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# FMRI correlates of different components of Braille reading by the blind

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ABSTRACT

Brain activations in early-blind subjects during Braille reading indicate considerable cross-modal neuroplasticity in posterior brain areas. Up to now it is, however, not clear how far such neuroplastic reorganization processes reach and whether a specific brain activation pattern corresponds to a specific component of the Braille reading task. Therefore, this fMRI study investigates whether different cortical areas are functionally specialized for different aspects of Braille reading. The comprehensive Braille reading task was contrasted to three control tasks representing subcomponents of Braille reading (passive tactile stimulation, active tactile pattern recognition, Braille imagery). Results in 14 early-blind subjects indicate that only occipital and basal temporo-occipital brain areas show specific fMRI correlates for Braille reading. Central rolandic brain activations correlated with basic somatosensory processing and superior temporal activations were associated with higher level stimulus-independent language processing. In these latter areas no indications for neuroplastic reorganizations specific for Braille reading were found, despite strong activations during the Braille reading task.



## 1. Introduction

More than two decades ago, pioneering research described considerable cross-modal neuroplastic processes in early-blind subjects in the occipital lobe (Uhl, Franzen, Lindinger, Lang, & Deecke, 1991; Uhl, Franzen, Podreka, Steiner, Deecke, & 1993; Uhl et al., 1994). The debate about functional specialization and neuroplastic processes has recently been intensified by further studies demonstrating multiple functional representations in the occipital lobe of blinds, including language processing (Amedi, Floel, Knecht, Zohary, & Cohen, 2014; Amedi, Raz, Pianka, Malach, & Zohary, 2003; Buchel, Price, Frackowiak, & Friston, 1998; Burton, Diamond, & McDermott, 2003; Ofan and Zohary, 2006; Roder, Stock, Bien, Neville, & Rosler, 2002), Braille reading (Burton et al., 2002a; Sadato, Okada, Honda, & Yonekura, 2002; Sadato et al., 1998), auditory processing (Arno et al., 2001; Ross, Olson, & Gore, 2003; Weeks et al., 2000), tactile processing (Amedi, Jacobson, Hendler, Malach, & Zohary, 2002; Burton, Sinclair, & McLaren, 2004; Sadato and Hallett, 1999; Sadato, Okada, Kubota, & Yonekura, 2004) and mental imagery (Lambert, Sampaio, Mauss, & Scheiber, 2004; Rauschecker, 2001; Vanlierde, De Volder, Wanet-Defalque, & Veraart, 2003).

In the primary "visual" cortex (V1) cross-modal neuroplasticity was demonstrated as early-blind subjects showed activation in V1 independent of language processes in a vibrotactile stimulation task (Burton et al., 2004) and a non-Braille tactile discrimination task (Sadato et al., 1998). The essential contribution of striate and extrastriate cortex to Braille reading was demonstrated in a blind subject suffering from bilateral occipital stroke (Hamilton et al., 2000). Inhibitory repetitive transcranial magnetic stimulation (TMS) of the occipital pole impaired Braille reading in early-onset and congenitally blind subjects (Cohen et al., 1997). In blind subjects reading of meaningful Braille letter strings activated the primary and secondary somatosensory cortex, motor and premotor areas (Burton et al., 2002a; Sadato et al., 1998), classical language areas such as the Broca and Wernicke area (Burton, Snyder, Diamond, & Raichle, 2002b), and several parietal (Sadato et al., 1998), temporal and occipital areas (Burton et al., 2002a) including the lateral occipital tactile-visual region (Amedi et al., 2002) and the primary visual cortex (Sadato et al., 2002).

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0941-9500/

The large number of posterior brain areas found active obviously reflects the complexity of the task. Braille reading requires processing of tactile input, association of this input with semantic memory, and all higher levels of language processing like phonologic, semantic and syntactic processing. Thus it combines several components of information processing in a parallel or sequential manner. Up to now it is not clear how far neuroplastic reorganization processes reach in the brain of blind humans and whether a specific brain activation pattern corresponds to a specific component of the Braille reading task. This study aims at providing first evidence on whether different components of Braille reading are associated with distinct fMRI correlates. Accordingly, three major components of Braille reading were identified: (1) unattended basic somatosensory processing of tactile information (Passive stimulation condition), (2) attended basic somatosensory processing by active pattern recognition (Blanks counting condition), and (3) language production without somatosensory processing (Braille Imagery condition). These tasks were used as control conditions for the different aspects of Braille reading and contrasted to the Braille Reading task in early-blind subjects. The goal was to describe different areas of cortex as functionally specialized for different aspects of Braille reading.

## 2. Materials and methods

### 2.1. Subjects

Fourteen early-blind subjects (mean age 33.0 ± 9.5 years, two females) participated in this study. All subjects were right-handed as assessed by a modified version of Oldfield's Edinburgh handedness inventory (Oldfield, 1971; Salmaso and Longoni, 1985), except for two subjects who showed left hand dominance (note that handedness inventories tend to be unreliable in the blind). Five subjects had minimal residual vision at the time of fMRI measurements. All of the early-blind subjects were proficient Braille readers. Since our primary goal was to provide a first investigation of the functional specialization of brain areas in early-blinds during Braille reading no normal vision subjects were included. Informed consent was given by all subjects in accordance with local guidelines. The protocol was approved by the ethical committee of the Medical University of Vienna. Details of subject characteristics are given in Table 1.

