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Visual Cortical Activation During Auditory Word Categorization: Evidence for Multiple Sensory Interaction From Normal Sighted Participants*

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Abstract Sensory substitution has been reported in recent brain imaging studies with blind people and others with sensory deficits so that sensory cortical regions traditionally considered unimodal respond to stimulation from other sensory modalities. Similar effects are also found for normal sighted people with sensory deprivation (blindfolded), indicative of pre-existing neuronal pathways for multiple sensory interactions. Such pathways are considered latent in that they only become unmasked or potentiated in the event of sensory deafferentation, although whether sensory deprivation is necessary to expose these pathways is unclear due to inconclusive evidence. With a relatively strong power in experimental design, visual cortical activation was observed when normal sighted participants (not blindfolded) judged whether auditorily-presented nouns referred to artificial or natural objects. The results suggest the above mentioned pathways can be exposed without sensory deafferentation and therefore are not totally latent. This establishes a boundary condition constraining theoretical models for the neural basis of multiple sensory interactions.

Key words visual cortex, auditory stimulation, functional MRI, cross-modality
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A significant recent progress in the study of neuroplasticity is the finding that sensory cortical areas previously thought to be unimodal can be recruited to process information of other sensory modalities. This was initially demonstrated with brain imaging techniques in deaf and blind people so that deaf participants showed activation in temporal cortex to purely visual stimuli[1~3] and blind participants showed primary visual cortex activation in a number of linguistic tasks [4~13], such as tactile Braille reading, auditory words perception, and verbal memorization. Such activations seem to have functional relevance as their disruption by repetitive transcranial magnetic stimulation (rTMS) during task performance produces behavioral consequences[14~16].

One explanation for this cortical functional reorganization is the establishment of new neural connections or pathways specific to the blind and the deaf population. Further studies suggest another possibility, that is, there are pre-existing latent pathways in the normal population between multiple sensory regions. These pathways can be unmasked or potentiated in the event of sensory deafferentation[17, 18].

With normal sighted participants blindfolded to simulate sensory deprivation, Pascual-Leone and Hamilton[19] reported gradually emerging activations in the visual cortex including the striate cortex during tone pitch judgment and Braille symbol discrimination tasks, over the course of a 5-day blindfold period. The

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activations were transient and reversible as they disappeared within 12～24 h following removal of the blindfold.

In the studies by Schlaug and colleagues [20, 21], there was a group of non-blindfolded normal participants who did not show visual cortical activations to the non-visual tasks, indicating that to expose the latent pathways in the normal population it was essential to have sensory deprivation. This conclusion was also supported by many of the studies on blind participants which similarly involved normal sighted participants as controls[5, 6, 8, 10, 22].

A few other studies however, reported visual cortical response to non-visual stimuli without sensory deprivation in normal participants. Amedi and colleagues[23] found that tactile perception of object shape activates the lateral occipital complex (LOC), an occipito-temporal region preferentially activated by visual objects. Blake and coworkers[24] discovered that mere touching of a rotating globe reliably activates the middle temporal visual area sensitive to shape from motion in vision. Martuzzi and colleagues[25] showed that nonsense auditory stimuli activated primary visual cortical regions.

Briefly, it remains understudied and unclear whether the latent pathways connecting two different sensory regions function when both senses are open to external stimulation without any information deprivation. The present study was intended to establish such a boundary condition, which should help to understand sensory functional reorganization, and more generally, multiple sensory interaction.

We assume that in the presence of normal visual simulation, any visual cortical activity induced by non-visual stimuli, if exists at all, would be a weak modulation of the background visual cortical activation. Consequently, more power would be needed to expose such weak effects. That many of the relevant studies failed finding such effects may be partly due to their small sample size, all being smaller or around 10 participants, not so adequate for reliable random-effect analysis. In addition, there could have been a general bias to focus on the blind/deaf population and to treat the normal sighted group only as a control where no effect was expected.

With a relatively large number of participants (n = 20), we used functional magnetic resonance imaging (fMRI) to compare an auditory word categorization task with a control task. Different from Martuzzi *et al.*[25] who were most interested in responses to simple meaningless stimuli, we used a linguistic task involving meaningful materials, as in most of the related studies on blind participants. Further, while Martuzzi *et al.*[25] adopted an event-related design, we used a block design to maximize detection power, as in most literature studies. A pure tone pitch judgment task as opposed to a resting baseline was used as the control condition to better match general attention and motor responses. There are some controversies in brain imaging research on the appropriateness of using resting as a baseline[26～28]. In addition, for the purpose of the present study, an ideal resting baseline should be a total silence devoid of any auditory stimulation, a condition in fact difficult to implement in the noisy scanner.

