

Brains of verbal memory specialists show anatomical differences in language, memory and visual systems



James F. Hartzell^{a,*}, Ben Davis^a, David Melcher^a, Gabriele Miceli^a, Jorge Jovicich^a, Tanmay Nath^b, Nandini Chatterjee Singh^b, Uri Hasson^a

^a Center for Mind/Brain Sciences (CIMeC), University of Trento, 38060, Italy

^b National Brain Research Centre, Manesar, Gurgaon Dist., Haryana 122 050, India

ARTICLE INFO

Article history:

Accepted 8 July 2015

Available online 15 July 2015

Keywords:

Cortical thickness

Gray matter density

Diffusion tensor imaging

Language

Memory

Plasticity

Hippocampus

ABSTRACT

We studied a group of verbal memory specialists to determine whether intensive oral text memory is associated with structural features of hippocampal and lateral-temporal regions implicated in language processing. Professional Vedic Sanskrit Pandits in India train from childhood for around 10 years in an ancient, formalized tradition of oral Sanskrit text memorization and recitation, mastering the exact pronunciation and invariant content of multiple 40,000–100,000 word oral texts. We conducted structural analysis of gray matter density, cortical thickness, local gyrification, and white matter structure, relative to matched controls. We found massive gray matter density and cortical thickness increases in Pandit brains in language, memory and visual systems, including *i*) bilateral lateral temporal cortices and *ii*) the anterior cingulate cortex and the hippocampus, regions associated with long and short-term memory. Differences in hippocampal morphometry matched those previously documented for expert spatial navigators and individuals with good verbal working memory. The findings provide unique insight into the brain organization implementing formalized oral knowledge systems.

© 2015 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

A large body of research has established that acquisition of certain long-term skill sets or knowledge is linked to plasticity in both grey matter (GM) and white matter (WM) in multiple cortical and subcortical regions (May, 2011; Zatorre et al., 2004). As reviewed by May (2011, see references within), various expert groups such as sportsmen, mathematicians, ballet dancers, and professional board-game players all show particular morphological features that may be related to learning and plasticity.

Our goal in the current work was to examine the potential impact of extensive memorization and verbal recital practice on brain plasticity, as identifying brain regions implicated in these functions can elucidate the functional capacities of both lateral and medial temporal regions, as detailed below. To investigate the potential impact of extensive memorization and verbal recital practice on brain plasticity we recruited a sample group of traditional Sanskrit learners—Yajurveda Sanskrit Pandits—who memorize and recite one set of the most ancient Sanskrit

texts, the Vedas and their subsidiary texts (*Vedāngas*). The Sanskrit Vedas are late bronze/early iron-age oral texts passed down for over 3000 years in an unbroken tradition in India. They form the core of the ancient Sanskrit knowledge system, which developed extensive oral and later written literature in a wide range of traditional subjects still taught in India's Sanskrit institutions using traditional oral memorization and recitation methods (Rashtriya Sanskrit Sansthan, 2014). Professional Vedic Pandits undergo rigorous training in exact pronunciation and invariant content of these oral texts for 7 or more years, with 8–10 h of daily practice (totaling ~10,080 h over the course of the initial training), starting in their childhood, and mastering multiple 40,000 to 100,000 word oral texts (compared to ~38,000 in the book of Genesis). The training methods strongly emphasize traditional face-to-face oral learning, and the Yajurveda recitation practice includes right hand and arm gestures to mark prosodic elements. After graduation from training, professional Yajurveda Pandits work as teachers or Vedic priests, with daily recitation reduced to ~3 h.

We note that while the ability of Yajurveda Pandits to perform large-scale, precise oral memorization and recitation of Vedic Sanskrit texts may, prima facie, appear extraordinary or bordering on impossible, textual memorization and recitation are in fact standard practice in traditional Sanskrit education in India (Rashtriya Sanskrit

* Corresponding author at: Center for Mind/Brain Sciences (CIMeC), Via delle Regole 101, Mattarello, TN, Italy.

E-mail address: James.Hartzell@unitn.it (J.F. Hartzell).

Sansthan, 2014).¹ Thus, while the Pandit's memorization capacity may appear unique to graduates of a Western educational system, it is one of several memorization-related study traditions current in the Indian subcontinent.

We had two predictions regarding brain systems possibly affected by the intense memorization and recitation routine practiced by the Pandits. First, we expected to see differences in cortical thickness or gray matter density of lateral temporal regions. These form the core system for speech processing at the phonemic and syllabic level (Zhuang et al., 2014), with left hemisphere regions of the superior temporal plane (STP) likely sampling information at a higher rate matching that of phonemic processing, and the right hemisphere STP sampling at a lower rate matching syllable-level processing (Giraud and Poeppel, 2012; Kotz and Schwartz, 2010; Morillon et al., 2012; Poeppel, 2003). Apart from their role in sublexical combinatorial processes, these regions also play a role in encoding sentential content to memory. Activity in these regions predicts whether sentential content will be subsequently remembered (a subsequent-memory effect, Hasson et al., 2007), and they show reduced activation for comprehension of repeated auditory sentences (repetition suppression (RS); Dehaene-Lambertz et al., 2006; Devauchelle et al., 2009). Particularly, sentential RS effects in these regions scale negatively with the temporal interval between sentence repetitions (Hasson et al., 2006). Thus, extensive memorization of language content, coupled with memory for sentential content could affect the structure of these regions.

In addition, plasticity effects linked to memory practice have been documented in the human hippocampus, which is involved in both the consolidation of prior experiences (e.g., Eichenbaum et al., 2007; Milner and Penfield, 1955; Scoville and Milner, 1957) and spatial navigation (e.g., Bird and Burgess, 2008; see also Eichenbaum and Cohen, 2014). Hippocampal plasticity has been linked to spatial navigation expertise, with greater posterior hippocampal volume and smaller anterior volume shown for expert urban navigators (Maguire et al., 2000). The hippocampus also mediates verbal memory (e.g., Fernandez et al., 1998; Grunwald et al., 1999), and is larger for individuals who perform better on declarative memory tasks for verbal materials (e.g., Ashtari et al., 2011; Pohlack et al., 2014). Poppenk and Moscovitch (2011) showed that better verbal memory for proverbs is related to greater posterior and smaller anterior hippocampal volume, a pattern similar to that seen for expert navigators. On the basis of this prior work we hypothesized that the intensive memorization demands of Pandit practice might be associated with changes to hippocampal volume or density.

To examine these issues, we studied a group of Pandits ($N = 21$) together with closely matched controls. We examined cortical-level data via voxel-based morphometry (VBM), cortical thickness (CT) and local gyrification index (LGI) analyses, and subcortical data via VBM and anatomically defined regional measurements. We also evaluated white matter data with diffusion tensor imaging (DTI) fractional anisotropy (FA) analysis, at a whole-brain level. The main purpose of the FA analysis was to evaluate whether WM changes would be found in the vicinity of areas linked to GM or CT differences. In particular, the frontal aslant tract (Catani et al., 2013) has been implicated in fluency and stuttering (Kronfeld-Duenias et al., 2014), as has the forceps minor in the anterior corpus callosum (Civier et al., 2015).

¹ There are today in India around 150,000 students engaged in traditional Sanskrit studies at approximately 5000 government and private institutions (Mishra, 1997; Rashtriya Sanskrit Sansthan, 2010–2011; Rashtriya Sanskrit Sansthan, 2014; Pathashala, 2014). The topics (and texts memorized) at these institutions include Sanskrit literature, grammar, law, history, philosophy, astronomy, yoga, logic, and Vedas, subsidiary Vedic disciplines, and Vedic commentary (Rashtriya Sanskrit Sansthan, 2014). There are in addition some 246 registered Ayurvedic traditional medical colleges in India where some 50,000 students memorize portions of Sanskrit core ("root") medical texts and subsidiary texts as part of their training (Central Council of Indian Medicine, 2014; Hartzell and Zysk, 1995). Specifically for Vedic studies, there are currently an estimated 34,000 Vedic Pandits in training in both government and non-government traditional Vedic schools (Shastri, 2014; Pathashala, 2014; Rashtriya Sanskrit Sansthan, 2014; Mishra, 1997).

Methods

Participants

Forty-two male volunteers participated in the study conducted at the National Brain Research Center in India. Twenty-one professionally qualified Pandits were recruited from government-supported Vedic Pandit schools in the greater New Delhi (India) area. They underwent an extensive semi-structured interview prior to scanning to evaluate their extent of training, family history, current practice routines, multilingualism, handedness and eye dominance. Professional qualification constituted demonstrable mastery, i.e. complete memorization and full recitation ability, of at least the ~40,000 word Yajurveda *Samhitā* text. All Pandits memorized part or all of one or more additional canonical texts (the length of these texts ranged from 1013 to 165,156 words but we could not quantify precisely how much of these additional texts was memorized by each Pandit). All began their training at an early age ($M = 12.33$, $SD = 1.59$, range 9–16), trained full-time for 7 years, for a total of approximately 10,080 h, and continued training and reciting at reduced daily hours for additional years ($M = 2.38$, $SD = 2.29$, range 0–8). From the interview reports, we estimated the total practice hours after competing the training ($M = 11,141$ h, $SD = 27,196$, range 2365–129,295). Note that Pandits enter training without any entrance exams, so there is no pre-selection for memory or recital abilities, and the dropout rate from the study program is only around 5% (Shastri, 2014). Thus, graduating the studies is not indicative of self-selection either prior to or during the studies themselves. Pandits had all either graduated from or were in the final year of professional Vedic Pandit training, and all were self-rated as fluent in speaking, reading and writing Sanskrit. None of the Pandits in our participant group came from traditional family lineages of reciters (see SI Methods). See Supplementary Information (SI Methods and SI Table 1) for additional Pandit demographics and practice specifics.

Twenty-one control volunteers were recruited to match the Pandit population in gender, age ($M_{\text{Pandits}} = 21.7$; $SD = 2.8$ vs. $M_{\text{controls}} = 22.8$; $SD = 3.6$, T-test, $P = .3$) and number of languages spoken ($M_{\text{Pandits}} = 3.1$; $SD = 0.8$ vs. $M_{\text{controls}} = 3.1$; $SD = 1.3$, T-test, $P = .9$). Participants in the control group were members of India's National Brain Research Centre community or students from a nearby technical college. All volunteers were right-handed, right-eye dominant, with no left-handed parent or sibling (Knecht et al., 2000). Multilingualism and handedness/eye-dominance were assessed by culturally-adapted Hindi versions of the Penn State Language History Questionnaire (v.2; Li et al., 2006), and Edinburgh Handedness questionnaire (Oldfield, 1971). (Adaptations and translations by N.C.S., T.N., J.H, and a fourth native Hindi/English speaker). The protocol was approved by India's National Brain Research Centre Ethics Committee and all participants provided written informed consent.

Image acquisition

Two T1-weighted 3D-MPRAGE sequences were acquired for each participant on a Philips Achieva 3 T scanner with an 8-channel head receive coil (FOV $256 \times 256 \times 176$ mm, voxel size $1 \times 1 \times 1$ mm), TE 3.2 ms, TR 934 ms, flip angle 9° , 176 sagittal-oriented slices, acceleration 2 (sense), total acquisition time 06:49.8. Image quality was evaluated immediately after each structural acquisition to control for motion effects or other artifacts. The two structural images of each participant were aligned using FSL's 4.1.8 FLIRT (Jenkinson et al., 2002; Jenkinson and Smith, 2001), and averaged to increase signal-to-noise ratio. Image intensity non-uniformities were corrected in AFNI (Cox, 1996). The resulting mean structural image was used for all subsequent analyses. Diffusion data were acquired for a subset of 15 Pandits and 15 controls using single-shot EPI during the same MRI session (FOV $256 \times 256 \times 128$ mm³, voxel size $2 \times 2 \times 2$ mm³), TE 75 ms, TR 8000 ms, flip angle 90° , 64 transverse slices, slice thickness 2 mm, fat

suppression, matrix 218×126 , 60 diffusion encoding directions (bvecs), b-value = $700 \text{ mm}^2/\text{s}$, 10 b0 volumes (saved as a single averaged volume), parallel imaging with acceleration factor 2 (sense), total acquisition time 10:59.6. Diffusion data was evaluated immediately upon acquisition to control for motion effects or other artifacts, and re-acquired if necessary (4 scans were reacquired). The b-value of 700 was chosen to be within the range of values considered optimal for human brain matter DTI analysis while favoring high SNR to facilitate the detection and correction of artifacts in the diffusion weighted images (Alexander and Barker, 2005; Ben-Amitay et al., 2012). Mean FA of the corpus callosum body (~ 0.52) matched values reported in the literature (Jovicich et al., 2014; see their Fig. 6).

