

Neural representation of self-concept in sighted and congenitally blind adults

Yina Ma and Shihui Han

Department of Psychology, Peking University, Beijing 100871, People's Republic of China

Correspondence to: Shihui Han, PhD,
Department of Psychology,
Peking University,
5 Yiheyuan Road,
Beijing 100871,
People's Republic of China
E-mail: shan@pku.edu.cn

The functional organization of human primary visual and auditory cortices is influenced by sensory experience and exhibits cross-modal plasticity in the absence of input from one modality. However, it remains debated whether the functional architecture of the prefrontal cortex, when engaged in social cognitive processes, is shaped by sensory experience. The present study investigated whether activity in the medial prefrontal cortex underlying self-reflective thinking of one's own traits is modality-specific and whether it undergoes cross-modal plasticity in the absence of visual input. We scanned 47 sighted participants and 21 congenitally blind individuals using functional magnetic resonance imaging during trait judgements of the self and a familiar other. Sighted participants showed medial prefrontal activation and enhanced functional connectivity between the medial prefrontal and visual cortices during self-judgements compared to other-judgements on visually but not aurally presented trait words, indicating that medial prefrontal activity underlying self-representation is visual modality-specific in sighted people. In contrast, blind individuals showed medial prefrontal activation and enhanced functional connectivity between the medial prefrontal and occipital cortices during self-judgements relative to other-judgements on aurally presented stimuli, suggesting that visual deprivation leads to functional reorganization of the medial prefrontal cortex so as to be tuned by auditory inputs during self-referential processing. The medial prefrontal activity predicted memory performances on trait words used for self-judgements in both subject groups, implicating a similar functional role of the medial prefrontal cortex in self-referential processing in sighted and blind individuals. Together, our findings indicate that self-representation in the medial prefrontal cortex is strongly shaped by sensory experience.

Keywords: neural plasticity; self; functional magnetic resonance imaging; medial prefrontal cortex; blindness

Abbreviation: BA = Brodmann area; MRI = magnetic resonance imaging

Introduction

Neural plasticity enables the human brain to change its functional architecture through different sensory experiences in order to adapt to environmental pressures (Bavelier and Neville, 2002; Pascual-Leone *et al.*, 2005). Studies of humans with visual or auditory deprivation have shown increasing evidence for modulations

of function of the primary visual and auditory cortices by sensory experience. The occipital cortex that is commonly involved in visual processing in sighted humans is activated by heard sounds/words (Burton *et al.*, 2002; Gougoux *et al.*, 2009) and by Braille reading in blind individuals (Sadato *et al.*, 1996; Büchel *et al.*, 1998; Burton *et al.*, 2002). Moreover, the occipital activity in early blind individuals predicts behavioural performances on auditory

tasks such as sound localization (Gougoux *et al.*, 2005) and verbal-memory (Amedi *et al.*, 2003). Similarly, auditory deprivation results in recruitment of the primary auditory cortex in the processing of vibrotactile stimuli (Levanen *et al.*, 1998) and sign language (Nishimura *et al.*, 1999) in deaf humans. The findings indicate that sensory experiences substantially shape the functions of primary sensory cortices to adapt to the processing of visual, auditory or tactile information.

However, observations regarding whether the functional organization of cortical structures involved in high-level social cognition are shaped by sensory experiences are inconsistent. The paracallosal cortex responds to both visual and auditory signals that indicate others' intention to communicate (Kampe *et al.*, 2003). The mirror neuron system in the premotor cortex, which responds both during performing an action and viewing others performing the same action (Rizzolatti and Sinigaglia, 2010), is activated by sounds produced by actions in both sighted and congenitally blind individuals (Ricciardi *et al.*, 2009). The temporoparietal junction that underlies inference of others' beliefs when reading and hearing stories in sighted subjects also engages in belief reasoning when early blind participants hear stories (Bedny *et al.*, 2009). Thus, it appears that these brain regions engage in social cognitive processing of others regardless of sensory modality and develop independently of visual experience. Apart from first-person visual experiences, hearing people talk about mental states may be a critical source of evidence about others' minds and result in development a similar neural network underlying the understanding of others' mental states in sighted and congenitally blind adults (Bedny *et al.*, 2009).

In contrast, evidence exists for modality specificity of the frontal activity involved in cognitive processes related to the self. Spatial localization of visual and auditory stimuli referenced to the self is dissociated in the superior and inferior regions of the middle frontal gyrus (Bushara *et al.*, 1999). Hearing one's own name activates the left middle frontal cortex (Carmodya and Lewis, 2006), which is, however, not engaged when seeing one's own name (Sugiura *et al.*, 2008). The results raise the possibility that functions of the frontal cortex engaged in self-related cognitive processes may be modality-specific and thus are influenced by modified sensory experience. Nevertheless, this has not been demonstrated by examining neural activity recorded from the same subject to visual and auditory stimuli that match in content.

The current work addressed this issue by assessing if neural activity in the medial prefrontal cortex related to self-concept representation (Northoff and Bermpoh, 2004) is modality-specific and shaped by sensory experiences. We employed a self-referential task that requires trait judgements of oneself and others (Rogers *et al.*, 1977), and can be conducted in both visual and auditory modalities. It has been shown that the medial prefrontal activity increases to trait judgements of the self compared to trait judgements of others (Kelley *et al.*, 2002; Lieberman *et al.*, 2004; Mitchell *et al.*, 2006; Zhu *et al.*, 2007) and increases more to highly self-descriptive trait words than less self-descriptive trait words (Macrae *et al.*, 2004; Moran *et al.*, 2006), suggesting an important role of the medial prefrontal cortex in self-concept representation. However, previous studies only showed self-related medial prefrontal activity to visually presented stimuli and left it

open as to whether such activity is visual modality-specific, and if so, whether visual deprivation leads to reorganization of medial prefrontal cortex function so as to be tuned to auditory modality during self-referential processing. To our knowledge, only one brain imaging study has employed aural stimuli for trait judgement tasks (Johnson *et al.*, 2002). This study showed increased activation in the contrast of self-judgements versus general knowledge judgements in the medial prefrontal cortex, which was associated with the processing of general personal knowledge. However, it did not report the results of the contrast of self-judgements versus other-judgements, leaving it an open issue as to whether the medial prefrontal cortex engages in self-referential processing of aurally presented stimuli.

According to the theory that self-concept is constructed as abstract symbolic knowledge (Sedikides and Skowronski, 1997; Kihlstrom *et al.*, 2003), the neural activity underlying self-concept representation should bear arbitrary relations to sensory input. However, there has been evidence that self-concept originates in processes of sensory perception that distinguish between self and non-self (Gibson, 1979; Butterworth, 1992) and visual input dominates information from other modalities in defining the primitive sense of self, such as the agency of an action and ownership of body parts (Bodvinik and Cohen, 1998; Lenggenhager *et al.*, 2007). If such primitive self-concept provides a basis for the representation of one's own traits, one may hypothesize that the medial prefrontal activity related to self-concept representation would be stronger to stimuli delivered through the visual rather than auditory modality. In addition, the medial prefrontal activity underlying self-representation should be taken over by the auditory modality in blind individuals for whom the auditory, rather than the visual, input dominates the distinction between self and non-self and thus may play a key role in the construction of one's self-concept.

To test these hypotheses, Experiment 1 scanned sighted participants using functional MRI during judgements of visually and aurally presented statements about one's own traits, a familiar other's traits, and word valence. Similar to the previous studies (Kelley *et al.*, 2002; Lieberman *et al.*, 2004; Mitchell *et al.*, 2006; Zhu *et al.*, 2007), the contrast of self-judgements versus other-judgements revealed neural activity underlying self-concept representation and the contrast of other-judgements versus valence-judgements identified neural activity associated with the processing of others' personal knowledge (Fig. 1). As Experiment 1 showed that the medial prefrontal activation associated with self-representation was specific to the visual modality, Experiment 2 further scanned congenitally blind individuals and sighted controls during self-, other- and valence-judgements of aurally presented stimuli to assess if lack of visual experience leads to functional reorganization of the medial prefrontal cortex so as to respond to auditory input during self-referential processing.

