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“Wrong Way Up”: Temporal and Spatial Dynamics of the Networks for Body Motion Processing at 9.4 T

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Abstract

Body motion delivers a wealth of socially relevant information. Yet display inversion severely impedes biological motion (BM) processing. It is largely unknown how the brain circuits for BM are affected by display inversion. As upright and upside-down point-light BM displays are similar, we addressed this issue by using ultrahigh field functional MRI at 9.4 T providing for high sensitivity and spatial resolution. Whole-brain analysis along with exploration of the temporal dynamics of the blood-oxygen-level-dependent response reveals that in the left hemisphere, inverted BM activates anterior networks likely engaged in decision making and cognitive control, whereas readily recognizable upright BM activates posterior areas solely. In the right hemisphere, multiple networks are activated in response to upright BM as compared with scarce activation to inversion. With identical visual input with display inversion, a large-scale network in the right hemisphere is detected in perceivers who do not constantly interpret displays as shown the “wrong way up.” For the first time, we uncover (1) (multi)functional involvement of each region in the networks underpinning BM processing and (2) large-scale ensembles of regions playing in unison with distinct temporal dynamics. The outcome sheds light on the neural circuits underlying BM processing as an essential part of the social brain.

Key words: body motion, BOLD response, display orientation, large-scale networks, point-light displays, temporal dynamics, ultrahigh field fMRI, whole-brain analysis

Introduction

Visual tuning to human body motion may serve a hallmark of daily-life social cognition, and a basis for nonverbal communication and social competence (Pavlova 2012). Effective social interaction often relies on detection of subtle cues revealed from body motion of a social counterpart (Krüger et al. 2013; Miller and Saygin 2013). The ability to correctly interpret body motion is impaired in many neurodevelopmental and psychiatric conditions such as autism (Klin et al. 2009; Kaiser et al. 2010). Human newborns at high risk of autism do not exhibit any visual preference for body motion as typically developing infants do (Di Giorgio et al. 2016). In experimental research, body motion is frequently represented as a set of moving dots on the joints of an invisible body (impoverished displays with point-light biological motion [BM], see Fig. 1) that helps to isolate information revealed by motion from other cues. A wealth
of brain imaging and neuropsychological work points to the distributed circuits engaged in BM processing with foci in the parieto-temporal junction and fusiform gyrus, and subcortical structures such as the cerebellum, with the pivot in the right superior temporal sulcus (STS) (Grossman et al. 2000; Vaina et al. 2001; Grossman and Blake 2002; Beauchamp et al. 2003; Saygin et al. 2004; Peuskens et al. 2005; Gobbini et al. 2007; Herrington et al. 2011; Sokolov et al. 2012, 2014; Han et al. 2013; Jastorff et al. 2016). In the right STS, this network likely topographically overlaps and communicates with the social brain, the neural circuits underpinning our ability for understanding emotions, drives, and dispositions of others (Pavlova 2012). Yet we are still far away from understanding proper functioning of these networks.

Visual psychophysics points to orientation specificity in BM perception (Pavlova and Sokolov 2000). Display inversion (180° rotation in the image plane) severely impedes performance on a variety of perceptual tasks (Sumi 1984; Shipley 2003; Troje and Westhoff 2006; Neri et al. 2007), and the inversion effect increases in elderly (Pilz et al. 2010). In the social domain, reading of body language from point-light displays representing dance (Dittrich et al. 1996), body expressions (Clarke et al. 2005), and interpersonal dialogue (Atkinson et al. 2007) is substantially weakened by upside-down presentation. Earlier work shows that inversion prevents human infants from discrimination of BM from similar displays (Bertenthal 1987). Even newly hatched chicks appear to have a predisposition for upright display orientation (Vallortigara and Regolin 2006), and 2-day-old human newborns prefer upright over inverted displays (Bardi et al. 2014). Infants aged 12 months share attentional tuning expressed by an upright oriented, but not by inverted point-light social agents (Yoon and Johnson 2009). At 14 months, infants detect other people’s interactions in BM displays, but not with inversion (Galazka et al. 2014).

The primary advantage of upside-down presentation is that an inverted display retains the same relational structure and amount of motion as an upright one, thereby, keeping the same amount of sensory information available. Equally important, neither with upright nor with inverted display orientations single components of point-light displays explicitly trigger body recognition process. These are 2 decisive reasons why inversion often serves as a control for proper BM processing in healthy perceivers and patients with neuropsychiatric disorders: in adolescents who were born preterm (Pavlova et al. 2006), children with autistic spectrum disorders (Klin et al. 2009), neurosurgical patients with cerebellar tumors (Sokolov et al. 2010), and patients with schizophrenia (Spencer et al. 2013).