Voxel-based morphometry (VBM)

Structural images were analyzed using the FSL's voxel-based morphometry (VBM) analysis pipeline (Ashburner and Friston, 2000; Good et al., 2001) with FSL-VBM tools (Douaud et al., 2007). Data consisted of the 21 aligned and averaged structural images acquired from Pandits and 21 from the control group. Brains were extracted using FSL's brain extraction tool (BET; Smith, 2002), with manual edits to control for extraction errors, and processed using FSL's VBM default pipeline. Note that in the FSL VBM pipeline, the single-participant data prior to alignment to common space reflects a voxel's probability of being gray matter (calculated by a combination of Hidden Markov Random Field and Expectation Maximization framework; see Zhang et al., 2001), and the final data, in common space, reflect an adjustment of that value by the Jacobian of the deformation applied to the participant's data when aligning to common space. Thus, this VBM implementation most closely reflects local volume differences. We spatially smoothed the final images by an isotropic Gaussian kernel (FWHM = 9.42 mm). Group-level statistical inference was achieved via nonparametric permutation using the FSL tool *randomise*. Family-wise error was controlled for at an alpha level of $P < .05$ by Threshold-Free Cluster Enhancement (TFCE; Smith and Nichols, 2009), in which cluster extent is constrained by cluster-like local spatial support. Age and whole brain Volume were included as covariates. References to anatomically defined regions within MNI space were established by intersecting the group's MNI gray matter template mask with FSL's pre-defined atlases. (See SI Methods for additional information.) To evaluate the impact of smoothing kernel, we also implemented Gaussian kernels of 2.35 mm, 4.71 mm, and 7.06 mm (sigma of 1, 2 and 3, respectively) and repeated the main analysis.

Cortical thickness analysis

Cortical thickness (CT) analysis was implemented in FreeSurfer (Dale et al., 1999), using the default processing pipeline, except for manually bypassing FreeSurfer's automatic skull stripping routines and using instead the skull-stripped brains created in the initial step of the VBM analysis described above. FreeSurfer's GM segmentation was verified manually for each participant, and no manual corrections were needed (for example participant's segmentation, see Inline Supplementary Figure S1). The CT estimates derived for each participant were imported into AFNI's surface-based analysis module, SUMA (Saad et al., 2004) for further analyses. CT values were spatially smoothed with a conservative (Pardoe et al., 2013) 10 mm smoothing kernel on the two dimension cortical surface using an iterative Heat Kernel method (Chung, 2004). The resulting CT values on the cortical surface were interpolated to a surface mesh that maintained the same number of vertices for all participants, in similar locations (using SUMA's *Mapicosahedron* procedure). The resulting meshes contained 156,252 vertices per hemisphere. Statistical analysis of CT values on the group level was performed using cluster-based thresholding that

was determined via a permutation procedure (following Nichols and Holmes, 2002; see SI Methods for details).

Inline Supplementary Fig. S1 can be found online at <http://dx.doi.org/10.1016/j.neuroimage.2015.07.027>.

Local gyrification index analysis

To examine potential gyrification differences between the two populations we used a method based on calculating an 'outer surface' (tangential to the folding points of the gyri), and then parcellating it into numerous circular patches covering the entire 2D cortical surface (Schaer et al., 2008, 2012). For each patch, the local gyrification index (LGI) computes the ratio of cortex within sulcal folds to the amount of visible cortex (tangent to the patch). Higher values indicate that a greater proportion of the pial matter under the patch is in sulci. The 2D surface maps generated by this method have, by definition, a strong degree of spatial smoothness (FWHM of ~ 30 mm) that is determined by the number of surface patches used. (Each patch has a radius of 20 mm, and the computed LGI value for each patch is propagated to all surface vertices overlapping with it, necessarily yielding less localized results than those seen for VBM or CT analyses.) Between-group statistical tests of LGI patterns were based on permutation tests as for the CT analysis. Permutation tests maintain the spatial autocorrelation of each participant's data and permit sensitivity to non-stationary changes in LGI across cortical regions.

Diffusion tensor imaging: fractional anisotropy

The 60 diffusion-encoding direction b-vectors were corrected individually for head motion using FSL's *rot_bvecs*, followed by eddy current and subject motion correction with affine registration to the averaged b0 image. Fractional Anisotropy (FA) images were created using FSL's Diffusion Toolbox (FDT) after brain-extraction using BET and manual edits to remove artifacts, then processed using FSL's Tract Based Spatial Statistics (TBSS; Smith et al., 2006) default settings. FSL's TBSS first erodes each participant's FA image. For registration to common space, we used an option that selects the best target image from among the subjects, performs a nonlinear alignment of all participants to that target, and then affine registers the resulting aligned files to MNI152 1 mm common space. Using the mean FA calculated from the participants' files in common space, TBSS creates a skeletonized representation of FA-derived tracts common to all subjects, by estimating the local surface perpendicular direction along the tracts and performing "non-maximum-suppression" along the perpendicular to the voxel with the highest FA value, which marks the center of the tract. The distance of each participant's FA voxel to this common skeleton is then calculated, with the distance calculation constrained to the nearest voxels, and the participant's maximum FA value in the already-calculated perpendicular to each skeleton voxel is projected into the skeleton. The aim of this method is to reduce variance from residual misalignments of each subject's FA to common space (Smith et al., 2006). Voxelwise cross-participant group-level statistics are then performed within a thresholded mean FA skeleton mask (we used a threshold of 0.3). The threshold reduces the effects of high inter-subject variability at the outer edges of the brain. We tested between group differences using 2D TFCE, controlling for family-wise error at an alpha level of $P < .05$ based on cluster extent constraints, with Age included as a covariate. References to anatomically defined white-matter regions within MNI space were established by intersecting the group's MNI template FA mask with FSL's predefined WM atlases (see SI Methods).

Hippocampal region-of-interest analysis

Hippocampus-optimized VBM

We also conducted a customized VBM analysis that was aimed directly at evaluating changes in the HF. This analysis consisted of the

following steps. First, the initial automatic segmentations of the HF as derived by FSL's FIRST subcortical alignment and segmentation procedures (Patenaude et al., 2011) were anonymized and then further manually evaluated and modified by one of the authors (J.H.). Segmentation was performed in original space, using advanced FIRST options to optimize the segmentation by algorithm-determined vertex numbers (modes) and internal reference to the thalamus for normalization. In the second step, we performed a nonlinear registration of these edited HF segmentations to MNI space (FSL's *MNI152 T1 1 mm* template) using high-resolution (6 mm^3) nonlinear warping (FNIRT) initialized with the affine matrix generated for each participant by FSL FIRST's subcortical alignment routine. After registration we multiplied the hippocampi by their Jacobians to modulate the GM, as in the standard VBM pipeline. Note that in contrast to the whole-brain analysis (which works with GM probabilities), the values multiplied by the Jacobian were the original T1 intensity values within the manually verified hippocampal segmentations. Steps 1 and 2 therefore provided a more precise inter-participant alignment of the HF specifically. Third, to evaluate the impact of various smoothing kernels (2.35 mm, 4.71 mm, 7.06 mm and 9.42 mm, sigma 1, 2, 3 and 4 respectively), we smoothed only *within* these MNI-registered right and left HF. Steps 1, 2 and 3 ensured that our between group tests focused only on the HF, thus obviating the chance of impacting the results from nearby regions. Then we performed voxel-wise tests inside the right and left hippocampal intersection masks (i.e. the hippocampal masks used in the *randomize* routine included only voxels to which all 42 subjects contributed values). We used TFCE testing, and included Age and whole-brain Volume as covariates at all four smoothing kernels. To evaluate the impact of using manually annotated hippocampi, we compared the results to those obtained when applying the same registration and analysis pipeline but using as inputs the FIRST automatic hippocampi segmentations produced in Step 1 above, as well as automatic hippocampi segmentations obtained from FreeSurfer for these participants.

Hippocampal local-volume analysis

We conducted an additional analysis to identify whether there were areas of the hippocampus whose local volume differed between groups. The method was based on FSL FIRST's vertex analysis (Patenaude et al., 2011), but modified to allow incorporation of manual edits on the hippocampal structure (following suggestions by Jenkinson, 2014). This analysis was not based on comparison of mesh-based segmentations of the hippocampus but rather on comparisons of the outer envelope of participants' hippocampi in common space. First, using the manually

annotated hippocampal segmentations from FIRST, we constructed a common core hippocampal 'shape' from the entire group of participants in common space (Pandits and controls). To this end, the individual hippocampal shapes from original space were projected to common space (*MNI152 T1 1 mm*) using a rigid body alignment to maintain size and shape differences. From the group average of these MNI-registered hippocampal shapes we then constructed a thresholded (0.9) group average boundary mask (this mask marks the outer edge of the common HF volume, in 3D space). For each voxel in this group-level boundary mask we then calculated its distance to the nearest boundary voxel of each participant's binarized hippocampal mask, whether inside or outside of the common boundary mask. This returned, for each group-level boundary-mask voxel, a vector reflecting the positive or negative distance to each participant's boundary voxel. Group-level tests were conducted on this 'signed distance' data. The result of this procedure, when applied to all participants, was a group-level statistical map showing those parts of the group-hippocampal boundary shape where (local) distances to the shape differed between the two groups. Note that as opposed to VBM this procedure implemented a strictly "local shape" analysis that (similarly to FSL's new vertex analysis) identifies geometric changes, is independent of any tissue-classification step, and does not involve any smoothing of the data.

Results

Evaluation of covariates

The VBM, CT, LGI and FA analyses included whole brain analyses for the Pandit group examining correlations of two covariates. These included Starting age of recitation training, and "Overall Practice Hours since Completion of Training" (OPHCT). OPHCT was included since, although all Pandits completed the common training, there was considerable variance in their subsequent practice routines, and it has been shown that even short-term cognitive and motor practice impacts neuroplasticity (e.g., Draganski et al., 2006; Driemeyer et al., 2008). None of the pair-wise correlations between Age, Start Age, and OPHCT approached significance (Correlation tests: Start Age and Age: $R = 0.23$, $P = .39$; OPHCT and Age: $R = 0.06$, $P = .7$; Start Age and OPHCT: $R = 0.22$, $P = .32$). Because age and whole brain volume are also known to correlate with changes in GM, we included Age and Volume as additional covariates in all analyses, including the between-group tests, with the exception of the CT, LGI, and FA analyses, where we used only Age as a covariate.

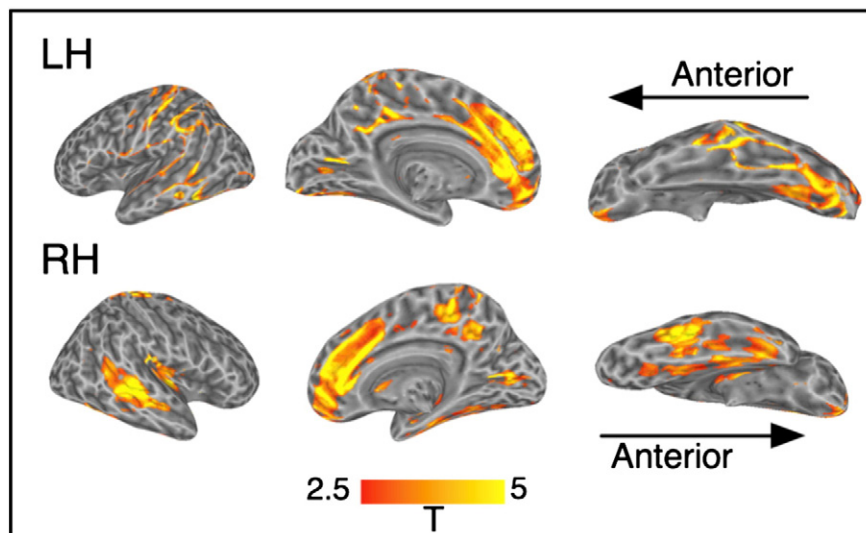


Fig. 1. Surface projection of areas where Pandits showed greater gray matter density/volume (GM) than controls as indicated by a whole brain Voxel Based Morphometry analysis. Analysis here and all other analysis corrected for family-wise error at $P < .05$, using FSL's TFCE cluster-extent correction (see SI Tables 2 and 3 for cluster details).

Voxel-based morphometry: whole brain analysis

The whole-brain VBM analysis revealed extensive GM differences in cortical, cerebellar and subcortical regions. In cortical regions Pandits demonstrated greater GM than controls in large portions of both left and right hemispheres (10.4% left and 12.5% right of total GM template cortical volume). To facilitate presentation, differences found in cortical regions were projected to an inflated cortical surface representation of a brain in MNI space (Fig. 1; see SI Tables 2 and 3 for complete cluster descriptives and local maxima). Differences were found bilaterally in both auditory and visual-stream regions, including lateral temporal cortices, ventral occipital cortices, angular gyri, pre- and post-central gyri, posterior cingulate, lingual gyri and precuneus. Greater Pandit GM was also found in large bilateral areas of the anterior cingulate (ACC) and ventromedial prefrontal cortices (vmPFC). We repeated the VBM analysis with spatial smoothing kernels of 2.35 mm, 4.71 mm, and 7.06 mm. The resulting statistical maps were almost identical, apart from an additional single cluster in the base of left STG, MTG that was only found for the 4.71 mm smoothing kernel (see SI Table 6 for additional smoothing kernel cluster specifics).

Within right lateral temporal cortex a large GM cluster was found that reached along the superior temporal sulcus (STS) into the STP, encompassing both the lateral transverse temporal gyrus and association cortices and extending deep into the ventral anterior temporal region. Pandits' GM was also larger in the right posteromedial insula and central operculum, the anterior and posterior parahippocampal gyri

and the right perirhinal cortex (PRC). As shown in Fig. 1 (and see SI Tables 2 and 3), in the left hemisphere GM differences in the lateral temporal cortex were found in posterior STG, MTG, and ITG, while in the STP, GM differences were found in the planum temporale (PT), extending into the angular gyrus and supramarginal gyrus in the parietal lobe.

In the cerebellum Pandits showed greater GM than controls in multiple bilateral structures (Fig. 2A), encompassing 34% of the total GM in the cerebellar template. The cerebellar subregions included both left and right Crus I, Crus II, V, VI, VIIb, VIIIa, VIIIb, IX and X, as well as several midline Vermis regions. Greater GM for Pandits was most dominant in Crus 1 and Crus II, VIIb and VIIIa (the cerebellar cluster regions and relative volume in each cerebellar sub-region for which GM was higher for Pandits is reported in SI Tables 3 and 4). In subcortical regions, we found a more heterogeneous result pattern, with Pandits showing greater GM than controls in a small cluster of the posteromedial right hippocampus (Fig. 2B), whereas they showed less GM than controls in a large cluster (62% of subcortical template GM) encompassing the more anterior portions of the hippocampus bilaterally and bilateral regions of the amygdala, caudate, nucleus accumbens, putamen and, thalamus (see Figs. 2C and D, and SI Table 3).

To directly compare our hippocampus results with prior literature that documented hippocampus-related volume changes in expert spatial navigators (London taxi drivers; Maguire et al., 2000), we isolated the Pandit > control cluster within the right hippocampus, and also established its left hemisphere mirror image. In each region we then calculated the mean GM change for Pandits and controls. Following

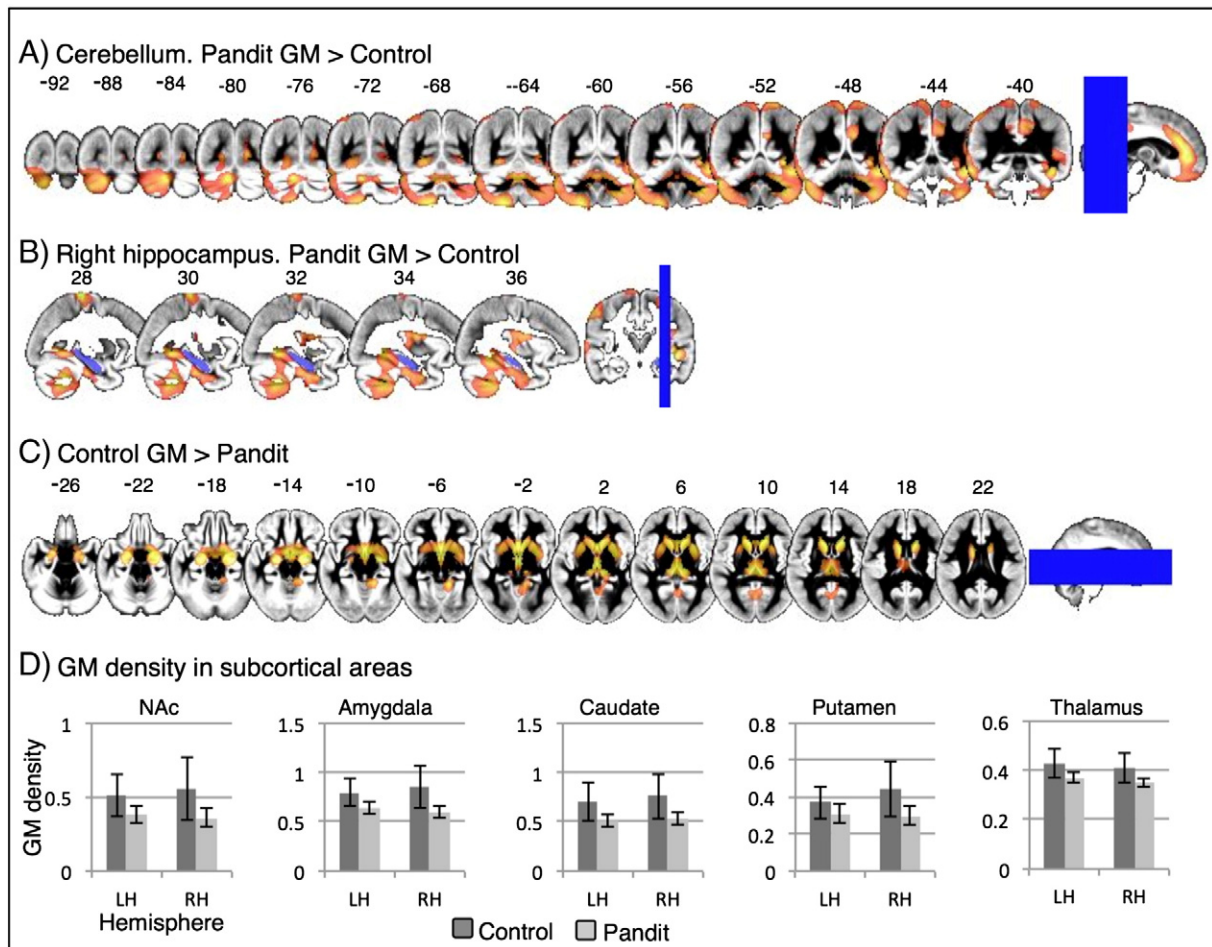


Fig. 2. Whole-brain VBM results in subcortical and cerebellar regions, overlaid onto the group GM template (left hemisphere on left). (A) Cerebellar subregions where Pandits showed greater GM than controls include, bilaterally, Crus I, Crus II, V, VI, VIIb, VIIIa, VIIIb, IX and X, as well as several midline Vermis regions (see SI Tables 3 and 4 for details). (B) Pandits showed greater GM than controls in the right medial posterior hippocampus; blue indicates anatomically-defined hippocampus mask. (C) Bilateral subcortical regions where Pandits showed less GM than controls: amygdala, caudate, anterior hippocampi, nucleus accumbens, putamen and thalamus. (D) Mean GM values for Pandits and controls for subcortical structures. All results $P < .05$, FWE-corrected.

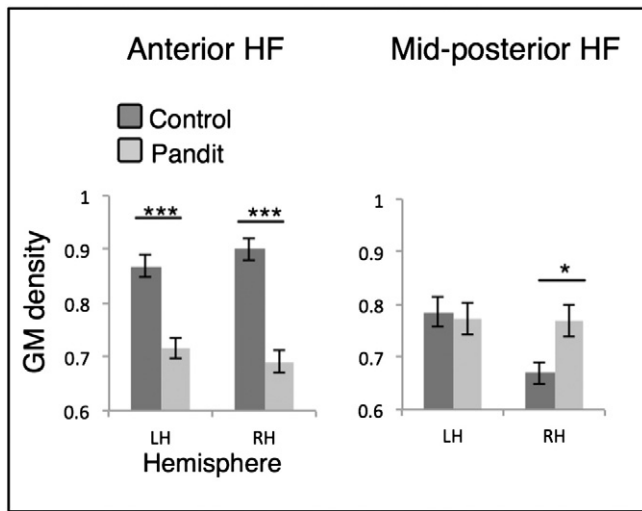


Fig. 3. Gray matter differences in hippocampi as indicated by a Whole Brain Voxel Based Morphometry analysis. Pandits showed less gray matter than controls in bilateral anterior hippocampal formation (left) and more gray matter than controls in a right middle-posterior hippocampal formation cluster (right). * = $P < .05$, *** = $P < .001$.

Maguire et al (2000), mean GM was also calculated for the anterior aspects of the hippocampus that fell within the large cluster where Pandits showed lower GM than controls. Fig. 3 bears out the greater density for controls in the anterior hippocampus, which is markedly absent, and even reversed, in the right mid-posterior hippocampus. (Note that diverging from our analysis, Maguire et al. did not include Age as covariate in the between-group tests, and doing the same in the current study revealed even stronger similarities to their findings; see SI Discussion and SI Fig. 2 for visual comparisons). We then evaluated whether these conclusions about the hippocampus would hold up if the whole brain VBM analysis was repeated at different smoothing kernels. The anterior hippocampal results (Pandits < controls) survived tests at additional FWHM Gaussian smoothing kernels of 2.35 mm, 4.71 mm, and 7.06 mm (sigma of 1, 2 and 3, respectively), while the right posterior hippocampus result (Pandits > controls) survived at the additional Gaussian kernel of 7.06 mm (sigma 3). We also conducted a whole brain analysis within the Pandit group to test whether GM density correlated with Start Age or with total post-training hours of Pandit recitation practice (OPHTC), both with Age and total brain Volume as covariates. We found no significant correlations.

Hippocampus-focused analyses

Given that the hippocampal data in the whole-brain analysis may reflect the impact of imperfect alignment or smoothing of data from outside the hippocampus, we implemented two additional analyses to

better study hippocampal differences between the groups. Both analyses considered the hippocampus as a region of interest, and examined VBM and local-volume changes in a more circumscribed manner. The implementation details of these analyses are described in the Methods. In brief, in both analyses we used accurate hippocampal segmentations in original space, obtained from FSL's automatic subcortical segmentation (FIRST; Patenaude et al., 2011), which were then further manually annotated. For the VBM analysis we implemented a high-resolution alignment to common space, optimized for subcortical structures. We used the Jacobians of the deformation to common space in order to modulate intensity values within each person's hippocampus. For the local-volume analysis we implemented a procedure similar to FSL FIRST's vertex-based subcortical shape analysis. This analysis was based on 3 main steps: i) aligning participants' hippocampi to common space, ii) producing a 'consensus shape' of hippocampal areas where participants overlapped, and iii) quantifying, for each point on the consensus shape's boundary, its distance to the nearest boundary of each person's hippocampus. (This analysis is identical to FSL FIRST's vertex-wise local distance calculations, but uses boundaries in voxel space rather than derived 2D meshes). Using this procedure we could determine, for each point on the consensus shape boundary, whether the two groups differed in local volume. In contrast to VBM, this analysis is immune to any spatial smoothing effects, and reflects strictly local volume differences.

The hippocampal-optimized VBM procedure indicated a large portion of the posterior-middle right HF where Pandits had greater GM than controls (see Fig. 4, and see Supplementary Table 7 for cluster specifics). The volume of this region formed between 73 and 98% of the hippocampal mask (depending on smoothing kernel; FWHM 2.35 mm = 73%, FWHM 4.71 mm = 80%, FWHM 7.06 mm = 92%, FWHM 9.42 mm = 98%; note that smoothing was implemented only within the hippocampal mask, thus obviating effects of nearby regions). At larger smoothing kernels (7.06 mm and 9.42 mm), we also found a cluster in the left posterior hippocampus where Pandits had greater GM than controls.

The hippocampal shape analysis revealed a portion of the right mid-anterior hippocampus with greater volume for the control group (see Inline Supplementary Figure S2). We then tested, within the Pandit group, whether hippocampal GM density or shape correlated with Pandit Start Age or with total post-training hours of recitation practice (OPHTC), both adjusted for Age and total brain Volume as covariates. We found no significant correlations.

Inline Supplementary Fig. S2 can be found online at <http://dx.doi.org/10.1016/j.neuroimage.2015.07.027>.