### 2.2. Functional and structural MRI measurements

Functional MRI data acquisition was performed on a 3 Tesla Medspec whole-body MR scanner (Bruker BioSpin, Ettlingen, Germany). Functional data were collected using a high-resolution, phase-corrected blipped gradient-recalled, single-shot echo-planar-imaging (EPI) sequence (TE/TR = 60/6000 ms, 128 × 128 matrix, 256 × 256 mm FOV (field of view), 30 axial slices parallel to the AC-PC-plane (anterior commissure—posterior commissure) as defined on sagittal structural T1-weighted images, slice thickness 3 mm). To achieve steady-state transverse magnetization, dummy scans were performed for 12 s prior to the start of a run of 990 s functional data recording (see Fig. 1). Structural images were acquired using an MDEFT sequence (32 slices, 256 × 256 matrix, 256 × 256 FOV, slice thickness 3 mm) with no slice offsets and slice angles identical to the functional data set. Individual custom-designed fixation helmets created at the screening visit served as a head-restraint system, minimizing motion artefacts and allowing for exact repositioning in each scanning session (Beisteiner, 2005;

**Table 1**
Characteristics of blind subjects.

| SN | Age (years) | Sex | Reading hand (S[a]/P[b]/G[c]) | HA[d] | Age at onset of blindness (years) | Years blind[e]/ reading[f] | Residual vision (years)[g] | Visual acuity[h] | Training Braille (h/day)[i] | Cause of blindness | Profession |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 29 | M | R/R1/no | R | 0 | 29/23 | 0 | 0 | 5 | Congenital anophthalmia | Musician |
| 2 | 34 | M | R/R1/no | R | 0 | 34/28 | 0 | 0 | 4 | Retinopathia pigmentosa | IT expert |
| 3 | 43 | M | L/B2/R | L | 0 | 43/37 | 0 | 0 | 1 | Retinopathia pigmentosa | Telephon operator |
| 4 | 44 | M | L/L1/no | L | 0 | 44/38 | 6 | 0 | 6 | Retrolental fibroplasia | Teacher |
| 5 | 46 | M | L/B2/R | R | 0 | 46/39 | 17 | 0 | 2 | unknown | Salesman |
| 6 | 18 | M | R/B4/no | R | 0 | 18/12 | 18 | LI | 1 | Glaucoma | n/a |
| 7 | 30 | F | R/B3/L | R | 0 | 30/23 | 30 | LI | 8 | unknown | Reader |
| 8 | 33 | M | L/B2/R | R | 0 | 33/26 | 33 | LI | 3 | Retrolental fibroplasia | Telephone operator |
| 9 | 35 | F | R/R1/no | R | 0 | 35/28 | 35 | MO, CO, LI | n/a | Retinopathia pigmentosa | Telephone operator |
| 10 | 37 | M | R/B2/L | R | 1 | 36/31 | 1 | 0 | 3 | Retinoblastoma | Singer, song writer |
| 11 | 19 | M | R/R2/no | R | 7 | 12/11 | 7 | 0 | 0.5 | Retinoblastoma | Telephone operator |
| 12 | 21 | M | L/L1/no | R | 7 | 14/13 | 9 | 0 | 5 | Glaucoma | Telephone operator |
| 13 | 20 | M | R/B2/L | R | 7 | 13/14 | 12 | 0 | 9 | Retinoblastoma | IT expert |
| 14 | 41 | M | R/B2/L | R | 9 | 32/34 | 41 | MO, LI | 4 | Retinopathia pigmentosa | Salesman |

[a] S: scanning, reading hand (index finger) during fMRI measurements (when asked to read Braille with one hand). L: left; R: right; B: both.
[b] P: preferred Braille reading hand(s) in business and private situations (number of fingers used including guiding hand).
[c] G: spatial guidance hand for Braille reading.
[d] HA: handedness, assessed by a modified version of Oldfield's Edinburgh handedness inventory.
[e] Blind: years of blindness for visual structures.
[f] Reading: years of Braille reading.
[g] Residual vision concerning perception of brightness.
[h] Visual acuity categories: the subjects had no remaining vision at the time of fMRI (0), could see only movements (MO) or colours (CO), had only perception of bright light (LI).
[i] Training of Braille reading including working hours (hours/day). n/a: not available; SN: subject number; M: male; F: female.

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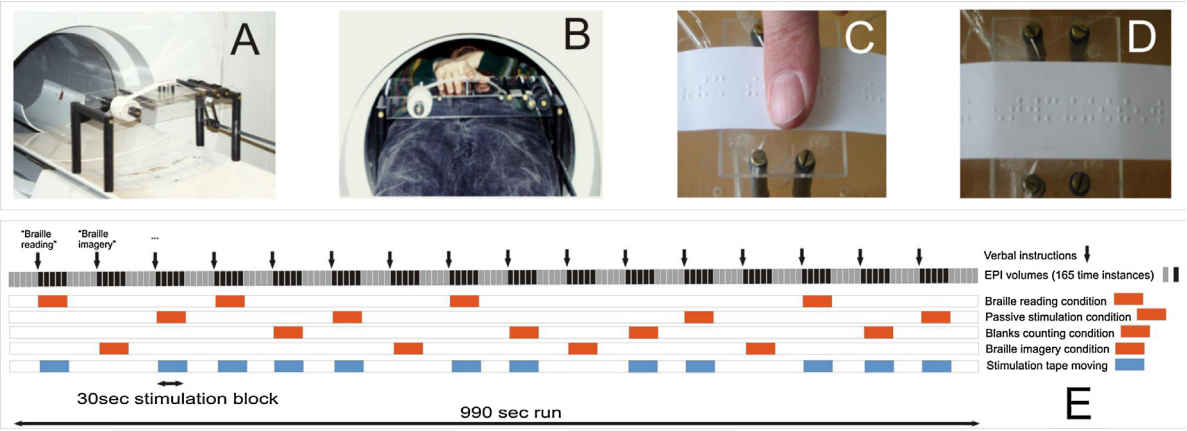


**Fig. 1.** Stimulation device and paradigm.

Beisteiner and Barth, 2005; Beisteiner et al., 2001; Edward et al., 2000).

### 2.3. Paradigm

Each subject performed six runs. Each run of the stimulation paradigm consisted of sixteen stimulation blocks alternating with rest (see Fig. 1). During rest, the stimulation tape was not moving and subjects were instructed to relax. Each block lasted 30 s, during which five brain volumes were recorded. This resulted in a total of 480 volumes recorded during stimulation (6 runs × 16 blocks × 5 volumes) and 480 volumes recorded during rest. In each stimulation block one of four task conditions (see Table 2,Fig. 1) was presented in a pseudorandom order. Conditions were designed to allow comparison of the comprehensive braille reading task with 3 control tasks representing major components of Braille reading in a general behavioral way.

Condition 1—passive stimulation: passive tactile stimulation by strings of 120 Braille-like random dot patterns, matched for dot number, size and presentation speed with the other conditions. No task was given and subjects were instructed to relax. This condition reflects processing of basic somatosensory stimulation without an explicit task and therefore without specifically directed attention. The critical difference to the reference state "rest" lies in the somatosensory stimulation by the moving tape. The major difference to Braille reading is the lack of specific attention and language processing.

Condition 2—blanks counting: tactile stimulation with attention focused on the blanks between Braille words. Subjects were instructed to count the blanks between words. Stimulus material was identical to Braille reading. This condition covers attended processing of basic somatosensory stimulation and basic language aspects (counting). The major difference to Braille reading is the lack of higher-level language aspects like complex semantic, syntactic and phonological processing. In addition, attention is shifted to a simple somatosensory stimulus pattern.

Condition 3—Braille imagery: mental imagery of the process of Braille reading without actual tactile stimulation using a Braille sentence presented previously. The reading finger rested motionless on the non-moving stimulation tape. Subjects were given clear and detailed instructions for standardized imagery at the screening visit. This included imagery of a fixed finger position and constant presentation speed of Braille characters comparable to the Braille reading condition. Subjects were asked to practice the imagery condition. This imagery task requires language production in a correct semantic, syntactic and phonological way. It lacks, however, all processes related to processing of real somatosensory input.

Condition 4—Braille reading: tactile stimulation engaging silent Braille reading of meaningful sentences. This task represented the integration of all subcomponents required for successful Braille reading.

For each task detailed instructions were given to minimize inter-individual variability. Prior to each block, short verbal instructions about the next block condition (e.g., "reading" or "imagery") were given via MR-compatible earphones. The subjects were instructed to close their eyes during all runs and conditions. For performance control, subjects were informed before scanning that they were to be asked about the number of blanks in the Blanks counting condition (condition 2) and about the contents of the sentences in the Braille reading condition (condition 4) after each run.

Stimuli were presented under the tip of the reading finger using a paper tape with embossed Braille characters moving at 2.4 cm/s (Fig. 1A–D). The presentation rate for non-contracted standard Braille characters was constant for all subjects (4 characters/s). In the Braille reading and the Blanks counting condition, subjects were stimulated by one Braille sentence per stimulation block consisting of 120 Braille letters. A total of 24 different sentences of about 18 words each, i.e., about 36 words per minute, were presented to each subject in six runs.

**Table 2**
Overview of conditions.

| No | Condition | Description | Stimulus (in each block) |
|---|---|---|---|
| 1 | Passive stimulation | Processing of basic somatosensory stimulation without specifically directed attention | String of 120 Braille-like random dot patterns |
| 2 | Blanks counting | Basic processing of tactile information with attention focused on the blanks between Braille letter strings | String of 120 Braille characters (meaningful sentence) |
| 3 | Braille imagery | Mental imagery of the process of Braille reading using a Braille sentence presented previously | No tactile stimulation |
| 4 | Braille reading | Tactile Braille reading with attention focused on the contents of Braille words | String of 120 Braille characters (meaningful sentence) |

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At the screening visit, subjects performed two runs outside the scanner as training. Our subjects generally exhibited considerable variability in Braille reading speed and style (one finger, two and more fingers of both hands) consistent to the literature (Burton, 2003; Millar, 1984a, 1984b). It has been argued that differences in reading speed might account for the differences in activation patterns between early- and late-blind subjects as found in several studies (Burton, 2003). In our study design, brain activation during Braille reading and several forms of tactile stimulation were contrasted, requiring stimulus presentation to be as comparable as possible across conditions. Reading speed and reading finger movement had to be controlled and, thus, constant Braille presentation rate and fixed finger position across the runs were used to minimize effects of tactile reading speed and reading finger movement. The Braille reading condition used in this study differs from the manner in which blind Braille readers usually perform Braille reading. Normally, blind subjects read Braille text by side-to-side finger movements, have a two to four times higher reading speed and many of them use multiple fingers and both hands (see Table 1). Nevertheless, all subjects studied were able to read the Braille sentences presented, as confirmed during debriefing.

### 2.4. Region of interest (ROI) analysis

This study was focusing on the occipital, temporal and parietal lobes of early-blind subjects, as well as the central rolandic area. Due to possible atrophies and considerable morphological variability in the blinds brains, consistent definition of neuroanatomical ROIs is a problematic task. Standard normalization and registration procedures may introduce considerable mislocalizations (White et al., 2001) reaching several centimeters, especially in pathological brains (Gartus et al., 2007). In contrast, an individual ROI definition allows exact designation of individual sulci including rami which might be morphologically modified by neuroplastic and neurodegenerative processes in congenitally and early-blind subjects (Breitenseher et al., 1998; Rakic, 1988; Shimony et al., 2005; Beisteiner et al., 2010). In addition, functional spatial resolution can be improved by smaller smoothing kernels (Geissler et al., 2005).