Materials and methods

Subjects

Twenty-five sighted participants were recruited in Experiment 1. Two sighted participants were excluded from data analysis due

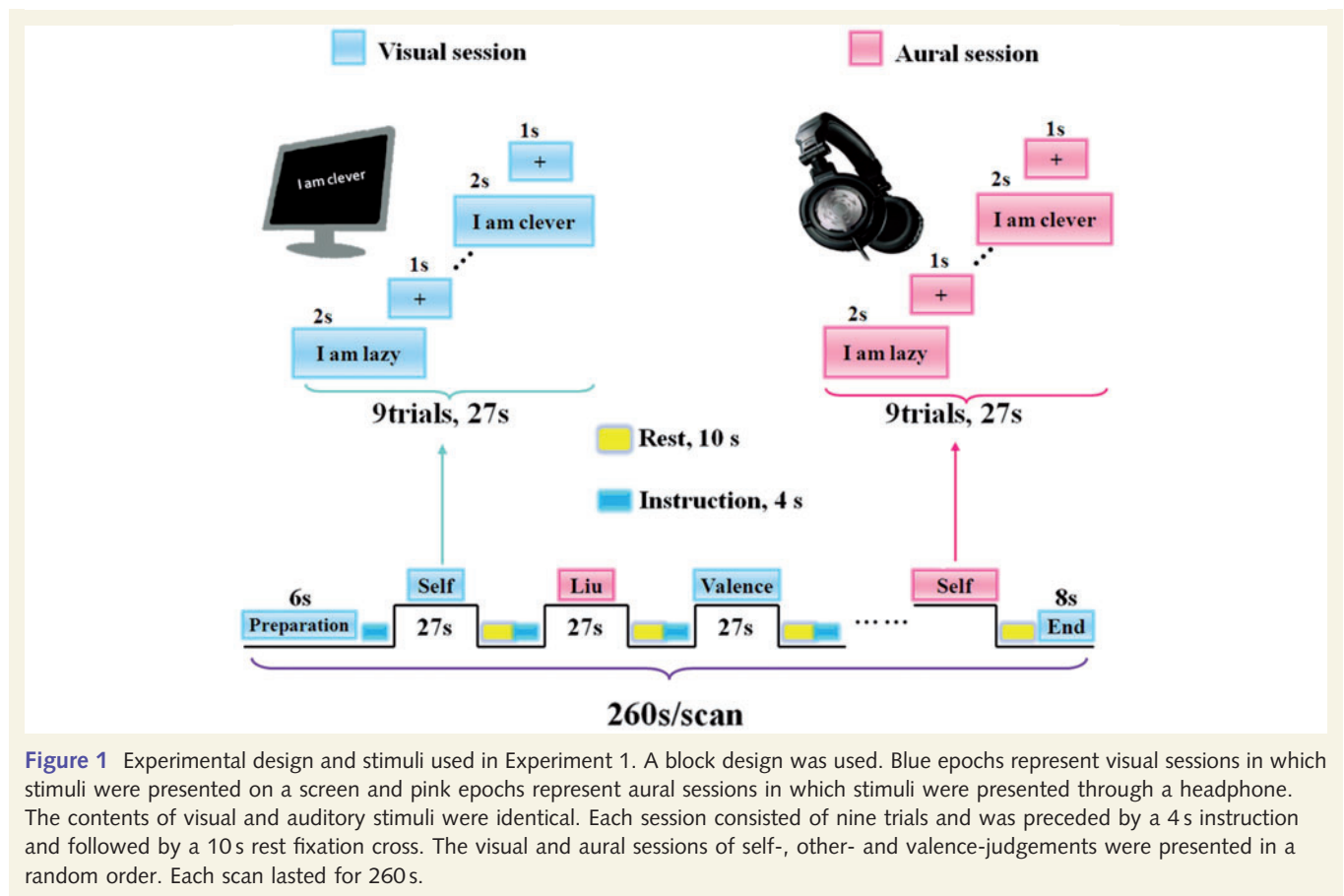


Figure 1 Experimental design and stimuli used in Experiment 1. A block design was used. Blue epochs represent visual sessions in which stimuli were presented on a screen and pink epochs represent aural sessions in which stimuli were presented through a headphone. The contents of visual and auditory stimuli were identical. Each session consisted of nine trials and was preceded by a 4 s instruction and followed by a 10 s rest fixation cross. The visual and aural sessions of self-, other- and valence-judgements were presented in a random order. Each scan lasted for 260 s.

to excessive head movement. The remaining 23 sighted individuals (11 males, 12 females; age range: 18–28 years, mean age = 22.0 years) were included in functional MRI data analysis. One of the subjects was left-handed, the others were right-handed. All sighted participants reported no history of neurological or psychiatric diagnoses and had normal or corrected-to-normal vision.

Twenty-one congenitally blind individuals and 22 sighted control participants were recruited for Experiment 2. Two blind and three sighted control participants were excluded from data analysis due to excessive head movement. Data from the remaining 19 congenitally blind participants (11 males, 8 females; age range: 18–28 years, mean age = 25.2 years) and 19 sighted control participants (9 males, 10 females; age range: 19–28 years, mean age = 23.2 years) were included in functional MRI data analysis. One blind participant was left-handed and the others were right-handed. All the participants had no history of neurological or psychiatric diagnoses. The causes of blindness included retinopathy of prematurity ($n=7$), cataracts ($n=5$), retrolental fibroplasia ($n=1$), genetic retinal pigmentation ($n=2$), nystagmus ($n=1$), microphthalmia ($n=1$) and congenital glaucoma ($n=2$). Informed consent, approved by a local ethics committee, was provided prior to the study. Informed consent was obtained verbally from blind participants.

Stimuli and procedure

In Experiment 1, stimuli used during the scanning procedure consisted of three types of statements in Chinese delivered through either a liquid crystal display projector onto a rear projection screen, which was viewed with an angled mirror positioned on the head-coil, or a magnetic resonance-compatible pneumatic headphone system

(22.05 kHz, 16 bit quantization, stereo, GoldWave Project). Visual stimuli consisted of short sentences written in white on a black background and auditory stimuli consisted of short-sentences read by a female. Each stimulus consisted of a statement about the self, a gender-matched Chinese athlete (Xiang Liu for male subjects and Xuan Liu for female subjects), or the valence of trait words. The statements delivered through the visual and auditory modalities were identical in content. Subjects were asked to make yes/no responses to self-judgements (e.g., 'I am brave'), other-judgements (e.g., 'Liu Xiang is lazy') and valence-judgements (e.g., 'smart is a positive word') by pressing one of the two buttons with the right index or middle finger. Prior to entering the scanner, participants were given practice trials to familiarize themselves with the tasks.

Each type of judgement was presented in a single session, using a block design. In each scan, each subject finished six functional scans with six sessions (i.e. auditory/visual self-judgements, auditory/visual other-judgements and auditory/visual valence-judgements). Different sessions in each scan were presented visually and aurally in a random order, resulting in 54 statements (six sessions of nine statements) in each condition. A 6 s prompt screen with 'The experiment is about to start, please concentrate on the task' preceded each scan. Each session of 31 s started with a 4 s instruction (instructions were presented on the screen for visual session and through headphones for auditory session), followed by nine trials. Each trial consisted of a 2 s statement, followed by a 1 s central fixation. The judgement tasks were intervened by rest sessions of 10 s during which participants viewed a white fixation on a black screen.

A total of 444 trait adjectives were selected from established personality trait adjective pools (Liu, 1990), each of which consisted

of two Chinese characters. Half of the words were positive adjectives, and the remaining ones were negative. Three hundred and twenty-four adjectives were randomly chosen to be used in 324 judgement statements for the functional scans and were randomly assigned to six lists of 54 words. The assignment of the lists to each condition was counterbalanced across subjects. Three lists of words were randomly chosen to be aurally delivered and the other three lists were visually presented. Each of the Chinese characters in the instructions and each statement subtended a visual angle of $0.34^\circ \times 0.45^\circ$ (width \times height) at a viewing distance of 80 cm.

After the scanning procedure, participants were given visual and auditory recognition memory tests. Subjects were presented with 60 old trait words (20 trait words from each judgement task) randomly chosen from visual or aural sessions and 60 new trait words. The order of visual and auditory memory tests was counterbalanced across subjects. Each word was presented individually for 2 s and participants indicated whether the presented word was old or new by a button press.

The stimuli and procedures in Experiment 2 were similar to those used in Experiment 1, except that only auditory sessions were included. Participants finished three scans, with two sessions of each condition in each scan. Sighted participants were masked with an eyepatch to block out visual input during the scanning procedure. After the scanning procedure, both blind participants and sighted controls performed the memory test on aurally presented trait words.

Imaging procedure

A GE 3 T scanner with a standard head coil was used to acquire blood oxygen level dependent (BOLD) gradient echo-planar images ($64 \times 64 \times 32$ matrix with $3.75 \times 3.75 \times 4$ mm³ spatial resolution, repetition time = 2000 ms, echo time = 30 ms, flip angle = 90° , field of view = 24×24 cm) while subjects were performing the trait judgement tasks. A high-resolution T_1 -weighted structural image ($256 \times 256 \times 128$ matrix with a spatial resolution of $0.938 \times 0.938 \times 1.4$ mm³, repetition time = 7.4 ms, echo time = 3 ms, inversion time = 450 ms, flip angle = 20°) was subsequently acquired.