Cortical thickness analysis

Several brain regions differed in CT between the Pandit and control group, and in all cases the Pandit group was associated with greater CT. Differences were found in right STS, right anterior temporal pole,

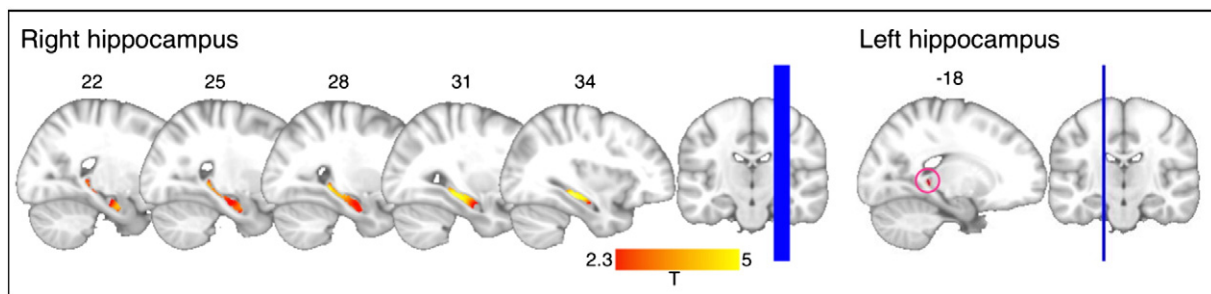


Fig. 4. Hippocampal region-of-interest analysis: areas within the right and left hippocampi where Pandits showed greater GM than controls. In addition to the whole brain analysis, we conducted a region-of-interest analysis using subcortex-optimized nonlinear alignment to MNI152 T1 1 mm common space. Greater GM density for Pandits was found in the mid-posterior right hippocampus, independent of spatial smoothing kernel. Greater GM density for Pandits was found in the posterior left hippocampus, but only when using 7.06 mm and 9.42 mm smoothing kernels. Statistical maps for both right and left hippocampus shown at 7.06 mm smoothing kernel, overlaid on MNI152-T1 1 mm template.

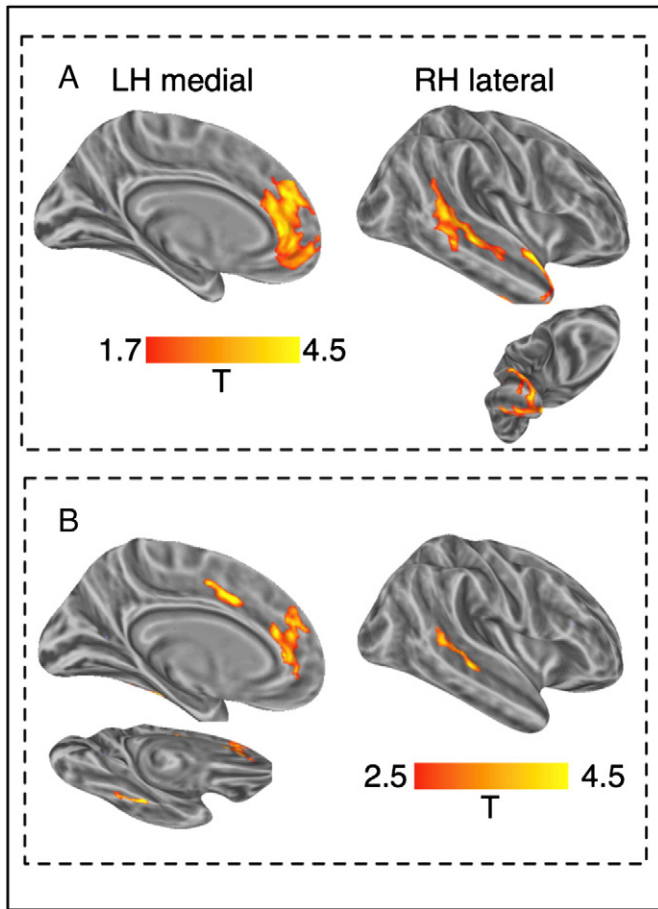


Fig. 5. Areas where Pandits demonstrated greater cortical thickness than controls. (A) Single vertex significance value set at uncorrected threshold of $P < .05$, corrected for family-wise error using cluster-extent thresholding. (B) Single vertex significance value set at uncorrected threshold of $P < .005$, corrected for family-wise error using cluster-extent thresholding (see *Methods*). LH = left hemisphere; RH = right hemisphere.

right occipito-temporal gyrus (OTG) and in the left rostral ACC extending into dorsomedial prefrontal cortex. Fig. 5 presents these regions as identified by two analyses, using two single voxel thresholds to identify both less localized clusters where all voxels passed the $P < .05$ threshold, and more highly localized clusters where all voxels passed a threshold of $P < .005$. We conducted a whole brain analysis to test, within the Pandit group, whether CT correlated with Start Age or total post-training hours of recitation practice (OPHTC), adjusted for Age as covariate. We found no significant correlations.

Differences in local gyrification

Two areas showed differences in local gyrification between the two groups. These were found in the inferior and middle occipital gyri on the left and middle occipital gyrus on the right. In both cases these cortical regions showed reduced gyrification for the Pandit group (see Fig. 6).

We also examined the relationship between the LGI and CT findings. Using the regions identified by the LGI analysis as masks, we quantified the mean CT within those regions per participant, and then evaluated these on the group level. There was absolutely no between-group difference in mean CT within those regions. In the right hemisphere LGI cluster, the mean CT for Pandits and controls was 2.65 mm ($SD = 0.18$) vs. 2.66 mm ($SD = 0.21$). In the left hemisphere cluster, the values were 2.08 mm ($SD = 0.13$) vs. 2.11 mm ($SD = 0.13$). In short, CT values were almost identical across groups in areas showing LGI differences. We also tested, within the Pandit group, for correlation of LGI with the

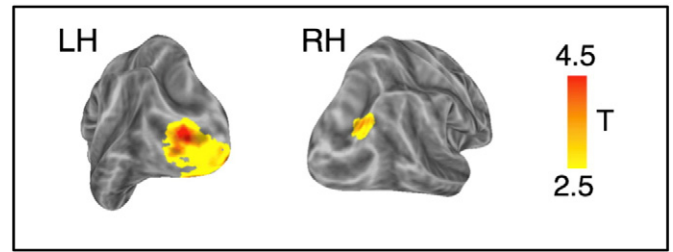


Fig. 6. Areas where Pandits showed less gyrification than controls.

Start Age or Practice (OPHTC) variables adjusted for Age as covariate. There were no significant correlations.

Differences in fractional anisotropy

Two adjacent clusters showed greater FA in Pandits compared to controls (see Fig. 7). No area showed the reverse pattern. The clusters were found in close proximity to the CT and GM differences we report for the left vmPFC/ACC (see Fig. 7), at the intersection of the left anterior thalamic radiation, the forceps minor, the left inferior fronto-occipital fasciculus (IFOF), the left anterior corona radiata (ACR), the genu of the corpus callosum, the left cingulum bundle, and the left uncinate fasciculus (UF). (See SI Methods, SI Table 5 for cluster details, and SI Fig. 1 for a brain map showing the location of these clusters overlaid on mean group FA map.) We also tested, within the Pandit group, whether either FA or skeletonized FA correlated with Pandit Start Age or with total post-training hours of recitation practice (OPHTC), both adjusted for Age as covariate. We found no significant correlations.

Discussion

Overall, we found considerable differences in the organization of the brains of professional Vedic Sanskrit Pandits. Specifically, they showed extensive cortical and cerebellar GM increase and subcortical GM decrease. The hippocampal GM differences followed a differential anterior/posterior pattern that has been linked to expert spatial navigation (Maguire et al., 2000), and to improved memory for verbal materials (Poppenk and Moscovitch, 2011). Cortical CT increases were extensive, and overlapped closely with GM differences in right temporal regions, left medial prefrontal, and left fusiform areas. Pandits also showed significantly less gyrification in bilateral occipital regions, and significantly larger FA in left inferior frontal WM clusters. Our findings are consistent with the possibility that the changes to medial-temporal and medial prefrontal regions, accompanied by changes to lateral temporal regions and cerebellum, reflect the impact of the Pandits' extensive verbal practices.

Hippocampus and ACC/mPFC

The Pandits' pattern of hippocampal differences as evident in a whole-brain VBM analysis were similar to those reported in the study of London taxi drivers (Maguire et al., 2000), showing a relative decrease in bilateral anterior hippocampi, and an increase in right (but not left) medial-posterior hippocampus. Our region-of-interest analyses identified a local reduction in volume in the right anterior HF for Pandits, accompanied by a VBM signature of increased GM in the medial-posterior right HF for this group, and an increased GM cluster in the posterior left hippocampus. Maguire et al (2000, p. 4398), who used whole brain VBM and HF pixel counting, suggested that the increases in the posterior hippocampus may indicate that this region stores a spatial representation for the environment and expands to accommodate this elaborated representation. A large body of subsequent research has shown, however, that the anterior and posterior

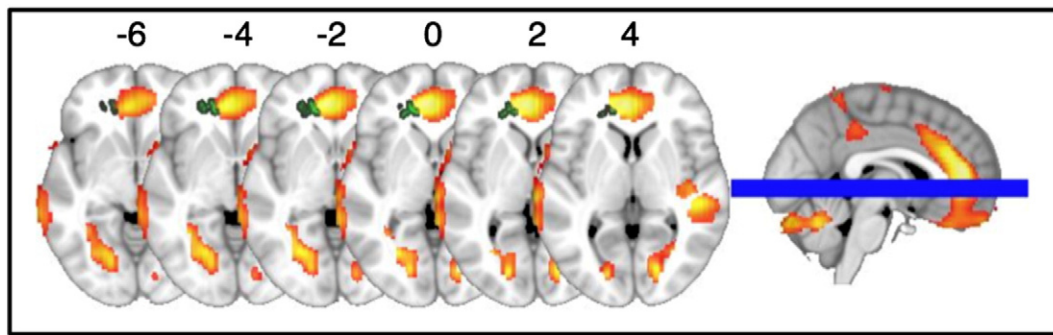


Fig. 7. Axial slices showing clusters (in green) where Pandits showed greater fractional anisotropy than controls. The statistical fractional anisotropy map (green) is overlaid on an MNI template, and shown alongside areas of the mPFC/ACC where Pandits showed greater GM than controls in the whole-brain analysis (red-orange), $P < 0.05$, FWE-corrected using Threshold Free Cluster Enhancement. Left hemisphere shown on left.

hippocampi play differential roles in a large range of cognitive processes including, but not limited to novelty processing (Daselaar et al., 2006; Kohler et al., 2005; Takashima et al., 2006), encoding of ongoing and recent experiences (Hartzell et al., 2014), and simulation of future events (van Mulukom et al., 2013; see Fanselow and Dong, 2010; Poppenk et al., 2013, and Strange et al., 2014 for reviews). Better memory for verbal materials has been associated with larger posterior and smaller anterior hippocampal segments (Poppenk and Moscovitch, 2011). One study found that the volume of the anterior hippocampus correlates positively with verbal memory (Hackert et al., 2002), but this was found for an age group (60–90 y.o.a.) for which the relation may reflect variations in the normal thinning patterns that the HF undergoes with increasing age. Our results, taken together with these prior studies, support the developing evidence that hippocampal regional changes may occur in various situations, beyond those necessitating memory for complex spatial scenes. We note that the training of London Taxi Drivers does in fact involve rote memorization of a large volume of preset verbal sequences: they are required to memorize street names and place names (30,000 landmarks) in 320 set route sequences totaling ~120,000 words, with part-time training over ~3–5 years (Transport.for.London, 2014). Their oral examinations necessitate precise rote verbal recall of route details between the landmarks.

Greater Pandit GM/CT in anterior cingulate cortex and medial temporal structures is also consistent with accommodating increased memory demands. Animal studies show long-term memory encoding in the mPFC/ACC (Weible et al., 2012; Teixeira et al., 2006), with short-term encoding in the hippocampus (Takehara-Nishiuchi and McNaughton, 2008), mediated by connections between perirhinal/parahippocampus and ACC (Insel and Takehara-Nishiuchi, 2013). In humans, patients with exclusive MTL lesions perform normally on remote autobiographical memory but poorly on recent memory tests (Bayley et al., 2005), while mPFC/ACC lesions conversely disrupt long-term memory, but not short-term memory for recent experiential learning (Squire and Bayley, 2007). Neuroimaging data from healthy human participants also suggest that recall for recent vs. remote experiences differentially relies, respectively, on hippocampal vs. medial frontal cortices (Takashima et al., 2006). Taken together with these animal and human studies, our findings suggest that Vedic Sanskrit oral text information may be initially encoded via the hippocampus, then stored in the mPFC/ACC regions, but a detailed longitudinal study is necessary to examine this issue.

