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Design and evaluation of an innovative MRI-compatible Braille stimulator with high spatial and temporal resolution

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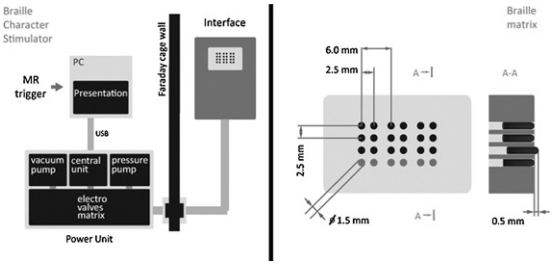
HIGHLIGHTS

- Experimental evaluation of the MRI-compatible tactile stimulator.
- Same-different discrimination task on Braille characters.
- Validity of using spatially and temporally precise tactile stimuli.

GRAPHICAL ABSTRACT



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ABSTRACT

Neural correlates of Braille reading have been widely studied with different neuroimaging techniques. Nevertheless, the exact brain processes underlying this unique activity are still unknown, due to suboptimal accuracy of imaging and/or stimuli delivery methods. To study somatosensory perception effectively, the stimulation must reflect parameters of the natural stimulus and must be applied with precise timing. In functional magnetic resonance imaging (fMRI) providing these characteristics requires technologically advanced solutions and there have been several successful direct tactile stimulation devices designed that allow investigation of somatotopic organization of brain sensory areas. They may, however, be of limited applicability in studying brain mechanisms related to such distinctive tactile activity as Braille reading.

In this paper we describe the design and experimental evaluation of an innovative MRI-compatible Braille Character Stimulator (BCS) enabling precise and stable delivery of standardized Braille characters with high temporal resolution. Our device is fully programmable, flexible in stimuli delivery and can be easily implemented in any research unit. The Braille Character Stimulator was tested with a same-different discrimination task on Braille characters during an event-related fMRI experiment in eleven right-handed sighted adult subjects. The results show significant activations in several cortical areas, including bilateral primary (SI) and secondary somatosensory (SII) cortices, bilateral premotor and supplementary motor areas, inferior frontal gyri, inferior temporal gyri and precuneus, as well as contralateral (to the stimulated hand) thalamus. The results validate the use of the BCS as a method of effective stimuli application in fMRI studies, in both sighted and visually impaired subjects.

1. Introduction

Functional magnetic resonance imaging (fMRI) is now a widely used non-invasive method to study the functional organization of the human brain. Besides its great scientific value, the

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MRI environment imposes a number of restrictions concerning the experimental design which renders transferring the real-life situations to laboratory a great challenge. In studies of somatosensory perception, several MRI-compatible direct tactile stimulation devices were designed, based mostly on electro- or vibrotactile stimuli. It has been shown that this type of stimulation can be effectively used to map the somatosensory system (Harrington et al., 2000; Golaszewski et al., 2002; Deuchert et al., 2002; Chakravarty et al., 2009). However, comparison of activations induced by tactile and vibrotactile stimuli revealed a difference in blood oxygenation level-dependent (BOLD) signal change i.e. in parietal operculum (secondary somatosensory cortex which is a higher-order area), in favor of the tactile stimuli (Li Hegner et al., 2010). Additionally, electro- and vibrotactile stimulation is rather uncommon in non-experimental reality and may have limited applicability in the investigation of pure tactile processing in the brain. This seems to be particularly important, since it has been shown that more naturalistic stimuli (mimicking real-life situations) produce more reliable and robust neuronal responses (Hasson et al., 2010). Moreover, detailed consideration of particular structures involved in somatosensory information processing has revealed the advantage of using naturalistic stimuli in tactile object recognition tasks (Reed et al., 2004).

One of the most distinctive but also commonly used tactile stimuli in neuroimaging studies are Braille characters. A few investigations on neural correlates of Braille reading and tactile recognition in blind and visually impaired people with electroencephalography and positron emission tomography yielded landmark reports of human brain capacity to undergo neuroplastic changes (e.g. Pascual-Leone and Torres, 1993; Sadato et al., 1998). A number of studies in this field have also been conducted using fMRI (Sadato et al., 2002; Gizewski et al., 2004), although Braille reading is a unique phenomenon and its specificity makes it hard to transfer into the MRI scanner bore. Braille characters, unlike visual letters, are not size-invariant. A single character consists of a specified number of pins of standard dimensions and distance. Active Braille reading involves hand movements from right to left in a horizontal plane, across text in front of the reader. These real-life Braille features need to be considered while investigating neural correlates of Braille reading.