Imaging analysis

SPM2 (the Wellcome Trust Centre for Neuroimaging, London, UK) was used for data analysis. The functional images were corrected for head movements. Six movement parameters (translation; x , y , z and rotation; pitch, roll, yaw) were included in the statistical model. The anatomical image was coregistered with the mean realigned image and then normalized to the standard T_1 Montreal Neurological Institute (MNI) template. The normalizing parameters were applied to the functional images, which were resampled to 2 mm of isotropic voxel size and spatially smoothed using an isotropic Gaussian kernel of 8 mm full-width half-maximum. The image data were modelled using a box-car function. Statistical analyses in SPM2 used a hierarchical random-effects model with two levels. In the first level of each subject, the onsets and durations of each session were modelled using a General Linear Model according to the condition types. All seven conditions (auditory/visual self-judgements, auditory/visual other-judgements, auditory/visual valence-judgements and rest) were included in the model. A box-car function was used to convolve with the canonical haemodynamic response in each condition. The design matrix also included the realignment parameters to account for any residual movement-related effect.

A region of interest analysis was first conducted in Experiment 1 to examine the involvement of the medial prefrontal cortex in

self-referential processing of visually and aurally presented stimuli in sighted participants. The medial prefrontal cortex was defined using a *priori* functionally-defined region of interest (a sphere with a radius of 5 mm centred at MNI coordinates 8, 56, 9 [Brodmann area (BA) 10] based on an entirely independent data set that also compared self- and other-judgements in Chinese participants) (Zhu *et al.*, 2007). The parameter estimates of signal intensity in association with different judgement tasks were calculated from sighted participants and subjected to a repeated-measures analysis of variance (ANOVA) with Modality (visual versus auditory) and Judgement (self-judgement versus other-judgement or other-judgement versus valence-judgement) as independent within-subjects variables.

Random effects analyses were also conducted based on statistical parameter maps from each individual participant to allow population inference. Contrasts of self- versus other-judgements and other- versus valence-judgements on visual and auditory stimuli were calculated. In order to identify brain regions that differentiated self- and other-judgements across different modalities, whole-brain statistical parametric mapping analyses were calculated to confirm the interaction between Modality (visual versus auditory) \times Judgement (self-judgements versus other-judgements) by calculating the contrast $1 -1 -1 1$ (visual self-judgements, visual other-judgements, auditory self-judgements and auditory other-judgements). Similarly, to identify brain regions that differentiate other- and valence-judgements across different modalities, the interaction between Modality (visual versus auditory) \times Judgement (other-judgement versus valence-judgement) was confirmed by calculating the contrast $1 -1 -1 1$ (visual other-judgement, visual valence-judgement, auditory other-judgement and auditory valence-judgement). Activations shown in the random-effects analyses were identified using a cluster level threshold at $P < 0.05$ (corrected for multiple comparisons).

A psychophysiological interaction analysis (Friston *et al.*, 1997) was performed in order to identify brain regions that showed significantly increased covariation (i.e. increased functional connectivity) with the medial prefrontal activity related to self-judgements compared to other-judgements. The coordinates of the peak voxel from the contrast of self- versus other-judgements were used to serve as a landmark for the individual seed voxels. The region of interest in each individual subject was defined as a sphere with 5-mm-radius centred at the peak voxel in the medial prefrontal cortex. The time series of each region of interest were then extracted, and the psychophysiological interaction regressor was calculated as the element-by-element product of the mean-corrected activity of this region of interest and a vector coding for differential task effects of self-judgements versus other-judgements. The psychophysiological interaction regressors reflected the interaction between psychological variable (self-judgement versus other-judgement) and the activation time course of the medial prefrontal cortex. The individual contrast images reflecting the effects of the psychophysiological interaction between medial prefrontal cortex and other brain areas were subsequently subjected to one-sample *t*-tests. The results of the group analysis identified brain regions in which the activity systematically showed increased correlations with the medial prefrontal activity during self-judgements compared to other-judgements. Given the prior hypothesis of visual specific medial prefrontal activity, a voxel-wise threshold of $P < 0.001$ and a spatial extent threshold of $k = 100$ were used to identify brain areas that showed significant functional connectivity with the seed region of interest.

In Experiment 2, region of interest analyses were first conducted to examine the differential medial prefrontal cortex involvement in self-referential processing of aurally presented stimuli in blind and sighted control participants. The medial prefrontal cortex was defined

in the brain regions that engaged more strongly in self-referential processing of visually than aurally delivered stimuli in sighted participants in Experiment 1. The parameter estimates of signal intensity linked to different judgement tasks were calculated and subjected to ANOVA with Judgement (self-judgement versus other-judgement or other-judgement versus valence-judgement) as an independent within-subjects variable and Group (blind participants versus sighted controls) as a between-subjects variable. Random effects analyses were also conducted to calculate contrasts of self-judgements versus other-judgements on auditory stimuli. Psychophysiological interaction analysis was conducted to examine brain areas that showed increased functional connectivity with the medial prefrontal cortex during self-judgements compared to other-judgements in the blind group who showed medial prefrontal cortex activity in the contrast of self-judgements versus other-judgements.

Results

Experiment 1: Brain imaging of sighted participants

The response accuracy of valence judgements was higher for visually than aurally presented stimuli [88 versus 82%, $F(1,22)=8.45$, $P=0.008$]. A 2 (Modality: visual versus aural) \times 3 (Judgment: self-, other-, and valence-judgements) ANOVA of the corrected recognition scores (the proportion of hits minus false alarms) showed a significant main effect of Modality [$F(1,22)=6.965$, $P=0.015$], suggesting that subjects remembered better trait words delivered through the visual than auditory modalities (Supplementary Table 1). There was also a significant main effect of Judgment

[$F(2,44)=5.273$, $P=0.009$]. However, the interaction of Modality \times Judgment was not significant ($F < 1$). To examine the self-reference effect in memory performance, we conducted a 2 (Modality: visual versus aural) \times 2 (Judgment: self- versus other-judgments) ANOVA, which showed a significant main effect of Judgment [$F(1,22)=11.25$, $P=0.003$], suggesting that subjects remembered better trait words associated with self-judgments than those with other-judgments.

To test if the medial prefrontal cortex is differentially involved in self-referential processing of trait words presented through visual and auditory modalities, a region of interest analysis was first conducted. Signal intensity of parameter estimates associated with different judgement tasks was calculated in the ventral region of the medial prefrontal cortex, which was previously shown to be involved in self-trait judgements in an independent study (MNI coordinates $x, y, z: 8, 56, 9$; Zhu *et al.*, 2007). The ANOVA with Modality (visual versus auditory) and Judgement (self-judgement versus other-judgement) as independent within-subjects variables showed a significant interaction of Modality \times Judgement [$F(1,22)=12.616$, $P=0.002$, Fig. 2A]. *Post hoc t*-tests confirmed that self-judgements significantly increased the medial prefrontal activity relative to other-judgements on visually presented stimuli [$t(1,22)=3.704$, $P=0.001$] but not on aurally presented stimuli [$t(1,22)=1.040$, $P=0.310$]. However, a 2 (Modality: visual versus auditory) \times 2 (Judgement: other-judgement versus valence-judgement) ANOVA did not show a significant interaction of Modality \times Judgement [$F(1,22)=0.655$, $P=0.427$], though the main effects of Judgement [$F(1,22)=44.646$, $P < 0.001$] and Modality [$F(1,22)=7.730$, $P=0.011$] were significant, suggested that the