Lateral-temporal and parietal cortices: potential indicators of language system differences

Our left and right temporal region cortical differences showed different topographies. The left postero-medial superior, middle, and inferior temporal gyri GM patterns were largely confined to gyral surfaces, reaching into the antero-medial PT. Many of these regions overlap

with presurgical speech interference sites (Roux et al., 2012), suggesting the observed differences may be related, at least in part, to recitation vocalization. These left posterior lateral temporal regions are also implicated in both lexical-phonological processing and semantic-syntactic integration in current cortical speech processing models (see e.g., Hickok and Poeppel, 2007; Friederici, 2012), while the PT/pSTG/SMG changes reach into areas linked to speech production (DeWitt and Rauschecker, 2012; Fedorenko and Thompson-Schill, 2014). On the right, greater GM/CT for Pandits reached into deep STS, and into lateral Heschl's gyrus/planum polare (HG/PP), dorsal posteromedial insula, OP2/OP3 of posteromedial operculum, and right ventral anterior lobe (vATL). Right HG/PP have been shown to sample acoustic information at a rate optimized for syllable-length acoustics (Kotz and Schwartz, 2010; Morillon et al., 2012; Altmann et al., 2007) and sound patterns (Altmann et al., 2007), with right STS linked to processing of human voices (Belin, 2006) and vocal identity (Petkov et al., 2009). The human vATL/anterior fusiform bilaterally is considered a hub for multi-modal/amodal semantic knowledge (Chan et al., 2011), linked with PRC for verbal memory construction (Bozeat et al., 2000). Greater Pandit GM in right posteromedial insula and operculum may reflect speech-sound processing (Cloutman et al., 2012), vocalization tuning (Remedios et al., 2009), and/or prosody detection (van Rijn et al., 2005).

The increased GM for Pandits in parietal regions suggests the possible involvement of cortical resources subserving Vedic recitation gestures, articulation, and multilingualism. Differences in the left superior and medial postcentral gyrus covered portions of the primary somatosensory cortex (Ruben et al., 2001) for the right arm, wrist, hand and fingers, face, mouth and tongue regions (Kaas et al., 1979; Nakamura et al., 1998), including areas known to be active during right hand and arm movement (Sereni and Huang, 2014). We also considered that while the Pandits and controls were matched for number of languages, the Pandits are highly competent in Sanskrit due to their training, and several of the areas where they demonstrate greater GM have been linked to multilingual abilities. The differences we documented in inferior parietal and superior lateral temporal cortices match well with greater GM found for bilinguals compared to monolinguals (Mechelli et al., 2004), and increased vocabulary is associated with increased GM in left posterior SMG (Richardson et al., 2010).

Notably absent were morphological differences in grey matter or cortical thickness in bilateral inferior frontal regions that have been linked to higher-level language functions. The left inferior frontal region has been linked repeatedly to semantic and syntactic processing (e.g., Bookheimer, 2002) or control processes during language (e.g., Fedorenko et al., 2012; Fedorenko and Thompson-Schill, 2014), whereas the right has been linked to discourse related functions (e.g., Menenti et al., 2009). We also found no WM changes in these regions of the sort previously associated with better grammar learning (Flöel et al., 2009). The absence of differences in inferior frontal cortices

could reflect the fact that the Pandits' memorization, recall and production of oral language content does not require putting ideas into words *de novo*, and so does not engage this particular use of these frontal regions that have been implicated in higher level language processing through studies typically not involving recited speech. Follow-up functional studies will be useful for clarifying the functional contribution of these temporal-parietal structural differences to the Pandits' verbal recitation practices.

Cerebellum

Pandit GM cerebellar differences were found in regions involved in cortico-cerebellar networks subserving language and memory (Marien et al., 2014), and executive function (Stoodley, 2012), and in which GM increases have been correlated with factors relevant to Vedic recitation: e.g. skilled hand movements with Vermis VI/VIIb (Di Paola et al., 2013) and bilingual semantic and phonemic fluency in left Crus II (Grogan et al., 2009). The large volume of Sanskrit memorized and recited by the Pandits, and their mastery of Sanskrit's complex morphology (Whitney, 1924) and semantics (Apte, 1890) may also contribute to the large increase in Pandit cerebellar GM (1/3rd of total cerebellar GM), a finding considerably larger than previously reported in cerebellar morphology analyses.

Visual system

Increased GM and CT in Pandits' visual/visual-association cortices may relate to their traditional multi-year training regimen that consists of close face-to-face oral instruction and repetition (including one-on-one training) and synchronized recitation gestures. Alternatively, or additionally, it may reflect the type of cross-modal plasticity and enhanced function previously documented in the visually impaired, such as ultra-fast speech comprehension and exceptional spatial acoustic cue detection in blind (Dietrich et al., 2013; Voss et al., 2004). One possibility, which necessitates further functional neuroimaging investigations, is that occipital regions are recruited to aid the extensive oral language-related computations performed by Pandits; these regions have been shown to have the potential for rapid functional plasticity even in healthy subjects (Merabet et al., 2008).

Subcortical and gyrification differences

To our knowledge, our study is the first to document comprehensive reduction of GM in subcortical structures in a population of healthy participants. While unexpected, one potential explanation of this finding is that it indicates a speeded maturation of these regions for Pandits. A developmental study of healthy children and adolescents (Wierenga et al., 2014) showed a linear age-related reduction of GM in caudate, putamen and nucleus accumbens (regions where Pandits had lower GM than controls), and inverted U-shaped curves in amygdala, thalamus, hippocampus and pallidum (the latter a region where we did not find clear differences between the two groups).

To our knowledge, the current work is also the first to document local gyrification differences between two healthy adult groups. Cortical gyrification complexity increases up through young adulthood with the occipital lobe showing both highest variability in preadolescents, and lowest complexity increase in adolescence (Blanton et al., 2001; Su et al., 2013). After adolescence, gyrification decreases steadily across much of the brain (Hogstrom et al., 2013). The Pandits in our study began training in late childhood or early adolescence, so their decreased occipital gyrification may indicate a training-related impact on the normal developmental curve of brain gyrification, specifically, a relatively more limited gyrification change attained in visual cortices.

WM structural differences

The WM tracts crossing through the Pandit FA clusters have been implicated in language processing. Increased FA in left forceps minor, genu of the corpus callosum, anterior thalamic radiation (ATR), and anterior corona radiata has been linked to mathematical ability (Navas-Sanchez et al., 2014), while stutterers have decreased FA in the forceps minor (Beal et al., 2013; Civier et al., 2015). Lesion studies have implicated left inferior frontal-occipital fasciculus (IFOF), left ATR, and left uncinate fasciculus (UF) in semantic processing (Han et al., 2013) and fluency (Almairac et al., *in press*), while in healthy participants left IFOF and UF are both prominently involved in amodal (domain general) semantic memory (de Zubicaray et al., 2011). As shown in Fig. 7, the FA clusters border the CT/GM Pandit increases in the mPFC/ACC, suggesting they may also be related to those structural differences.

Convergence and divergence between morphometric measures

The different measures we used provided convergent information regarding changes in several brain regions, but several also identified unique change patterns. The VBM results highlighted extensive differences in bilateral temporal regions, vmPFC and lateral occipital regions, and the CT findings documented similar changes in vmPFC, the right lateral temporal regions and right occipito-temporal regions, though less extensively than VBM. However, the right temporal pole areas identified by the CT analysis were not identified by VBM, and conversely, occipital and posterior midline regions identified by VBM were not identified by CT. With respect to FA findings, there was a good overlap between the diffusion results and the mPFC/ACC cluster identified in both the CT and VBM analysis. Finally, within the clusters showing LGI changes, we did not find any changes in CT.

While it is interesting to find convergence in some aspects of the results, it is important to note that prior work suggests that VBM, CT and LGI target at least partially different organizational aspects of structural morphometry. We first address the relation between VBM and CT. Whereas CT, as implemented in FreeSurfer, loads strictly on the local cortical thickness, FSL's VBM analysis, which includes modulation by the Jacobian to account for stretching and compression, reflects (based on GM probability metrics from the GM segmentation step) a combination of thickness, surface area and differences in folding. For this reason VBM has sometimes been interpreted as measuring "overall local volume" (Hutton et al., 2009). Prior studies that have used both VBM and CT to study a single dataset show their divergent, rather than strictly convergent nature. Blankstein et al. (2009), Voets et al. (2008), and Bermudez et al. (2009) are good examples of such work. Voets et al., who compared VBM and surface-based morphometry (SBM), concluded that, "VBM-style approaches are sensitive to a combination of cortical thickness, surface area and shape measures. SBM, on the other hand, uses an explicit model of the neocortex, offering independent measures of thickness, surface area and folding patterns. Thus, areas of significant difference in VBM GM density may be found without a corresponding change in SBM-derived cortical thickness" (Voets et al., p. 667).

Formal attempts at relating VBM and CT have been only moderately successful. Voets et al. (2008) tried examining the Jacobian of the warp field, or dividing CT by change in metric distortion on the vertex wise level, but these did not account well for the divergence between VBM and CT. Palaniyappan and Liddle (2012) used a region of interest analysis and found that between-group differences in VBM data were only moderately mediated by different surface morphometry features such as CT, LGI and surface area: a large proportion of VBM-related variance (between 36% and 80%) was not accounted for by these surface measures. Furthermore, depending on brain region, different surface features accounted for the between-group VBM differences. VBM and surface measures therefore appear to target partially different aspects of brain morphometry; this may have to do with the fact that these measures are related to separate genetic traits (e.g., Winkler et al., 2010).

With respect to LGI and CT, while one might expect that the two measures would generally be negatively correlated, this relationship appears modest, and also varies spatially. As part of this study, Hogstrom et al. (2013) examined the relationship between LGI, and CT. While there was a negative relation between LGI and CT in all lobes, it was relatively weak ($-0.17 < R < -0.08$), with significant correlations limited to medial prefrontal cortex, superior frontal gyrus, and precuneus. In all, prior work highlights the utility of using multiple measures for understanding changes to different facets of brain morphometry, and our current findings are largely consistent with the import of that body of work.

Potential limitations and future directions

As in any cross-sectional study, one cannot claim with absolute certainty that structural differences are caused by experience-related changes, rather than reflecting a genetic predisposition. However, several unique features of the Pandit selection and training very strongly argue against explanations grounded in self-selection or genetic predisposition: there are no pre-entrance selection exams to Pandit studies so that memorization ability is not tested as a pre-condition; the attrition rate from studies is only ~5%, arguing against self-selection during training itself; and none of our specific participants came from Vedic Pandit families, with very few having any relatives who recite (See SI Table 1). All these are highly consistent with an experience-related explanation rather than one based on genetic predisposition (of the sort licensed for musicians, athletes, piano tuners and other special populations).

A second apparent interpretive challenge is the absence of statistically significant correlations between Pandits' practice estimate or starting age and GM/CT/LGI/FA measures. We consider power, limited range, and possible ceiling effects as the reasons for this null result. First, given the sample size ($N = 21$), to satisfy a single-voxel criteria of $P < .005$, correlations would need to exceed a level of 0.56 (Pearson's R) in each voxel within a cluster, which is a high standard that even if found would likely be an inaccurate documentation of the actual effect size in the population (Yarkoni, 2009). Second, while all the Pandits had completed the basic training course, 12 of those were within 1 year of graduation, and 5 others within 3 years of graduation, resulting in a limited range of the post-training Practice variable (OHPTC; see SI Table 1). Third, given the reported total hours of basic training of 10,080 h (See SI Methods), it is also possible that the lack of correlation is due to a ceiling or plateau effect, wherein training-driven plasticity asymptotes, as is seen in motor and cognitive skill acquisition studies (Macnamara et al., 2014, see references therein; Karni et al., 1998; Anderson, 1981). Further elucidation of the issue will require follow-up longitudinal studies during the training period, and/or recruitment of a larger subject pool of qualified Pandits with a wider range of post-training practice.

We note that a recent (Kalamangalam and Ellmore, 2014) smaller scale study (Pandit $N = 11$) examined cortical thickness differences between Pandits and a control group and reported different results for this measure (the study reports 2 clusters limited to inferior temporal and orbito-frontal cortex, regions not typically associated with speech, language or memory processing). That study could not examine hippocampal or subcortical differences due to its focus on the cortical fold, and surprisingly, did not document differences in lateral temporal regions implicated in speech processing (STG, STS, STP), or regions implicated in memory for verbal materials, concluding that those regions are not impacted by memory training (VBM analysis was not conducted). The markedly divergent results in our work are probably the result of a more powerful sample and control for confounding variables.² For

these reasons, we cannot directly compare that particular prior work with the current findings.

