Latency time variability hinders ASL fMRI analyses

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Target Audience

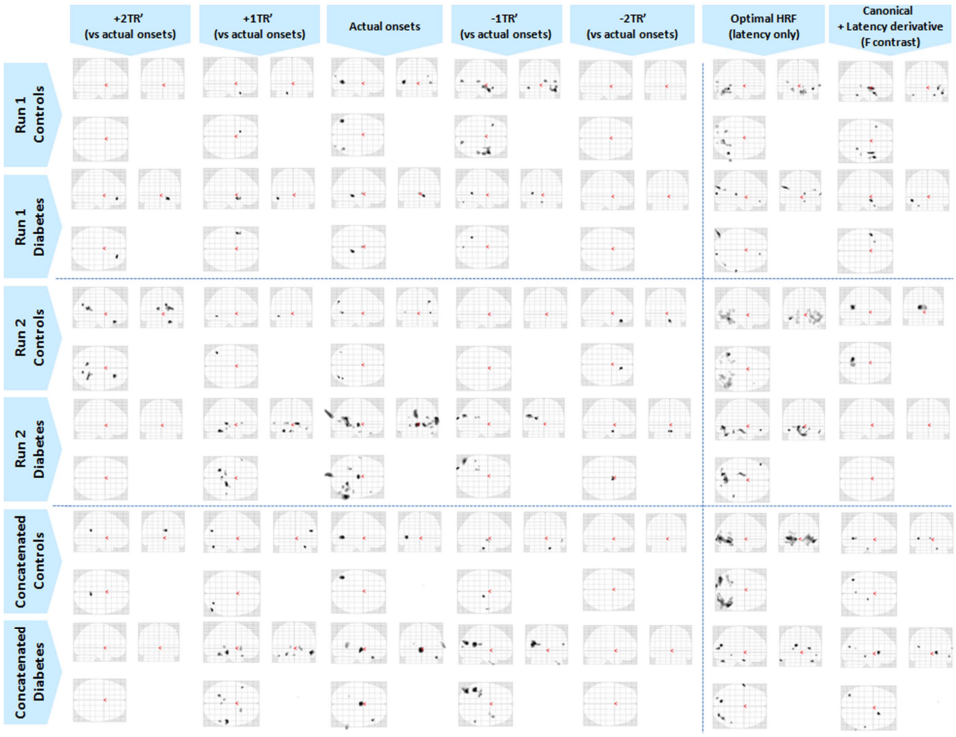
This work will benefit any researcher who works with Arterial Spin Labeling (ASL) in a functional MRI (fMRI) context, as well as those working with brain imaging of diabetes type 2 (DM2) patients.

Purpose

For functional imaging purposes, Arterial Spin Labeling (ASL) has the advantage of measuring activity directly related to neuronal activation with greater localizing sensitivity than the more common BOLD signal analyses (1). The application of ASL in the fMRI context has, however, been blighted by subpar performances (2). The hypothesis here is that this is related to variability in the hemodynamic response function (HRF) latency time, which is not fully captured in standard analyses. In order to assess this, a cohort of DM2 patients was study as well as a group of healthy cohorts, as this pathology is known to affect brain vasculature (3). It is therefore sensible to expect that the HRF is also affected in this pathology, which could be a challenge for adequate ASL analyses.

Methods

A group of 18 controls and 18 DM2 subjects had two runs of 174 pulsed-arterial spin labeling (pASL) scans acquired with PICORE Q2T (TR=2.5s) (4) on a Siemens Trio 3T scanner. A visual speed discrimination paradigm was used, with 15 blocks of fixation and 14 blocks of movement perception (moving dots). Scans were processed using SPM8 in MNI space, with the ASL Data Processing toolbox. The optimal HRF latency was estimated for the MT visual region, for each subject, by maximizing the correlation of the observed signal with estimates of the underlying model with different latencies. For each subject, the statistical analysis was performed using i) the actual stimuli onsets, ii) the onsets shifted by one (1TR' in ASL=2TR=5s) scan in either direction, iii) an F-contrast with the latency derivative, iv) the optimal HRF latency estimated for each subject. A second level random effects analysis was performed for each case, using an 8mm FWHM Gaussian smoothing kernel.



Results

The Figure shows, for both cohorts, the glass brain second level analyses results of (in rows) the first run, the second run, and the concatenation of both runs, using (in columns, in order) the models with an HRF latency between -1TR' and +1TR', the statistics based on the estimated optimal latency HRF, and the statistics based on an F-contrast coupling the canonical HRF with its latency time derivative.

Discussion

The results with the actual onsets were mostly as expected in the control cohort but not in the DM2 cohort. The shifting of onsets revealed that, in the latter, the latency of the HRF could be the responsible for the differences. The modeling of the latency derivative was not enough to deal with this issue, but the estimation of the optimal latency yielded good results in general, for both cohorts.

Conclusions

The optimisation of the latency time of the HRF was necessary to produce adequate and biologically plausible results in all ASL analyses. ASL critically depends on the latency time, which varies from subject to subject, and possibly also between runs: the standard HRF model may therefore be inadequate, and the modeling of the latency derivative may not be enough to solve this issue. It is suggested that any ASL study should start with a basic visual or motor paradigm used to calculate a proxy for the latency time of the HRF, which should then inform the statistical model rather than relying on the generally assumed default values.

References

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