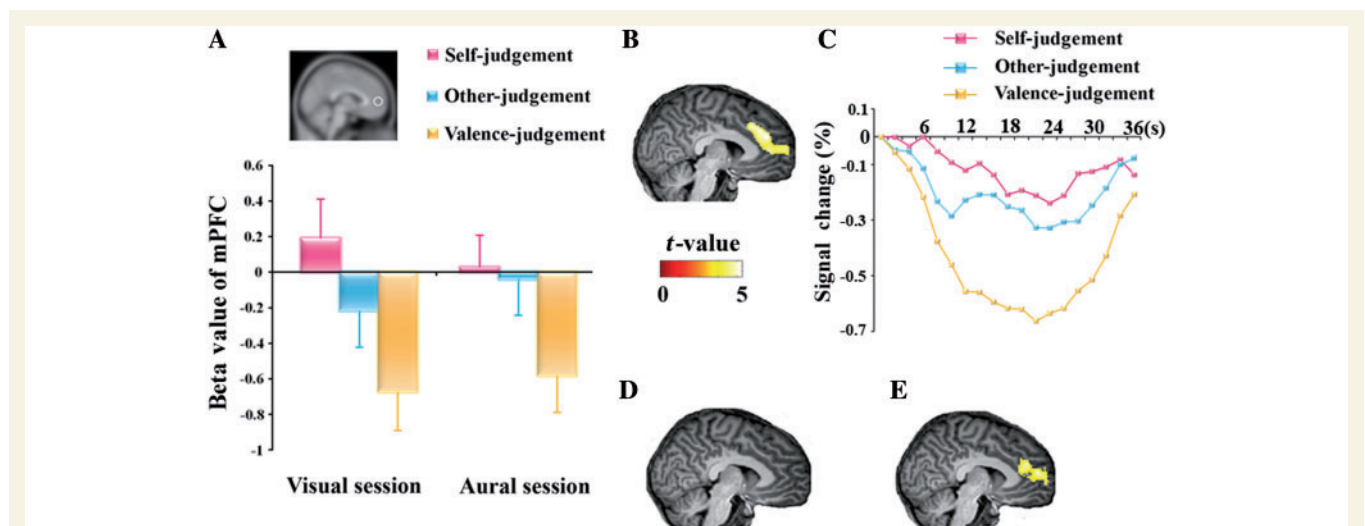


Figure 2 Results of region of interest and random effect analyses in Experiment 1. (A) The results of the region of interest analysis. The region of interest in the medial prefrontal cortex (mPFC) is illustrated in an echo-planar image template. Signal intensity of parameter estimates of the medial prefrontal cortex associated with self-, other- and valence-judgement tasks in the visual and aural sessions are shown separately. (B) The results of the random effects analysis. The contrast of self- versus other-judgements on visually presented stimuli showed activation in the ventral medial prefrontal cortex and anterior cingulate cortex. (C) Signal changes in the medial prefrontal cortex associated with self-, other-, and valence-judgments. (D) The results of the random effects analysis. The contrast of self- versus other-judgements on aurally presented stimuli failed to show any activation. (E) The results of the interaction analysis. The comparison of the two contrasts (self- versus other-judgements of visually and aurally presented stimuli) showed significantly enhanced activation in the medial prefrontal cortex and anterior cingulate cortex.

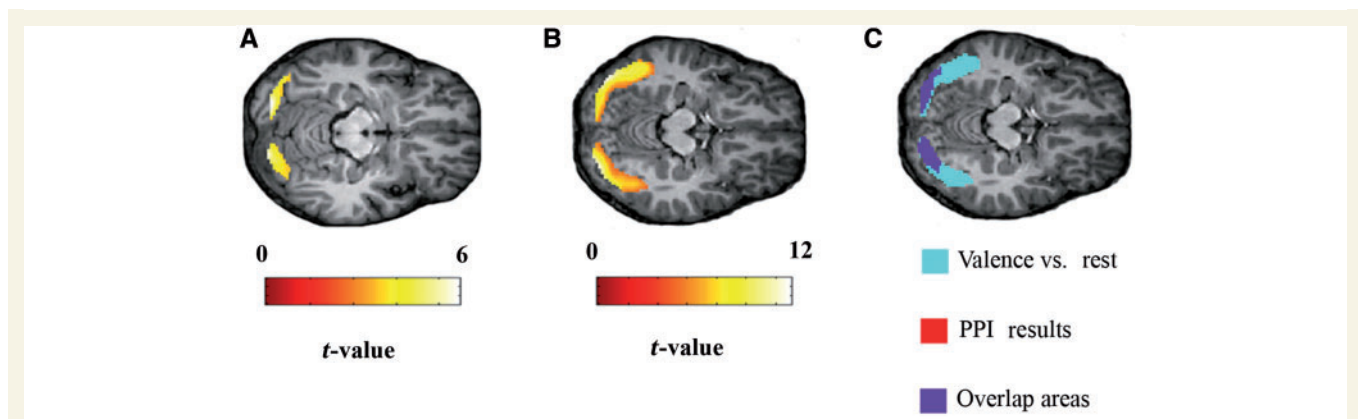


Figure 3 Results of psychophysiological interaction (PPI) analysis in Experiment 1. (A) Increased functional connectivity between the medial prefrontal cortex and bilateral occipital cortex was observed during self-judgements compared to other-judgement. (B) The visual activation during valence-judgement in the visual sessions. The contrast of valence-judgement versus rest showed activations in the bilateral visual cortex. (C) The overlap between visual activation and occipital activity that showed enhanced functional connectivity with the medial prefrontal cortex during self-judgements. The purple areas illustrate the overlapped areas.

medial prefrontal activity was greater to other-judgements than to valence-judgements and was greater to aural than visual stimuli. The results indicated that medial prefrontal cortex activity related to self-referential processing was specific to the visual modality whereas the medial prefrontal activity associated with the processing of others' personal knowledge did not differ significantly between the two modalities.

A whole-brain statistical parametric mapping analysis was conducted to further confirm the differential medial prefrontal activity associated with self-referential processing of visually and aurally presented stimuli. The contrast of self-judgements versus other-judgements of visually presented stimuli revealed significant activation in the ventral medial prefrontal cortex extending to the anterior cingulate cortex ($x, y, z: 8, 56, 10$ and $6, 42, 24$, BA 10, 32 and BA 24, $Z=3.61$, Fig. 2B and 2C). However, the contrast of self-judgements versus other-judgements of aurally presented statements failed to show any significant activation even under a voxel-wise threshold of $P < 0.001$ and an extend threshold of 50 voxels (Fig. 2D). An interaction analysis that compared the two contrasts (self-judgement versus other-judgement of visually versus aurally presented stimuli) was also conducted to confirm differential involvement of the medial prefrontal cortex in self-referential processing in the two modalities. This showed significant activation in the medial prefrontal cortex and anterior cingulate cortex ($x, y, z: 8, 56, 12$ and $4, 44, 24$, BA 10, 32 and BA 24, $Z=3.53$, Fig. 2E). No cortical regions showed greater activity to other-judgements than to self-judgements on either visually or aurally delivered stimuli. The results of all contrasts are listed in Supplementary Table 2.

As the results suggested that the medial prefrontal activity underlying self-referential processing was visual modality-specific, we reasoned that there might be enhanced functional connectivity between the medial prefrontal cortex and visual cortex during self-referential processing of visually delivered statements. This was tested using the psychophysiological interaction analysis, which confirmed increased functional connectivity between the

medial prefrontal cortex and bilateral occipital cortex during self-judgements compared to other-judgement ($x, y, z: 22, -88, -16$ and $-18, -88, -16$, BA 18, $Z = 3.77$ and 3.60 , a voxel-wise threshold of $P < 0.001$ and an extend threshold of 100 voxels, Fig. 3A). To examine in more detail the relationship between the occipital cortex, which showed enhanced functional connectivity with the medial prefrontal cortex, and the visual cortex that was initially activated by the visual stimuli, we calculated the contrast of valence-judgements versus rest. This identified the visual areas that were activated by visual stimuli in bilateral occipital cortices ($x, y, z: 38, -82, -12$ and $-22, -90, -12$, BA 17, 18, $Z=6.28$ and 6.39 , Fig. 3B). These were then superimposed with the occipital cortex observed in the psychophysiological interaction analysis. As can be seen in Fig. 3C, the regions of the occipital cortex that showed enhanced functional connectivity with the medial prefrontal cortex were located inside bilateral visual areas that were initially activated by the visual stimuli (the overlapped regions are depicted in purple), suggesting coherent neural responses in the medial prefrontal cortex and visual areas during self-referential processing.

To estimate whether sensory input also modulates neural activity associated with the processing of others' personal knowledge, we calculated contrasts of other-judgements versus valence-judgements on visually and aurally presented statements. We found a set of regions that showed higher activity to other-judgements than to valence-judgements on visually delivered stimuli. These include the dorsal medial prefrontal cortex ($x, y, z: 4, 58, 16$, BA 9, 10, $Z=5.57$), posterior cingulate cortex ($x, y, z: 4, -52, 28$, BA 23, 31, $Z=5.30$) and bilateral middle and superior temporal gyri (right: $x, y, z: 52, 2, -18$, BA 22, $Z=5.13$; left: $x, y, z: -44, -8, 2$, BA 42, $Z=5.34$, Supplementary Fig. 1A). Similarly, the contrast of other-judgements versus valence-judgements on aurally presented stimuli uncovered activations in the dorsal medial prefrontal cortex ($x, y, z: 2, 56, 18$, BA 9, 10, $Z=5.24$) and posterior cingulate cortex ($x, y, z: 6, -48, 32$, BA 23, 31, $Z=5.61$, Supplementary Fig. 1B). To examine whether

these brain regions were differentially involved in processing visually and aurally presented stimuli, we conducted an interaction analysis that compared the two contrasts (other- versus valence-judgements of visually or aurally presented stimuli). This, however, did not reveal any significant activation, suggesting that the medial prefrontal activity related to the representation of others' personal knowledge did not differ significantly between visual and auditory modalities.