What is happening in the brain when we see BM presented upside-down? It is still largely unclear how brain networks underpinning upright BM processing are affected by displays presented the “wrong way up.” An easily recognizable upright point-light walker robustly elicits consecutive peaks of oscillatory magnetoencephalographic (MEG) cortical activity over the left occipital, bilateral parietal and right temporal cortices. Yet under inverted conditions, the boosts of oscillations are topographically restricted to the left occipital cortex (Pavlova et al. 2004). This outcome points to importance of the bilateral parietal and right temporal cortices for veridical BM processing. Previous very few fMRI studies (Grèzes et al. 2001; Grossman and Blake 2001; Peuskens et al. 2005) that used magnetic field strength of 1.5 T and, thereby, with limited sensitivity and
rather coarse spatial resolution, were mainly restricted to analysis of activation in predefined regions of interests (ROIs), such as the posterior STS (pSTS) and might have been incapable to capture alterations in the whole-brain activation. At higher magnetic field strengths, fMRI sensitivity increases substantially (Duyn 2012), and is expected to enable revealing whole-brain activation even under subtle variations in functional signals. As upright and inverted BM displays are rather similar, fine-grained modulation of brain circuits driven by cognitive processing of comparable visual input can presumably be detected. The motivation of the present work was to uncover alterations in the brain circuits underlying BM processing elicited by display inversion, and thereby, better understand networks underlying proper BM processing. We intended to clarify: (1) whether and, if so, how neural circuits are affected by inversion and (2) how brain activity in response to inverted BM differs as a function of display interpretation. With this purpose in mind, by using whole-brain coverage, we conducted ultra-high field fMRI recording at magnetic field strength of 9.4 T providing for high sensitivity and spatial resolution. Previous fMRI work has been entirely restricted to localization of brain areas involved in BM processing. Yet for understanding proper functioning of neural circuits, one has to consider dynamical changes in brain activation unfolding over time: distinct networks can be topographically similar, but differ from each other in terms of temporal dynamics. Therefore, after identification of the key brain areas involved, we analyzed temporal dynamics of the blood-oxygen-level-dependent (BOLD) response by dividing the entire display duration into intervals. This analysis was motivated by a desire to characterize the (multi)functional role of the brain areas playing in unison at different time points and, thus, making up diverse neural circuits engaged in BM processing.

Material and Methods

Participants

In total, 25 paid right-handed male volunteers with normal or corrected vision were enrolled in the study. As BOLD response in females fluctuates with menstrual cycle, sex-specific influences may be potentially expected. Sex differences are reported in both hemodynamic (Anderson et al. 2013) and neuromagnetic (Pavlova et al. 2015) brain responses to BM. For attaining a homogeneous BOLD signal, therefore, male volunteers only were recruited. One of participants did not follow instruction, and in the other one the lower parts of occipital cortices were not properly covered. This left the data sets from 23 participants aged 26.75 ± 7.72 years (mean ± SD). None had a history of neurological or psychiatric disorders, nor regular drug intake (medication). They were naïve as to the purpose of the study. Informed written consent was obtained from all participants in accordance with the requirements of the local Ethics Committee at the University of Tübingen Medical School.

Stimuli, Task, and Experimental Design

Point-light stimuli used are described in detail elsewhere (Pavlova et al. 2004). Participants were presented with a canonical point-light walker consisting of 11 dots placed on the head and main joints of an invisible human figure shown either with upright or inverted (180° rotation in the image plane) orientation (Fig. 1). The walking figure, facing either right or left, was seen moving as if on a treadmill. A gait cycle was completed in 40 frames with frame duration of 31 ms that produced a walking speed of about 48 cycles per minute. The configurations were generated by Cutting’s algorithm (Cutting 1978), and subtended a visual angle of 4° in height and 3.5° in width at the most extended point of a gait cycle. In 3 separate runs, participants were presented with a pseudorandomized set of 48 displays (2 orientations [upright/inverted] × 2 facing directions [right/left] × 4 times × 3 runs) using the Presentation software (Neurobehavioral Systems, Inc., Albany, CA, USA). Outside the scanner (just before recording sessions), examples of movies were shown to acquaint participants with the stimuli. All participants easily recognized an upright walker. Participants had to perform a 2-alternative forced-choice (2AFC) task; by pressing a respective key, they indicated whether an upright point-light walker facing right or left, or control configurations (the same displays shown upside-down that participants were not informed about) were presented. This task obligates attention to both types of stimuli and, therefore, reduces possible attention effects on recorded brain activity. To minimize possible influences of motor responses on recorded activity, participants had to respond following the offset of each stimulus. Participants were asked to visually fixate an area where a white cross in the middle of the screen appeared between trials. Each stimulus appeared for 20 s on a blank screen with an inter-stimulus interval of 16 s. Following the whole recording session, participants were debriefed outside the scanner indicating any stimulus interpretations they might have had.

