Brain ^{18}F-FDG PET-MRI coregistration: iconographic essay*

PET-RM neurológico com FDG-^{18}F: ensaio iconográfico

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Abstract **The combination of positron emission tomography (PET) with magnetic resonance imaging (MRI) has been the subject of several studies in recent years. Positron emission tomography is the most sensitive and specific imaging modality in the detection of metabolic changes, but presents limited spatial resolution. On the other hand, MRI presents a significant spatial resolution, besides evaluating soft tissues signal intensity with excellent contrast resolution. The present iconographic essay is aimed at demonstrating the potential clinical application of PET/MRI coregistration. The studies were performed in a dedicated PET unit with ^{18}F-fluorodeoxyglucose (FDG) as radiopharmaceutical and coregistered with 1.5 T or 3 T brain MRI. The brain images fusion software presents an already well-established accuracy, so a significant synergy between a functional PET study and an excellent MRI anatomical detail is achieved. The most attractive clinical applications of this approach are the following: epileptogenic zone assessment in patients refractory to drug therapy, identification of patients with cognitive impairment at higher risk for progression to dementia and differentiation of dementias and Parkinsonian syndromes.**

Keywords: Fluorodeoxyglucose; FDG; Positron emission tomography; PET; Magnetic resonance imaging; Fusion; Clinical neurology.

Resumo **A integração da tomografia por emissão de pósitrons (PET) com a ressonância magnética (RM) tem sido alvo de diversos estudos nos últimos anos. O PET é a modalidade de imagem mais sensível e específica na detecção de alterações metabólicas, entretanto, apresenta limitada resolução espacial. Por outro lado, a RM apresenta importante resolução espacial, além de avaliar estruturas com intensidade de sinal de partes moles com excelente contraste. O objetivo deste estudo é demonstrar, na forma de ensaio iconográfico, as potenciais aplicações clínicas da fusão de imagens de PET e RM. Os exames foram realizados em aparelho PET dedicado utilizando como radiofármaco a fluordeoxiglicose-^{18}F (FDG) e corregistrados com RM de 1,5 T ou 3 T do encéfalo. A fusão por programa de imagens do cérebro tem acurácia já bem estabelecida. Consegue-se, assim, importante sinergia de um estudo funcional de PET com excelente detalhamento anatômico da RM. As aplicações clínicas mais atraentes dessa abordagem são a avaliação da zona epileptogênica em pacientes refratários ao tratamento medicamentoso, identificação dos pacientes com déficit cognitivo com maior risco de progressão para demência e distinção de demências e síndromes parkinsonianas.**

Unitermos: Fluordeoxiglicose; FDG; Tomografia por emissão de pósitrons; PET; Imagem por ressonância magnética; Fusão; Neurologia.

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INTRODUCTION

Recent clinical studies have demonstrated that combined positron emission tomography/computed tomography (PET/CT) offers higher accuracy in the evaluation of patients with suspicion of malignancy and disease staging than other methods where the study is made through interpretation of PET or CT images alone[(1)]. In clinical practice, the use of multimodality imaging methods has already become a reality, particularly in the field of nuclear medicine, and practically the whole range of PET equipment, actually, represents integrated PET and CT systems. The interpretation of PET images alone without fusion with other imaging modalities with a better anatomical definition such as CT or magnetic resonance imaging (MRI), presents a low specificity and decreased positive predictive value. In the last few years, a lot has been researched on PET/MRI coregistration[(2)]. A high potential is estimated for these methods integration in the diagnosis of neurological diseases, because PET is highly sensitive for detecting metabolic changes, but presents a limited spatial resolution. On the other hand, MRI presents a high spatial resolution in the

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evaluation of structures with soft tissues signal such as the brain, additionally to the functional capability of the method.

TECHNICAL ASPECTS

Basically, there are three systems for integrating PET and MRI[3], as follows: 1) independent PET and MRI apparatuses in separate rooms. The images coregistration is performed with dedicated softwares, which generates flexibility, considering that both methods can be separately utilized; 2) sequential images acquired in different apparatuses, but the patient remains on a single examination table that is used on both the systems. Therefore, this is a hardware-fused system; 3) a completely integrated systems where the images are simultaneously acquired, for example, with a single examination table positioning, neither the patient nor the table is moved in the process of images acquisition.