1 Methods

1.1 Participants

Twenty healthy undergraduates (mean age= 21.3 years, SD=1.8) participated in the present study with written informed consent. All were right-handed female to reduce possible handedness and gender effects although such effects cannot be excluded a priori without further study. All had normal hearing, normal or corrected-to-normal vision, and none had any history of neurological or psychiatric disorders. The experiment was conducted following a protocol approved by the Human Subject Committee of the Institute of Psychology, The Chinese Academy of Sciences.

1.2 Stimuli and task

The study included a single 12-minute run using a block design in which each participant completed 6 word blocks and 6 pure tone blocks with the block order counterbalanced across-subject. During each word block lasting 60 s, 20 concrete two-syllable Chinese nouns were presented auditorily, each for 1 000 ms with a 2 000 ms inter-stimulus-interval (ISI). Participants were to pay attention to each word and decided whether the word referred to a natural or an artificial object. The same set of 20 words was used in the 6 word blocks, with their presentation order pseudo-randomized in each block.

During each pure tone block lasting 60 s, 10 pairs of pure tones were presented, each for 1 000 ms with a 2 000 ms ISI. Each pair was either a low-high sequence, consisting of a low tone of 500 Hz and a high tone of 2 000 Hz, or a high-low sequence, consisting of a high tone of 2 000 Hz and a low tone of 500 Hz. The two types of sequences were randomly intermixed and participants were to judge whether each pair was a low-high or a high-low sequence.

For both the word block and the pure tone block, participants indicated their responses with either a left or a right buttonpress. Prior to the testing, there was a stage for sound volume adjustment so that every participant heard the word and tones at a clear and comfortable level. Practice trials were also given outside the scanner to familiarize the participants with the task.

1.3 Image acquisition and analysis

All MR images were collected in a 1.5 T Siemens SONATA scanner. For functional images, 20 axial images parallel to the AC/PC line and covering the whole brain were acquired for each TR with a T2* gradient echo planner imaging (EPI) pulse sequence sensitive to blood oxygenation level dependent contrast (TR = 2 s, TE = 60 ms, FOV = 22 cm, matrix = 64 × 64, flip angle = 90°, slide thickness = 5 mm, gap = 1.5 mm). Co-plannar T1-weighted anatomic images were collected with spin echo (SE) pulse sequence (TR = 447 ms, TE = 15 ms, matrix = 256 × 256). A fast low angle shot (FLASH) sequence (TR = 30 ms, TE = 1.17 ms, FOV = 32.5 cm, matrix = 192 × 256, slice thickness = 1.3 mm, gap = 0.26 mm, 128 sagittal slices) was also used to acquire a high-resolution 3D anatomic whole brain image for reconstruction and spatial normalization.

The imaging data were analyzed using the AFNI software package[29]. Preprocessing consisted of stages including slice acquisition correction, head motion correction, linear drift removal, and spatial smoothing (8 mm FWHM Gaussian kernel).

Hemodynamic responses for the two types of blocks, or conditions, were then estimated for each participant using the multiple regression analysis, with the six motion parameters (x, y, z translations, roll, pitch, and yaw) as covariates to remove residual motion artifacts. The estimated coefficients were normalized as percent signal changes, and the resulting images were then transformed to the Talairach space, re-sampled to 3 mm × 3 mm × 3 mm voxel size. A random-effect group analysis was then conducted using t-test to identify brain regions that showed significantly ($P < 0.05$, corrected) different responses across the two conditions.

2 Results

Mean performance accuracy was high, being 94.5% (SD=5.9) for the word condition and essentially 100% for the tone condition. Response speed was slower to the word stimuli (986 ms, SD=288) than to the tone stimuli (918 ms, SD=298).

As shown in Figure 1, significantly greater activity was observed for the word condition relative to the tone condition in left frontal, occipital, temporal, parietal regions and right insula.

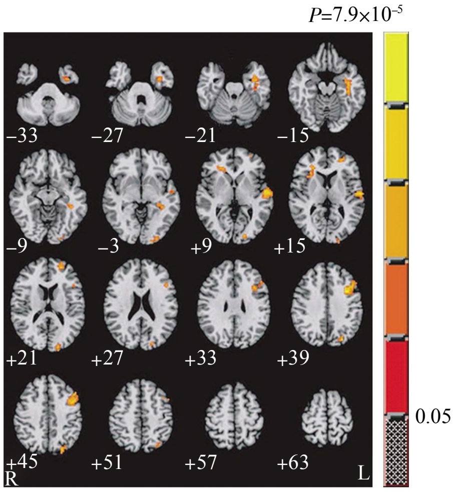

Fig. 1 Brain areas showing significantly stronger activity in the word task than in the tone task

Left is right and the numbers show z-axis coordinates for each slice.