fMRI Recording and Data Preprocessing

Measurements were performed at a 9.4 T scanner equipped with whole-body gradients (Siemens Medical Systems, Erlangen, Germany) and a head coil with a 16-channel, dual row transmit array and 31-channel receive array (Shajan et al. 2014) operating in the circularly polarized transmit mode. The measurement protocol consisted of scout imaging, B0 shimming, mapping of the B1 transmit field, and adjustment based on flip angle values found in cortical areas, anatomical imaging, and acquisition of 3 runs of fMRI recording. B1 mapping was performed by using the Actual Flip Angle Method (Yarnykh 2007) with the following parameters: repetition time (TR) 20/100 ms; echo time (TE) 7 ms, 3 × 3 × 5 mm² voxel size, nominal flip angle (FA) 60°; total acquisition time (TA) 3 min 45 s. For anatomical imaging, the MP2RAGE sequence was used with an isotropic resolution of 0.8 mm, inversion time (TI): 700/2500 ms; TR: 8894 ms, TE: 2.3 ms, FA: 4°/5°; gradient echo TR: 6 ms, Grappa factor 3, partial Fourier acquisition ¼, TA: 8 min 53 s. Prior to image segmentation, the MP2RAGE contrast images were corrected for deviations of the read-out flip angle and the inversion efficiency (Hagberg et al. 2017). Standard image segmentation and normalization into MNI space were then conducted by using SPM12 (http://www.fil.ion.ucl.ac.uk/spm), without need for additional bias correction. fMRI scanning was performed using a 3D EPI sequence (Poser et al. 2010) with TR: 1287 ms, TE: 18 ms, isotropic voxel size: 1.5 mm, and 8-fold acceleration (2 directions, 2 × 4); FA = 15°. For each run, a total of 450 images were acquired (TA: 581.4 s – 10 min). During each run, stimulus onset, stimulus type, key-press responses, and start of each EPI volume were recorded using the Presentation software.

For each participant, preprocessing was performed with SPM12 (revision 6470). After conversion of DICOM files to NIfTI-1 data, and manual setting of the anterior commissure location to the origin of the coordinate system based on the MP2RAGE contrast images, tissue segmentation was performed. The EPI images were motion corrected (linear realignment), and a mean functional image was generated across all runs. This image was then used for tissue segmentation including bias intensity correction. Co-registration of the functional EPI scans
to the anatomical MP2RAGE image was made by estimating the transformation matrix from segmented images (sum of the gray and white matter tissues masks). For image transformation to the common MNI brain atlas, calculation of nonlinear transforms were made with DARTEL (Ashburner 2007). Within this framework, a study specific template was derived from all participants based on the MP2RAGE contrast image prior to linear registration to the MNI template. Finally, the resulting flow fields were used to transform the coregistered EPI images to MNI space prior to spatial smoothing (by means of an isotropic Gaussian blurring kernel with a FWHM of 3 mm).

fMRI Analysis

For calculation of the statistical model used for the first (individual) level analysis, the onsets of the different stimuli were extracted from the individual Presentation log files with an in-house Matlab script. In order to analyze the task-related temporal dynamics of the BOLD response during display exposure, the 20 s stimulus interval was subdivided into 4 sub-intervals, each lasting 5 s (timeBins 1–4). Each time bin was convolved with the canonical hemodynamic response function, resulting in 8 regressors (4 for the upright and 4 for the inverted BM conditions) for each run (Runs 1–3) included in the design matrix. This yielded a total of 24 (= 8 x 3) regressors along with 3 regressors of no-interest for the mean value of each run.

For the second (group) level analysis, 2 models were generated for evaluation of additionally smoothed (6 mm FWHM) first level contrast images. (The additional smoothing takes into account the residual variability of the brain areas after spatial normalization.) By using the first model, condition-dependent main effects, difference contrasts, and the temporal dynamics of the BOLD response were analyzed, whereas a second model was used to additionally assess interaction effects between factors Bin and Group. Based on the outcome of subsequent debriefing, participants were subdivided into perceivers who did not recognize an inverted control display as BM and/or reported multiple display configurations (the same displays shown the "wrong way up" that participants were not informed about) and perceivers who did recognize an inverted display as BM (Group 2/G2; N2 = 10).

The first statistical model represented an analysis of variance, ANOVA, with factors Bin (1–4), Run (1–3), Condition (upright/ inverted BM), and Group (G1/G2) resulting in 48 regressors for a total of 552 input images (23 participants with 24 first-level contrast images for each). The factor Run was included, because effects of implicit learning and attentional fluctuation may be potentially expected in the course of recording session consisting of 3 runs. By using this model, condition-dependent main effects (for either upright or inverted BM compared with baseline) and display orientation-specific difference contrasts (upright vs. inverted and inverted vs. upright BM) were analyzed. The second statistical model was created to assess the interaction effect between the Bin and Group factors. This analysis was based on first-level contrast images generated as the bin-specific difference between inverted and upright BM conditions averaged across all 3 runs. In addition to the factors Group, Bin, and Participant, the model contained the Group x Bin interaction term, resulting in 37 (2 + 4 + 23 + 2 x 4) regressors for 92 (4 x 23) first-level contrast images. Finally, for better evaluation of factors’ contribution and their interaction, individual parameter estimates in significantly activated brain areas were analyzed by ANOVAs with the software package JMP (V11.1 SAS Institute Inc. 2013; Cary, NC). For each participant, the contrast estimates within each activated brain area were extracted from the contrast image and averaged using in-house Matlab code. The outcome of these analyses is given in Supplementary Materials.