A few attempts have been made to deliver tactile stimuli representing Braille characters in fMRI studies. Most of them used either a plastic or a paper panel with embossed standard Braille symbols (e.g. Gizewski et al., 2004). This allowed a presentation of words and texts and thereby investigation of processes accompanying Braille reading per se. However, a severe limitation of this method is that it can only be employed in block-design fMRI experiments. Event-related paradigms, which enable characterization of the hemodynamic response and allow particular brain processes to be assessed (e.g. related to emotions or memory) cannot be used. This method of Braille presentation, furthermore, excludes using such powerful technique as functional magnetic resonance-adaptation (repetition supression) which enables investigation of functional properties of specific neuronal populations (Grill-Spector and Malach, 2001; Tal and Amedi, 2009). Additional problems include: (i) brain activations related to wide range of hand-movements and (ii) not fully controllable number of signs/words palpated by the subject.

In another study fingertip stimulation was delivered by a manually driven plastic rail with standard Braille characters embossed (Sadato et al., 2002). Inadequacy of this solution involves a passive way of stimuli application and an unnatural position of the hand, which does not correspond to the natural way of reading Braille. Additionally, experimenter-driven stimulation may affect the timing precision.

Some more controllable devices for fMRI were also developed, such as pneumatically driven spherical points (4 mm in diameter) arranged in a matrix (80 mm × 80 mm) (Zappe et al., 2004). This technically advanced, computer-controlled device enables application of a custom combination of stimuli. However, this tactile stimulation still cannot be regarded as a direct Braille equivalent, as the character dimensions exceed more than twice the standard Braille symbols and the real-life arrangement of characters cannot be displayed.

Here we describe the design and experimental evaluation of an innovative MRI-compatible Braille Characters Stimulator (BCS) enabling precise and stable delivery of standardized Braille characters with high temporal resolution. We also present data obtained from an fMRI experiment involving eleven subjects performing a same-different discrimination task on Braille characters displayed on the BCS.

2. Material and methods

2.1. The Braille Characters Stimulator: design and control

The BCS was designed to be used predominantly within Magnetic Resonance Imaging (MRI) environment. Fulfilling this objective required technically advanced solutions. The device is composed of two subunits: (a) an interface and (b) a power unit (Fig. 1A). The main part of the interface, and the whole stimulator as well, is the pins matrix (Fig. 1B and C). The pins matrix consists of three cells of eight blunt-ended pins each (2 × 4), with standard Braille character dimensions (Marburg Medium, Fig. 1B). Braille characters are typically combined of six points (2 × 3). In the BCS, one additional row of pins can represent letters with diacritics (common in many languages) or meaningless characters. This greatly expands the spectrum of the experimental tasks. The system enables application of three characters simultaneously. The BCS pins matrix is enclosed in a PVC housing (Fig. 1C). The interface is connected with the power unit with 24 tubes (1 mm in inside diameter; Tygon®, Saint-Gobain Corporation) with a length of 6 m. The power unit is composed of a vacuum and a pressure pump, a matrix of 24 electrovalves [all elements were custom-made], and a microcontroller (ATmega Family). The power unit supplies the interface with working pressure in the range of −0.5 to 0.7 bars. The pressure is controlled by pressure sensors. The microcontroller shuts off the pumps after reaching the set value. The BCS does not require any external compressors and pressure regulators. The frequency standing of pins is ≤1 Hz (displayed pattern of pins can be changed once per second).

Communication with BCS is managed by a RS-232 Serial Port with a default baud rate of 115,200 bit/s. This type of connection is commonly used providing maximum flexibility in connectivity with any external systems and makes BCS compatible with all of the most popular software for stimuli presentation in neuroimaging studies (e.g. Presentation®, e-Prime®, Matlab®, nordicActiva®), as well as with custom scripts written in many programming languages (e.g. C, C++, Python, Java). The BCS can be set with all possible combinations of pins, for each of three characters separately. Data can be provided by a binary or a text protocol. Synchronization with the MRI unit is provided by an external device, e.g. SyncBox® (NordicNeuroLab, Norway, Bergen). The BCS requires a power supplier of 230 V/50 Hz. A universal method of controlling and connecting to the MRI scanner makes the BCS easily implementable in any research unit.

