to excessive head movement. The remaining 23 sighted individuals (11 males, 12 females; age range: 18–28 years, mean age = 22.0 years)

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 wasstatements fo.2 (on)-4halanc57.8 (6o)-4across.5 (judgesubves)59 (Th8he)- li8ts to the wa5e

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 dur (of-780.1 (s)-e5ov13 of-780.1 (s)-e5oi785.2 (pref (wit69.6603o)-445.160and)--judgements)

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

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

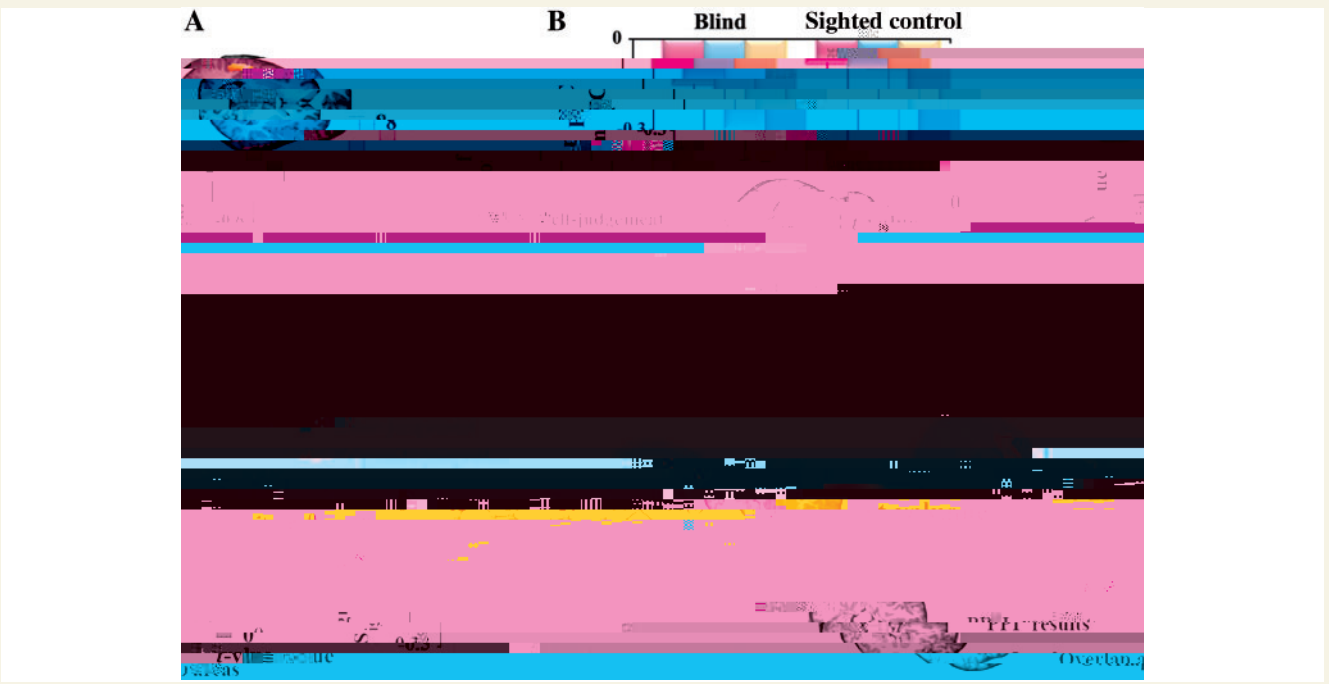

Figure 4 Results of Experiment 2. (**A**) The activation elicited by auditory stimuli in blind individuals. The contrast of valence-judgements versus rest showed activations in bilateral occipital and superior temporal cortices. (**B**) The results of the region of interest analysis. Signal intensity 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-judgments 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

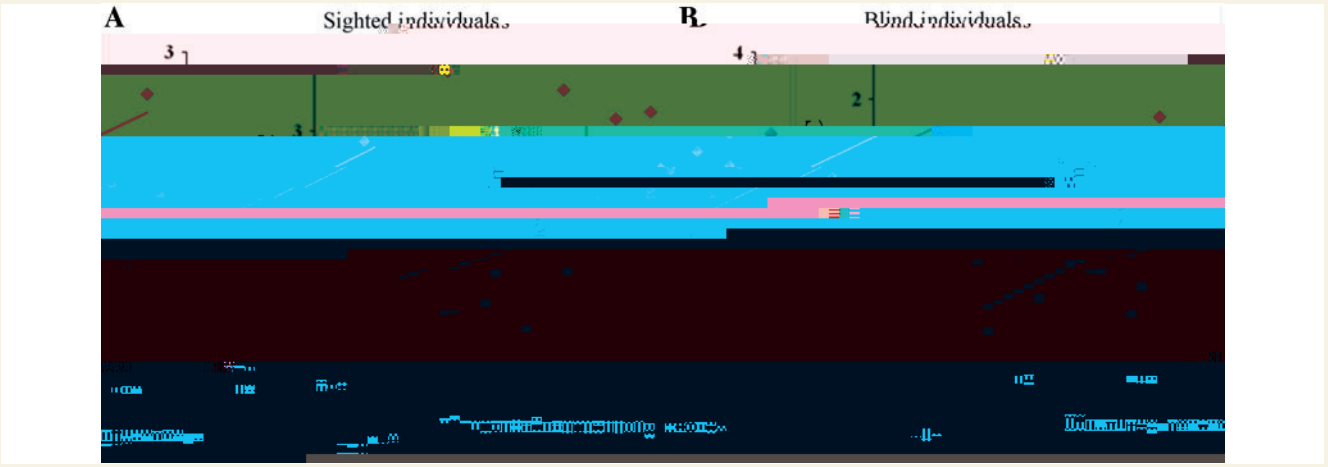

Figure 5 Results of correlation analysis. (**A**) Results of the correlation analysis in Experiment 1. Medial prefrontal cortex (mPFC) activity

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.

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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.

Lenggenhager B, Tadi T, Metzinger T, Blanke O. Video ergo sum: