Diagnosis of Alzheimer's Disease Through Identification of Abnormality Patterns in FDG PET Data

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Background: In machine learning classification methods developed for dementia studies, neuroimaging features, e.g. glucose consumption extracted from PET images, are often used to draw the border that differentiates normality from abnormality. However, these features are affected by the anatomical and metabolic variabilities present in the population, which acts as a confounding factor making the task of finding the frontier between normality and abnormality very challenging.

Methods: To reduce the confounding impact of these variabilities when trying to distinguish disease versus normal ageing, we developed a method able to extract for each individual the signal characteristic of abnormality from ^{18}F-FDG PET data. Instead of comparing the patient's PET image to a population of healthy controls as usually done, this framework consists of creating a patient-specific model of healthy PET appearance, and comparing the patient's PET image to the model via a Z-score [1]. The resulting voxel-wise Z-score map can be interpreted as an *abnormality map*, as it statistically evaluates the localised deviation of the patient-specific uptake with respect to the healthy uptake distribution. We applied this method to 298 ADNI2 subjects (103 cognitively normal, 105 late MCI and 90 Alzheimer's disease subjects). The abnormality maps generated with the proposed method were then used as features to feed a classification algorithm based on linear support vector machines. We compared the classification results obtained using the abnormality maps to the classification results obtained using features from the native PET images, and using state-of-the-art Z-maps.

Results: The balanced accuracy obtained with the proposed method when differentiating CN from late MCI and AD (80.5% and 91.6%, respectively) was found to be higher than the balanced accuracy obtained using PET SUVR values (78.3% and 88.9%) and the state-of-the-art Z-maps (78.7% and 89.6%) as features. The same trend was observed when differentiating amyloid positive from amyloid negative subjects (73.9% vs 71.5% and 71.4%).

Conclusions: The high classification accuracy obtained when using the abnormality maps as features demonstrates that the proposed pipeline is able to extract for each individual the signal characteristic of dementia from FDG PET data. Instead of trying to find the frontier between normality and abnormality at the population level, by transporting the problem to the individual level, the proposed method appears to offer a more effective way of differentiating dementia stages.

References: [1] Burgos et al.: Subject-specific models for the analysis of pathological FDG PET data. In: MICCAI 2015, pp.651-658 (2015)

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Table: Balanced accuracy obtained when using PET standardised uptake value ratio (SUVR) images, state-of-the-art Z-maps (obtained by comparing the patient's PET image to a population of healthy controls), and proposed abnormality maps (obtained by comparing the patient's PET image to a patient-specific model of healthy PET appearance) as features of the linear support vector machine classification algorithm.

	CN vs AD	CN vs LMCI	Aß$^{+}$ vs Aß$^{-}$
PET SUVR images	88.9%	78.3%	71.5%
State-of-the-art Z-maps	89.6%	78.7%	71.4%
Proposed abnormality maps	91.6%	80.5%	73.9%

CN: cognitively normal – AD: Alzheimer's disease – LMCI: late mild cognitive impairment – Aß$^{+}$: amyloid positive (AV45 SUVR $>$ 1.11) – Aß$^{-}$: amyloid negative (AV45 SUVR $<$ 1.11)

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