Figure 2 shows brain regions with greater activity in the tone condition relative to the word condition,

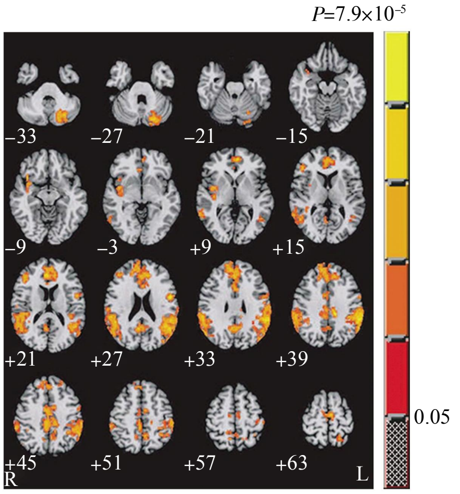

Fig. 2 Brain areas showing significantly stronger activity in the tone task than in the word task

Left is right and the numbers show z-axis coordinates for each slice.

including regions mainly in the cingulate gyrus, and the parietal lobule, but there was no activation in the visual cortex. Detail information for these regions of activation is provided in Table 1.

Table 1　List of brain regions ($P<0.05$, corrected) and their peak activation Talairach coordinates from group analysis ($n=20$) for the word > tone and tone > word contrasts

Region	BA	Coordinates			Word > tone		Tone > word	
		x	*y*	*z*	*t* value	Volume	*t* value	Volume
L. occipital gyrus	18	−16	−87	17	2.55	1 755	–	–
L. precuneus	7	−25	−76	35	2.62	1 242	–	–
L. superior frontal gyrus	10	−22	52	14	2.65	999	–	–
L. middle frontal gyrus	9	−34	8	32	2.77	4 428	–	–
L. superior temporal gyrus	22	−52	−10	2	2.81	2 349	–	–
L. parahippocampal gyrus	36	−31	−10	−12	2.62	3 915	–	–
R. insula	13	25	32	8	2.56	1 215	–	–
Cingulate gyrus	24/31/23	−13	−31	33	–	–	2.62	40 176
L. inferior parietal lobule	40	−53	−40	30	–	–	2.73	29 943
R. inferior parietal lobule	40	56	−35	29	–	–	2.61	21 519
L. cerebellum	–	−28	−67	−36	–	–	2.76	6 885
R. insula	13	40	−3	−1	–	–	2.57	3 213
L. precentral gyrus	6	−49	−1	20	–	–	2.74	2 538

The visual cortical activation, peaking within primary visual cortex and also covering cuneus, is highlighted in Figure 3.

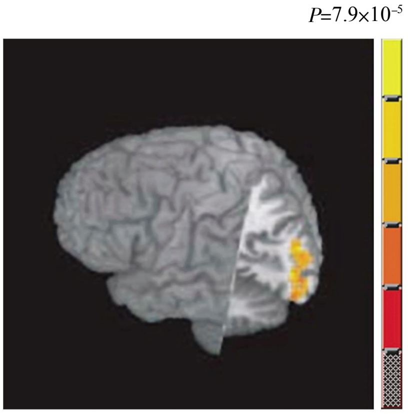

Fig. 3　Highlight of the visual cortical activation which showed significantly greater activity for the word task than for the tone task

3　Discussions

Conforming to general expectations, the word categorization task produced a clearly left lateralized pattern of activations with several temporal and frontal regions known to be involved in language processing. The superior temporal gyrus seems to be responsible for word comprehension and semantic information retrieval [30] and the inferior and middle prefrontal regions for semantic judgment [31]. Parahippocampal regions may also contribute to the retrieval process[32]. The few regions activated more in the pure tone condition were mostly part of the ‘default mode’ network [33] typically seen when an easier task was compared with a more difficult task.

The key finding was the visual cortical activation from the word *vs*. tone contrast, indicating recruitment of the visual sensory modality in processing linguistic materials from the auditory modality in normal participants who were not blindfolded. The reversed contrast did not show any visual cortical activation.