The temporal dynamics of the BOLD response was analyzed within the brain areas exhibiting activation during processing of upright (vs. inverted) and inverted (vs. upright) BM. First, independent of display condition, temporal contrasts of each bin with respect to the weighted average of 3 other bins were evaluated, either with positive (for a relative increase, “inc”) or negative (for a relative decrease, “dec”) weights resulting in 8 temporal (bin-related) contrasts. We then calculated t-values for each of these temporal contrasts at each peak of activation from the parameter estimates extracted for each individual participant (Supplementary Material, Table S2). As indicated by this analysis, significance (P < 0.01, uncorrected) was reached for 4 out of 8 temporal contrasts in: BinInc [1, −1/3, −1/3, −1/3], Bin2dec [1/3, −1/3, −1/3, −1/3], Bin3dec [1/3, 1/3, −1, −1/3], and Bin4inc [−1/3, −1/3, −1/3, 1] (temporal contrast, see Supplementary Material, Table S2).

Second, within each bin, we assessed whether activation exhibited display-orientation specificity, or, in other words, whether within each single time bin a significant difference (P < 0.01, uncorrected) occurred between either upright versus inverted or inverted versus upright BM. For this purpose, we calculated t-values for the display-orientation contrasts within single time bins (“condition contrast,” see Supplementary Material, Table S2). Similar analysis had been conducted for brain areas with a significant Group effect in the first statistical model; we evaluated temporal dynamics of the BOLD response in these areas by using the first-level contrast images from the first statistical model (see Supplementary Material, Table S3).

For determination of the anatomical labels for the activated brain areas, the Automated Anatomical Labeling (AAL) Atlas (Tzourio-Mazoyer et al. 2002) was used.

Results

Performance: Behavioral Data

Participants were administered a 2-alternative forced-choice (2AFC) task: by pressing a respective key, they indicated whether an upright point-light walker or control configurations (the same displays shown the "wrong way up" that participants were not informed about) were presented. They performed the task with great accuracy, reaching ceiling level of performance. On overall, the percentage of errors was negligible: only 0.27% misses (no response) and 0.64% incorrect responses (either “control display” to an upright walker or vice versa). This indicates that participants were alert during the whole recording session.

BM Presented Upright and Upside-Down

The whole-brain analysis of display-specific main effects (upright BM vs. baseline and inverted BM vs. baseline) revealed that both upright and inverted BM elicited topographically similar and partly overlapping clusters of activation in the occipital cortices including bilateral superior and middle occipital gyri, right calcarine fissure, cuneus, and the left middle occipital gyrus (Fig. 2A). Beyond the occipital cortices, several clusters were activated bilaterally in the inferior and superior parietal gyri, precuneal, postcentral and frontal cortices, in the right middle and superior temporal gyri, and in the left fusiform gyrus (P < 0.05, FWE; see also Supplementary Material, Table S1). Bilateral activation in response to both upright and inverted BM was also observed in such deep structures of the brain as the hippocampus and thalamus including...
Figure 2. Functional MRI activation to biological motion presented upright and upside-down. (A) Left column: areas of overlapping fMRI activation (yellow) in response to upright (green) and inverted (orange) biological motion (BM), middle and right columns: t-values for the main effects of the whole-brain fMRI activation in response to upright and inverted BM, respectively. Upright and inverted displays elicit overlapping clusters of activation with greater voxel numbers for upright BM with the only exception of the left fusiform gyrus. The activated regions are displayed as maximum intensity projections (MIP) to the corresponding planes. For separation of the regions from each other, different thresholds were adopted as shown on the right side; they are also represented as black contours in the middle and right rows. (B) Examples of 2 patterns of topographical overlapping in activation for upright and inverted BM: (1) "an egg sunny-side up": areas of activation for either inverted BM (upper row, the left fusiform gyrus) or upright BM (middle row, the left lingual gyrus) that are surrounded by activated voxels for either upright or inverted BM and (2) "a double mushroom": partly overlapping areas of activation for upright and inverted BM, also possessing voxels activated for upright or inverted BM separately in the right inferior parietal gyrus (lower row). Activation is shown on the anatomical slices of one representative participant. For MNI coordinates, see Supplementary Material, Table S1.
the pulvinar. The right thalamus along with the pulvinar was involved stronger than hippocampus (50% vs. 16% voxels of the activated area, respectively) or the left thalamus (25% of voxels), whereas the left thalamus and hippocampus were almost equally engaged. In all these areas, upright BM activated greater numbers of voxels as compared with inverted displays, with the only exception of the left fusiform gyrus, where a greater number of voxels was found for inverted BM (see Supplementary Material, Table S1). Figure 2B illustrates 2 patterns of topographical overlap in peaks of activation in response to upright and inverted BM: (1) an "egg sunny-side up": areas of activation for either inverted or upright BM that are surrounded by activated voxels either for upright or inverted BM and (2) a "double mushroom": partly overlapping areas of activation in response to both upright and inverted BM, also possessing voxels activated either for upright or inverted BM separately. These 2 patterns occur equally often across activated areas: whereas in some regions inverted BM simply activates fewer voxels, in other regions peaks of activation for upright and inverted BM are topographically shifted relative to each other (see Supplementary Material, Table S1).