The definition of sulci and rami was done by three anatomically experienced raters and based on the atlas published by Ono and colleagues describing anatomical variations and sulcal patterns in detail (Ono, Kubik, & Abernathey, 1990). The order of data sets to be analyzed was randomized between raters and interrater agreement was computed. Three-dimensional drawing of individual ROIs and volumetric measurements were performed with the MRIcro software package (http://www.sph.sc.edu/comd/rorden/mricro) and included the following steps:

First, sulci and their rami were identified, manually traced and cross-checked on 3D rotatable individual brain surface models (Fig. 2) and coronal, sagittal and axial high-resolution structural MR slices (Fig. 2B). Compared to superficial structures, improved identification of developmental patterns is possible in the depths of the sulci, resulting in more accurate differentiation of primary, secondary and tertiary sulci (Armstrong, Schleicher, Omran, Curtis, & Zilles, 1995; Naidich, Valavanis, & Kubik, 1995). Anatomical landmarks were found on different sections, e.g. the inverted omega-shape representing the central sulcus is best seen in axial views, the “M”-like pattern (intraparietal, primary and secondary intermediate sulci) in sagittal planes, and the intraoccipital sulcus in coronar sections (Naidich et al., 1995; Ono et al., 1990).

Second, colour-coded sulci on high-resolution structural axial slices (Fig. 2B) were assigned on corresponding axial EPI slices (Fig. 2C). Based on this sulcal definition, ROIs including bordering cortices were drawn on axial EPI slices (Fig. 2C) resulting in three-dimensional ROI volumes (Fig. 2D) for ROI-dependent voxel-counting. A total of thirty different regions of interest were drawn on each hemisphere. Details of regions investigated including standard errors are given in Table 3. Each ROI was drawn separately in both hemispheres to account for interhemispheric neuroanatomical differences. As shown in Fig. 2D, ROIs included over 90% of occipital, parietal and temporal cortical areas to exclude a spatial bias.

### 2.5. Data analysis

Preprocessing including 3D-realignment and smoothing (isotropic Gaussian kernel of 6 mm FWHM) as well as single-subject

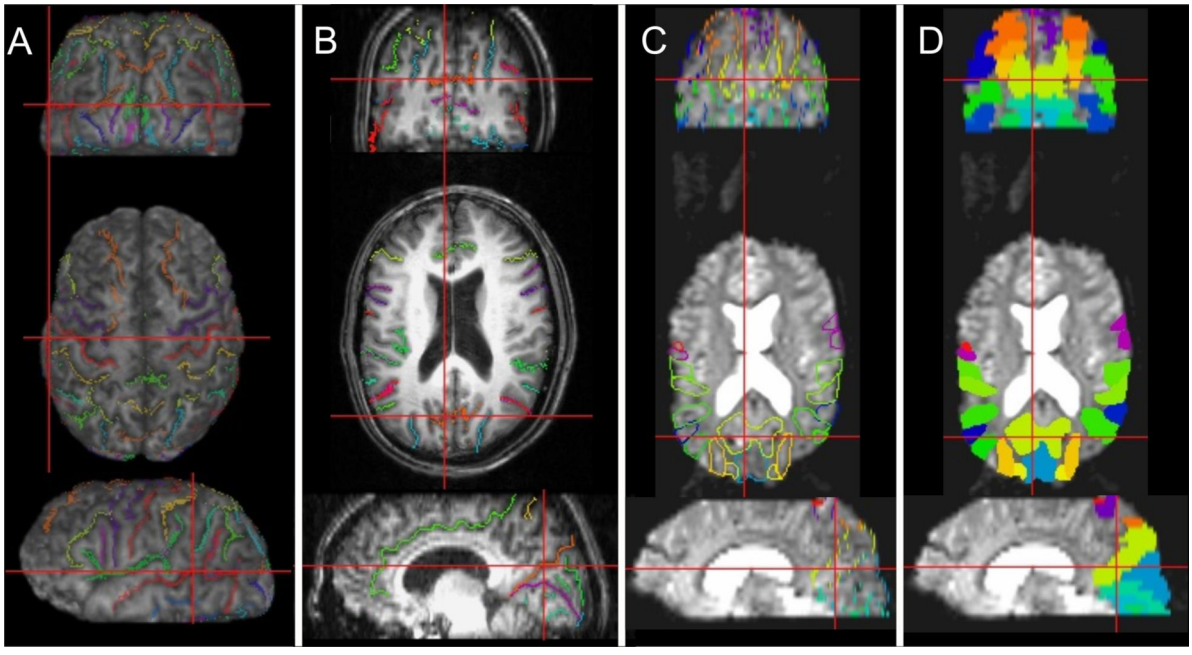


**Fig. 2.** Delineation of regions of interest.

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**Table 3**
Activation patterns in different conditions.