The BCS tests were performed using a phantom and with recording background noise in the following scanners: 3 T Philips Achieva, 3 T Siemens Magnetom Trio and 1,5 T Siemens Avanto. No effects of radiofrequency interference were found. The results indicate that the BCS can be safely used in any MRI environment.

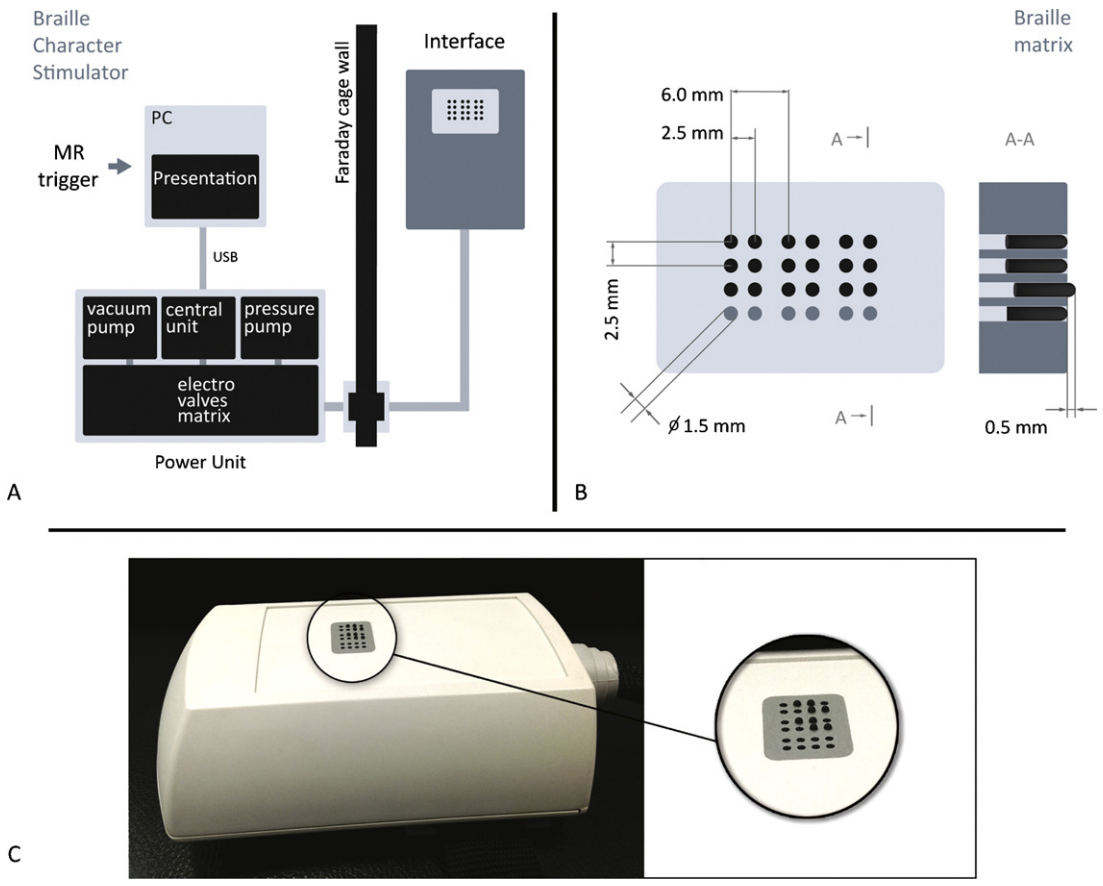

Fig. 1. Schematic illustration of The Braille Characters Stimulator system (A) and matrix (B), photograph of the actual interface of the BCS (C).

2.2. *fMRI testing protocols*

Eleven right-handed sighted subjects (5 women, 6 men, mean age: 24.1 ± 2.1) with no history of neurological or psychiatric disorders, participated in the study. All participants gave their informed consent prior to the start of the experiment. The study was approved by the Ethics Committee of the Medical University of Warsaw.