Experiment 2: Brain imaging of blind participants and sighted controls

Response accuracy of valence judgements was slightly lower for blind than sighted participants [72 versus 78%, $F(1,36)=4.820$, $P=0.035$]. A 2 (Group: blind versus sighted control) \times 3 (Judgment: self-, other-, and valence-judgments) ANOVA of the corrected recognition scores showed a significant main effect of Judgment [$F(2,72)=13.39$, $P < 0.001$]. However, the interaction of Group \times Judgment was not significant ($F < 1$, Supplementary Table 1). Post hoc analyses suggested that trait words associated with self- and other-judgments were remembered better than those associated with valence-judgments [$F(1,36)=22.67$ and 16.84 , both $P < 0.001$]. Sighted controls showed a trend to

remember better trait words associated with self-judgments than those associated with other-judgments of auditory trait words. Such difference, however, did not reach significance, possibly due to that fewer trait words required for remembering in Experiment 2 than Experiment 1, facilitated memory performances in both self- and other-judgment conditions.

A whole-brain statistical parametric mapping analysis was first conducted to evaluate functional reorganization of the sensory cortices in our blind participants by calculating the contrast of valence-judgements versus rest. This identified significant activations in the bilateral occipital ($x, y, z: 18, -78, -8$, BA 18, 19, $Z=4.06$; $x, y, z: -20, -68, -18$, BA 18/19, $Z=3.98$) and superior temporal cortices ($x, y, z: 48, -32, 14$, BA 41, 42, $Z=5.29$; $x, y, z: -62, -24, 10$, BA 41, 42, $Z=5.25$, Fig. 4A), consistent with the findings of the previous studies (Burton *et al.*, 2002; Gougoux *et al.*, 2009).

We then assessed whether medial prefrontal cortex underlying self-referential processing in sighted individuals undergoes cross-modal plasticity in the absence of visual input. A region of interest analysis was first conducted to calculate signal intensity of parameter estimates from blind participants and sighted controls in the medial prefrontal cortex that engaged more strongly in self-referential processing of visually than aurally delivered

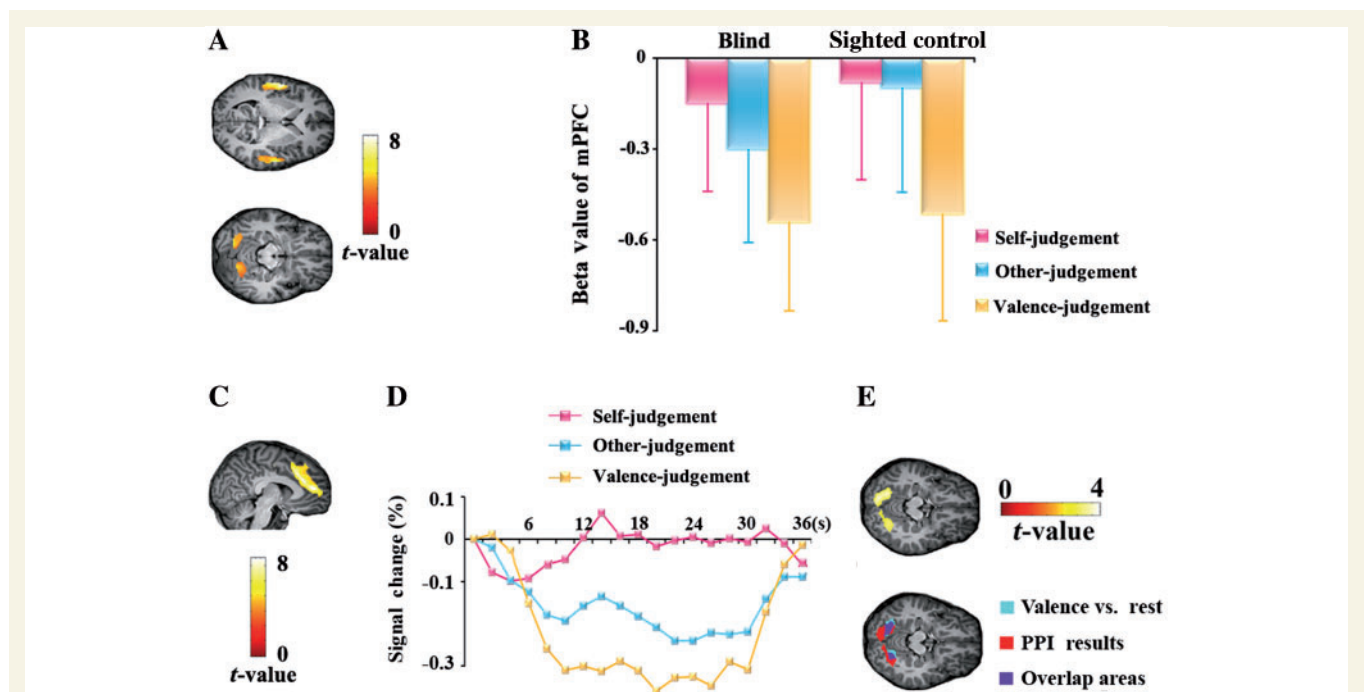


Figure 4 Results of Experiment 2. (A) The activation elicited by auditory stimuli in blind individuals. The contrast of valence-judgements versus rest showed activations in bilateral occipital and superior temporal cortices. (B) The results of the region of interest analysis. Signal intensity of parameter estimates associated with self-, other- and valence-judgement tasks in the medial prefrontal cortex (mPFC) are shown separately for blind and sighted controls. (C) The results of the random effects analysis in blind participants. The contrast of self-versus other-judgements on aurally presented stimuli showed activation in the ventral medial prefrontal cortex and anterior cingulate cortex. (D) Signal changes in the medial prefrontal cortex associated with self-, other-, and valence-judgments in blind participants. (E) The results of the psychophysiological interaction analysis (PPI). The top figure shows increased functional connectivity between the medial prefrontal cortex and bilateral occipital cortex during self-judgements compared to other-judgements in blind participants. The bottom figure shows the overlap between activations elicited by auditory stimuli and the occipital activities that showed enhanced functional connectivity with the medial prefrontal cortex during self-judgements. The purple areas illustrate the overlapped areas.

stimuli in Experiment 1 ($x, y, z: 8, 56, 12$). The ANOVA with Judgement (self- versus other-judgements) as a within-subjects variable and Group (blind participants versus sighted controls) as a between-subjects variable showed a significant interaction between Judgement and Group [$F(1,36) = 4.972, P=0.032$, Fig. 4B], suggesting that the medial prefrontal activity was greater to self-judgements than to other-judgements in blind individuals [$F(1,18)=15.657, P=0.001$] but not in sighted controls [$F(1,18)=0.071, P=0.793$]. The ANOVA with Judgement (other-judgement versus valence-judgement) and Group (blind versus sighted controls), however, failed to show a significant interaction between Judgement and Group [$F(1,36)=1.350, P=0.253$, Fig. 4B]. These results indicate that medial prefrontal cortex was engaged in aural self-referential processing in blind participants but not in sighted controls whereas the medial prefrontal activity related to the processing of others' personal knowledge did not differ between the two subject groups. A whole-brain statistical parametric mapping analysis was also conducted to confirm the involvement of the medial prefrontal cortex in the self-referential processing in blind participants. The contrast of self-judgements versus other-judgements revealed significant activation in the ventral medial prefrontal cortex and anterior cingulate cortex ($x, y, z: 6, 50, 12, BA 10, Z=4.06, P < 0.05$, corrected for multiple comparisons, Fig. 4C and 4D) in blind participants. However, no significant activation was observed in sighted controls even at a voxel-wise threshold of $P < 0.001$ and an extend threshold of 50 voxels. The results of all contrasts for blind individuals and sighted controls are listed in Supplementary Tables 3 and 4, respectively.

Given the findings of Experiment 1, we hypothesized that self-judgements of aurally presented statements in blind individuals may increase functional connections between the medial prefrontal cortex and the sensory cortex. This was tested by conducting a psychophysiological interaction analysis that compared self-judgements and other-judgements. We found that

self-judgements caused increased functional connectivity between the medial prefrontal cortex and bilateral occipital cortex ($x, y, z: 18, -80, -18$ and $-28, -78, 34, BA 18, Z=3.22$ and 3.39 ; a voxel-wise threshold of $P < 0.001$ and an extent threshold of 100 voxels, Fig. 4E). Figure 4E illustrates the overlap of the brain areas that were activated by auditory stimuli and those that showed enhanced functional connectivity with the medial prefrontal cortex during self-judgements in blind participants.