| ROI no | Region of interest (ROI) | ROI ($cm^3$) | ROI (%) | Braille reading | Passive stimulation | Blanks counting | Braille imagery |
|---|---|---|---|---|---|---|---|
| 1 | Central sulcus | 30.95 ± 1.7 | 8.8 | 7.7** ± 1.3 | 7.7** ± 1.0 | 11.0* ± 1.5 | 14.6 ± 2.9 |
| 2 | Superior postcentral sulcus | 16.75 ± 2.1 | 4.8 | 5.2* ± 0.9 | 6.9** ± 1.1 | 7.5* ± 1.6 | 4.1 ± 0.9 |
| 3 | Inferior postcentral sulcus | 18.22 ± 1.8 | 5.2 | 6.2*** ± 0.7 | 10.1*** ± 2.0 | 12.5*** ± 2.0 | 3.2 ± 0.9 |
| 4 | Anterior intraparietal sulcus | 23.99 ± 2.0 | 6.8 | 8.3*** ± 0.9 | 12.0*** ± 1.5 | 12.2** ± 2.4 | 6.2 ± 1.2 |
| 5 | Posterior intraparietal sulcus | 13.52 ± 1.7 | 3.9 | 4.5*** ± 0.6 | 6.1** ± 1.0 | 4.8** ± 0.9 | 3.9 ± 0.9 |
| 6 | Intraoccipital sulcus | 16.93 ± 1.1 | 4.8 | 6.0*** ± 0.4 | 6.1** ± 0.7 | 4.3* ± 0.6 | 4.1 ± 0.7 |
| 7 | Transverse occipital sulcus | 7.48 ± 0.9 | 2.1 | 3.0*** ± 0.5 | 2.7** ± 0.5 | 1.9 ± 0.5 | 2.3 ± 0.5 |
| 8 | Parieto-occipital sulcus | 27.65 ± 1.9 | 7.9 | 5.9** ± 0.7 | 5.5** ± 0.7 | 5.0 ± 0.8 | 5.2 ± 1.1 |
| 9 | Lateral fissure. posterior ascending branch | 10.83 ± 0.9 | 3.1 | 2.1* ± 0.3 | 2.4* ± 0.3 | 2.6* ± 0.6 | 2.7 ± 0.5 |
| 10 | Lateral fissure. middle part including SII | 15.61 ± 2.3 | 4.4 | 4.2* ± 0.9 | 4.5** ± 1.0 | 6.0* ± 0.8 | 8.4** ± 3.2 |
| 11 | Superior temporal sulcus. posterior ascending branch | 16.13 ± 1.5 | 4.6 | 2.6*** ± 0.3 | 1.9* ± 0.3 | 2.8 ± 0.5 | 5.1* ± 0.7 |
| 12 | Superior temporal sulcus. posterior horizontal branch | 8.81 ± 1.5 | 2.5 | 2.1** ± 0.3 | 1.5 ± 0.4 | 1.9 ± 0.5 | 1.8 ± 0.5 |
| 13 | Superior temporal sulcus. middle part (Wernicke) | 23.17 ± 1.8 | 6.6 | 5.9*** ± 0.7 | 3.2** ± 0.5 | 2.4 ± 0.7 | 6.2* ± 1.1 |
| 14 | Collateral sulcus | 11.66 ± 0.9 | 3.3 | 4.2*** ± 0.5 | 2.9* ± 0.5 | 2.3 ± 0.5 | 3.0* ± 0.7 |
| 15 | Transverse collateral sulcus | 5.43 ± 0.8 | 1.5 | 1.9** ± 0.4 | 1.3 ± 0.3 | 0.8 ± 0.3 | 1.1 ± 0.5 |
| 16 | Calcarine sulcus | 12.88 ± 1.1 | 3.7 | 5.6*** ± 0.8 | 2.5* ± 0.5 | 1.9 ± 0.6 | 3.9 ± 1.1 |
| 17 | Retrocalcarine sulcus | 2.78 ± 0.5 | 0.8 | 1.0* ± 0.3 | 0.6 ± 0.2 | 0.5 ± 0.2 | 0.7 ± 0.3 |
| 18 | Lingual sulcus and gyrus | 8.04 ± 0.9 | 2.3 | 3.2*** ± 0.5 | 1.4 ± 0.3 | 1.0 ± 0.3 | 3.4** ± 0.9 |
| 19 | Cuneus | 9.18 ± 0.7 | 2.6 | 4.0*** ± 0.5 | 3.0** ± 0.4 | 2.1 ± 0.5 | 2.1 ± 0.4 |
| 20 | Anterior occipital sulcus | 3.83 ± 0.7 | 1.1 | 1.2 ± 0.3 | 1.3 ± 0.3 | 1.1* ± 0.3 | 1.3 ± 0.3 |
| 21 | Temporo-occipital junction | 7.68 ± 1.4 | 2.2 | 2.7** ± 0.6 | 2.7* ± 0.5 | 2.4 ± 0.6 | 2.4 ± 0.6 |
| 22 | Primary intermediate sulcus | 6.23 ± 0.9 | 1.8 | 0.4 ± 0.1 | 1.4** ± 0.3 | 0.8 ± 0.2 | 1.6 ± 0.5 |
| 23 | Secondary intermediate sulcus | 2.87 ± 0.5 | 0.8 | 0.4 ± 0.1 | 0.5±0.1 | 0.4 ± 0.1 | 0.5 ± 0.2 |
| 24 | Lateral occipital sulcus | 9.78 ± 1.4 | 2.8 | 3.3* ± 0.6 | 3.1 ± 0.7 | 2.8* ± 0.5 | 2.8* ± 0.6 |
| 25 | Lunate sulcus | 5.70 ± 0.8 | 1.6 | 1.8*** ± 0.3 | 1.4 ± 0.3 | 1.0 ± 0.3 | 1.4 ± 0.7 |
| 26 | Transverse parietal sulcus | 10.56 ± 1.3 | 3.0 | 1.5* ± 0.3 | 1.9 ± 0.6 | 2.9* ± 0.5 | 1.9 ± 0.7 |
| 27 | Inferior temporal sulcus | 8.14 ± 1.1 | 2.3 | 1.4** ± 0.2 | 2.0** ± 0.4 | 1.4 ± 0.5 | 2.9 ± 1.3 |
| 28 | Inferior occipital sulcus | 3.11 ± 0.7 | 0.9 | 0.7 ± 0.2 | 0.5 ± 0.2 | 0.2 ± 0.1 | 0.4 ± 0.2 |
| 29 | Lateral occipito-temporal sulcus | 9.78 ± 1.4 | 2.8 | 2.2* ± 0.5 | 1.9 ± 0.5 | 1.9 ± 0.6 | 1.8 ± 0.7 |
| 30 | Subcentral sulcus | 3.15 ± 0.4 | 0.9 | 0.9** ± 0.2 | 1.1** ± 0.2 | 1.5** ± 0.3 | 0.9 ± 0.3 |

* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

analyses were done with SPM (http://www.fil.ion.ucl.ac.uk/spm). As outlined above, no normalization procedures and no data filtering were applied prior to analysis. To allow a comprehensive picture of activation results, the first and second level data analysis was performed in two ways.