In some cases, simultaneous images acquisition is essential, considering that certain radiopharmaceuticals present a different pharmacokinetics. For example, H_2O-^{15}O passes through the region of interest in a matter of minutes, thus in this case this type of acquisition is required. On the other hand, fluorodeoxyglucose (FDG) takes about 45 minutes to be biodistributed, so simultaneous images acquisition is not relevant in this case.

Images fusion was already utilized even before the introduction of hybrid systems. In fact, it was this method that paved the way to images coregistration by hybrid systems.

Brain images coregistration with software is already validated because of the static nature of this organ[4]. A comparison of several softwares available for MRI and PET/CT fusion, demonstrated a 2–3 mm accuracy that is smaller than the size of one PET pixel[4]. Thus, the fusion of brain FDG-PET images and MRI becomes an attractive method for noninvasive evaluation of neurological diseases.

PET/MRI COREGISTRATION IN COGNITIVE IMPAIRMENT/ DEMENTIA

Recently, the concept of mild cognitive impairment (MCI) was introduced to describe a memory deficit similar to, but without other criteria of Alzheimer's disease[5]. Patients with mild cognitive impairment present a rate of conversion to Alzheimer's disease of approximately 10–15% per year. For this reason, the recognition of such patients is important so that a treatment can be defined as the earliest as possible.

About 60–70% of patients with mild cognitive impairment and presenting mild to severe association cortex hypometabolism (Figure 1), even with a mini mental statement examination (MMSE) scored as