To assess whether a similar neural network was engaged in the processing of others' personal knowledge in blind participants and sighted controls, we calculated the contrast of other-judgements versus valence-judgements. This revealed significant activations in the dorsal medial prefrontal cortex ($x, y, z: -4, 54, 20, BA 10, Z=5.46$) and posterior cingulate cortex/precuneus ($x, y, z: -6, -58, 24, BA 23, 31, Z=5.96$, Supplementary Fig. 2A) in blind individuals. A similar neural circuit was observed in sighted controls [medial prefrontal cortex ($x, y, z: -6, 58, 24, BA 10, Z=5.00$)] and posterior cingulate cortex/precuneus ($x, y, z: -6, -56, 20, BA 23, 31, Z=4.23$, Supplementary Fig. 2B), suggesting that visual deprivation does not influence the medial prefrontal activity related to the processing of others' personal knowledge.

To examine if the medial prefrontal activity could predict individual differences in behavioural performances during the memory test, we calculated correlations between the medial prefrontal cortex activity associated with self-judgements and the recognition scores of trait words (hits minus false alarms) used during self-judgements. As can be seen in Fig. 5, the medial prefrontal cortex activity extracted from the brain region defined in the contrast of self- versus other-judgements positively correlated with the recognition scores in both sighted (medial prefrontal coordinates: $x, y, z: 8, 56, 10; r=0.566, P=0.005$) and blind participants (medial prefrontal coordinates: $x, y, z: 6, 50, 12; r=0.483, P=0.036$). The larger the medial prefrontal activity, the better participants remembered trait words used in self-judgements. To test whether the medial prefrontal activity can predict memory

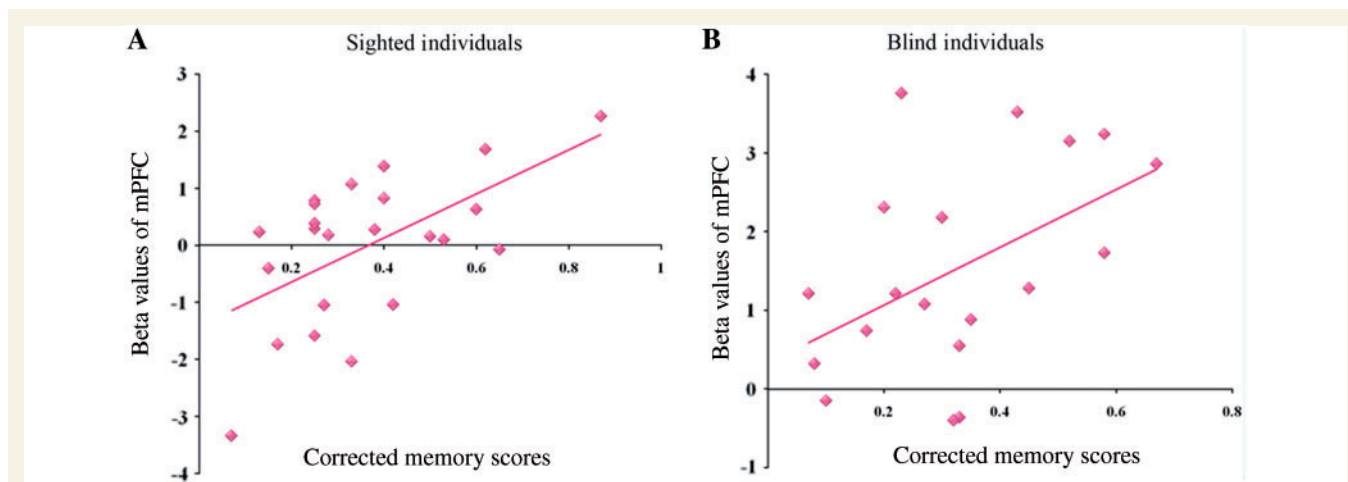


Figure 5 Results of correlation analysis. (A) Results of the correlation analysis in Experiment 1. Medial prefrontal cortex (mPFC) activity associated with self-judgements in the visual session positively correlated with the corrected memory scores of trait words (hits minus false alarms) used during self-judgements. (B) Results of the correlation analysis in Experiment 2. Medial prefrontal cortex activity associated with self-judgements in blind participants positively correlated with the corrected memory scores of trait words (hits minus false alarms) used during self-judgements.

performance related to others, we calculated the correlation between the medial prefrontal activity related to the processing of others' personal knowledge and the recognition scores of trait words used for other-judgements in both sighted and blind participants. This failed to show any significant results for sighted (visual session: $r=0.170$, $P=0.438$; aural session: $r=-0.061$, $P=0.789$) or blind participants ($r=-0.152$, $P=0.533$), suggesting that the medial prefrontal cortex's function of encoding information during trait judgements was specific to the self rather than general to any person.

Discussion

Our functional MRI results provide evidence that the medial prefrontal activity underpinning self-concept representation is specific to the visual modality in sighted individuals and exhibits cross-modal plasticity in the absence of visual experience in congenitally blind individuals. Our findings on sighted participants making trait judgements on visually presented stimuli replicate the results of previous work (Kelley *et al.*, 2002; Lieberman *et al.*, 2004; Mitchell *et al.*, 2006; Zhu *et al.*, 2007), showing that self-judgements activate the ventral region of the medial prefrontal cortex relative to other-judgements. Surprisingly, we found that the medial prefrontal activity associated with self-referential processing was eliminated when stimuli for judgements were presented aurally, indicating that the medial prefrontal activity involved in self-concept representation in sighted individuals is visual modality-specific. Consistent with this finding, self-judgements induced enhanced functional connectivity between the medial prefrontal cortex and visual cortex relative to other-judgements, suggesting task-related cortico-cortical coherence and enhanced information exchange between the medial prefrontal cortex and visual cortex during self-referential processing of visually presented stimuli. Previous studies showed that the prefrontal cortex is directly connected with secondary or 'association' but not primary sensory cortex (Miller and Cohen, 2001). However, these studies did not exclude the possibility that the prefrontal cortex is connected indirectly with the primary sensory cortex as the prefrontal cortex is also connected with other cortical regions that are themselves sites of multimodal convergence. Indeed, a recent diffusion spectrum imaging study has shown evidence that the prefrontal cortex is indirectly connected with the pericalcarine cortex and the superior temporal cortex that correspond with the primary visual and auditory cortex (Hagmann *et al.*, 2008). Thus the functional connectivity between the medial prefrontal cortex and the occipital cortex observed in our work might be mediated by the indirect structural connections between the two brain areas.

It is commonly known that human sensory cortices are modality-specific so that the occipital cortex engages in the initial encoding of visual features of stimuli and the posterior superior temporal cortex processes auditory features of stimuli. Such modality specificity is also observed in the parietal and lateral frontal cortices in that spatial localization of visual and auditory stimuli recruits distinct sub-regions in these brain areas (Bushara *et al.*, 1999). Our findings provide evidence that high-level social

cognitive processes related to the self, subserved by the medial prefrontal cortex, strongly depend on sensory input and are visual modality-specific in sighted people.

In addition, our functional MRI results demonstrate cross-modal plasticity of the medial prefrontal activity underlying self-referential processing. We showed that medial prefrontal cortex activity underlying self-referential processing of visually delivered stimuli in sighted people was modulated similarly by aurally delivered stimuli in congenitally blind individuals when they performed self-judgements. This is akin to the functional reorganization of the occipital cortex by visual deprivation observed in the current and previous studies (Burton *et al.*, 2002; Gougoux *et al.*, 2009). In line with the medial prefrontal cortex cross-modal reorganization, the psychophysiological interaction analysis confirmed increased functional connectivity between the medial prefrontal cortex and occipital cortex during self-judgements in blind individuals. Interestingly, the medial prefrontal activity related to self-judgements observed in both blind and sighted groups was able to predict individual differences in memory performances on trait words used during self-judgements, indicating that the medial prefrontal cortex played a similar functional role in elaborating self-related information in visual and auditory modalities in sighted and blind individuals, respectively. While the neural plasticity of the sensory cortex after visual or auditory deprivation has been demonstrated (Finney *et al.*, 2001; Nishimura *et al.*, 1999; Burton *et al.*, 2002; Gougoux *et al.*, 2009), our findings from blind individuals indicate that visual deprivation leads to functional reorganization of the medial prefrontal cortex so as to be tuned by auditory input during self-referential processing. The results implicate that visual dominance in shaping medial prefrontal cortex function of self-concept representation in sighted people is not innately determined, but rather strongly dependent on one's sensory experiences.