We tested BCS using an fMRI event-related design stimulation protocol. Subjects were asked to compare two (same-different) simultaneously applied Braille characters (Fig. 2A). One pair of signs was presented for 4 s. During the experimental session subjects were asked to hold their right hand on the interface of the stimulator and touch its surface (pins array) only with the index finger. They were also requested to constantly look at the fixation cross ('+') located in the center of a black screen visible through MRI-compatible goggles. The change of the fixation point color was used as a cue for subjects. The sequence of colors in a single experimental trial was as follows: (a) yellow "+" is presented for 2 s as a 'get ready' cue, (b) the "+" turns green and at the same time characters are applied by the stimulator, (c) after 4 s "+" turns white (basic color), (d) after few seconds (see details below) "+" becomes red which is the signal to respond, (e) "+" changes again to white (Fig. 2B). Inter- and intra-trial intervals varied across tasks and were administered randomly for 4–6 s and 4–10 s, respectively (i.e. jittered). Subjects submitted their answers by pushing an appropriate button on a ResponsePad® (SMIT-LAB, www.smit-lab.eu) with left hand (with the index finger when characters were the same, with the middle finger when they were different). In the rest condition trials the 'get ready' cue was presented in blue and the subjects were asked not to move their finger and then give a random response. The delay between the stimulation and the response cue was carefully chosen in order to obtain 'pure' activation from unilateral stimulation. The constant display of a fixation cross that changed its color depending on the task, was used as a way to keep the subject's attention and reduce head movements. A total of 34 pairs of Braille

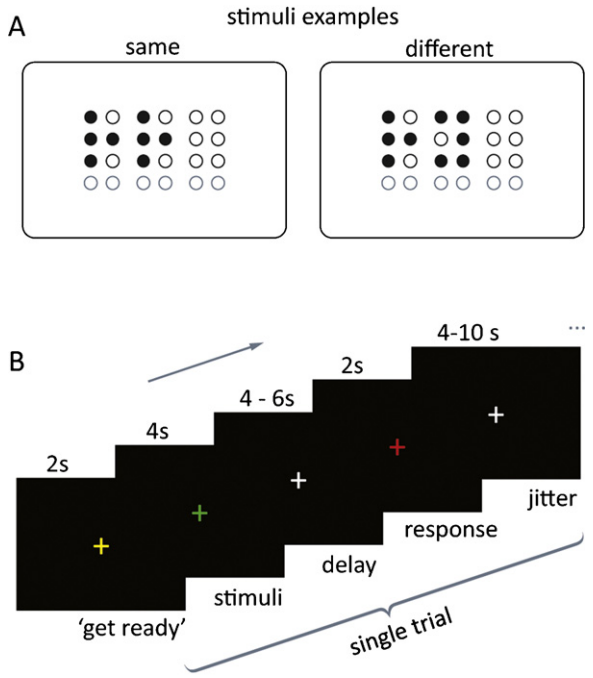

Fig. 2. Examples of Braille characters same-different pairs (A) schema of the protocol (a single trial) used in the study (B).

