Spatial normalization transforms an individual brain into a standard stereotaxic space in order to compare imaging results across individuals. However, most approaches rely on information from a template composed from one or more adult brains, with the applicability of this adult data depending on the differences between the populations making up the template (adult) and the brains to be normalized (pediatric). Therefore, spatial misregistration must be expected especially in younger children. To provide a closer template, we created gender-specific pediatric templates from a large collection of healthy children and examined their differences. These templates can be integrated into SPM99.

**Subjects & Methods**

200 healthy children were included in this study. Institutional review board approval and informed consent were obtained for all subjects. Exclusion criteria were: previous neurological or psychiatric illness, psychiatric illness in a first-degree relative, learning disability, head trauma with loss of consciousness, current or past psychostimulant medication, pregnancy, IQ < 80 (WISC III), prematurity, abnormal findings on clinical neurological examination, and clinical or technical contraindications to an MRI-examination (including orthodontic braces). All MRI scans were read by a qualified pediatric neuroradiologist.

Children were imaged with a Bruker Biospec 30/60 3 Tesla MRI scanner. A whole-brain, 3D T1-weighted Modified Driven-Equilibrium Fourier Transform (MDEFT) image was acquired (TR = 15 ms, TE = 4.3 ms, t time = 550 ms, flip angle = 20º, matrix = 128 x 256 x 96, FOV = 19.2 x 25.6 x 14.4 cm, resolution = 1.5 x 1 x 1.5 mm).

Images were rated (regarding arterial blood flow-artifacts and motion artifacts) on a scale from 0 (no flow artifact, no motion artifact) to 4 (strong flow or motion artifact). Images with a rating of 3 or 4 were excluded from further analysis. The only manual step in data processing was the identification of the anterior commissure to allow for optimal normalization starting estimates. This was done by a single investigator for all images. Images were resliced to 1 x 1 x 1 mm isotropic voxels to reduce partial volume effects in further processing and to achieve a better fit with the axially oriented templates. As in all of the other processing steps within SPM99, a sinc-interpolation algorithm was used if possible.

Images were automatically transformed into stereotaxic space within SPM99 by a 12-parameter affine-only, linear transformation. All images from female and male subjects were then averaged independently, resulting in two templates ($T_{female}$ & $T_{male}$). To provide pediatric normative data for segmentation, we segmented our images into gray matter, white matter, and cerebro-spinal fluid maps and averaged these. The brain mask (to mask out non-brain tissue) was derived from the averaged gray and white matter maps using the "brain extract" function of SPM99.

**Results**

Data from 52 children was rejected due to insufficient image quality, technical failure, or pathological findings. This left data from 148 children, 79 girls and 69 boys. Their demographical data was not significantly different (girls: mean age = 140.23 ± 42.44 months, right-handed = 74, left-handed = 5, ethnic origin: 72 were Caucasian, 3 Asian, 3 African American, and 1 was Hispanic; boys: mean age = 130.87 ± 41 months, right-handed = 59, left-handed = 10, ethnic origin: 60 were Caucasian, 2 Asian, 3 African American, 1 Native American, 2 Multi-Ethnic, and 1 was Hispanic). Differences in tissue distribution (girls>boys and boys>girls) were only considered valid if the pixel intensity difference between the tissue maps (equaling the likelihood to find tissue at this particular location) was more than 10%.

**Discussion**

We examined a large sample of normal, healthy children. The differences between the tissue probability maps indicate that although boys have on average a higher gray matter volume, this relation is inversed in specific brain areas. This pattern is reversed for white matter. These differences are in line with earlier observation of striking gender-effects in pediatric brain morphology [2] and suggest that a more appropriate normalization and/or segmentation result might be achieved if not only pediatric, but gender-specific pediatric templates are used. We could recently show that a pediatric template leads to less deformation during normalization [3], and considering gender might further enhance this effect. To allow for the exploration of such effects, the templates are available for download [4].

**References:**


**Construction of gender-specific pediatric templates for spatial normalization within SPM99**

M. Wilke, V. J. Schmithorst, and S. K. Holland

Imaging Research Center, Cincinnati Children’s Hospital Medical Center, OH, USA