Interestingly, our data suggest that cross-modal plasticity is specific to the ventral medial prefrontal cortex involved in self-referential processing. The activity in the dorsal medial prefrontal cortex in association with the processing of others' personal knowledge was likewise observed in the visual and auditory modalities in sighted and in the auditory modality in blind participants. Similarly, previous studies have shown that the neural substrates employed for understanding others' mental states is not sensory modality-specific and can develop independently of visual experience (Kampe *et al.*, 2003; Bedny *et al.*, 2009; Ricciardi *et al.*, 2009). The findings suggest that social cognitive processes related to others are susceptible to sensory experiences to a much less degree than social cognitive processing of the self. Moreover, unlike self-trait judgements, trait judgements of others activated the posterior cingulate cortex and precuneus, which have been associated with retrieval of information from episodic memory (Cavanna and Trimble, 2006). This is consistent with the proposal that, relative to trait judgement of the self, trait judgements of others may require enhanced episodic memory retrieval to provide information for evaluation processes (Klein *et al.*, 2002).

Traditionally, self-concept is considered to be socially constructed and emerges as a by-product of social interaction (Hogg, 2003). In accordance with this proposition, social

psychological research has shown ample evidence that self-concept differs remarkably across cultures (Marsella *et al.*, 1985; Markus and Kitayama, 1991). In addition, recent brain imaging studies have shown evidence that cultural experiences also influence self-concept representation in the human brain (Zhu *et al.*, 2007; Han and Northoff, 2008; Chiao *et al.*, 2010). For example, the medial prefrontal cortex engages in representations of the self and close others in Chinese individuals, but represents exclusively the self in Westerners (Zhu *et al.*, 2007). While previous functional MRI studies suggest cultural influences on neural representations of the self in the prefrontal cortex, the present study demonstrates that sensory experiences also play a pivotal role in shaping the neural substrates underlying self-representation in the medial prefrontal cortex. Humans live in an environment that relies heavily on vision. The ecological approach to sensory perception suggests that information used in distinguishing between self and non-self is inherently encoded in perception, and the visual modality dominates other sensory modalities in representation of the 'physical self' by providing information for movement of the self (Gibson, 1979). Consistent with this, people intend to attribute a visible rubber hand, which is stroked synchronously with their own unseen hand, to themselves (Botvinik and Cohen, 1998). Conflicting visual-somatosensory input in virtual reality environments even make humans feel as if the self is located inside a virtual body seen in front of them (Lenggenhager *et al.*, 2007). Sensory experiences may affect the neural representation of the mental aspect of self (e.g. trait) through modulations of the basic sense of self (e.g. the bodily self that constitutes an independent bounded entity). Visual input in sighted humans plays a stronger role compared to auditory input in constructing the bodily self that may provide a basis for self-concept representation in the medial prefrontal cortex. However, auditory input in congenitally blind individuals plays a dominant role in accumulating sensory experiences to differentiate self versus non-self in daily life. Consequently, the medial prefrontal activity was taken over by auditory stimuli for self-referential processing in blind individuals, as suggested by our finding of cross-modal plasticity in the medial prefrontal activity related to self-referential processing.

A possible account of the medial prefrontal activity related to self-referential processing in blind participants is that, compared to sighted participants, blind individuals possess superior skills in auditory tasks (Roder *et al.*, 1999; Gougoux *et al.*, 2004) and may be able to hear the statements more clearly during the aural sessions. However, our data contradict this explanation because sighted participants made over 80% correct judgements on word valence in Experiment 1. Sighted controls in Experiment 2 also showed higher response accuracy on valence judgements than blind participants, indicating that the noise of the scanner was unable to mask the auditory stimuli in sighted participants and did not produce stronger interference on the sensory-perceptual processing of auditory stimuli in sighted than in blind participants. An alternative explanation is that auditory language processing is different between sighted and blind individuals and results in differential involvement of the medial prefrontal cortex in self-referential processing. However, previous research has identified comparable activations in the frontal and temporal gyri in

blind and sighted subjects during auditory language processing (Burton *et al.*, 2002), suggesting similar auditory language processing in blind and sighted people. Similarly, one may argue that the absence of medial prefrontal activity related to self-referential processing of aurally delivered stimuli in sighted participants might arise from the difference in semantic processing of stimuli between visual and auditory modalities (Booth *et al.*, 2002). In contrast to this argument, recent work has shown similar activations in the left parietal and frontal cortex associated with the phonology and semantic processing of Chinese words delivered through both visual and auditory modalities (Liu *et al.*, 2008), suggesting modality independent Chinese language processing in sighted individuals. Even if this difference in language processing of visual and auditory stimuli existed in our work, it should be the same for self-judgements and other-judgements. Our interaction analysis confirms the modality-specific differences in self-referential processing, excluding the potential influences of modality differences in language processing. Taken together, the difference in language processing cannot account for the distinct medial prefrontal activity underlying self-referential processing between visual and auditory modalities in sighted people, and between sighted and blind individuals in the auditory modality.

Recent brain imaging studies have accumulated evidence for functional and structural reorganization of the human brain as a consequence of visual deprivation (Bavelier and Neville, 2002; Noppeney, 2007). However, evidence for functional reorganization resulting from the absence of visual input is limited to the primary visual cortex. The same medial-to-lateral organization of the ventral occipitotemporal cortex in categorization of living and non-living stimuli is observed in sighted adults when the stimuli are presented through both visual and auditory modalities and in blind individuals when the stimuli are delivered through the auditory modality (Mahon *et al.*, 2009). The frontal and parietal cortices involved in high-level cognitive processes such as language processing (Burton *et al.*, 2002) and understanding of others' intentions and beliefs (Kampe *et al.*, 2003; Bedny *et al.*, 2009; Ricciardi *et al.*, 2009) seem to function independently of sensory modalities and develop properly in people without visual experience. While our data complement previous studies by showing that cross-modal plasticity resulting from visual deprivation can also take place in the prefrontal cortex, cross-modal plasticity of the medial prefrontal activity may be different from that of the sensory cortex in that modality specificity of medial prefrontal activity is true only for a specific task (e.g. self-trait judgements) but not for a task domain (e.g. trait judgements of people in general). Thus only the medial prefrontal activity underlying self-concept representation shows cross-modal plasticity. In addition, there has been no evidence for structural reorganization of the prefrontal cortex in blind individuals whereas visual deprivation leads to both grey and white matter changes in the visual, somatosensory and motor systems (Emmorey *et al.*, 2003; Penhune *et al.*, 2003).

Using a similar trait judgement task, Moran and colleagues (2006) found that the medial prefrontal activity was greater to trait words that were self-descriptive but did not differ as a function of the valence of the trait. However, the anterior cingulate activity was greater to positive than negative trait words when

they were judged to be self-relevant. The results disentangled the cognitive and affective components of self-reflective thoughts in the medial prefrontal cortex and anterior cingulate cortex, respectively. Similarly, our study also showed greater activity in both the medial prefrontal cortex and anterior cingulate cortex to self-judgements than to other-judgements. Moreover, the neural activity in both brain areas showed similar variation as a function of sensory modality and similar cross-modal plasticity, suggesting that both the cognitive and affective components of self-referential processing are strongly influenced by sensory experiences.

In conclusion, our brain imaging results provide new insight into the relation between sensory experience and self-concept representation in the medial prefrontal cortex. Our data demonstrate visual modality specificity of the medial prefrontal activity in self-concept representation in sighted individuals and cross-modal plasticity of the medial prefrontal activity associated with self-concept representation in congenitally blind individuals. The medial prefrontal cortex activity in congenitally blind individuals plays a similar functional role of elaborating and encoding self-relevant information as seen in sighted individuals. These findings indicate that the neural substrates underlying complicated social processes such as self-reflective thinking can be shaped by sensory experience in a fashion similar to that observed in the primary sensory cortex. Thus, neural plasticity is exhibited in the functional architecture of the brain regions involved in both low-level sensory processing and high-level social cognitive processing.

Acknowledgements

The authors thank Zhenhao Shi, Yifan Li and Gang Wang for helping with data collection. They are grateful to B. Waxler, W. Yund and S. Liew for comments on an early draft of this article, and to Jianqiao Ge for helping with preparation of the auditory stimuli.

Funding

National Natural Science Foundation of China (Project 30630025, 30828012, 30910103901), National Basic Research Program of China (973 Program 2010CB833903) and the Fundamental Research Funds for the Central Universities.

Supplementary material

Supplementary material is available at *Brain* online.