**Contrasts Upright Versus Inverted BM**

As seen in Figure 3, the whole-brain analysis indicates that upright BM as compared with upside-down presentation elicits 2 most pronounced areas of activation in the upper part of the occipital cortices, namely, (1) superior (48% of voxels) and middle (44%) occipital gyri, and calcarine fissure (8%) in the left hemisphere and (2) the cuneus (49% of voxels), superior occipital gyrus (35%), and calcarine fissure (12%) in the right hemisphere ($P < 0.05$, FWE). The opposite contrast results in 2 areas of activation in the lower parts of the occipital cortices: (1) the left lingual gyrus (73% of voxels), calcarine fissure (19%), and fusiform gyrus (5%) and (2) the right lingual gyrus (98% of voxels) ($P < 0.05$, FWE). With both contrasts, therefore, activation in the right and left hemispheres are not topographically symmetrical.

This also holds true for the strength of activation. For both contrasts, the individual parameter estimates averaged within activated regions were submitted to an analysis of variance, ANOVA, with subsequent post hoc comparisons (Supplementary Material). Although with the contrast inverted versus upright BM, activation in the left and right hemispheres was of the same strength, with the opposite contrast, activation in the right hemisphere was greater than in the left one (Tukey HSD, $Q = 2.573$, $P < 0.05$).

Additional brain areas with greater activation either for upright or inverted BM ($P < 0.01$ unc.) are listed in Supplementary Material, Table S2 and shown in Figures 3–5. As seen in Figure 5, in the left hemisphere, inverted displays activate several anterior brain areas, whereas upright BM elicited activation in posterior brain areas solely. In the right hemisphere, more areas are activated in response to upright than inverted BM.

**Figure 3.** Contrasts between upright and inverted biological motion. (A and B) Whole-brain contrast between upright and inverted BM, (A) the same areas of activation $2 \times$ zoomed. (C and D) Whole-brain contrast between inverted and upright BM, (D) the same areas of activation $3 \times$ zoomed. As seen on the rendered brain representations, upright BM elicits most pronounced activation in the bilateral superior occipital gyri and cuneus, whereas the inverted BM results in bilateral activation of lower occipital cortices, primarily, the lingual gyrus ($P < 0.05$, FWE). Additional regions (on the slices, $P < 0.01$ unc.) with greater activation for upright BM: the right fusiform gyrus, left inferior temporal gyrus, portions of bilateral middle temporal gyrus, portions of the left middle occipital gyrus, right superior temporal gyrus, bilateral precuneus, left medial cingulate gyrus, left inferior parietal gyrus, bilateral inferior frontal gyrus, left inferior parietal gyrus, right middle frontal gyrus. Regions with greater activation for inverted BM: the right inferior temporal gyrus, bilateral superior occipital gyrus, portions of the left precentral gyrus and the right anterior cingulate gyrus, left middle temporal gyrus, left middle and superior frontal gyrus, and bilateral superior parietal gyrus. Activation is shown on the anatomical slices of one representative participant. For MNI coordinates, see Supplementary Material, Table S2.
Temporal Dynamics of the BOLD Response

Within the brain areas activated during processing of upright (vs. inverted) and inverted (vs. upright) BM, we analyzed the temporal dynamics of the BOLD response. By doing so, one better understands involvement of each region in the networks underpinning BM processing. Many brain areas are multifunctional, and at different time points they may be recruited by distinct networks subserving different stages of display processing (such

Figure 4. Examples of temporal dynamics patterns. Left column: Activation amplitude exhibits distinct temporal dynamics during stimulus duration: pattern (A), a decrease in activation in the second 5 s of stimulus duration (time Bin 2) with a recurrent increase afterwards in the right lingual gyrus (contrast inverted vs. upright BM); pattern (B), a decrease in the second 5 s (time Bin 2) with a subsequent increase in the last 5 s (time Bin 4) of stimulus duration in the right inferior frontal gyrus (contrast upright vs. inverted BM); and pattern (C), an increase in the last 5 s (time Bin 4) of stimulus duration in the right superior parietal gyrus (contrast inverted vs. upright BM). Parameter estimates (PE) in arbitrary units (au) averaged over participants for each temporal interval of 5 s (time bin) are plotted with ± SD, standard deviations (thin vertical bars), for upright (dark green lines and bars) and inverted (orange lines and bars) BM. Right column: Brain activation is overlaid onto anatomical slices of the whole brain (top), and 3× zoomed (bottom) for each panel. (Areas of partial signal drop-out related to B1 transmit field are seen in the cerebellum and to a lesser extent in the inferior temporal cortex, see Discussion.)
Fluctuations in temporal dynamics of the BOLD response can also exhibit display-orientation specificity; in each single time interval, the BOLD response may be greater for either upright or inverted BM.

Figure 4 illuminates 3 main patterns of temporal dynamics (independent of the first 5 s, Bin 1, where the BOLD response always increases).

Pattern A represents a decrease in the second 5 s of stimulus duration (Bin 2), with a recurrent increase afterwards (Fig. 4A). This pattern of activation is typical for the regions that are known to be involved in sensory and cognitive BM processing. For contrast upright versus inverted BM, such areas are 2 portions of the left middle occipital gyrus, and the right superior occipital and middle temporal gyrus (Fig. 5, see Supplementary Material, Table S2). For a portion of the left middle occipital gyrus and the right middle temporal gyrus, this decrease is display-orientation specific. For the opposite contrast, the bilateral lingual gyri and right superior occipital gyrus exhibit this pattern.

