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Predictive pre-operative diagnostic added value of ^1H Magnetic Resonance Spectroscopy, interictal ^{18}F -Fluorodesoxyglucose Positron Emission Tomography and ictal Single Photon Emission Computed Tomography for localization and lateralization of the epileptogenic zone and for outcome in the evaluation of candidates for epilepsy surgery: A meta-analysis from January 1992 to July 2003

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By a systematic literature review and a subsequent patient-based meta-analysis considering publications from January 1992 to July 2003 we aimed to assess the additional diagnostic predictive value of widely used functional diagnostic imaging (FDI) methods like ^1H MRS, ^{18}F -FDG PET and ictal SPECT for the pre-surgical evaluation of the epileptogenic zone (EZ). We considered the following four points: Firstly they do not add information in well-localized patients by ictal scalp EEG (iEEG) and MRI. Secondly they do not provide useful information in conflicting iEEG and MRI cases. Thirdly they do not allow prognostic information regarding the post-operative outcome. Finally they do not reduce the need for invasive EEG recording (DEEG).

Inclusion criteria were: (a) Reported classified post-operative outcome; (b) Detailed reported diagnostic test results; (c) English publications. Studies exclusively reporting on patients with brain tumors or on patients younger than 18 years were excluded.

From more than 1300 PubMed citations and an extensive hand search 78 studies were included in the systematic literature review and 18 in the patient-based meta-analysis which was only possible for PET. In the studies the EZ was mainly defined by EEG data and the final surgical side. Great heterogeneity among studies regarding methodological and technical aspects and concerning the evaluation and interpretation of FDI data was observed. Only two studies really assessed the impact and additional value, one for PET and one for ictal SPECT respectively.

For MRS only temporal lobe epilepsy (TLE) patients were presented. 64% of all patients and 72% of the patients with good outcome had an ipsilateral MRS abnormality (IMRSA) localizing the EZ. The positive predictive value (PPV) of all patients with IMRSA for good outcome was 82%. An odds ratio weighted by inverse variance showed a 4.891 better chance [CI = 1.965-12.172; Q = 2,748; df = 5; critical χ^2 value = 11.07] to become seizure-free if the patient had an IMRSA when comparing to a patient with bilateral MRS abnormality. Conflicting MRS studies were found for patients with negative MRI. One study stressed the use of MRS in patients with bilateral hippocampal atrophy at MRI.

For PET highest concordance values with other diagnostic tests and highest PPVs were seen in TLE patients ranging from 70-90%. The PPV for good outcome was 86% in all patients, in patients with normal MRI 80%, with non-localizing iEEG 72% and in patients localized by DEEG 74%. Contralateral or bilateral hypometabolism was rare and most of these patients had good outcome. In extratemporal lobe epilepsy values for PET were lower, but included studies were too rare to calculate overall values.

In the patient-based meta-analysis about PET of 153 adult TLE patients with a follow-up of at least 12 months and without mass lesions good inter-diagnostic test agreement was seen and similar PPVs for seizure freedom as in the review for good outcome were calculated for localizing PET scans, but also for normal PET findings. All odds ratios for seizure freedom of concordant versus non-concordant PET findings were not statistically significant, even in two or three test combinations.

For ictal SPECT and for the comparison of PET with ictal SPECT the attempt totally failed due to insufficient literature data. In four studies comparing MRS and PET patients were well-localized and almost all had good outcome. PET showed often unilateral hypometabolism and MRS was able to detect

more often bilateral abnormalities. A superiority of one FDI method for difficult iEEG or MRI cases can not be obtained.

MRS still remains a research tool with clinical potential. Our findings may indicate the connection of IMRSA to good outcome in an unspecified population. PET seems to be a good confirmatory test, but our data support that the significance and the extent of hypometabolism is still unclear. Data for ictal SPECT did not allow conclusions and many critical points regarding the conduction of studies were found, but SPECT seems to be more accurate than PET.

So we concluded that the FDI methods are not useful in patients well-localized by iEEG and MRI. They may be useful in patients with non-localizing iEEG or negative MRI. Their ability for prediction of post-operative outcome may depend on the assessed population. From the literature it is uncertain if the FDI methods can reduce the need for DEEG. Prospective studies limited to non-localized iEEG or MRI-negative patients are required for validation of these data.