Cerebral perfusion and vascular reactivity in insulin resistance and obesity

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The obesity epidemic is responsible for the increasing prevalence of Type 2 diabetes, with its corresponding micro- and macrovascular comorbidities. Using a high-resolution arterial-spin labeling (ASL) 3T MRI technique, we present evidence that brain perfusion and vascular reactivity (VR) are affected in the early (insulin resistance) stage of this disease.

Methods
82 middle-aged (age range 35-59) volunteers included 35 healthy controls (HC), 24 insulin-resistant non-diabetics (IR), and 23 diabetics (DB). The groups were matched for age and gender, but both IR and DB patients were significantly more obese than the HC group (see table). The insulin resistance index QUICKI was significantly lower for IR than HC, and also lower for DB than IR patients.

Results and Discussion
Resting cerebral blood flow (CBF) was fitted well by a linear regression model that included end-tidal CO2 as the continuous dependent variable and group membership as the categorical variable. There was a significant improvement in fit when we entered the CO2 * group interaction, with overall residual standard error 5.5 ml/100g/min, F-statistic 5.578, and p-value 0.002. Plots of gray matter perfusion vs end-tidal CO2 (figures below) supports the notion that as a group, IR subjects (slope = 0.243) and diabetic patients (slope = 0.448) show reduced vascular reactivity as compared with healthy brains (slope = 0.794).

<table>
<thead>
<tr>
<th>group</th>
<th>BMI</th>
<th>waist/height</th>
<th>QUICKI</th>
</tr>
</thead>
<tbody>
<tr>
<td>HC</td>
<td>25.3</td>
<td>5.0</td>
<td>0.54</td>
</tr>
<tr>
<td>IR</td>
<td>32.3</td>
<td>7.5</td>
<td>0.62</td>
</tr>
<tr>
<td>DB</td>
<td>33.1</td>
<td>4.9</td>
<td>0.66</td>
</tr>
</tbody>
</table>

CBF distribution previously measured in diabetic patients using PET 15O, the gold standard, and transcranial Doppler [2], a commonly used technique. Interestingly, the variability of our ASL technique (62.4±4.8 for DB group) was several times lower than for PET and Doppler methods, indicating superior precision, required for detection of subtle functional impairments.

The unexpected finding of larger impairment in IR than in DB group may be explained by the beneficial effect of aggressive drug treatment in diabetics. While many details remain unknown, our findings suggest that cerebral blood flow and vascular reactivity changes resulting from obesity and insulin resistance are reversible.