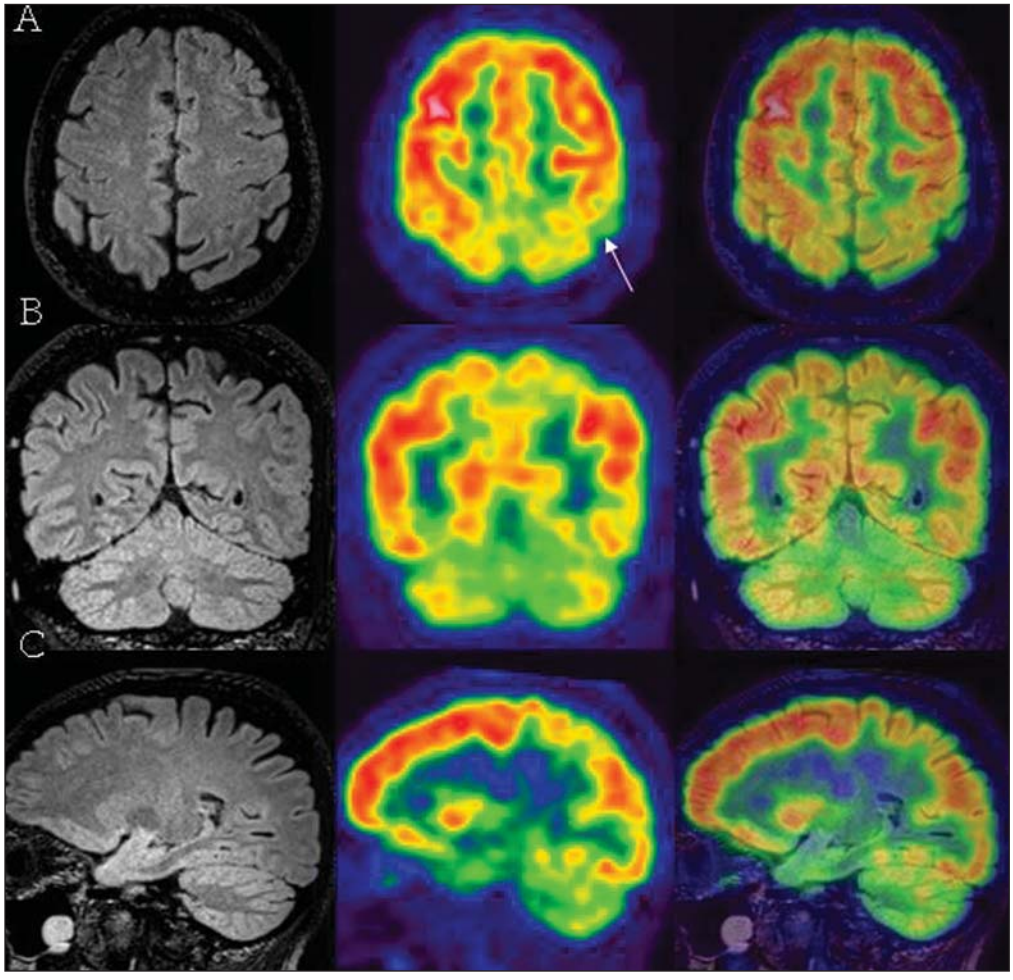

Figure 1. W.T.L., a 49-year-old patient presenting episodes of subtle forgetfulness observed by his wife. Normal neurological evaluation with mini mental statement examination score 27 (N > 24), but presenting selective impairment of declarative memory. Lines **A**, **B** and **C** represent MRI, PET images and PET/MRI coregistration. MRI demonstrates subtle changes in the posterior parietal sulci, with a nonspecific aspect corroborated by the metabolism asymmetry due to a more noticeable hypo-uptake at left (arrow).

normal, may progress to dementia within two years. Early Alzheimer's disease tends to present hypometabolism in the parietal, temporal lobes and posterior cingulate cortex. This change can be easily identified at FDG-PET (Figure 2)[6].

The relevance of the fusion of FDG-PET images and MRI is associated with the identification of metabolic changes in small-sized structures that are difficult to be anatomically localized at PET, such as the hippocampus, for example (Figure 3),

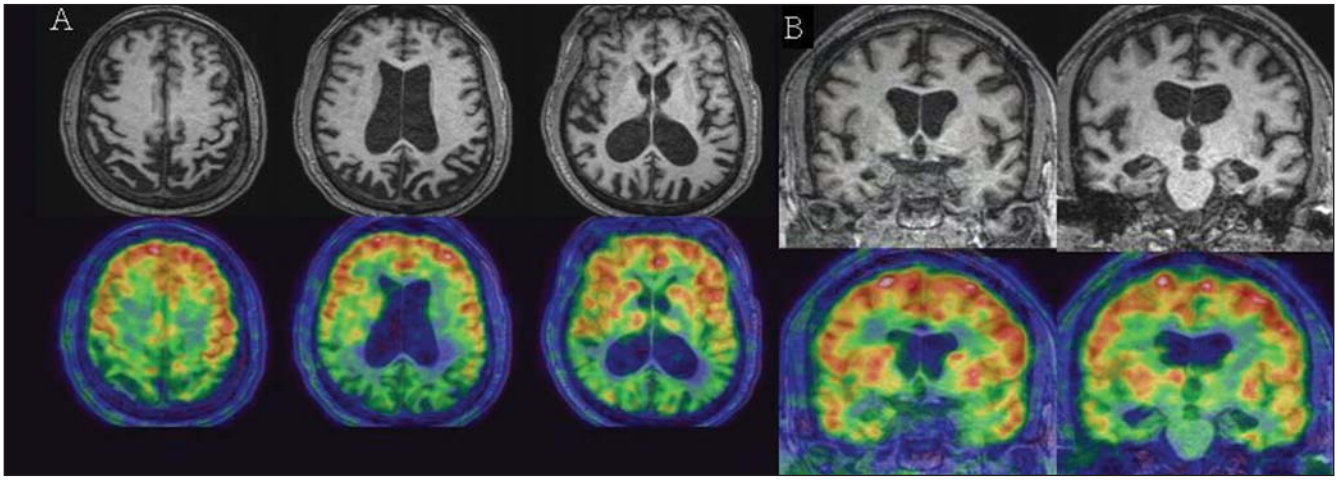

Figure 2. J.C.L.M., a 45-year-old patient with a history of cognitive impairment with slow and progressive worsening, particularly in the last three years. MRI axial (**A**) and coronal (**B**) sections and PET/MRI coregistration demonstrating a significant increase of parietal sulci associated with a more relevant hypometabolism in these lobes as compared with the temporal lobes, suggestive of Alzheimer's disease. Additionally, a relatively preserved metabolism can be observed in the frontal lobes.