References

- Amedi A, Raz N, Pianka P, Malach R, Zohary E. Early visual cortex activation correlates with superior verbal memory performance in the blind. *Nat Neurosci* 2003; 6: 758–66.
- Bavelier D, Neville HJ. Cross-modal plasticity: where and how? *Nat Rev Neurosci* 2002; 3: 443–52.
- Bedny M, Pascual-Leonea A, Saxe R. Growing up blind does not change the neural bases of Theory of Mind. *Proc Natl Acad Sci USA* 2009; 106: 11312–17.
- Booth JR, Burman DD, Meyer JR, Gitelman DR, Parrish B, Mesulam MM. Functional anatomy of intra- and cross-modal lexical tasks. *Neuroimage* 2002; 16: 7–22.
- Botvinick M, Cohen J. Rubber hands ‘feel’ touch that eyes see. *Nature* 1998; 391: 756.
- Büchel C, Price C, Frackowiak RS, Friston K. Different activation patterns in the visual cortex of late and congenitally blind subjects. *Brain* 1998; 121: 409–19.
- Burton H, Snyder AZ, Diamond JB, Raichle ME. Adaptive changes in early and late blind: a fMRI study of verb generation to heard nouns. *J Neurophysiol* 2002; 88: 3359–71.
- Bushara KO, Weeks RA, Ishii K, Catalan M, Tian B, Rauschecker JP, et al. Modality-specific frontal and parietal areas for auditory and visual spatial localization in humans. *Nat Neurosci* 1999; 2: 759–66.
- Butterworth G. Origins of self-perception in infancy. *Psychol Inquiry* 1992; 3: 103–11.
- Carmody DP, Lewis M. Brain activation when hearing one’s own and others’ names. *Brain Res* 2006; 1116: 153–8.
- Cavanna AE, Trimble MR. The precuneus: a review of its functional anatomy and behavioural correlates. *Brain* 2006; 129: 564–83.
- Chiao JY, Harada T, Komeda H, Li Z, Mano Y, Saito D, et al. Dynamic cultural influences on neural representations of the self. *J Cogn Neurosci* 2010; 22: 1–11.
- Emmorey K, Allen JS, Bruss J, Schenker N, Damasio H. A morphometric analysis of auditory brain regions in congenitally deaf adults. *Proc Natl Acad Sci USA* 2003; 100: 10049–54.
- Finney EM, Fine I, Dobkins KR. Visual stimuli activate auditory cortex in the deaf. *Nat Neurosci* 2001; 4: 1171–73.
- Friston KJ, Büchel G, Fink GR, Morris J, Rolls E, Dolan RF. Psychophysiological and modulatory interactions in neuroimaging. *Neuroimage* 1997; 6: 218–29.
- Gibson JJ. *The ecological approach to visual perception*. Boston: Houghton Mifflin; 1979.
- Gougoux F, Lepore F, Lassonde M, Voss P, Zatorre RJ, Belin P. Neuropsychology: pitch discrimination in the early blind. *Nature* 2004; 430: 309.
- Gougoux F, Belin P, Vossa P, Lepore F, Lassonde M, Zatorre RJ. Voice perception in blind persons: a functional magnetic resonance imaging study. *Neuropsychologia* 2009; 47: 2967–74.
- Gougoux F, Zatorre RJ, Lassonde M, Voss P, Lepore F. A functional neuroimaging study of sound localization: visual cortex activity predicts performance in early-blind individuals. *PLoS Biol* 2005; 3: e27.
- Hagmann P, Cammoun L, Gigandet X, Meuli R, Honey CJ, Wedeen VJ, et al. Mapping the structural core of human cerebral cortex. *PLoS Biol* 2008; 6: e159.
- Han S, Northoff G. Culture-sensitive neural substrates of human cognition: a transcultural neuroimaging approach. *Nat Rev Neurosci* 2008; 9: 646–54.
- Hogg MA. Social identity. In: Leary MR, Tangney JP, editors. *Handbook of self and identity*. New York: The Guilford Press; 2003. p. 462–79.
- Johnson SC, Baxter LC, Wilder LS, Pipe JG, Heiserman JE, Prigatano GP. Neural correlates of self-reflection. *Brain* 2002; 125: 1808–14.
- Kampe KKW, Frith CD, Frith U. “Hey John”: signals conveying communicative intention toward the self activate brain regions associated with “mentalizing,” regardless of modality. *J Neurosci* 2003; 23: 5258–63.
- Kelley WM, Macrae CN, Wyland CL, Caglar S, Inati S, Heatherton TF. Finding the self? An event-related fMRI Study. *J Cogn Neurosci* 2002; 14: 785–94.
- Kihlstrom JF, Beer JS, Klein SB. Self and identity as memory. In: Leary MR, Tangney JP, editors. *Handbook of self and identity*. New York: Guilford Press; 2003. p. 68–90.
- Klein SB, Cosmides L, Tooby J, Chance S. Decisions and the evolution memory: multiple systems, multiple functions. *Psychol Rev* 2002; 109: 306–29.

- Lenggenhager B, Tadi T, Metzinger T, Blanke O. Video ergo sum: manipulating bodily self-consciousness. *Science* 2007; 317: 1096–9.
- Levanen S, Jousmaki V, Hari R. Vibration-induced auditory-cortex activation in a congenitally deaf adult. *Curr Biol* 1998; 8: 869–72.
- Lieberman MD, Jarcho JM, Satpute AB. Evidence-based and intuition-based self-knowledge: an fMRI study. *J Pers Soc Psychol* 2004; 87: 421–35.
- Liu Y. Modern lexicon of Chinese frequently-used word frequency. Beijing: Space Navigation Press; 1990.
- Liu L, Deng X, Peng D, Cao F, Ding G, Jin Z, et al. Modality- and task-specific brain regions involved in Chinese lexical processing. *J Cogn Neurosci* 2008; 21: 1473–87.
- Macrae CN, Moran JM, Heatherton TF, Banfield JF, Kelley WM. Medial prefrontal activity predicts memory for self. *Cereb Cortex* 2004; 14: 647–54.
- Mahon BZ, Anzellotti S, Schwarzbach J, Zampini M, Caramazza A. Category-specific organization in the human brain does not require visual experience. *Neuron* 2009; 63: 397–405.
- Marsella AJ, De Vos GA, Hsu FLK. Culture and self: Asian and Western perspectives. New York: Tavistock Publications; 1985.
- Markus HR, Kitayama S. Culture and the self: implication for cognition, emotion and motivation. *Psychol Rev* 1991; 98: 224–53.
- Miller EK, Cohen JD. An integrative theory of prefrontal cortex function. *Annu Rev Neurosci* 2001; 24: 167–202.
- Mitchell JP, Macrae CN, Banaji MR. Dissociable medial prefrontal contributions to judgments of similar and dissimilar others. *Neuron* 2006; 50: 655–63.
- Moran JM, Macrae CN, Heatherton TF, Wyland CL, Kelley WM. Neuroanatomical evidence for distinct cognitive and affective components of self. *J Cogn Neurosci* 2006; 18: 1586–94.
- Nishimura H, Hashikawa K, Doi K, Iwaki T, Watanabe Y, Kusuoka H, et al. Sign language 'heard' in the auditory cortex. *Nature* 1999; 397: 116.
- Noppeney Y. The effects of visual deprivation on functional and structural organization of the human brain. *Neurosci Biobehav Rev* 2007; 31: 1169–80.
- Northoff G, Bermpoh F. Cortical midline structures and the self. *Trends Cogn Sci* 2004; 8: 101–7.
- Pascual-Leone A, Amedi A, Fregni F, Merabet LB. The plastic human brain cortex. *Annu Rev Neurosci* 2005; 28: 377–401.
- Penhune VB, Cismaru R, Dorsaint-Pierre R, Petitto LA, Zatorre RJ. The morphometry of auditory cortex in the congenitally deaf measured using MRI. *Neuroimage* 2003; 20: 1215–25.
- Ricciardi E, Bonino D, Sani L, Vecchi T, Guazzelli M, Haxby JV, et al. Do we really need vision? How blind people "see" the actions of others. *J Neurosci* 2009; 29: 9719–24.
- Rizzolatti G, Sinigaglia C. The functional role of the parieto-frontal mirror circuit: interpretations and misinterpretations. *Nat Rev Neurosci* 2010; 11: 264–74.
- Roder B, Teder-Salejarvi W, Sterr A, Rosler F, Hillyard SA, Neville HJ. Improved auditory spatial tuning in blind humans. *Nature* 1999; 400: 162–6.
- Rogers TB, Kuiper NA, Kirker WS. Self-reference and the encoding of personal information. *J Pers Soc Psychol* 1977; 35: 677–88.
- Sadato N, Pascual-Leone A, Grafman J, Ibanez V, Deiber MP, Dold G, et al. Activation of the primary visual cortex by Braille reading in blind subjects. *Nature* 1996; 380: 526–8.
- Sedikides C, Skowronski JJ. The symbolic self in evolutionary context. *Person Soc Psychol Rev* 1997; 1: 80–102.
- Sugiura M, Sassa Y, Jeong H, Horie K, Sato S, Kawashima R. Face-specific and domain-general characteristics of cortical responses during self-recognition. *Neuroimage* 2008; 42: 414–22.
- Zhu Y, Zhang L, Fan J, Han S. Neural basis of cultural influence on self representation. *Neuroimage* 2007; 4: 1310–17.