During first level analysis, individual data sets were analyzed by contrasting each task to the resting condition using the GLM as implemented in SPM99. Fixed response boxcar functions convolved with a hemodynamic response function were used. Only voxels surpassing a standard statistical threshold ($p < 0.05$, corrected) were accepted as representing "true positive" activations in a statistical sense (thresholded analysis). Various kinds of such a thresholded data analysis are widely used to compare ROI activations and data indicate that this approach may be adequate for a variety of cognitive tasks (Jansen et al., 2006; Lee and Dapretto, 2006; Sommer et al., 2006). On the other hand, it is obvious that results of this technique depend on the threshold applied to the statistical parametrical maps, the intrinsic smoothness of the data and other parameters not directly related to activation per se. To control for these effects, a second, additional first level analysis was done by calculating the mean parameter estimate value within an ROI for every condition, every ROI and every subject (non-thresholded analysis). This approach includes signal contributions from all ROI voxels.

**Table 4**
Areas showing significant differences between conditions.

| Between condition differences | Braille reading > passive stimulation | Braille reading > blanks counting | Braille reading > Braille imagery | Blanks counting > Braille imagery | Passive stimulation > Braille imagery |
|---|---|---|---|---|---|
| Inferior postcentral sulcus | | | 0.0133* | 0.0095** | 0.0038** |
| Subcentral sulcus | | | 0.0110* | 0.0273* | 0.0052** |
| Intraoccipital sulcus | | | 0.0233* | | |
| Collateral sulcus | | 0.0253* | 0.0242* | | |
| Transverse collateral sulcus | | 0.0167* | 0.0020** | | |
| Cuneus | | 0.0064** | 0.0005*** | | |
| Calcarine sulcus | 0.0468* | 0.0019** | 0.0009*** | | |
| Lingual sulcus and gyrus | 0.0128* | 0.0031** | 0.0097** | | |
| Superior temporal sulcus. middle part (Wernicke) | 0.0186* | 0.0066** | | | |
| Lateral occipital sulcus | 0.0270* | | | | |
| Temporo-occipital junction | | | | | |
| Transverse occipital sulcus | | | | | |

* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

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Following the first level analysis, two second-level analyses were done: (1) testing for significant ROI activation across subjects in a specific condition (second-level-analysis-I). (2) Testing for significant ROI activation differences between conditions across subjects (second-level-analysis-II). Both second-level analyses were done twice—either including the number of significantly activated voxels per ROI per subject (thresholded analysis) or including the mean parameter estimates per ROI per subject (non-thresholded analysis). For second level random effects analysis voxel counts or mean parameter estimates were submitted to *t*-tests using SPSS 12.0 after normal distribution (via Kolmogorov–Smirnov testing) and equality of variance (via Levene's test) were established. Condition specific ROI activations (second-level-analysis-I, Table 3) were evaluated by one-sample *t*-tests ($p < 0.05$, two-tailed) for each of the four conditions. These *t*-tests were corrected for multiple comparisons using Bonferroni correction. Differences between the four conditions (second-level-analysis-II), were calculated using paired *t*-tests ($p < 0.05$, two-tailed) and significance levels were again Bonferroni-corrected for multiple comparisons (Table 4).

## 3. Results

All subjects met the task requirements as demonstrated during the training sessions and performance controls described in Section 2. Significant brain activation was found for every participant (see Fig. 3) and no data set had to be excluded. A comparison of the thresholded with the non-thresholded analysis revealed very similar results, with analogous activation pattern. The number of ROIs showing statistically significant activation was, however, reduced in the non-thresholded analysis. In detail, the second-level-analysis-I (which assessed significantly activated ROIs separately for each condition) showed 62 significant results with the thresholded analysis, and 25 significant results with the non-thresholded analysis (all 4 conditions taken together, see Table 3). The overlap was 96% (24 of the non-thresholded significances overlapped with the significances achieved with the thresholded analysis). The most comprehensive task (Braille reading) showed the strongest brain activation (thresholded data: 26/30 ROIs active). Sparse activation was found with the Braille Imagery condition (6/30 ROIs active). Passive stimulation and Blanks counting lay in-between (19/30, 12/30 ROIs active). Details of activated areas in different conditions including interindividual variability measures (mean ± SEM) are given in Table 3. Second-level-analysis-II (indicating significant differences between conditions) revealed 22 significant results in the thresholded analysis (i.e., all possible comparisons taken together), whereas the non-thresholded analysis showed 18 significant results (see Table 4). Here, the overlap between both analysis approaches was 72% (13 of the non-thresholded significancies overlapped). All details are shown in Table 4.

A combined analysis of all second-level results allows inferences about fMRI activations correlating specifically with certain tasks. Basic somatosensory processing is required for Passive stimulation, Blanks counting and Braille reading but not for Braille Imagery. FMRI correlates for basic somatosensory processing should therefore be found with all tasks except Braille Imagery. This was indeed found for central rolandic activations. In contrast to basic somatosensory processing, Braille reading includes also stimulus-independent high-level language processing (semantic, syntactic, phonologic processes). Such fMRI correlates should show similar activation with Braille reading and Braille Imagery—both of them requiring "internal speech". Further, stimulus-independent fMRI correlates should activate much stronger with internal speech tasks (Braille reading, Braille imagery) than with tactile stimulation tasks (Blanks counting, Passive stimulation). This pattern was found for temporal activations.

FMRI correlates specifically representing processing of Braille characters beyond basic somatosensory processing and beyond higher-level language processing should activate consistently stronger for Braille reading in contrast to all three control tasks.