Pattern B exemplifies a decrease in the second 5 s (Bin 2) with substantial increase in the last 5 s (Bin 4) along with an (either abrupt or steady) increase in Bin 3 (Fig. 4B). Brain areas with this pattern are likely to be multifunctional, and engaged in both cognitive processing and decision making. For contrast upright versus inverted BM, these areas are shown in Figure 5A. A decrease in Bin 2 is display-orientation specific for the bilateral precuneus, right cuneus and inferior frontal gyrus, left medial cingulate/paracingulate gyrus, and the left middle occipital gyri (Fig. 5A, see Supplementary Material, Table S2). In other words, in Bin 2, these brain areas differentiate between upright and inverted BM. For the opposite contrast, 2 portions of the precentral gyrus, superior parietal gyrus, and the middle frontal gyrus in the left hemisphere, and the anterior cingulate/paracingulate gyrus, and inferior temporal gyrus in the right hemisphere.
hemi- nosphere show this pattern (Fig. 5B). In 2 portions of the left precentral cortex, increase in Bin 4 is display-orientation specific.

Pattern C represents an increase in the last 5 s of stimulus duration (Bin 4). This pattern is specific for the regions which are known to be involved in decision making and readiness to motor responses (Fig. 4C). For the contrast upright versus inverted BM, these areas are the right middle frontal and temporal gyri (Fig. 5A). For the opposite contrast, these areas are the right anterior cingulate/paracingulate gyri and superior parietal gyrus, both of which differentiate between upright and inverted BM (Fig. 5B).

Figure 5 provides the overview of regions exhibiting similar temporal dynamics, and thus playing in unison. These areas form up large-scale networks underpinning processing of upright and inverted BM. In the left hemisphere, inverted BM primarily activates anterior networks engaged in decision making, and cognitive control, whereas upright BM elicits activation in posterior brain areas exclusively. In the right hemisphere, multiple networks are activated in response to upright BM as compared with a few areas activated in response to inverted displays.

**Brain Activation as a Function of Display Interpretation**

All participants readily reported seeing the upright walker. Despite the same visual input under inverted conditions, part of them (Group 1/G1) either did not recognize an inverted display as a walker (they reported 3D rotation, double helix DNA or flies hovering in circle) or provided multiple interpretations of the display with spontaneous switch from one interpretation to another. Other participants (Group 2/G2) reported seeing the same point-light walker presented the "wrong way up."

G1 exhibited greater activity in response to an inverted display than G2 in the right hemisphere with peaks of activation in the (1) lingual gyrus, (2) postcentral gyrus, and (3) rolandic operculum (P < 0.05, FWE; Fig. 6). An ANOVA along with post hoc analyses (Supplementary Material) indicated that with upright orientation, there was a lack of difference in activation between G1 and G2 whereas with inversion, activation was greater in G1 for all 3 brain areas (Q = 2.572, P < 0.05). This dissociation points to the percept-related specificity of activation in these areas. Temporal dynamics of activation also varied within the areas: the right lingual gyrus demonstrated a typical stimulus-specific decrease in Bin 2 (pattern A), whereas both the right postcentral gyrus and rolandic operculum exhibited stimulus nonspecific increase in Bin 4 (pattern C) (Fig. 6). The same outcome delivers the analysis of temporal dynamics as reported in Supplementary Material, Table S3. To sum up, in perceivers who did not constantly interpret BM as shown the "wrong way up," we detected peaks of activation in the right brain hemisphere forming up a large-scale network of regions with distinct functional involvement. The fine-grained modulation of brain activation of this network is driven solely by cognitive processing of identical point-light stimuli under the same task demands.

**Discussion**

The present work was aimed at uncovering alterations in the whole-brain circuits elicited by inversion of BM displays, and thereby, at better understanding the networks underlying proper BM processing. As upright and inverted BM displays are rather similar, we used whole-brain ultrahigh field fMRI at 9.4 T with high sensitivity and spatial resolution taking advantage of high field strength.

**BM Presented Upright and “Wrong Way Up”**

Both upright and inverted BM (as compared with baseline) elicited rather similar patterns of activation with a greater number of activated voxels for upright BM (Fig. 2, see Supplementary Material, Table S1). The only region with a greater number of activated voxels for inverted BM was the left fusiform gyrus. This region is reported to be engaged in body mental rotation (Tomasino and Greimese, 2016). Several of the activated brain regions (such as fusiform gyrus, calcine sulcus, middle occipital and temporal gyrus, right superior temporal gyrus) have been previously reported to be responsive to upright BM (Grossman et al. 2000; Vaina et al. 2001; Grossman and Blake 2002; Beauchamp et al. 2003; Saygin et al. 2004; Peuskens et al. 2005; Gobbini et al. 2007; Herrington et al. 2011; Sokolov et al. 2012, 2014; Han et al. 2013; Jastorff et al. 2016; for meta-analyses, see Grosbras et al. 2012; Engell and...
McCarthy 2013). This is of much importance, as the topography of whole-brain activation revealed by 9.4 T dovetails well with patterns uncovered by standard field fMRI and other imaging modalities.