Summary

The data demonstrate that there exist extensive morphological differences in the brains of professional Vedic Sanskrit Pandits, which are in some cases identifiable by both VBM and CT measures, and in some cases only by one of these two metrics. These findings are consistent with a role for medial temporal regions and medial prefrontal cortex in large-scale language, memory and information processing. These data further suggest that inferior frontal and lateral temporal regions play different roles in their ability to subservise rehearsed speech. Finally, the results raise interesting questions about the potential of intensive, specialized expertise training to substantially drive plasticity in healthy adult brains, and possibly alter natural developmental curves.

Acknowledgments

We thank Prof. R.K Shastri of the Ministry of Human Resource Development, Government of India, for information regarding the current state of Vedic training at government-supported institutions in India. We also thank Krishna Miyapuram, India Institute of Technology, Gandhinagar, for helpful discussions and assistance with translation of the survey forms. This research has received funding from the India-Trento Program for Advanced Research. U.H was supported by a European Council Starting Grant (ERC-STG #263318).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.neuroimage.2015.07.027>.

References

- Alexander, D.C., Barker, G.J., 2005. Optimal imaging parameters for fiber-orientation estimation in diffusion MRI. *Neuroimage* 27, 357–367. <http://dx.doi.org/10.1016/j.neuroimage.2005.04.008>.
- Almairac, F., Herbet, G., Moritz-Gasser, S., de Champfleury, N.M., Duffau, H., 2014. The left inferior fronto-occipital fasciculus subserves language semantics: a multilevel lesion study. *Brain Struct. Funct.* <http://dx.doi.org/10.1007/s00429-014-0773-1> (in press).
- Altmann, C.F., Bledowski, C., Wibrall, M., Kaiser, J., 2007. Processing of location and pattern changes of natural sounds in the human auditory cortex. *NeuroImage* 35, 1192–1200. <http://dx.doi.org/10.1016/j.neuroimage.2007.01.007>.
- Anderson, J.R. (Ed.), 1981. *Cognitive Skills and Their Acquisition*. Carnegie Mellon Symposium on Cognition Series. Taylor & Francis, New York.
- Apte, V., 1890. *The Practical Sanskrit-English Dictionary, Containing Appendices on Sanskrit Prosody and Important Literary and Geographic Names of Ancient India. Revised and Enlarged edition.* Motilal Barnasidass, Delhi.
- Ashburner, J., Friston, K.J., 2000. Voxel-based morphometry—the methods. *NeuroImage* 11, 805–821.
- Ashdari, M., Avants, B., Cyckowski, L., Cervellione, K.L., Roofeh, D., Cook, P., Gee, J., Sevy, S., Kumra, S., 2011. Medial temporal structures and memory functions in adolescents with heavy cannabis use. *J. Psychiatr. Res.* 45, 1055–1066. <http://dx.doi.org/10.1016/j.jpsychires.2011.01.004>.
- Bayley, P.J., Gold, J.J., Hopkins, R.O., Squire, L.R., 2005. The neuroanatomy of remote memory. *Neuron* 46, 799–810. <http://dx.doi.org/10.1016/j.neuron.2005.04.034>.
- Beal, D.S., Gracco, V.L., Brettschneider, J., Kroll, R.M., De Nil, L.F., 2013. A voxel-based morphometry (VBM) analysis of regional grey and white matter volume abnormalities within the speech production network of children who stutter. *Cortex* 49, 2151–2161. <http://dx.doi.org/10.1016/j.cortex.2012.08.013>.
- Belin, P., 2006. Voice processing in human and non-human primates. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 361, 2091–2107. <http://dx.doi.org/10.1098/rstb.2006.1933>.
- Ben-Amity, S., Jones, D.K., Assaf, Y., 2012. Motion correction and registration of high b-value diffusion weighted images. *Magn. Reson. Med.* 67, 1694–1702. <http://dx.doi.org/10.1002/mrm.23186>.
- Bermudez, P., Lerch, J.P., Evans, A.C., Zatorre, R.J., 2009. Neuroanatomical correlates of musicianship as revealed by cortical thickness and voxel-based morphometry. *Cereb. Cortex* 19 (7), 1583–1596. <http://dx.doi.org/10.1093/cercor/bhn196>.
- Bird, C.M., Burgess, N., 2008. The hippocampus and memory: insights from spatial processing. *Nat. Rev. Neurosci.* 9, 182–194. <http://dx.doi.org/10.1038/nrn2335>.
- Blankstein, U., Chen, J.Y., Mincic, A.M., McGrath, P.A., Davis, K.D., 2009. The complex minds of teenagers: neuroanatomy of personality differs between sexes. *Neuropsychologia* 47 (2), 599–603. <http://dx.doi.org/10.1016/j.neuropsychologia.2008.10.014>.
- Blanton, R.E., Levitt, J.G., Thompson, P.M., Narr, K.L., Capetillo-Cunliffe, L., Nobel, A., Singerman, J.D., McCracken, J.T., Toga, A.W., 2001. Mapping cortical asymmetry and

² The study by Kalamangalam and Ellmore was conducted in Houston, Texas, with local control participants, and does not report control for eye-dominance or multilingualism in the experimental and control groups, nor Vedic lineage and assessment of Vedic competence, and does not report control for Age in the analysis pathway.