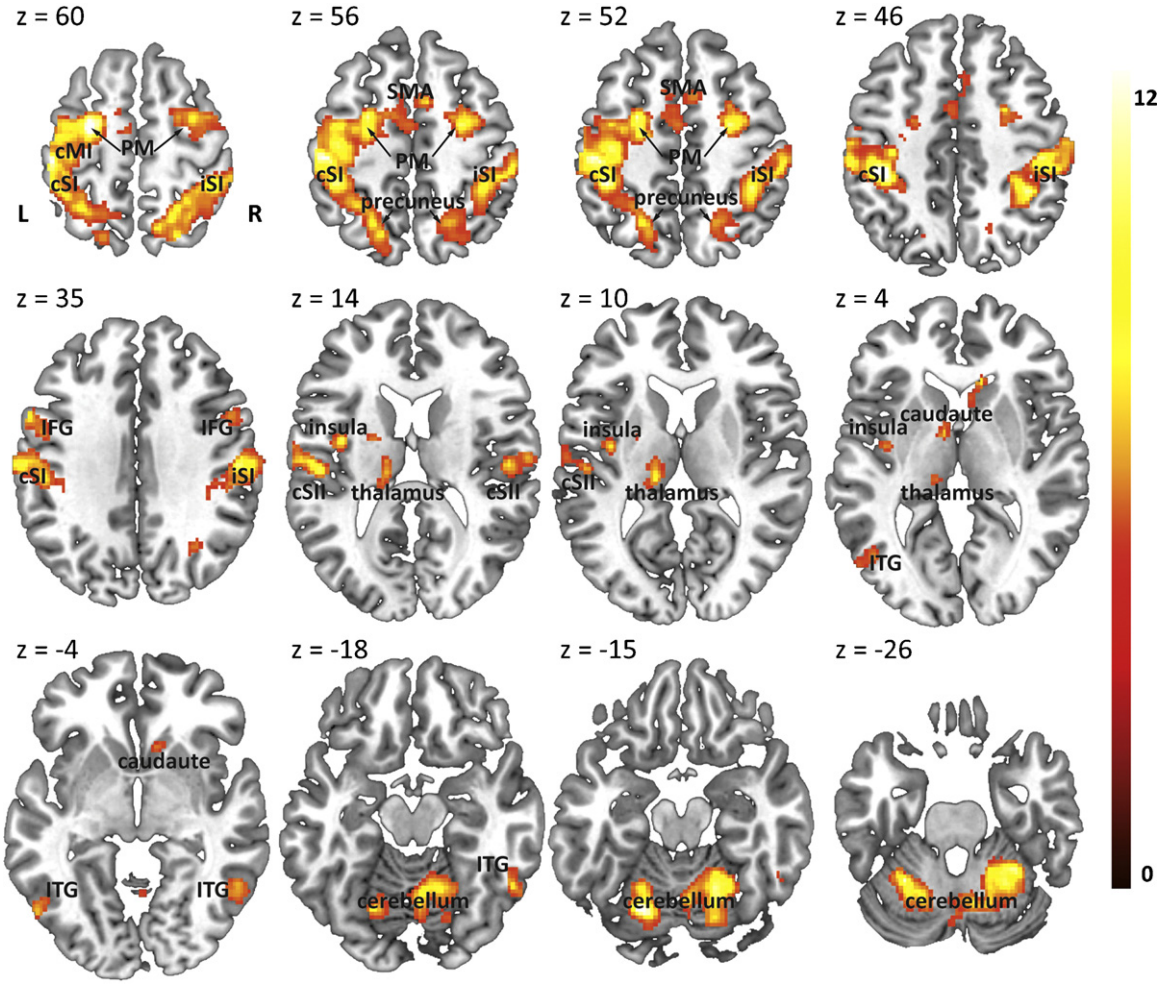

Fig. 3. Group-level analysis of an fMRI Braille characters discrimination task superimposed on a template image in MNI space (touch vs rest). Abbreviations: SII, secondary somatosensory cortex; SI, primary somatosensory cortex; MI, primary motor cortex; PM, premotor cortex; IFG, inferior frontal gyrus; ITG, inferior temporal gyrus; c, contralateral to stimulated hand; i, ipsilateral; L – left side, R – right side.

characters were presented (half of which were the same) randomly, alternating with 20 rest trials. The final set of stimuli and timings was chosen on the basis of a pilot study ($n = 9$). Analysis of preliminary results and detailed interviews revealed that for people naïve to Braille, 4 s of the stimuli application is an optimal timing. Examples of characters are shown in Fig. 2A. The software package Presentation® (Neurobehavioral Systems, Albany, CA) was used to synchronize BCS with the MRI-scanner and to present instructions.