Yet we found bilateral activation also in several deep structures of the brain such as the hippocampus and thalamus including the pulvinar (Fig. 2A) that have not been previously reported. The right thalamus was stronger engaged than the hippocampus or left thalamus. The pulvinar is a part of the thalamus that is known to be involved in visual processing of biologically or socially relevant stimuli. Damage to the pulvinar impairs facial expressions recognition (Ward et al. 2005), and its response does not require intact visual cortex or awareness (Cleghorn et al. 2015). It appears therefore intriguing to further examine whether the network underlying BM processing also includes a direct contribution from early visual processing in the pulvinar as a new route in addition to the canonical input from early visual areas.

In a series of studies, the cerebellum and, in particular, the left lateral cerebellum, has been reported to engage in the network underpinning visual processing of human locomotion (Grossman et al. 2000; Vaina et al. 2001; Sokolov et al. 2012, 2014; Jack et al. 2017). Despite whole-brain imaging, we did not find any reliable activation in the cerebellum. The most plausible explanation for this is the inhomogeneity of the radiofrequency transmission field at high magnetic field strengths (Pohmann et al. 2016). Here we were limited to the circular polarized transmission mode described in detail earlier (Hagberg et al. 2017): this mode generates spin excitation in a central 3D elliptic shaped “sweetspot,” where the flip angle is high and surrounded by areas of reduced transmit field. In other words, spin excitation may vary across the brain and hereby the BOLD contrast-to-noise ratio might also be modulated. In the present study, the signal was particularly low in the cerebellum (e.g., the partial signal drop-out is visible in Fig. 4). Another contributing factor is that in some participants the cerebellum was not properly covered by the radiofrequency coil due to its geometry.

The pattern of fMRI activation in response to upright BM agrees well with the topographical pattern of the oscillatory response revealed by MEG (Pavlova et al. 2004). These findings lend support to the notion that high-frequency oscillatory activity is topographically related to fMRI response (Niessing et al. 2005).

Contrasts Between Upright and Upside-Down BM

Earlier very few fMRI studies, which used magnetic field strength of 1.5 T with coarse spatial resolution and low sensitivity, were mainly restricted to analysis of difference in activation between upright and inverted BM in predefined ROIs. In a 1-back repetition task, an upright walker elicited an increased BOLD response over the right pSTS, the region assumed to be heavily involved in BM processing, whereas with display inversion, the BOLD signal over the pSTS was diminished by about one half (Grossman and Blake 2001). During detection of a walker’s facing (right or left), the increased BOLD response to an upright walker’s facing as compared with inverted displays occurred in the left orbitofrontal and frontal cortices, and in the right cingulate gyrus (Grèzes et al. 2001). The opposite contrast resulted in activation in the right inferior and middle frontal gyrus, intracopcular sulcus, bilateral posterior intraparietal sulcus, and the left superior parietal lobule. When upright and inverted displays were presented in a sequence along with similar displays (scrambled BM, 3D rotation, and a static walker), the ROIs such as the right hMT/V5 and STS were stronger activated by upright BM (Peuskens et al. 2005).

Here we conducted the whole-brain analysis contrasting activation in response to upright and inverted BM. The outcome indicates that both contrasts yield pronounced peaks of activation already at early stages of visual processing: upright BM as compared with upside-down presentation results in activation in the upper occipital cortices, whereas the opposite contrast reveals activation in the lower occipital cortices, primarily in lingual gyri. At first glance, one possible explanation for this pattern of activation is that lower or upper parts of the display corresponding to the legs of either an upright or an inverted walker (that contain the most amount of absolute motion, Takahashi et al. 2011) might have elicited these peaks of activation. Yet in this case, one would expect topographical symmetry and equal strength of activation in both hemispheres. The findings, however, show that although with inverted BM, activation in the left and right hemispheres is of the same strength, with upright display, activation is greater in the right hemisphere. This agrees well with the right hemispheric lateralization of BM processing with wide repertoires of actions (Grosbras et al. 2012; Engell and McCarthy 2013). For processing of upright point-light BM stimuli, the right hemispheric dominance has been also reported for nonhuman species (Rugani et al. 2015). Moreover, with both orientations, the areas of activation are not topographically symmetrical. Most plausible account would be that the topography of activation reflects different stages of feature binding; lower occipital regions may be involved in processing of coherent structures emerging from the array of moving dots in accord with such percept as “flies hovering in circle,” while upper occipital cortices are responsible for processing of the whole configuration, Gestalt of a walker.

Additional regions activated when contrasting upright versus inverted BM (such as the right superior temporal gyrus and bilateral inferior frontal gyrus) have been earlier reported for contrasts with spatially scrambled BM (Grossman and Blake 2002; Peuskens et al. 2005; Gobbin et al. 2007; Herrington et al. 2011). As contrast with scrambled BM is more pronounced than with inverted BM, leading to stronger differences in the functional BOLD response, it had been used furthermore in previous imaging studies. The present study uncoveres differences in whole-brain activation despite subtle variations in functional signals when contrasting rather upright with inverted BM. Activation in some brain areas such as the superior parietal lobule in the left hemisphere was observed earlier (Grèzes et al. 2001). This region is consistently reported to be involved in mental rotation, in particular in male observers (Hugdahl et al. 2006), including mental rotation of bodies and body parts (Tomasi and Greimese 2016). Taken together, the whole-brain analysis of activation in response to upright BM and the same display rotated 180° uncovered brain activation in response to displays with highly comparable visual input and tiny sensory information.