- complexity patterns in normal children. *Psychiatry Res.* 107, 29–43. [http://dx.doi.org/10.1016/S0925-4927\(01\)00091-9](http://dx.doi.org/10.1016/S0925-4927(01)00091-9).
- Bookheimer, S., 2002. Functional MRI of language: new approaches to understanding the cortical organization of semantic processing. *Annu. Rev. Neurosci.* 25, 151–188. <http://dx.doi.org/10.1146/annurev.neuro.25.112701.142946>.
- Bozeat, S., Lambon Ralph, M.A., Patterson, K., Garrard, P., Hodges, J.R., 2000. Non-verbal semantic impairment in semantic dementia. *Neuropsychologia* 38, 1207–1215. [http://dx.doi.org/10.1016/S0028-3932\(00\)00034-8](http://dx.doi.org/10.1016/S0028-3932(00)00034-8).
- Catani, M., Mesulam, M.M., Jakobsen, E., Malik, F., Martersteck, A., Wieneke, C., Rogalski, E., 2013. A novel frontal pathway underlying verbal fluency in primary progressive aphasia. *Brain* 136 (Pt 8), 2619–2628. <http://dx.doi.org/10.1093/brain/awt163>.
- Central Council of Indian Medicine, 2014. <http://ccimindia.org> (accessed 1 October 2014).
- Chan, A.M., Baker, J.M., Eskandar, E., Schomer, D., Ulbert, I., Marinkovic, K., Cash, S.S., Halgren, E., 2011. First-pass selectivity for semantic categories in human anteroventral temporal lobe. *J. Neurosci.* 31, 18119–18129. <http://dx.doi.org/10.1523/JNEUROSCI.3122-11.2011>.
- Chung, M., 2004. Heat kernel smoothing and its application to cortical manifolds. Technical Report. Department of Statistics, U. W. Madison.
- Civier, O., Kronfeld-Duenias, V., Amir, O., Ezrati-Vinacour, R., Ben-Shachar, M., 2015. Reduced fractional anisotropy in the anterior corpus callosum is associated with reduced speech fluency in persistent developmental stuttering. *Brain Lang.* 143, 20–31. <http://dx.doi.org/10.1016/j.bandl.2015.01.012>.
- Cloutman, L.L., Binney, R.J., Drakesmith, M., Parker, G.J., Lambon Ralph, M.A., 2012. The variation of function across the human insula mirrors its patterns of structural connectivity: evidence from in vivo probabilistic tractography. *NeuroImage* 59, 3514–3521. <http://dx.doi.org/10.1016/j.neuroimage.2011.11.016>.
- Cox, R.W., 1996. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. *Comput. Biomed. Res.* 29, 162–173. <http://dx.doi.org/10.1006/cbmr.1996.0014>.
- Dale, A.M., Fischl, B., Sereno, M.I., 1999. Cortical surface-based analysis. I. Segmentation and surface reconstruction. *NeuroImage* 9, 179–194. <http://dx.doi.org/10.1006/nimg.1998.0395>.
- Daselaar, S.M., Fleck, M.S., Cabeza, R., 2006. Triple dissociation in the medial temporal lobes: recollection, familiarity, and novelty. *J. Neurophysiol.* 96, 1902–1911. <http://dx.doi.org/10.1152/jn.01029.2005>.
- de Zubicaray, G.L., Rose, S.E., McMahon, K.L., 2011. The structure and connectivity of semantic memory in the healthy older adult brain. *NeuroImage* 54, 1488–1494. <http://dx.doi.org/10.1016/j.neuroimage.2010.08.058>.
- Dehaene-Lambertz, G., Dehaene, S., Anton, J.L., Campagne, A., Ciuciu, P., Dehaene, G.P., Denghien, I., Jobert, A., LeBihan, D., Sigman, M., Pallier, C., Poline, J.B., 2006. Functional segregation of cortical language areas by sentence repetition. *Hum. Brain Mapp.* 27, 360–371. <http://dx.doi.org/10.1002/hbm.20250>.
- Devauchelle, A.D., Oppenheim, C., Rizzi, L., Dehaene, S., Pallier, C., 2009. Sentence syntax and content in the human temporal lobe: an fMRI adaptation study in auditory and visual modalities. *J. Cogn. Neurosci.* 21, 1000–1012. <http://dx.doi.org/10.1162/jocn.2009.21070>.
- DeWitt, I., Rauschecker, J.P., 2012. Phoneme and word recognition in the auditory ventral stream. *Proc. Natl. Acad. Sci. U. S. A.* 109, E505–E514. <http://dx.doi.org/10.1073/pnas.1113427109>.
- Di Paola, M., Caltagirone, C., Petrosini, L., 2013. Prolonged rock climbing activity induces structural changes in cerebellum and parietal lobe. *Hum. Brain Mapp.* 34, 2707–2714. <http://dx.doi.org/10.1002/hbm.22095>.
- Dietrich, S., Hertrich, I., Ackermann, H., 2013. Ultra-fast speech comprehension in blind subjects engages primary visual cortex, fusiform gyrus, and pulvinar—a functional magnetic resonance imaging (fMRI) study. *BMC Neurosci.* 14, 74. <http://dx.doi.org/10.1186/1471-2202-14-74>.
- Douaud, G., Smith, S., Jenkinson, M., Behrens, T., Johansen-Berg, H., Vickers, J., James, S., Voets, N., Watkins, K., Matthews, P.M., James, A., 2007. Anatomically related grey and white matter abnormalities in adolescent-onset schizophrenia. *Brain* 130, 2375–2386. <http://dx.doi.org/10.1093/brain/awm184>.
- Draganski, B., Gaser, C., Kempermann, G., Kuhn, H.G., Winkler, J., Buchel, C., May, A., 2006. Temporal and spatial dynamics of brain structure changes during extensive learning. *J. Neurosci.* 26 (23), 6314–6317. <http://dx.doi.org/10.1523/JNEUROSCI.4628-05.2006>.
- Driemeyer, J., Boyke, J., Gaser, C., Buchel, C., May, A., 2008. Changes in gray matter induced by learning—revisited. *PLoS One* 3 (7), e2669. <http://dx.doi.org/10.1371/journal.pone.0002669>.
- Eichenbaum, H., Cohen, N.J., 2014. Can we reconcile the declarative memory and spatial navigation views on hippocampal function? *Neuron* 83, 764–770. <http://dx.doi.org/10.1016/j.neuron.2014.07.032>.
- Eichenbaum, H., Yonelinas, A.P., Ranganath, C., 2007. The medial temporal lobe and recognition memory. *Annu. Rev. Neurosci.* 30, 123–152.
- Fanselow, M.S., Dong, H.W., 2010. Are the dorsal and ventral hippocampus functionally distinct structures? *Neuron* 65, 7–19. <http://dx.doi.org/10.1016/j.neuron.2009.11.031>.
- Fedorenko, E., Thompson-Schill, S.L., 2014. Reworking the language network. *Trends Cogn. Sci.* 18, 120–126. <http://dx.doi.org/10.1016/j.tics.2013.12.006>.
- Fedorenko, E., Nieto-Castanon, A., Kanwisher, N., 2012. Syntactic processing in the human brain: what we know, what we don't know, and a suggestion for how to proceed. *Brain Lang.* 120, 187–207. <http://dx.doi.org/10.1016/j.bandl.2011.01.001>.
- Fernandez, G., Weyerts, H., Schrader-Bolsche, M., Tendolkar, I., Smid, H.G.O.M., Tempelmann, C., Hinrichs, H., Scheich, H., Elger, C.E., Mangun, G.R., Heinze, H.J., 1998. Successful verbal encoding into episodic memory engages the posterior hippocampus: a parametrically analyzed functional magnetic resonance imaging study. *J. Neurosci.* 18, 1841–1847.
- Flöel, A., de Vries, M.H., Scholz, J., Breitenstein, C., Johansen-Berg, H., 2009. White matter integrity in the vicinity of Broca's area predicts grammar learning success. *NeuroImage* 47, 1974–1981. <http://dx.doi.org/10.1016/j.neuroimage.2009.05.046>.
- Friederici, A.D., 2012. The cortical language circuit: from auditory perception to sentence comprehension. *Trends Cogn. Sci.* 16, 262–268. <http://dx.doi.org/10.1016/j.tics.2012.04.001>.
- Giraud, A.L., Poeppel, D., 2012. Cortical oscillations and speech processing: emerging computational principles and operations. *Nat. Neurosci.* 15, 511–517. <http://dx.doi.org/10.1038/nn.3063>.
- Good, C.D., Johnsrud, I.S., Ashburner, J., Henson, R.N., Friston, K.J., Frackowiak, R.S., 2001. A voxel-based morphometric study of ageing in 465 normal adult human brains. *NeuroImage* 14, 21–36. <http://dx.doi.org/10.1006/nimg.2001.0786>.
- Grogan, A., Green, D.W., Ali, N., Crinion, J.T., Price, C.J., 2009. Structural correlates of semantic and phonemic fluency ability in first and second languages. *Cereb. Cortex* 19, 2690–2698. <http://dx.doi.org/10.1093/cercor/bhp023>.
- Grunwald, T., Beck, H., Lehnertz, K., Blumcke, I., Pezer, N., Kurthen, M., Fernandez, G., Van Roost, D., Heinze, H.J., Kutas, M., Elger, C.E., 1999. Evidence relating human verbal memory to hippocampal N-methyl-D-aspartate receptors. *Proc. Natl. Acad. Sci. U. S. A.* 96, 12085–12089. <http://dx.doi.org/10.1073/pnas.96.21.12085>.
- Hackert, V.H., den Heijer, T., Oudkerk, M., Koudstaal, P.J., Hofman, A., Breteler, M.M., 2002. Hippocampal head size associated with verbal memory performance in nondemented elderly. *NeuroImage* 17 (3), 1365–1372.
- Han, Z., Ma, Y., Gong, G., He, Y., Caramazza, A., Bi, Y., 2013. White matter structural connectivity underlying semantic processing: evidence from brain damaged patients. *Brain* 136, 2952–2965. <http://dx.doi.org/10.1093/brain/awt205>.
- Hartzell, J.F., Zysk, K.G., 1995. Columbia University Dharam Hinduja Indie Research Center Conference: Health, Science, and the Spirit: Veda and Ayurveda in the Western World. *J. Altern. Complement. Med.* 1, 297–301. <http://dx.doi.org/10.1089/acm.1995.1.297>.
- Hartzell, J.F., Tobia, M.J., Davis, B., Cashdollar, N.M., Hasson, U., 2014. Differential lateralization of hippocampal connectivity reflects features of recent context and ongoing demands: an examination of immediate post-task activity. *Hum. Brain Mapp.* <http://dx.doi.org/10.1002/hbm.22644>.
- Hasson, U., Nusbaum, H.C., Small, S.L., 2006. Repetition suppression for spoken sentences and the effect of task demands. *J. Cogn. Neurosci.* 18, 2013–2029. <http://dx.doi.org/10.1162/jocn.2006.18.12.2013>.
- Hasson, U., Nusbaum, H.C., Small, S.L., 2007. Brain networks subserving the extraction of sentence information and its encoding to memory. *Cereb. Cortex* 17, 2899–2913. <http://dx.doi.org/10.1093/cercor/bhm016>.
- Hickok, G., Poeppel, D., 2007. The cortical organization of speech processing. *Nature Reviews Neuroscience* 8, 393–402. <http://dx.doi.org/10.1038/nrn2113>.
- Hogstrom, L.J., Westlye, L.T., Walhovd, K.B., Fjell, A.M., 2013. The structure of the cerebral cortex across adult life: age-related patterns of surface area, thickness, and gyrification. *Cereb. Cortex* 23, 2521–2530. <http://dx.doi.org/10.1093/cercor/bhs231>.
- Hutton, C., Draganski, B., Ashburner, J., Weiskopf, N., 2009. A comparison between voxel-based cortical thickness and voxel-based morphometry in normal aging. *NeuroImage* 48 (2), 371–380. <http://dx.doi.org/10.1016/j.neuroimage.2009.06.043>.
- Insel, N., Takehara-Nishiuchi, K., 2013. The cortical structure of consolidated memory: a hypothesis on the role of the cingulate-entorhinal cortical connection. *Neurobiol. Learn. Mem.* 106, 343–350. <http://dx.doi.org/10.1016/j.nlm.2013.07.019>.
- Jenkinson, M., 2014. <https://www.jiscmail.ac.uk/cgi-bin/webadmin?A2=ind14111&FSL&P=R16234&1=FSL&9=A&J=on&d=No+Match%3BMatch%3BMatches&z=4>.
- Jenkinson, M., Smith, S., 2001. A global optimisation method for robust affine registration of brain images. *Med. Image Anal.* 5, 143–156. [http://dx.doi.org/10.1016/S1361-8415\(01\)00036-6](http://dx.doi.org/10.1016/S1361-8415(01)00036-6).
- Jenkinson, M., Bannister, P., Brady, M., Smith, S., 2002. Improved optimization for the robust and accurate linear registration and motion correction of brain images. *NeuroImage* 17, 825–841. <http://dx.doi.org/10.1006/nimg.2002.1132>.
- Jovicich, J., Marizzoni, M., Bosch, B., Bartres-Faz, D., Arnold, J., Benninghoff, J., Wiltfang, J., Roccatagliata, L., Picco, A., Nobili, F., Blin, O., Bombois, S., Lopes, R., Bordet, R., Chanoine, V., Ranjeva, J.P., Didic, M., Gros-Dagnac, H., Payoux, P., Zoccatelli, G., Alessandrini, F., Beltramello, A., Bargallo, N., Ferretti, A., Caulo, M., Aiello, M., Ragucci, M., Soricelli, A., Salvadori, N., Tarducci, R., Floridi, P., Tsolaki, M., Constantinidis, M., Drevolegas, A., Rossini, P.M., Marra, C., Otto, J., Reiss-Zimmermann, M., Hoffmann, K.T., Galluzzi, S., Frisoni, G.B., 2014. Multisite longitudinal reliability of tract-based spatial statistics in diffusion tensor imaging of healthy elderly subjects. *NeuroImage* 101, 390–403. <http://dx.doi.org/10.1016/j.neuroimage.2014.06.075>.
- Kaas, J.H., Nelson, R.J., Sur, M., Lin, C.S., Merzenich, M.M., 1979. Multiple representations of the body within the primary somatosensory cortex of primates. *Science* 204, 521–523. <http://dx.doi.org/10.1126/science.107591>.
- Kalamangalam, G.P., Ellmore, T.M., 2014. Focal cortical thickness correlates of exceptional memory training in Vedic priests. *Front. Hum. Neurosci.* 8, 833. <http://dx.doi.org/10.3389/fnhum.2014.00833>.
- Karni, A., Meyer, G., Rey-Hipolito, C., Jezzard, P., Adams, M.M., Turner, R., Ungerleider, L.G., 1998. The acquisition of skilled motor performance: fast and slow experience-driven changes in primary motor cortex. *Proc. Natl. Acad. Sci. U. S. A.* 95, 861–868. <http://dx.doi.org/10.1073/pnas.95.3.861>.
- Knecht, S., Dräger, B., Deppe, M., Bobe, L., Lohmann, H., Floel, A., Ringelstein, E.B., Henningsen, H., 2000. Handedness and hemispheric language dominance in healthy humans. *Brain* 123 (Pt 12), 2512–2518. <http://dx.doi.org/10.1093/brain/123.12.2512>.
- Kohler, S., Danckert, S., Gati, J.S., Menon, R.S., 2005. Novelty responses to relational and non-relational information in the hippocampus and the parahippocampal region: a comparison based on event-related fMRI. *Hippocampus* 15, 763–774. <http://dx.doi.org/10.1002/hipo.20098>.
- Kotz, S.A., Schwartz, M., 2010. Cortical speech processing unplugged: a timely subcortical-cortical framework. *Trends Cogn. Sci.* 14, 392–399. <http://dx.doi.org/10.1016/j.tics.2010.06.005>.

