Presence of AVA in High Frequency Oscillations of the Perfusion fMRI Resting State Signal

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\[ \text{variance(peaks)} = \frac{\sigma^2_{\text{peaks}}}{\sigma^2_{\text{pits}}} \]

\[ \text{log} \]

Image of brain scans with regions of interest highlighted.
AVA in perfusion fMRI

Motivation

• Elements of resting state activity (RSA) described by high-frequency and non oscillatory properties are non-random and functionally relevant\(^1\).

• Variance of BOLD fluctuations within short time frames contain important information for understanding RSA\(^1\).

1) Garrett DD et al. J Neurosc 2010;30:4914
AVA in perfusion fMRI

Motivation

• We have recently proposed a novel metric that quantifies the asymmetry between values of local maxima and local minima in the BOLD signal: this amplitude variance asymmetry (AVA) shows strong age-related development in well defined networks, and, in children, correlations between AVA and IQ\(^3\).

3) Davis et al. Cereb Cortex 2014; 24:1332
AVA in perfusion fMRI

Motivation

• However, it remains unclear the extent to which BOLD AVA reflects CBF changes or the more complex coupling of CBF and CMRO$_2$.

AIMS OF THE STUDY

• Our main goal was to determine whether AVA patterns would be identified in the ASL data, in sensory regions, as previously found for BOLD data. Our second goal was to see whether there are systematic differences in AVA profiles for BOLD and ASL data.
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Data acquisition

• Subjects: 35 healthy volunteers (25.0±5.3 years old)
• MRI Scanner: Bruker 4T Medspec, birdcage Tx, 8-channel Rx
• MRI Sequences:
  - 3D T1-weighted MP-RAGE: TR/TE=2700/4.18 ms, 1x1x1 mm³, 176 slices
  - 2D GE EPI: TR/TE=2200/30 ms, 3x3x3 mm³, 37 slices
  - 2D EPI PASL-Q2TIPS: TR/TE/TI1/TI2/T1s=2000/17/700/1400/1050 ms, 3x3x7 mm³, 9 slices
• Participants fixating on a centrally presented visual cross during both the BOLD and the perfusion sequence.
AVA in perfusion fMRI

Data preprocessing with FSL and AFNI
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AVA analysis

**Amplitude Variance Asymmetry test per voxel:**

**Null Hypothesis:** Voxel Ratio (VR) = \( \sigma^2(\text{peaks})/\sigma^2(\text{pits}) = 1 \)

**Group-level test:** Mean(log(VR\(_1\)), log(VR\(_2\))...log(VR\(_n\))) \neq 0

**Single-participant test:** Levene's \( W > F(df_a, df_b) \)
\[
\begin{align*}
df_a &= 1; \\
\text{df}_b &= N(\text{peaks}) + N(\text{pits}) - 1.
\end{align*}
\]

For 3 time series

1. PureBOLD
2. PerfBOLD
3. PerfCBF
AVA in perfusion fMRI

Comparison of BOLD AVA and CBF AVA

1. How similar are pureBOLD AVA and perfBOLD and perfCBF AVA in spatial distribution?
2. How close are perfCBF and perfBOLD clusters with significant AVA in gray matter (GM)?
3. Are AVA CBF patterns more localized in GM than perfBOLD?
4. Does the magnitude of AVA as measured by BOLD and CBF sequences originate from similar sources?
AVA in perfusion fMRI

- The group analysis was limited to the common brain volume covered in all subjects in both BOLD and perfusion fMRI data.
AVA group maps (n=35)

Note: partial brain volume coverage
AVA clusters: spatial correspondance between perfBOLD and perfCBF

AVA clusters did not fully overlap but the euclidean distance between cluster centroids was small (6.6 mm) relative to the voxel size and significantly smaller than the distance that could be obtained by chance.

- Nearest distance between perfBOLD and perfCBF clusters:
  - 6.6±0.5 mm
- Nearest distance between Random GM voxels and perfCBF clusters
  - 8.4±0.9 mm
- Are these distances different?
  - Yes: t=9.6, p<0.0001 , paired t-test
AVA clusters: gray matter specificity in the different modalities

PerfCBF AVA clusters showed a significantly higher gray matter specificity (more AVA voxels in GM) relative to perfBOLD. The comparison was restricted to ASL data to minimize spatial resolution confounds.

<table>
<thead>
<tr>
<th>Percentage of voxels with significant AVA in GM (p&lt;0.05 Levene’s test)</th>
<th>PerfCBF</th>
<th>PerfBOLD</th>
</tr>
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<tbody>
<tr>
<td>47±9</td>
<td></td>
<td>39±3</td>
</tr>
</tbody>
</table>

\[
t=3.62, \ p=0.001, \ \text{paired t-test}
\]
AVA intensity distributions in the different modalities

AVA distribution values showed that perfCBF was more dissimilar to the AVA values measured in any of the two BOLD based modalities, which were more similar between themselves.

**Similarity analysis of AVA distribution values**

*Distribution of 2 samples Kolmogorov Smirnov values (D):*
- perfBOLD and pureBOLD (0.09 ±0.07)
- perfCBF and pureBOLD (0.12 ±0.07)
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• PureBOLD AVA results are consistent with a recent study\(^3\).
• PureBOLD and perfBOLD show very similar AVA patterns, despite different contrast and spatial/temporal resolution in the acquisitions.
• PerfCBF shows significant AVA clusters. There are differences relative to perfBOLD AVA in terms of: extent of activation, gray matter specificity and AVA distribution values:
• PerfCBF shows a reduced extent of AVA activation compared to perfBOLD.

3) Davis et al. Cereb Cortex 2014; 24:1332
AVA in perfusion fMRI

- PerfCBF AVA shows higher gray matter specificity.
- PerfCBF shows one negative AVA cluster, something not seen before in BOLD AVA\(^3\). In fact the distributions of AVA values are significantly different between perfCBF and the other two BOLD modalities.
- Study limitations: partial brain coverage, use of pASL
- Altogether our results suggest that AVA patterns exist in CBF and that these show general correspondence to BOLD AVA patterns.
- Above-chance closeness between perfBOLD and perfCBF in cluster centers suggests that BOLD AVA clusters reflect neuronal rather than physiological origins.

3) Davis et al. Cereb Cortex 2014; 24:1332
Thank you for your attention. Feedback welcome: domenico.zaca@unitn.it