An Example Using PET for Statistical Parametric Mapping

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Example PET Study

- Interest in brain areas active in stutters
- Stuttering can be quantified using stuttered interval count or SI count
- SI count is the # of 4-second intervals containing stuttered speech
- SI count can serve as an external measure for correlation with CBF in PET study
- Need group design study to see subtle effects
Example Study PET Acquisition

- CTI/Siemens scanner
- Attenuation correction using Ge-68/Ga-68 rod transmission source
- 10-min interval between scans
- Head immobilized to reduce motion
- 40 second uptake phase initiated when tracer enters the brain followed by 50 second initial washout phase
- Images were of the combined 90 second period which represents CBF with good SNR
- Text for reading presented on video monitor
- Reading started at time of injection and lasted for 60 seconds
- Six scans each task repeated twice
Example PET Study Design

<table>
<thead>
<tr>
<th></th>
<th>Subject 1</th>
<th>Subject 2</th>
<th>Subject 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scan 1</td>
<td>mono</td>
<td>oral</td>
<td>mono</td>
</tr>
<tr>
<td>Scan 2</td>
<td>ECR</td>
<td>ECR</td>
<td>ECR</td>
</tr>
<tr>
<td>Scan 3</td>
<td>oral</td>
<td>mono</td>
<td>oral</td>
</tr>
<tr>
<td>Scan 4</td>
<td>ECR</td>
<td>ECR</td>
<td>ECR</td>
</tr>
<tr>
<td>Scan 5</td>
<td>oral</td>
<td>mono</td>
<td>oral</td>
</tr>
<tr>
<td>Scan 6</td>
<td>mono</td>
<td>oral</td>
<td>mono</td>
</tr>
</tbody>
</table>

- oral - solo reading of text passage
- mono - spontaneous monologue (speaking without text passage)
- ECR - eyes closed rest

Full study had 12 subjects.
Preprocessing of MRI for PET studies is similar to fMRI, but most PET studies use group analyses so average MRI images are created, often at the lower pixel spacing seen with PET studies.

Group SPMs are overlaid onto the group average MR images.
PET O-15 water Scans 1-6
2 - Monolog
2 - Solo Reading
2 - Eyes Closed Rest

Value Normalization required for PET studies (deals with scans and subject differences in radiotracer levels).

Raw group average of six scans after correction for movement

• ROI delimiting brain tissue is defined using the raw group average image
• Each scan adjusted to the same average value within the brain (often 1000)

<table>
<thead>
<tr>
<th>Value before normalization</th>
<th>Value after normalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>3102.4</td>
<td></td>
</tr>
<tr>
<td>3850.3</td>
<td></td>
</tr>
<tr>
<td>3293.3</td>
<td></td>
</tr>
<tr>
<td>3768.2</td>
<td></td>
</tr>
<tr>
<td>2928.8</td>
<td></td>
</tr>
<tr>
<td>3480.4</td>
<td></td>
</tr>
</tbody>
</table>
Spatial Normalization MRI

Manual (landmark based) approach with high resolution MRI
Automated Spatial Normalization MRI

Average 2 mm MRI from study.

2 mm MRI template.

FLIRT to align
PET Spatial Normalization

Convex Hull surfaces similar for MRI and PET images.

- All subject’s PET scans are corrected for motion and averaged
- Dotted outline is from the average PET scan
- Solid outline is from spatially normalized MRI of the subject
- A 4x4 affine transform is iteratively adjusted to seek best fit between the two outlines (minimum mean square error)
- Alternatively can use FLIRT with normalized correlation cost function
- Resulting transform is applied to all PET scans for the subject
- Repeat for all subjects fitting a common template
Overlays of PET from individual subjects onto the average MRI for the study demonstrates how well fitting of PET images to MR images works. All images are now spatially normalized and Talairach coordinates can be used to provide candidate labels from coordinates.
Simple Contrast

- After value and spatial normalization
- All subject’s solo reading minus all eyes closed rest as simple contrast.
- Pool the SD from this subtraction to estimate z-score
- Voxel-by-voxel z-score $\sim \frac{\text{reading} - \text{rest}}{\text{SD}}$
Task-Task provides estimate of SD
Task - Task provides estimate of SD
Single-subject single-trial contrast of Solo reading vs. Eyes closed rest

- Image thresholded to illustrate large changes
- Poor SNR
- Does not deal with task performance variability (single trial)
- Doesn’t address issue of where in brain (single subject)
- Poor estimate of standard deviation for subtraction
Simple Group Contrast

Solo reading vs. Eyes closed rest two trials per task and n=12 subjects. Thresholded at z-score > 3.
### Table Used for Correlation

<table>
<thead>
<tr>
<th>Subject</th>
<th>Task</th>
<th>SI Count</th>
<th>Scan</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>solo reading</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>1</td>
<td>solo reading</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>1</td>
<td>eyes closed rest</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>eyes closed rest</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>solo reading</td>
<td>83</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>solo reading</td>
<td>89</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>eyes closed rest</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>eyes closed rest</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>solo reading</td>
<td>17</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>solo reading</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>eyes closed rest</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>eyes closed rest</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>

- Four SI count samples per subject and full study was of 12 subjects.
- Voxel-by-voxel correlation with the SI count pattern
- Correlation coefficients converted to z-scores for use as SP maps
Simple Contrast Compared With Performance Correlation

Reading vs. Eyes closed rest

SPI threshold \( z > 2.5 \).

Voxel-by-voxel correlation with SI count.

Images at Talairach coordinate \( z = 56 \).
Simple Contrast Compared With Performance Correlation

Reading vs. Eyes closed rest
SPI threshold z > 2.5.

Images at Talairach coordinate z = 38.
For More Details on PET Processing similar to what was used in this example see