- Kronfeld-Duenias, V., Amir, O., Ezrati-Vinacour, R., Civier, O., Ben-Shachar, M., 2014. The frontal aslant tract underlies speech fluency in persistent developmental stuttering. *Brain Struct. Funct.* <http://dx.doi.org/10.1007/s00429-014-0912-8>.
- Li, P., Sepanski, S., Zhao, X., 2006. Language history questionnaire: a web-based interface for bilingual research. *Behav. Res. Methods* 38, 202–210.
- Macnamara, B.N., Hambrick, D.Z., Oswald, F.L., 2014. Deliberate practice and performance in music, games, sports, education, and professions: a meta-analysis. *Psychol. Sci.* 25, 1608–1618. <http://dx.doi.org/10.1177/0956797614535810>.
- Maguire, E.A., Gadian, D.G., Johnsrude, I.S., Good, C.D., Ashburner, J., Frackowiak, R.S., Frith, C.D., 2000. Navigation-related structural change in the hippocampi of taxi drivers. *Proc. Natl. Acad. Sci. U. S. A.* 97, 4398–4403. <http://dx.doi.org/10.1073/pnas.070039597>.
- Marien, P., Ackermann, H., Adamaszek, M., Barwood, C.H., Beaton, A., Desmond, J., De Witte, E., Fawcett, A.J., Hertrich, I., Kuper, M., Leggio, M., Marvel, C., Molinari, M., Murdoch, B.E., Nicolson, R.I., Schmahmann, J.D., Stoodley, C.J., Thurling, M., Timmann, D., Wouters, E., Ziegler, W., 2014. Consensus paper: language and the cerebellum: an ongoing enigma. *Cerebellum* 13, 386–410. <http://dx.doi.org/10.1007/s12311-013-0540-5>.
- May, A., 2011. Experience-dependent structural plasticity in the adult human brain. *Trends Cogn. Sci.* 15, 475–482. <http://dx.doi.org/10.1016/j.tics.2011.08.002>.
- Mechelli, A., Crinion, J.T., Noppeney, U., O'Doherty, J., Ashburner, J., Frackowiak, R.S., Price, C.J., 2004. Neurolinguistics: structural plasticity in the bilingual brain. *Nature* 431, 757. <http://dx.doi.org/10.1038/431757a>.
- Menenti, L., Petersson, K.M., Scheeringa, R., Hagoort, P., 2009. When elephants fly: differential sensitivity of right and left inferior frontal gyri to discourse and world knowledge. *J. Cogn. Neurosci.* 21, 2358–2368. <http://dx.doi.org/10.1162/jocn.2008.21163>.
- Merabet, L.B., Hamilton, R., Schlaug, G., Swisher, J.D., Kiriakopoulos, E.T., Pitskel, N.B., Kauffman, T., Pascual-Leone, A., 2008. Rapid and reversible recruitment of early visual cortex for touch. *PLoS One* 3, e3046. <http://dx.doi.org/10.1371/journal.pone.0003046>.
- Milner, B., Penfield, W., 1955. The effect of hippocampal lesions on recent memory. *Trans. Am. Neurol. Assoc.* 42–48.
- Mishra, K.K. (Ed.), 1997. *Sanskrit Studies in India: On the Occasion of 10th World Sanskrit Conference, Bangalore, Jan 3–9, 1997*. Rashtriya Sanskrit Sansthan, New Delhi, India.
- Morillon, B., Liegeois-Chauvel, C., Arnal, L.H., Benar, C.G., Giraud, A.L., 2012. Asymmetric function of theta and gamma activity in syllable processing: an intra-cortical study. *Front. Psychol.* 3, 248. <http://dx.doi.org/10.3389/fpsyg.2012.00248>.
- Nakamura, A., Yamada, T., Goto, A., Kato, T., Ito, K., Abe, Y., Kachi, T., Kakigi, R., 1998. Somatosensory homunculus as drawn by MEG. *NeuroImage* 7, 377–386. <http://dx.doi.org/10.1006/nimg.1998.0332>.
- Navas-Sanchez, F.J., Aleman-Gomez, Y., Sanchez-Gonzalez, J., Guzman-De-Villoria, J.A., Franco, C., Robles, O., Arango, C., Desco, M., 2014. White matter microstructure correlates of mathematical giftedness and intelligence quotient. *Hum. Brain Mapp.* 35, 2619–2631. <http://dx.doi.org/10.1002/hbm.22355>.
- Nichols, T.E., Holmes, A.P., 2002. Nonparametric permutation tests for functional neuroimaging: a primer with examples. *Hum. Brain Mapp.* 15, 1–25. <http://dx.doi.org/10.1002/hbm.1058>.
- Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9, 97–113. [http://dx.doi.org/10.1016/0028-3932\(71\)90067-4](http://dx.doi.org/10.1016/0028-3932(71)90067-4).
- Palaniyappan, L., Liddle, P.F., 2012. Differential effects of surface area, gyrification and cortical thickness on voxel based morphometric deficits in schizophrenia. *NeuroImage* 60 (1), 693–699. <http://dx.doi.org/10.1016/j.neuroimage.2011.12.058>.
- Pardoe, H.R., Abbott, D.F., Jackson, G.D., 2013. Sample size estimates for well-powered cross-sectional cortical thickness studies. *Hum. Brain Mapp.* 34, 3000–3009. <http://dx.doi.org/10.1002/hbm.22120>.
- Patenaude, B., Smith, S.M., Kennedy, D.N., Jenkinson, M., 2011. A Bayesian model of shape and appearance for subcortical brain segmentation. *NeuroImage* 56, 907–922. <http://dx.doi.org/10.1016/j.neuroimage.2011.02.046>.
- Pathashala, Veda, 2014. *Traditional Vedic Schools*. <http://sanskritdocuments.org> (accessed October 1, 2014).
- Petkov, C.I., Logothetis, N.K., Obleser, J., 2009. Where are the human speech and voice regions, and do other animals have anything like them? *Neuroscientist* 15, 419–429. <http://dx.doi.org/10.1177/1073858408326430>.
- Poeppel, D., 2003. The analysis of speech in different temporal integration windows: cerebral lateralization as 'asymmetric sampling in time'. *Speech Comm.* 41, 245–255. [http://dx.doi.org/10.1016/S0167-6393\(02\)00107-3](http://dx.doi.org/10.1016/S0167-6393(02)00107-3).
- Pohlack, S.T., Meyer, P., Cacciaglia, R., Liebscher, C., Ridder, S., Flor, H., 2014. Bigger is better! Hippocampal volume and declarative memory performance in healthy young men. *Brain Struct. Funct.* 219, 255–267. <http://dx.doi.org/10.1007/s00429-012-0497-z>.
- Poppenk, J., Moscovitch, M., 2011. A hippocampal marker of recollection memory ability among healthy young adults: contributions of posterior and anterior segments. *Neuron* 72, 931–937. <http://dx.doi.org/10.1016/j.neuron.2011.10.014>.
- Poppenk, J., Evensmoen, H.R., Moscovitch, M., Nadel, L., 2013. Long-axis specialization of the human hippocampus. *Trends Cogn. Sci.* 17, 230–240. <http://dx.doi.org/10.1016/j.tics.2013.03.005>.
- Rashtriya Sanskrit Sansthan, 2010–2011. *Annual Report. Rashtriya Sanskrit Sansthan (Deemed University)*, Government of India, New Delhi.
- Rashtriya Sanskrit Sansthan, 2014. <http://www.sanskrit.nic.in> (accessed October 1, 2014).
- Remedios, R., Logothetis, N.K., Kayser, C., 2009. An auditory region in the primate insular cortex responding preferentially to vocal communication sounds. *J. Neurosci.* 29, 1034–1045. <http://dx.doi.org/10.1523/JNEUROSCI.4089-08.2009>.
- Richardson, F.M., Thomas, M.S., Filippi, R., Harth, H., Price, C.J., 2010. Contrasting effects of vocabulary knowledge on temporal and parietal brain structure across lifespan. *J. Cogn. Neurosci.* 22, 943–954. <http://dx.doi.org/10.1162/jocn.2009.21238>.
- Roux, F.E., Durand, J.B., Jucla, M., Rehaut, E., Reddy, M., Demonet, J.F., 2012. Segregation of lexical and sub-lexical reading processes in the left perisylvian cortex. *PLoS One* 7, e50665. <http://dx.doi.org/10.1371/journal.pone.0050665>.
- Ruben, J., Schwiemann, J., Deuchert, M., Meyer, R., Krause, T., Curio, G., Villringer, K., Kurth, R., Villringer, A., 2001. Somatotopic organization of human secondary somatosensory cortex. *Cereb. Cortex* 11, 463–473. <http://dx.doi.org/10.1093/cercor/11.5.463>.
- Saad, Z.S., Reynolds, R.C., Argall, B., Japee, S., Cox, R.W., 2004. SUMA: an interface for surface-based intra- and inter-subject analysis with AFNI. *2004 2nd IEEE International Symposium on Biomedical Imaging: Macro to Nano*, pp. 1510–1513.
- Schaer, M., Cuadra, M.B., Tamarit, L., Lazeyras, F., Eliez, S., Thiran, J.P., 2008. A surface-based approach to quantify local cortical gyrification. *IEEE Trans. Med. Imaging* 27, 161–170. <http://dx.doi.org/10.1109/TMI.2007.903576>.
- Schaer, M., Cuadra, M.B., Schmansky, N., Fischl, B., Thiran, J.P., Eliez, S., 2012. How to measure cortical folding from MR images: a step-by-step tutorial to compute local gyrification index. *J. Vis. Exp.* e3417. <http://dx.doi.org/10.3791/3417>.
- Scoville, W.B., Milner, B., 1957. Loss of recent memory after bilateral hippocampal lesions. *J. Neurol. Neurosurg. Psychiatry* 20, 11–21.
- Sereno, M.I., Huang, R.S., 2014. Multisensory maps in parietal cortex. *Curr. Opin. Neurobiol.* 24, 39–46. <http://dx.doi.org/10.1016/j.conb.2013.08.014>.
- Shastri, R.K., 2014. personal communication, October 15.
- Smith, S.M., 2002. Fast robust automated brain extraction. *Hum. Brain Mapp.* 17, 143–155.
- Smith, S.M., Nichols, T.E., 2009. Threshold-free cluster enhancement: addressing problems of smoothing, threshold dependence and localisation in cluster inference. *NeuroImage* 44, 83–98. <http://dx.doi.org/10.1016/j.neuroimage.2008.03.061>.
- Smith, S.M., Jenkinson, M., Johansen-Berg, H., Rueckert, D., Nichols, T.E., Mackay, C.E., Watkins, K.E., Ciccarelli, O., Cader, M.Z., Matthews, P.M., Behrens, T.E., 2006. Tract-based spatial statistics: voxelwise analysis of multi-subject diffusion data. *NeuroImage* 31, 1487–1505. <http://dx.doi.org/10.1016/j.neuroimage.2006.02.024>.
- Squire, L.R., Bayley, P.J., 2007. The neuroscience of remote memory. *Curr. Opin. Neurobiol.* 17, 185–196. <http://dx.doi.org/10.1016/j.conb.2007.02.006>.
- Stoodley, C.J., 2012. The cerebellum and cognition: evidence from functional imaging studies. *Cerebellum* 11, 352–365. <http://dx.doi.org/10.1007/s12311-011-0260-7>.
- Strange, B.A., Witter, M.P., Lein, E.S., Moser, E.I., 2014. Functional organization of the hippocampal longitudinal axis. *Nat. Rev. Neurosci.* 15, 655–669. <http://dx.doi.org/10.1038/nrn3785>.
- Su, S., White, T., Schmidt, M., Kao, C.Y., Sapiro, G., 2013. Geometric computation of human gyrification indexes from magnetic resonance images. *Hum. Brain Mapp.* 34, 1230–1244. <http://dx.doi.org/10.1002/hbm.21510>.
- Takahima, A., Petersson, K.M., Rutters, F., Tendolkar, I., Jensen, O., Zwarts, M.J., McNaughton, B.L., Fernandez, G., 2006. Declarative memory consolidation in humans: a prospective functional magnetic resonance imaging study. *Proc. Natl. Acad. Sci. U. S. A.* 103, 756–761. <http://dx.doi.org/10.1073/pnas.0507774103>.
- Takehara, N., Nishiyuchi, K., McNaughton, B.L., 2008. Spontaneous changes of neocortical code for associative memory during consolidation. *Science* 322, 960–963. <http://dx.doi.org/10.1126/science.1161299>.
- Teixeira, C.M., Pomedii, S.R., Maei, H.R., Kee, N., Frankland, P.W., 2006. Involvement of the anterior cingulate cortex in the expression of remote spatial memory. *J. Neurosci.* 26, 7555–7564. <http://dx.doi.org/10.1523/JNEUROSCI.1068-06.2006>.
- Transport for London, 2014. www.tfl.gov.uk (accessed May 6, 2014).
- van Mulukom, V., Schacter, D.L., Corballis, M.C., Addis, D.R., 2013. Re-imagining the future: repetition decreases hippocampal involvement in future simulation. *PLoS One* 8. <http://dx.doi.org/10.1371/journal.pone.0069596>.
- van Rijn, S., Aleman, A., van Diessen, E., Berckmoes, C., Vingerhoets, G., Kahn, R.S., 2005. What is said or how it is said makes a difference: role of the right fronto-parietal operculum in emotional prosody as revealed by repetitive TMS. *Eur. J. Neurosci.* 21, 3195–3200. <http://dx.doi.org/10.1111/j.1460-9568.2005.04130.x>.
- Voets, N.L., Hough, M.G., Douaud, G., Matthews, P.M., James, A., Winmill, L., Webster, P., Smith, S., 2008. Evidence for abnormalities of cortical development in adolescent-onset schizophrenia. *NeuroImage* 43, 665–675. <http://dx.doi.org/10.1016/j.neuroimage.2008.08.013>.
- Voss, P., Lassonde, M., Gougoux, F., Fortin, M., Guillemot, J.P., Lepore, F., 2004. Early- and late-onset blind individuals show supra-normal auditory abilities in far-space. *Curr. Biol.* 14, 1734–1738. <http://dx.doi.org/10.1016/j.cub.20.04.09.0.5.1>.
- Weible, A.P., Rowland, D.C., Monaghan, C.K., Wolfgang, N.T., Kentros, C.G., 2012. Neural correlates of long-term object memory in the mouse anterior cingulate cortex. *J. Neurosci.* 32, 5598–5608. <http://dx.doi.org/10.1523/JNEUROSCI.5265-11.2012>.
- Whitney, D., 1924. *Sanskrit Grammar, Including Both the Classical Language and the Older Dialects of Veda and Brahmana*. 5th ed. Breitkopf & Hartel, Leipzig.
- Wierenga, L., Langen, M., Ambrosino, S., van Dijk, S., Oranje, B., Durston, S., 2014. Typical development of basal ganglia, hippocampus, amygdala and cerebellum from age 7 to 24. *NeuroImage* 96C, 67–72. <http://dx.doi.org/10.1016/j.neuroimage.2014.03.072>.
- Winkler, A.M., Kochunov, P., Blangero, J., Almasy, L., Zilles, K., Fox, P.T., Duggirala, R., Glahn, D.C., 2010. Cortical thickness or grey matter volume? The importance of selecting the phenotype for imaging genetics studies. *NeuroImage* 53, 1135–1146. <http://dx.doi.org/10.1016/j.neuroimage.2009.12.028>.
- Yarkoni, T., 2009. Big correlations in little studies: inflated fMRI correlations reflect low statistical power—commentary on Vul et al. (2009). *Perspect. Psychol. Sci.* 4, 294–298. <http://dx.doi.org/10.1111/j.1745-6924.2009.01127.x>.
- Zatorre, R.J., Bouffard, M., Belin, P., 2004. Sensitivity to auditory object features in human temporal neocortex. *J. Neurosci.* 24, 3637–3642. <http://dx.doi.org/10.1038/nn.3045>.
- Zhang, Y., Brady, M., Smith, S., 2001. Segmentation of brain MR images through a hidden Markov random field model and the expectation-maximization algorithm. *IEEE Trans. Med. Imaging* 20, 45–57.
- Zhuang, J., Tyler, L.K., Randall, B., Stamatakis, E.A., Marslen-Wilson, W.D., 2014. Optimally efficient neural systems for processing spoken language. *Cereb. Cortex* 24, 908–918. <http://dx.doi.org/10.1093/cercor/bhs366>.