2.3. fMRI data acquisition and analysis

Both anatomical and functional images were acquired with 3 T MRI scanner (Magnetom Trio, Siemens Healthcare, Germany) using a 12-channel phased array coil. Prior to the study phase, detailed anatomical data (T1-weighted) were obtained with 0.9 mm isotropic resolution (TR = 1900 ms/TE = 2.2 ms/FA = 9°.). In the functional run a total of 340 volumes were collected during Echo-Planar Imaging sequences with the following parameters: TR = 3000 ms/TE = 30 ms/voxel: 2 mm × 2 mm × 3 mm/FA = 90°. SPM8 (http://www.fil.ion.ucl.ac.uk/spm/) was used for data preprocessing and analysis. First, functional images were motion corrected. Then, structural images from single subjects were coregistered to the mean functional image. As a next step, the normalization to the MNI (Montreal Neurological Institute) T1 image was performed with voxel size 2 mm × 2 mm × 2 mm. Next, data were smoothed using 6-mm Gaussian FWHM algorithm. A 128-s high-pass filter was applied to remove low-frequency fluctuations in the BOLD response. For each subject, the onsets and stimuli durations were entered into the design matrix and modeled in a general linear model according to different event types. Regressors were convolved with the canonical hemodynamic response function. Specific condition effects were assessed by the application of linear contrasts, where parameter estimates for events, i.e. discrimination of Braille characters, were compared to the 'rest' condition. In a group analysis parameter estimates for each subject's first-level analysis ('discrimination of Braille characters' and 'rest') were entered into a one-way ANOVA (stimulation × rest). The statistical threshold was set at $p < 0.001$ and corrected to $p < 0.05$ for multiple comparisons (Family Wise Error, FWE) at the cluster-level using cluster size (extent threshold at $k = 100$ voxels). Detailed results of the ANOVA analysis with MNI coordinates for peak activations and exact values used as extent thresholds are presented in Table 1. Areas of activations that survived the $p < 0.05$ (FWE) threshold at voxel level are indicated with *. Anatomical localization of activated regions was verified on the basis of MNI Space Utility (MSU, http://www.ihb.spb.ru/~pet_lab/msu/msumain.html).

3. Results

Eleven sighted subjects performed a same-different discrimination task on Braille characters while in an fMRI scanner. The analysis revealed that tactile stimulation accompanying active touching of

Table 1
Areas significantly activated during Braille characters discrimination task (touch vs. rest).

	Cluster size (k)		MNI coordinates (mm)			T (peak)
			x	y	z	
PM*	L	8632	−26	−8	60	12.64
SI*	L		−48	−24	56	11.45
SI*	L		−40	−32	46	11.94
MI*	L		−35	−20	48	9.75
Inferior Frontal Gyrus	L		−62	6	28	9.58
SII*	L		−50	−20	14	8.17
SMA*	L/R		8	6	56	8.00
Precuneus	L		−22	−58	54	7.36
Cerebellum*	L	5177	−22	−68	−18	11.94
Cerebellum*	R		8	−72	−48	10.34
Cerebellum*	L		−28	−52	−26	9.96
SI*	R	4517	56	−18	36	9.76
SI*	R		46	−24	46	8.99
Precuneus	R		20	−54	62	8.71
SII*	R		52	−18	16	7.28
PM*	R	356	26	−6	52	9.13
Inferior Frontal Gyrus*	R	520	50	8	20	7.79
Inferior Temporal Gyrus*	R	474	56	−56	−8	7.95
Thalamus*	L	327	−14	−24	10	7.29
Caudate	R	284	12	26	4	6.66
Caudate	R		8	8	4	4.47
Claustrum	R		24	30	0	4.04
Inferior Temporal Gyrus	L	264	−46	−68	2	6.15
Caudate	L	250	−18	12	20	7.06
Lentiform Nucleus	L		−20	−4	16	5.42
Thalamus	L	218	−8	0	4	6.35
Insula	L	196	−38	−4	14	8.31
Lingual Gyrus	L	159	−28	−78	4	4.60
Cuneus	L		−10	−84	10	4.49
Middle Frontal Gyrus	R	126	46	44	16	4.99
Lingual Gyrus	R	100	16	−78	10	5.14
Cuneus	R		4	−68	10	3.77

MNI coordinates, peak activation and volume are presented at the estimated significance threshold. T-values and a percentage of BOLD signal change of the peak activations (touch vs rest), $p < 0.001$ (correction for multiple comparisons at cluster level) with an extent threshold of $k = 100$ voxels and height threshold $T = 3.55$. SI: primary somatosensory cortex; SII: secondary somatosensory cortex; MI: primary motor cortex; PM: premotor cortex; SMA: supplementary motor area.