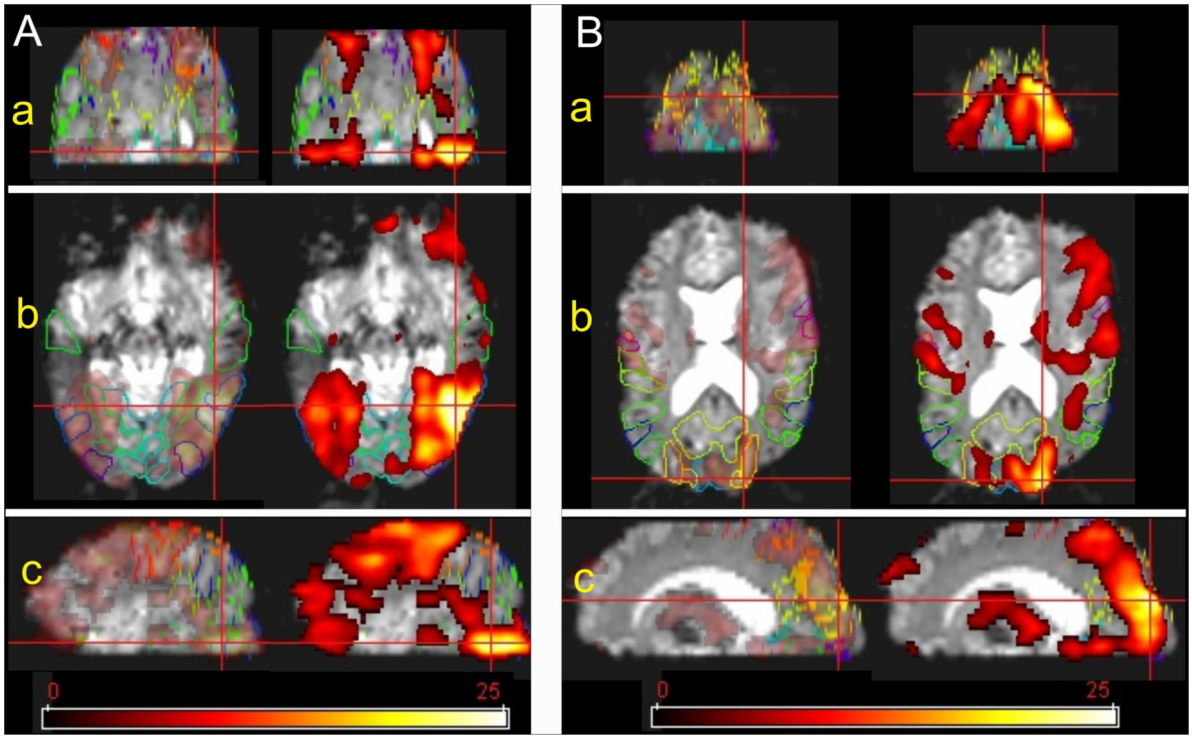


**Fig. 3.** Activation patterns in the braille reading condition.

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This was indeed found for the visual cortex and inferior temporo-occipital areas.

In frontal areas we did not find any task specific activation differences.

## 4. Discussion

Previous studies about Braille reading indicated considerable functional reorganizations in the brains of blind subjects as a basis for effective accomplishment of this task. Here we provide a first assessment of the degree of functional reorganization and functional specialization by investigating different aspects of the Braille reading task. Our goal was to reveal different cortical areas, which are functionally specialized for different aspects of Braille reading.

In order to meet this challenging task appropriately, several methodological efforts concerning standardization of experimental setup, validation of neuroanatomical localization, maximization of signal gain and reliability of the statistical results were included in this study. Behavioral overlap between blocks was avoided by precise verbal instructions given prior to each stimulation block and by performance controls done with each subject. Activation differences related to uncontrolled variations of the external stimulation were minimized by a highly standardized Braille stimulation setup with a non-moving reading finger. Although this approach generates a somewhat artificial reading situation for the participating blinds, it guarantees constant reading conditions throughout all tasks.

A correct delineation of small neuroanatomical ROIs is essential to allow for detailed analyses of activation patterns, as differences between tasks may concentrate on subcomponents of larger neuroanatomical or functional units. Since standard registration procedures are very likely to produce mislocalizations in our brain cohort, we extended previous approaches by providing an individualized neuroanatomical ROI delineation methodology with every brain and compared individualized ROI specific activations. Signal gain was maximized by performing this study at high-field (3 Tesla), employing a blocked design and extensive data acquisition periods (for every condition 12 min of data recording was applied per subject). This resulted in good contrast-to-noise ratios and rather high individual *t*-values. Reliable statistical results were obtained by two separate analysis methods, using either thresholded statistical maps corrected for multiple comparisons or a threshold-independent approach based on ROI-specific contrast values (parameter estimates). Both methods revealed congruent results. In the following, inferences about fMRI correlates of the different components of Braille reading are drawn from a combined analysis of all results but with concentrating on the thresholded data.

### *4.1. FMRI activations correlating with basic somatosensory processing*

Brain activations specifically correlated with basic tactile processing should demonstrate similar activations with Passive stimulation, Blanks counting and Braille reading. In addition, all these tasks should generate stronger activations when compared with a task lacking tactile components (Braille Imagery). This is indeed demonstrated for the central rolandic area of the blind's brains (inferior postcentral sulcus, subcentral sulcus). Here the contrasts Braille reading > Braille imagery, Blanks counting > Braille imagery and Passive stimulation > Braille imagery all reveal significant differences. In addition, no difference is found between Braille reading and Passive stimulation, Braille reading and Blanks counting, Blanks counting and Passive stimulation, indicating similar processing demands in these areas for all tactile tasks. Basic somatosensory processing is therefore correlated with central rolandic brain activations.

Our results negate specific processing for Braille characters or Braille reading in these areas (no difference between Braille character tasks and random-dot tasks: Blanks counting vs. Passive stimulation, Braille reading vs. Passive stimulation). Correspondingly, there is no evidence for basic somatosensory processing in the occipital lobe, which, however, activates with more elaborate processing requirements (see below).