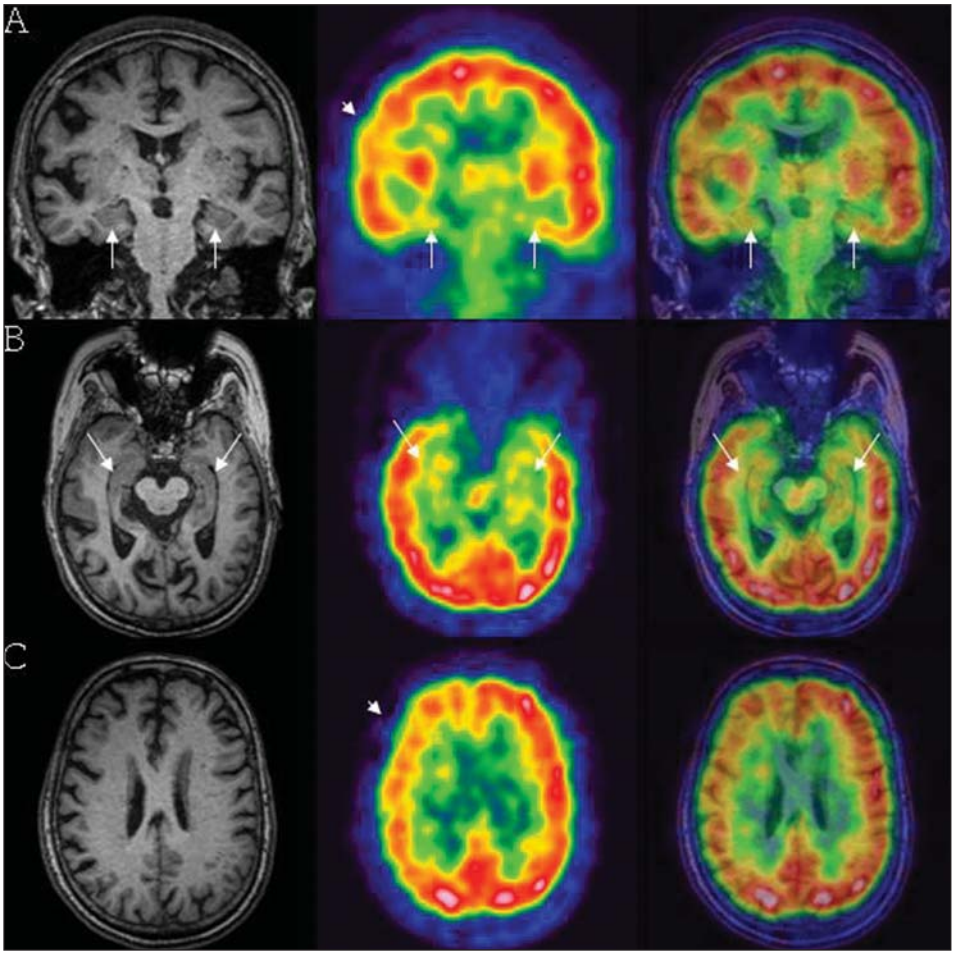

Figure 3. G.M.R., a 62-year-old patient presenting progressive memory loss for one year. Mini mental statement examination score of 22 (N > 24). Lines **A**, **B** and **C** represent MRI and PET images and PET/MRI coregistration. Both hippocampi present a subtle metabolism decrease (arrows on **A** and **B**). Additionally, a mild hypometabolism can be observed in the frontotemporoparietal cortex at right (arrowheads on **A** and **C**).

that is intimately related to a future cognitive impairment and Alzheimer's disease, as well as the angular gyrus and the precuneus.

Frontotemporal dementia is not a specific clinical entity, comprising a spectrum including from a classic Pick's disease to a primary progressive aphasia. It can be identified with PET in the presence of either frontal or frontotemporal hypometabolism (Figure 4).

The clinical diagnosis of vascular dementia represents a diagnostic challenge, since a consensus is still to be reached and the convergence among specialists is poor. Additionally, about 20–40% of patients vascular dementia is associated with Alzheimer's disease[7]. Considering that MRI is highly sensitive in the evaluation of structural lesions, but poorly specific for Alzheimer's disease, the diagnosis of vascular dementia is frequently tendentious. For this reason, the fusion of metabolic PET images with structural MRI emerges as a relevant tool in the correct classification of these dementias.