Brain Activation as a Function of Display Interpretation

By changing orientation of point-light BM or in other words, by using the same stimuli under conditions providing for different possibilities for reconstruction of “hidden” meaning (i.e., easily recognizable, “pop-up” upright BM representing a human figure, and inverted display allowing for a plenty of perceptual interpretations), we revealed key nodes of the network that is active in perceivers who failed to constantly interpret BM as shown the “wrong way up.” This network peaked in the right hemisphere.
including the lingual and postcentral gyr, and the rolandic operculum. With identical visual input, activation in these brain areas was driven solely by fine-grained cognitive processing. In our study, the right lingual gyrus is shown to be generally involved in processing of inverted BM (see above). On the basis of the temporal dynamics of the BOLD response in these areas, one can assume that the postcentral cortex and rolandic operculum are most likely engaged in cognitive control and decision making (see Supplementary Material, Table S3 and Fig. 6). The rolandic operculum is also known to be involved in speech processing and articulation (Behroozmand et al. 2015), and may reflect interplay between switching in display interpretations.

Temporal Dynamics

On the basis of temporal dynamics of the BOLD response, we figured out: (1) the (multi)functional role each region plays in the networks underpinning BM processing and (2) ensembles of brain regions making up neural networks that play in unison at different processing stages (Fig. 5). Three main patterns of temporal dynamics were revealed (Figs 4 and 5). To the best of our knowledge, the present study is the first that characterizes the bunch of brain areas activated by BM analyzing the temporal dynamics of the BOLD response. This helps to better understand the (multi)functional role these areas play in proper BM processing. For instance, it had been earlier heatedly debated that portions of the frontal premotor cortices, in particular, the inferior frontal cortex, are engaged in visual processing of BM reflecting involvement of the mirror neuron system (MNS) (Saygin et al. 2004; Herrington et al. 2011; Lingnau and Petris 2013). The MNS involvement suggests that by observing actions, perceivers activate parietal and premotor areas that may also be recruited by performing actions by perceivers themselves. The present analysis indicates that indeed, a portion of the inferior frontal cortex is not only involved in decision making and motor response preparation for both upright and inverted BM, but exhibits stimulus-specific decrease in activation, differentiating between upright and inverted BM already at earlier stages of BM processing. This temporal dynamics pattern suggests, therefore, that this brain area is engaged in cognitive BM processing, though it leaves open the precise machinery of this involvement. The motor system may be engaged either in “filling in” impoverished point-light displays in accordance with the MNS nature of this region (Saygin et al. 2004) or in biologically plausible action understanding (Lingnau and Petris 2013). The temporal dynamics of the BOLD response is rarely taken into account, though it provides indispensable information for understanding formation of the functional brain networks.

Regions exhibiting similar temporal dynamics, and thus playing in harmony, form up large-scale networks underpinning BM processing. As shown in Figure 5, in the left hemisphere, inverted BM primarily activates anterior networks engaged in decision making and cognitive control, whereas upright BM elicits activation in posterior brain areas. In the right hemisphere, multiple networks are activated in response to upright BM, whereas only parsimonious activation is found in response to inverted displays.

Resume

In a nutshell, by using high-sensitive ultrahigh field fMRI at 9.4 T along with whole-brain analysis, we revealed differences in the brain circuits underpinning upright and inverted BM processing despite subtle variations in the functional signal. In the left hemisphere, inverted BM primarily activates anterior networks engaged in decision making and cognitive control, whereas upright BM activates posterior brain areas solely. In the right hemisphere, multiple networks are activated in response to upright BM as compared with scarce activation to inverted displays. The differences in the brain-wide networks activated for upright and inverted BM may be summarized in terms of hemispheric laterality and antero-posterior brain axis.

Moreover, in perceivers who did not constantly interpret BM as shown the “wrong way up,” we detected peaks of activation in the right brain hemisphere forming up a distributed network of regions with distinct functional involvement. This fine-grained modulation of brain activation was driven solely by cognitive processing of identical visual input.

Most important, for the first time, on the basis of the temporal and spatial dynamics of the BOLD response, we uncovered (1) functional involvement of each region in the networks underpinning BM processing and (2) distributed ensembles of regions playing in unison. The outcome provides novel insights on the brain networks underlying proper BM processing as an essential part of the social brain.

To the best of our knowledge, this is the first fMRI study at 9.4 T that gauges fine-grained cognitive processing.

Supplementary Material

Supplementary Materials are available at Cerebral Cortex online.

Authors’ Contributions

M.A.P., M.E., G.E.H., and J.L. performed the measurements; M.A.P., M.E., G.E.H., and A.N.S. analyzed the data; M.A.P. and K.S. supervised the whole project; all co-authors contributed to writing the article.

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Notes

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