### *4.2. FMRI activities correlating with stimulus-independent language processing*

Changing from basic to the top level of Braille processing, data were analyzed with respect to representation of stimulus-independent higher-level language components (semantic, syntactic, phonologic processes). Such areas should show similar activation with the "internal speech tasks" Braille reading and Braille imagery. At the same time, activations should be stronger with internal speech tasks (Braille reading, Braille imagery) compared to tactile stimulation tasks (Blanks counting, Passive stimulation). This is found for the superior temporal lobe (superior temporal sulcus). Here, activations were similar with Braille reading and Braille imagery. In addition, tasks with an internal speech component showed stronger activation compared to tactile stimulation tasks. This effect was significant for the contrasts Braille reading > Passive stimulation and Braille reading > Blanks counting. Although Braille imagery showed low activations per se (only 6 ROIs active, see Table 3) and no significant differences compared to Passive stimulation and Blanks counting, 5 of the 6 active areas were found within the temporal lobe. Furthermore, Braille Imagery activations comprised all superior temporal sulcus ROIs and showed stronger activation than tactile stimulation tasks. Braille imagery results, therefore, strongly support the hypothesis that stimulus-independent language processing correlates with superior temporal lobe activations.

Similar activation patterns during Braille reading and Braille imagery within the superior temporal cortex of early-blind subjects are consistent with language studies in sighted subjects where the superior temporal sulcus was found to be specifically activated in the silent reading of visually presented words, i.e. associated with processing of word comprehension (Ashtari et al., 2005; Xu et al., 2002). Ashtari and colleagues reported activation in the posterior superior temporal sulcus contrasting sentence-completion based on semantic meaning with completion of non-linguistic letter strings (Ashtari et al., 2005). Xu et al. (2002) demonstrated that the mid-temporal region integrates semantic representations and found this area consistently activated during the processing of word meaning of visually presented words. In addition, multisensory integration has been demonstrated in the superior temporal sulcus for meaningful visual and auditory but not tactile stimuli in sighted subjects (Beauchamp, 2005). Therefore, the superior temporal sulcus might be specifically engaged in semantic or other high level language processes (syntactic, phonologic) in both sighted and early-blind subjects.

### *4.3. FMRI activities correlating with Braille reading*

Brain areas which activate consistently stronger with Braille reading relative to all three control tasks should represent core areas for the Braille reading process, i.e., these areas should represent task components beyond basic processing of tactile stimuli and beyond stimulus-independent higher level language processing. Our results show that the visual cortex and inferior temporo-occipital areas represent such core areas for Braille reading (Table 3). This is especially true for the primary visual

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cortex (V1) and the lingual sulcus and gyrus, which showed significant differences to all three control tasks. Corresponding results (although less significant) were also found for the collateral sulcus, the transverse collateral sulcus and the cuneus. They all showed considerably stronger activation for Braille reading compared to the three control tasks. Between-condition contrasts, however, reached significance only for 2 of the comparisons (Braille reading > Blanks counting, Braille reading > Braille imagery). The findings suggest a cross-modal change from visual to higher level somatosensory processing in early-blinds in occipital and inferior temporo-occipital areas. Previous literature indicates however, that the representations within the calcarine cortex are special. A significant part of neurons in the adult visual cortex of sighted mammals responds not only to visual, but also to acoustic and/or tactile stimuli (Pascual-Leone and Hamilton, 2001). FMRI studies in long term blindfolded sighted subjects showed activation of visual cortex during tactile and auditory stimulation (Pascual-Leone, Amedi, Fregni, & Merabet, 2005). There are dense reciprocal projections between the striate cortex and the superior temporal cortex, including the polysensory temporal area, indicating multimodal integration in primate striate cortex ( Falchier, Clavagnier, Barone, & Kennedy, 2002). By applying repetitive transcranial magnetic stimulation (rTMS) targeting the primary somatosensory cortex, Wittenberg, Werhahn, Wassermann, Herscovitch, & Cohen (2004) verified functional connectivity between S1 and early "visual" areas in early-blind subjects in a PET study. Burton et al. (2005) found activation in visual areas V1 and V2 during reading of embossed capital letters. Combining this previous neurophysiological evidence and our data, the most likely interpretation seems to be an enhancement of preexisting connections and functions of the calcarine cortex in the early-blind (Pascual-Leone et al., 2005)

Activations found in other occipital and temporo-occipital areas are supported by a variety of previous studies on sighted and blind subjects. A study by Reich, Szwed, Cohen, & Amedi, (2011) demonstrated that the Visual Word Form Area (fusiform gyrus) is similarly located and active with Braille reading in blinds than with ordinary reading in sighted. Ashtari et al. (2005) performed an analogous visual paradigm in sighted subjects where the calcarine sulcus, lingual cortex and cuneus were activated when sentence-completion based on semantic meaning was contrasted with completion of non-linguistic letter strings. Investigating cross-modal integration of tactile and visual stimulation with small spherical ellipsoids Hadjikhani and Roland (1998) localized the representation of visual shapes in the lingual and fusiform cortex as well as in the occipital lobe in sighted subjects. Imagery of animals after listening to their names versus listening to abstract words activated the striate cortex and basal temporal areas in congenitally blinds (Lambert et al., 2004) demonstrating object-related representations in both areas. Altogether, these studies indicate that visual cortex and inferior temporo-occipital areas in early-blinds are critically engaged in associating Braille characters to semantic contents.

In conclusion, there are three main results of our study: (1) Braille reading specifically activates occipital and basal temporo-occipital brain areas with particular importance of the primary visual cortex. Activation in these areas shows no correlation with basic somatosensory processing or high-level stimulus-independent language processing. (2) Central rolandic brain areas activate with basic somatosensory tasks. These areas show no activation specific for processing of Braille characters. (3) Superior temporal brain areas activate with stimulus-independent language processing (e.g., semantic, syntactic, phonologic). These areas show no activation specific for the tactile component of the Braille reading task.

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