PET/MRI COREGISTRATION IN EPILEPSY

The drug therapy for epilepsy is ineffective in a considerable number of patients. Complete resection of the epileptogenic

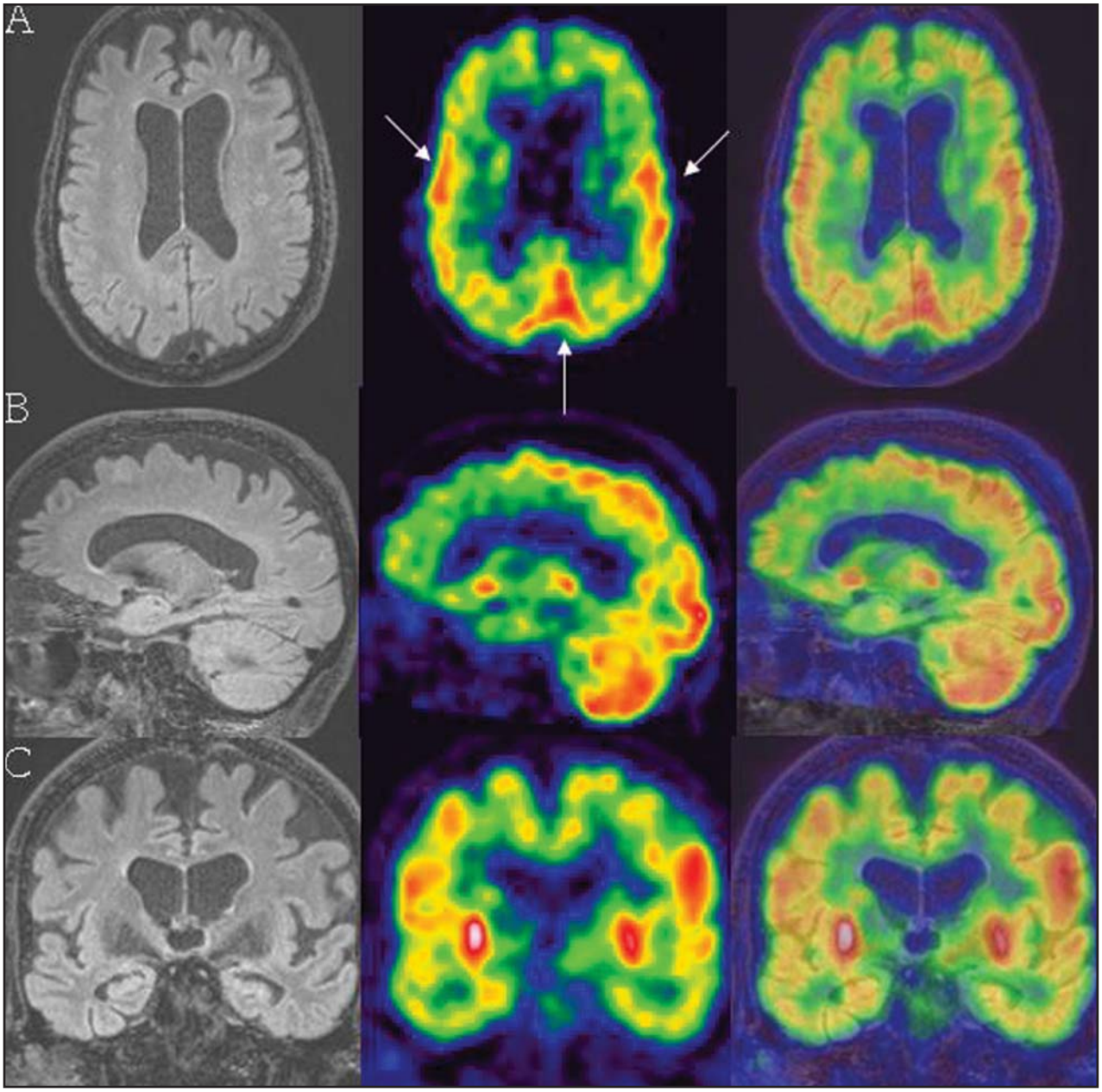

Figure 4. E.J.M., a 68-year-old patient with clinical diagnosis of frontotemporal dementia for four years. MRI axial (**A**), sagittal (**B**) and coronal (**C**) sections, PET images and PET/MRI coregistration. A pronounced hypometabolism is observed, principally in the frontal lobes, with a less pronounced presentation in the parietal and temporal lobes. Preserved metabolism can be observed in the sensory-motor and visual cortex (arrows). A discrepancy is observed between PET and MRI findings, the latter demonstrating dilated supratentorial ventricles and more noticeable sulci.

focus may prevent future seizures in 90% of patients with mesial temporal lobe epilepsy, and in up to 70% of patients with cortical dysplasia.