As described in the introduction, the study by Martuzzi *et al*.[25] was the only study we could identify showing such a visual-auditory sensory substitution in the absence of any sensory deprivation. That study, however, was designed to study non-linguistic stimuli and did not use a language task. Their results therefore may not be directly compared with most of the related studies that did use language tasks with blind or blindfolded participants. In addition, their event-related design intermixing visual stimulus trials and auditory stimulus trials may not provide maxim power to separate the sluggish BOLD signals for the auditory events from those for the visual events.

However, in the present study, we used a block design where only auditory stimuli were presented. The fact that we were still able to obtain a sensory substitution effect provides a strong piece of evidence for the notion that there are pre-existing neural pathways in normal sighted people between the visual and auditory sensory cortical areas and such pathways can be exposed without resorting to sensory deprivation, provided the experiment had adequate power.

Our results strengthen and extend the conclusion from Martuzzi *et al.*[25]. Together, this line of study implies a modification of the view that such inter-cortical pathways are totally latent and only come to surface in the event of deafferentation and suggests that these pathways may be always functioning. To speculate, the activities produced from these pathways may be weak and therefore usually overshadowed by the background activity from sensory stimulation.

This interpretation is not to deny that, as shown in the blindfold studies, the visual activation develops gradually following sensory deprivation suggesting a time course over while the neural plasticity gets potentiated. Our results only constrain this potentiation process to indicate that functionally it starts from a non-zero level. It is interesting to note in our results that the visual cortical activation is left lateralized. When looking at the individual data, 15 out of the total 20 participants showed activation only in the left visual cortex, 1 only in the right, 2 in both left and right, and 2 in neither. This lateralized pattern has not been reported in the literature of sensory substitution. One may attempt to link this to the left lateralization of language processes as we used linguistic materials. However, many studies[4, 5, 8～13, 18, 19, 22] with blind or blindfolded participants using languages tasks did show bi-lateral visual cortical activations, indicating that the inter-cortical pathways should be at least anatomically present for both the left and the right visual cortices. Therefore, our results suggest slightly stronger connection strength in the left visual-auditory pathways than that in the right, pending on further confirmation in future research.

As proposed in similar studies with blind or blindfolded participants[34], one alternative explanation of the present results is that the visual cortex activation observed may reflect brain processes associated with mental imagery of the objects the words depicted. Post-test report from our participants did not indicate explicit use of mental imagery of the objects involved, although introspection is not a reliable measure of the actual processing. Further, it is unclear why mental imagery would have engaged the left hemisphere but not the right in the present study. In an influential line of research, Kosslyn and colleagues[35] have convincingly demonstrated that the mental imagery elicited when participants were explicitly instructed to imagine concrete objects from spoken words, recruited both the left and the right visual cortex. However, the nature of the present task, doing semantic categorization of concrete objects could easily cue a response strategy based on mental imagery which would result in slow and effortful responses, consistent with the long response time (around 1s) we found. Therefore, whether mental imagery did play a role in the present study needs to be clarified with further empirical data, particularly when some researchers[36] propose that it may not be mutually exclusive from the sensory substitution account.

In summary, with a relatively large sample size and a block design to maximize power, we found visual cortical activation when non-blindfolded normal sighted participants performed an auditory word categorization task. This finding indicates that the inter-cortical neuronal pathways responsible for sensory substitution can be exposed under normal sensory stimulation and therefore are not totally latent. This result provides an important constraint on theorization of the neural basis of multiple sensory interaction.

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明视人听词分类任务时的视皮层激活*

——跨感觉通道的新证据

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摘要 近期的脑成像研究在盲人等感官缺陷被试者身上发现了感觉替换现象，即传统上认为仅对单一感觉通道刺激反应的皮层区域也参与其他感觉通道的信息加工．类似的效应在感觉剥夺(蒙住眼睛)的明视人被试中也被观察到，提示脑内可能预存着多感觉交互作用的神经通路．通常认为，上述神经通路在常态的人脑中是以潜伏形式存在的，只有当感觉剥夺时才显露出来或得到加强．但是，感觉剥夺是否是该类神经通路发挥作用的必要条件，已有的研究尚缺乏确切的证据．采用统计力度较强的实验设计，给未蒙眼明视人被试听觉呈现一组名词，要求其对听到的每一个词语做出是人工物体还是自然物体的语义判断．对同步采集的功能磁共振信号进行统计分析，观察到视皮层脑区有显著激活．这些结果表明，跨感觉通道的神经通路在未实施感觉剥夺的条件下依然能够显示出来，因而在常态人脑中也不是完全以潜伏形式存在的．上述研究为建立多感觉交互作用神经机制的具体理论模型提供了一个约束条件．

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