Improved Inter-Subject Functional Registration Using DARTEL in Individuals Prenatally Exposed to Alcohol

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INTRODUCTION

On account of the multifaceted structural damage induced by prenatal alcohol exposure (PAE), MR image registration problems have been a roadblock in the detailed analysis of images from this population. The recently introduced DARTEL (diffeomorphic anatomical registration through exponentiated lie algebra) algorithm [1] is thought to improve inter-subject functional image registration, but has not been previously applied to the PAE population. The present study examines the applicability of DARTEL to functional image registration in the PAE population using images derived from a vibrotactile stimulation task with contralateral hand response.

METHODS

Participants were healthy control (n=18) and dysmorphic PAE (n=14) individuals recruited from a longitudinal cohort. PAE subjects were characterized as prenatally exposed to alcohol based on repeated physical examination for growth retardation and dysmorphia, IQ testing, and by screening of the maternal population for alcohol use [2]. The functional paradigm consisted of a vibrotactile stimulation delivered by piezo-electric buzzer to the participants' right hand, upon which the participants were asked to respond with the left hand. All acquisition was performed on a 3T Siemens Trio scanner (Siemens Medical Solutions, Erlangen, Germany). Anatomical scan (T1-MPRAGE) parameters: TR/TI/TE of 2600ms/900ms/3.93ms, flip angle of 8°, field of view of 256 × 224 × 176 mm3. Functional scan (EPI-BOLD sequence) parameters: 120 axial images (30, 4mm thick slices), TR/TE/FA/FOV of 2000ms/35ms/90º/22 cm. For the functional data run, preprocessing was performed in AFNI (http://afni.nimh.nih.gov/afni/) and included slice-timing correction, motion correction, and spatial smoothing (using a 5mm FWHM). Activation maps were generated by a multiple linear regression analysis evaluating the goodness of the fit. Functional data was warped to either Talairach space (using automatic Talairach transformation command provided by AFNI) or to the customized space created by the DARTEL toolbox in SPM8b (http://www.fil.ion.ucl.ac.uk/spm/) using the gray matter template and its associated transformation matrix for warping from native space. Difference maps were then generated to compare between the two exposure groups. To determine whether difference maps generated by Talairach warping or DARTEL are more representative of the alcohol exposure effect, exposure-related measures (dysmorphic score, brain size, isthmus fractional anisotropy (FA) and splenium FA) were correlated, respectively, with the magnitude of activation at a region of significant difference (SMA) between the two groups by the DARTEL method.

RESULTS

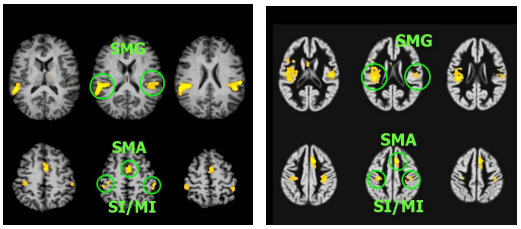

Figure 1. PAE group task-activation maps derived by Talairach (left) and DARTEL (right) registration methods. SMG: supramarginal gyrus; SMA: supplementary motor area; S1/M1: primary sensory/motor areas.

Activation maps created by Talairach transformation indicate significant activation in bilateral SMG, bilateral S1/M1, and SMA regions (Fig 1, left). Corresponding regions can be indentified in activation maps created from DARTEL template warping (Fig 1, right). Difference maps between groups indicate higher activation in the PAE group as compared to the control group by both methods (Fig 2). More differences are revealed by the DARTEL warp method than Talairach, with significant clusters located in the regions identified in Figure 1. The difference cluster at the SMA (identified by pink circle in Figure 2) was used for subsequent correlation analysis. Positive correlation with dysmorphic score and negative correlation with brain size and splenium FA were significant, while negative correlation with isthmus FA was not significant (Table 1).

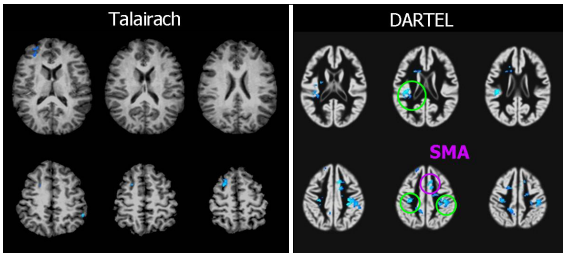

Figure 2. Difference maps (Control-PAE) of activation derived by Talairach and DARTEL registration methods. SMA region used for subsequent correlation analysis is highlighted.

Table 1. Pearson's correlation of group activation in the SMA derived with Talairach (TAL) and DARTEL registration methods with exposure-related measures. The p-values are given in parentheses. *significant correlation (p<0.05).

Registration Method	**Exposure-related measure correlation: r (p-value)**			
	Dysmorphic score	**Brain size**	**FA isthmus**	**FA splenium**
TAL	-0.018 (0.935)	0.266 (0.209)	0.329 (0.116)	-0.329 (0.116)
DARTEL	0.448 (0.028*)	-0.500 (0.013*)	-0.221 (0.300)	-0.439 (0.032*)

DISCUSSION

DARTEL improved spatial normalization of functional images from the PAE population, indicated by detecting more regional differences between groups and more significant correlation of signal intensity with known exposure-related characteristics. Thus it is possible that studies of the PAE population would benefit from alignment to a customized space (e.g, DARTEL method) rather than a standardized common space.

REFERENCES: [1] Ashburner J 2007 Neuroimage 38(1):95-113. [2] Coles, C.D., et al. 2002 Feb;26(2):263-71.

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