MRI is the method of choice in the investigation of epileptogenic lesions. FDG-PET adds relevant prognostic information, since it is known that hypometabolism restricted to the temporal lobe is correlated with surgical healing in 75% of these patients, as compared with only 45% of patients with extratemporal hypometabolism (Figures 5 and 6)[8].

A relevant role is played by FDG-PET/MRI coregistration in the identification of

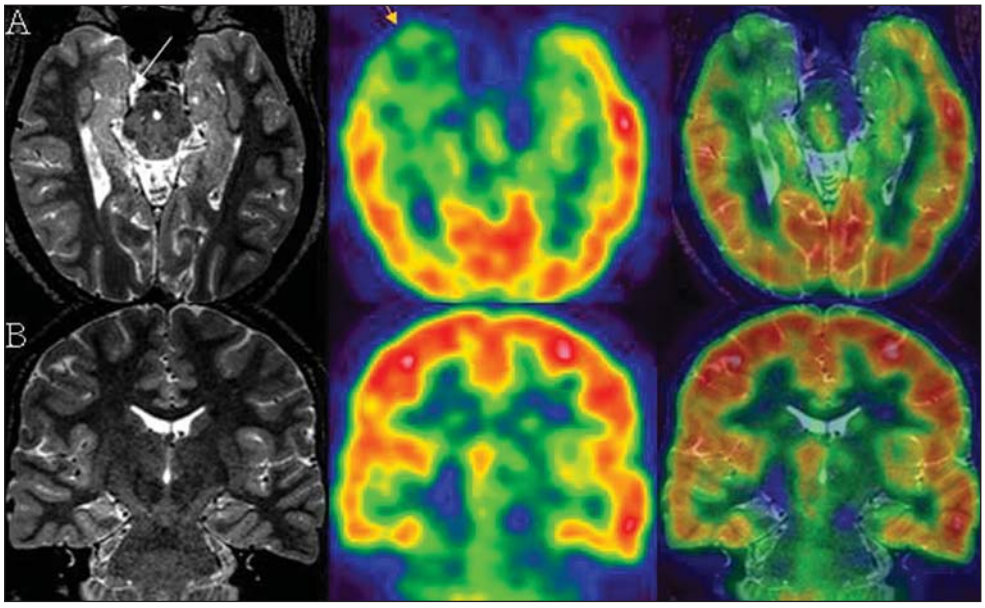

Figure 5. D.M.F.P, a 18-year-old patient with epilepsy refractory to drug therapy. MRI axial (**A**) and coronal (**B**) T2-weighted sequences, PET images and PET/MRI coregistration. PET demonstrates right temporal lobe hypometabolism associated with a subtle hypersignal on the right hippocampus at MRI T2-weighted sequences, suggesting mesial sclerosis (white arrow). Note that the hypometabolic change is more extensive than the dimensions of the anatomical finding, suggesting the presence of a functional deficit zone restricted to the right temporal lobe (better prognosis). The patient was submitted to surgery and is currently seizure-free.

