dysfunctions in prediction and sense of agency[10, 43].

In sum, our results point towards alterations in the encoding of parametric force in the motor and somatosensory domain in patients affected by schizophrenia. Particularly affected seems to be the processing of the somatosensory feedback associated to parametric force, putatively linked to defective prediction and sensory integration mechanisms. This study also confirms the utility of using functional imaging to probe cortical response to elementary sensorimotor stimuli, in addition to the more conventional investigation of higher order cognitive processing. We suggest that future research on the topic would benefit from the investigation of the specific functional features involved in motor and somatosensory processing. In particular, mapping alterations in these components with the different motor profile of patients may increase our understanding of these often under-recognised symptoms[46].

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Table 1

Demographic and clinical characteristics	**SCZ (n = 21)**	**HC (n = 26)**	**Test statistic**	**P value**
Age: mean (SD)	36.1 (8.23)	32.23	t (44) = 1.05	0.3

		(8.46)		
Gender/male: n (%)	3 (14.29)	11 (42.31)	FET	0.06
Handedness/right: n (%)	21 (100)	26 (100)	--	--
PANSS Positive: mean (SD)	18.25 (5.64)	--	--	--
PANSS Negative: mean (SD)	13.2 (3.14)	--	--	--
PANSS General: mean (SD)	33.65 (5.96)	--	--	--
Medication: mean (SD)[a]	315.33 (270.35)	--	--	--

SCZ: volunteers diagnosed with schizophrenia, HC: healthy controls, SD: standard deviation, PANSS: Positive and Negative Syndrome Scale, FET: Fisher's Exact Test.
[a] Chlorpromazine equivalent (mg per day) – all volunteers were on stable atypical medication

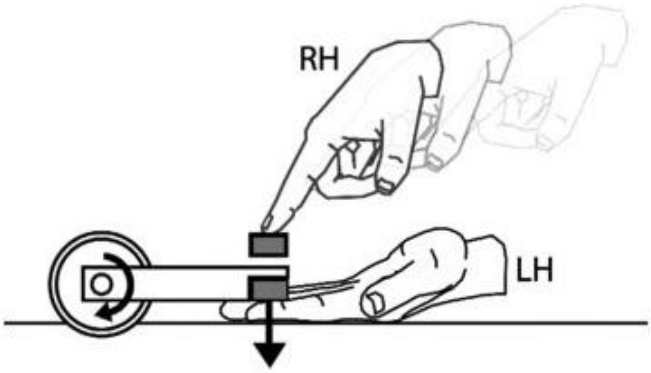
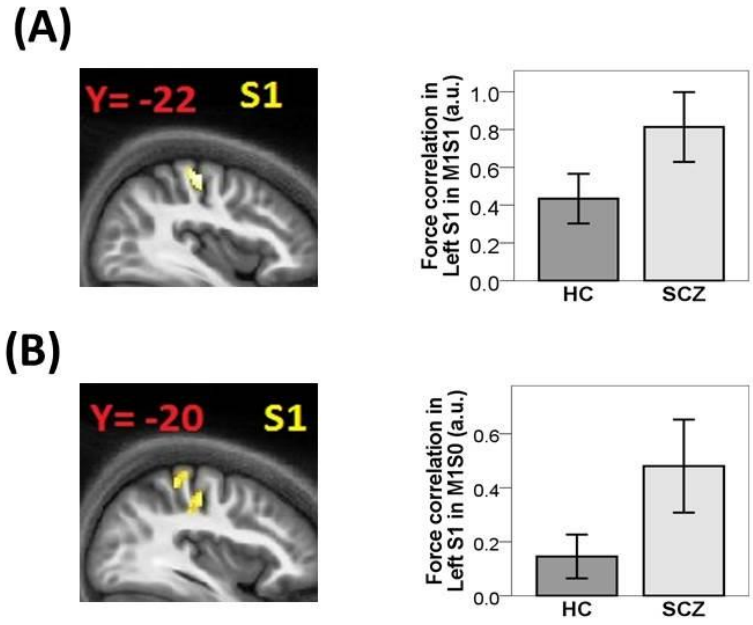


Figure 1

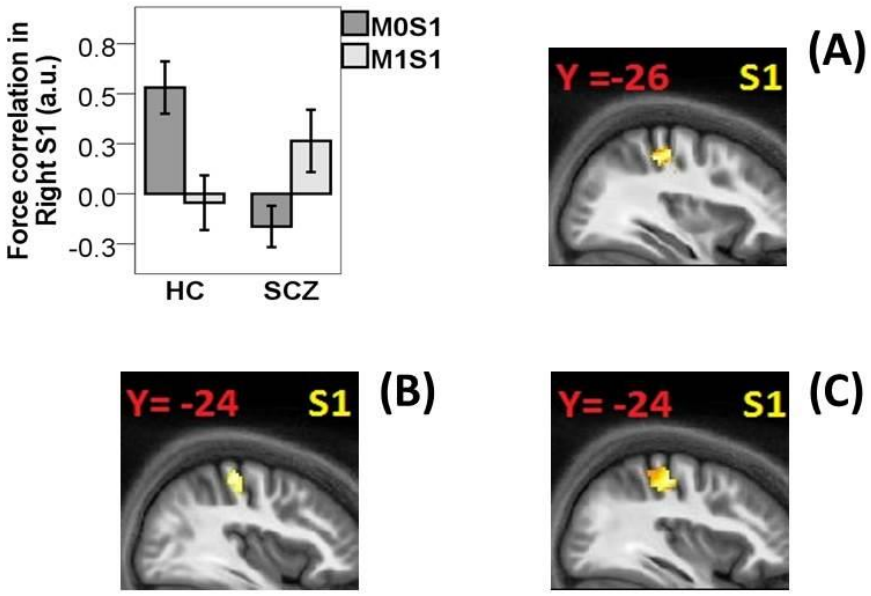
The apparatus permitted to transmit a force generated by the right index finger to the left index finger (M1S1) or not (M1S0), due to the ability of the torque motor to move so as to reflect (on the left finger) the movement performed by the right finger or to remain still. Likewise, a tactile sensation caused by the lever pressing against the left index finger could be caused by a self-initiated movement with the right finger (M1S1) or by the movement of the torque motor without any involvement of the right finger (M0S1). In movement conditions (M1S1 and M1S0), force increments were achieved by asking participants to press a lever in order to match a visual force target on the screen, in that different visual target levels corresponded to different force levels. In M0S1, force increments on the left finger were automatically delivered by the apparatus and participants viewed randomly selected replays of target force movements from previous press blocks. The latter was done to match conditions on visual stimulation, while predicting unpredictability of force intensity.

Figure 2



(A) Activation in left S1 comparing patients vs. controls for the correlation of parametric force for motor condition in M1S1 (right finger performing the movement); (B) Activation in left S1 comparing patients vs. controls for the correlation of parametric force for motor condition in M1S0 (right finger performing the movement). Figures show the peak voxel statistics for the between groups contrasts within the ROI (SVC, $p < 0.05$ FWE).

Figure 3



(A) Activation in right S1 comparing externally-generated (M0S1) vs. self-generated (M1S1) parametric sensation in controls for the correlation of parametric tactile sensation (left finger receiving tactile sensation); (B) Activation in right S1 comparing self-generated (M1S1) vs. externally-generated (M0S1) in patients for the correlation of parametric tactile sensation (left finger receiving tactile sensation); (C) Activation in right S1 comparing controls vs. patients for the correlation of parametric tactile sensation in M0S1 (left finger receiving tactile sensation). Figures show the peak voxel statistics within the ROI (SVC, $p < 0.05$ FWE).