* $p < 0.05$ (correction for multiple comparisons at voxel level $k = 1$).

characters during the task induces highly significant ($p < 0.05$, FWE) activations in several cortical areas, including bilateral primary (SI) and secondary somatosensory (SII) cortices, bilateral premotor and supplementary motor area, inferior frontal gyri, inferior temporal gyri and precuneus as well as contralateral thalamus. Additional activations were found in the contralateral insula, the ipsilateral middle frontal gyrus and bilateral caudaute, the cuneus, the lingual gyrus and the cerebellum and several other regions (for details see Table 1).

Group results superimposed on an anatomical MNI T1 template are shown in Fig. 3. The list of the individual subject activations with peak-values and percentage of BOLD signal change for contra- and ipsilateral SI and SII with significance thresholds is presented in Table 2. All subjects demonstrated significant activations in cSI, iSI and cSII; nine subject showed activations in iSII. Results of exemplary individual subjects results, one male and one female, are shown in Fig. 4.

4. Discussion

The main goal of constructing the Braille Characters Stimulator was to create an MRI-compatible tool for spatially and temporally precise application of standard Braille characters. The BCS is fully programmable and flexible in stimuli delivery, thereby ensuring an optimal control during the course of an experiment. We successfully tested mechanical resistance and performance of the stimulator and its application in functional MRI studies. Notably highly significant results were obtained using an event-related

Table 2
Results for each subjects. Peak activation and percentage of BOLD signal change for contra- and ipsilateral primary (SI) and secondary (SII) somatosensory cortex are presented at the estimated significance threshold.

Subject	Gender	cSI	iSI	cSII	iSII	Threshold (T)
A	m	15.01 (1.8%)	10.95 (0.6%)	8.74 (0.9%)	7.19 (0.8%)	5.09
B	m	9.98 (1.65%)	8.83 (1.25%)	8.98 (1.7%)	7.53 (1.6%)	5.09
C	m	11.6 (1.72%)	11.03 (1.55%)	8.61 (0.82%)	6.18 (0.7%)	5.08
D	f	13.03 (1.45%)	10.47 (1.1%)	8.21 (0.75%)	–	5.08
E	m	7.93 (1.2%)	8.58 (1.3%)	5.39 (0.5%)	7.94 (1.0%)	5.07
F	m	12.98 (1.25%)	11.16 (1.1%)	6.6 (0.85%)	7.22 (0.9%)	5.07
G	m	11.88 (1.8%)	11.47 (1.2%)	5.9 (0.7%)	5.17 (0.6%)	5.06
H	f	6.1 (0.9%)	6.57 (0.85%)	5.53 (0.5%)	–	5.05
I	f	10.62 (1.5%)	10.8 (1.75%)	7.68 (0.7%)	5.86 (0.45%)	5.04
J	f	10.32 (1.5%)	9.9 (0.9%)	9.62 (0.85%)	8.17 (0.7%)	5.04
K	f	9.53 (1.2%)	7.6 (0.7%)	4.45 (0.45%)	4.4 (0.42%)	5.03

T-values of peak activations at $p < 0.05$ level (FWE corrected at voxel level), extent threshold set at $k = 5$ voxels. c, contralateral to the stimulated hand; i, ipsilateral.