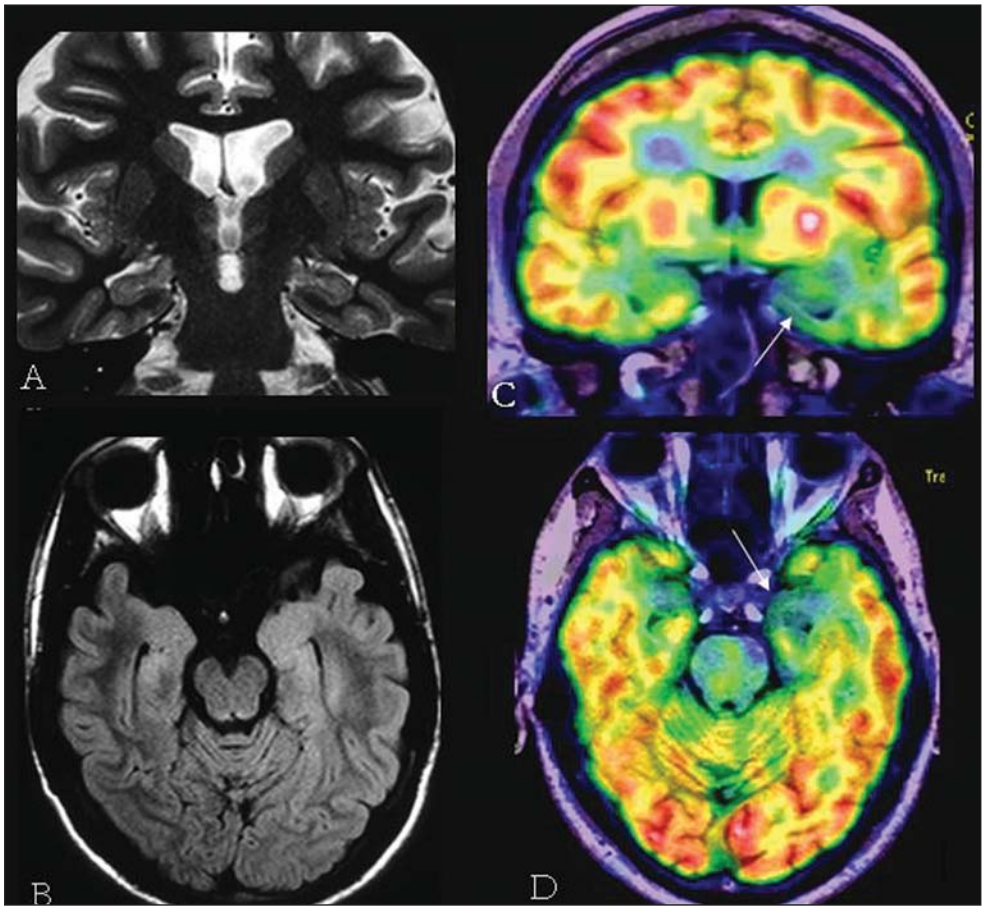

Figure 6. R.C.D., a 22-year-old patient with refractory epilepsy. MRI STIR (**A**) and FLAIR (**B**) sequences have not demonstrated any change. Coronal (**C**) and axial (**D**) sections of PET/MRI coregistration have demonstrated a hypometabolic area in the hippocampus at left (arrows). The patient was submitted to surgery and is currently seizure-free.