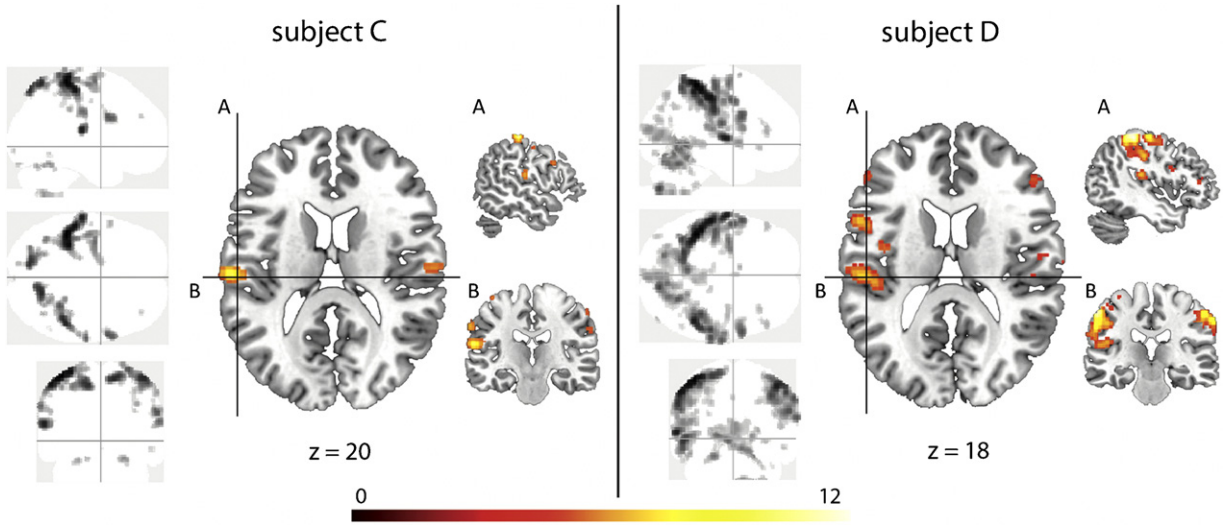

Fig. 4. Results from single subjects; male (C) and female (D), $p < 0.05$ level, FWE corrected at voxel level, threshold set at $k = 5$ voxels.

design in an acquisition sequence lasting only 15 min and 30 s. Relatively short time needed to obtain significant results is an additional advantage of our device, as a short duration of a study may be crucial while testing any clinical population and not just control subjects. Taking into account the timings and other characteristics of the procedure used in the study, it is very likely that significant activations may be achieved with a sequence of an even shorter duration. It should also be emphasized that our results were obtained using a particular experimental paradigm (discrimination task) which is just an example of a wide range of possible applications of the BCS to the functional neuroimaging studies. The device may also be applied to the very particular field of neuroimaging, which is presurgical mapping of brain functional regions, especially in blind and visually impaired subjects.

4.1. fMRI results

Experimental evaluation of the BCS effectiveness revealed that in the same-different discrimination task brain activations were localized in the expected structures. We consider as particularly important the significant activations found bilaterally in the primary and secondary somatosensory cortex and in the thalamus, and we interpret this results as a prominent evidence of successful BCS application. The crucial role of these structures in perception, transfer and analysis of the somatosensory input have been well documented. Bilateral activations in SII induced by unilateral stimulation have been revealed (Simoes and Hari, 1999; Karhu and Tesche, 1999; Maldjian et al., 1999), but SI used to be reported as manifesting mainly contralateral responsiveness (Deuchert et al., 2002). Only recently, several papers have demonstrated bilateral SI engagement in somatosensory information processing (Blatow et al., 2007).

Our findings are consistent with the latter reports. It can be hypothesized that bilateral involvement of the primary somatosensory cortex may be related to the task complexity. In our experimental procedure the challenging tactile exercise engaged working memory systems (due to the required delayed response) and involved interference caused by submitting answers with the hand opposite to the one engaged in touching the stimuli. Execution of the tasks obviously engaged wide intra- and interhemispheric neuronal networks. Since existence of reciprocal SI and SII connections as well as callosal SI–SI and SII–SII projections is well documented (Carvell and Simons, 1987), the bilateral activation of SI seems to be a natural consequence of brain processing of this specific tactile stimulation.

Moreover, activations associated with the Braille discrimination task found in SI, SII, the inferior frontal gyrus, the inferior temporal gyrus, the supplementary motor area, the premotor area and the thalamus stay in line with patterns of activation observed in a study by Reed et al. (2004) investigating neural correlates of tactile object recognition. Braille reading could also be considered as a task of this kind.

4.2. Limitations

Braille reading by its nature is performed actively, which makes it hard to transfer into laboratory environment. Self-exploration of Braille characters by the subject limits the control of the experimental conditions and appears to be an intrinsic limitation of any device similar to BCS. However, the BCS is just a prototype. Further modifications and improvements, such as adding sensors monitoring the range of finger movements (since the elimination of the movements is not advisable for the reasons described earlier) and expansion of the interface with more Braille cells, are possible.

5. Conclusion

In conclusion, we demonstrated that the BCS with the protocol used in this experiment, based on touching single Braille characters, induced significant activations in somatosensory and motor pathways, as well as associative cortices. The results indicate the validity of using such a precise – in terms of a presentation timing, stimuli size and resolution – method of stimuli application in fMRI studies, in sighted and blind subjects. We therefore recommend the Braille Characters Stimulator as an effective method of delivering tactile stimulation.

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