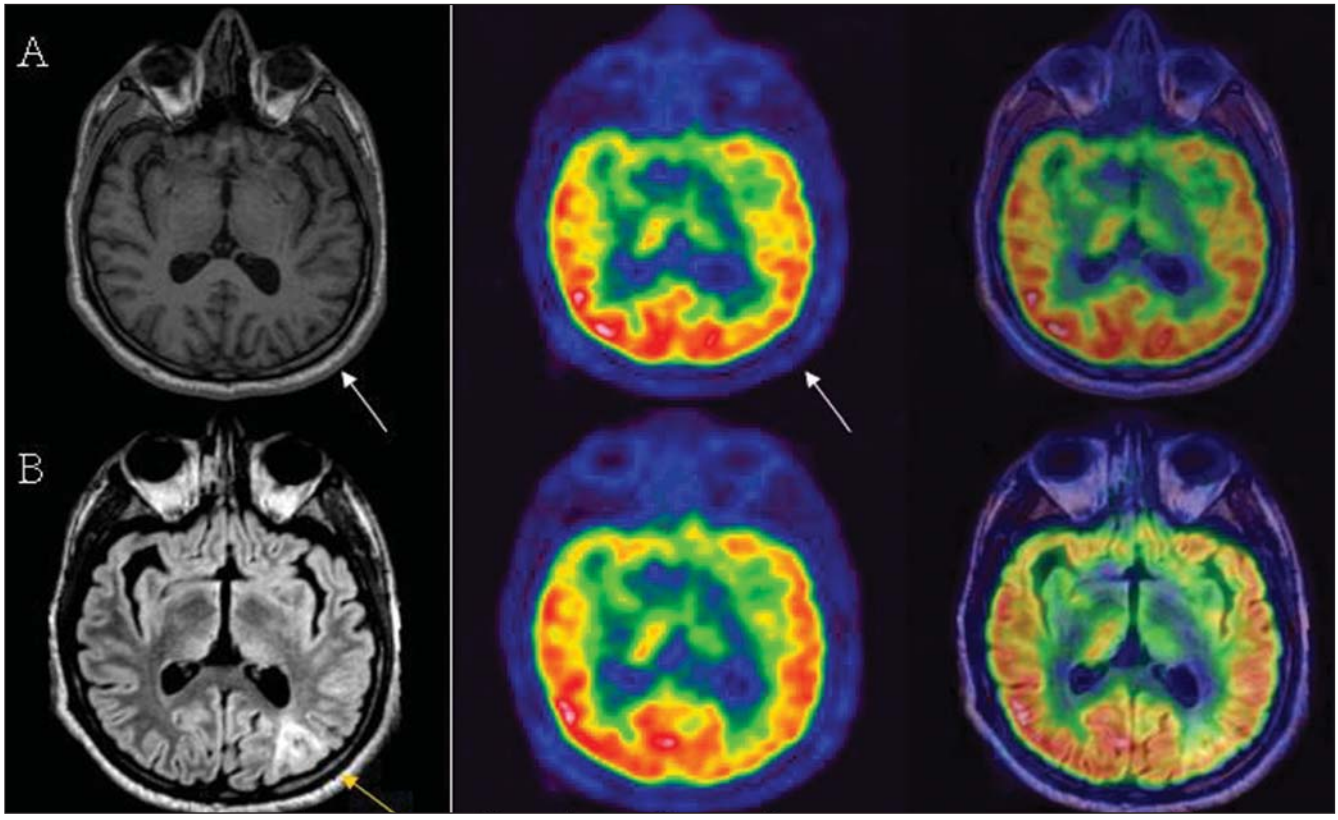

Figure 7. G.M.R., a 30-year-old patient with epilepsy refractory to drug therapy. On line **A**, a subtle hypo-uptake is observed in the occipito-parietal lobe at left, with no change at MRI T1-weighted sequence (white arrows). On the FLAIR sequence (line **B**) a cortical thickening can be observed in association with hypersignal compatible with cortical dysplasia (yellow arrow). The patient was submitted to surgery and is currently seizure-free.

cortical dysplasia (Figure 7), particularly in patients with Palmini type 1 focal cortical dysplasia, leading to an increase of 18% in the detection of this disease[9].

PET/MRI COREGISTRATION IN PARKINSONISM

Clinically differentiating among parkinsonian syndromes may be very difficult. Morphological studies such as CT and MRI are usually used to rule out other causes that may be leading to parkinsonism. FDG-PET may be utilized in dubious cases (Figure 8)[10].

Besides the already described Parkinson's disease, other types of parkinsonism such as progressive supranuclear palsy, multiple system atrophy and corticobasal degeneration may be investigated.

Radiotracers such as FDOPA-^{18}F and ^{11}C-Raclopride are more specific since they can indicate the function and integrity of pre- and postsynaptic dopaminergic terminals. However, these radiopharmaceuticals are not available yet to the Brazilian market.

CONCLUSION

Considering that the fusion of brain images with software is highly accurate, the most sensitive and specific modality for detection of metabolic changes (PET) can be associated with other modality with high spatial resolution, besides evaluating structures with soft tissues signal intensity with excellent contrast resolution (MRI). Therefore, brain PET/MRI coregistration becomes an extremely attractive noninvasive method for evaluating neurological diseases.

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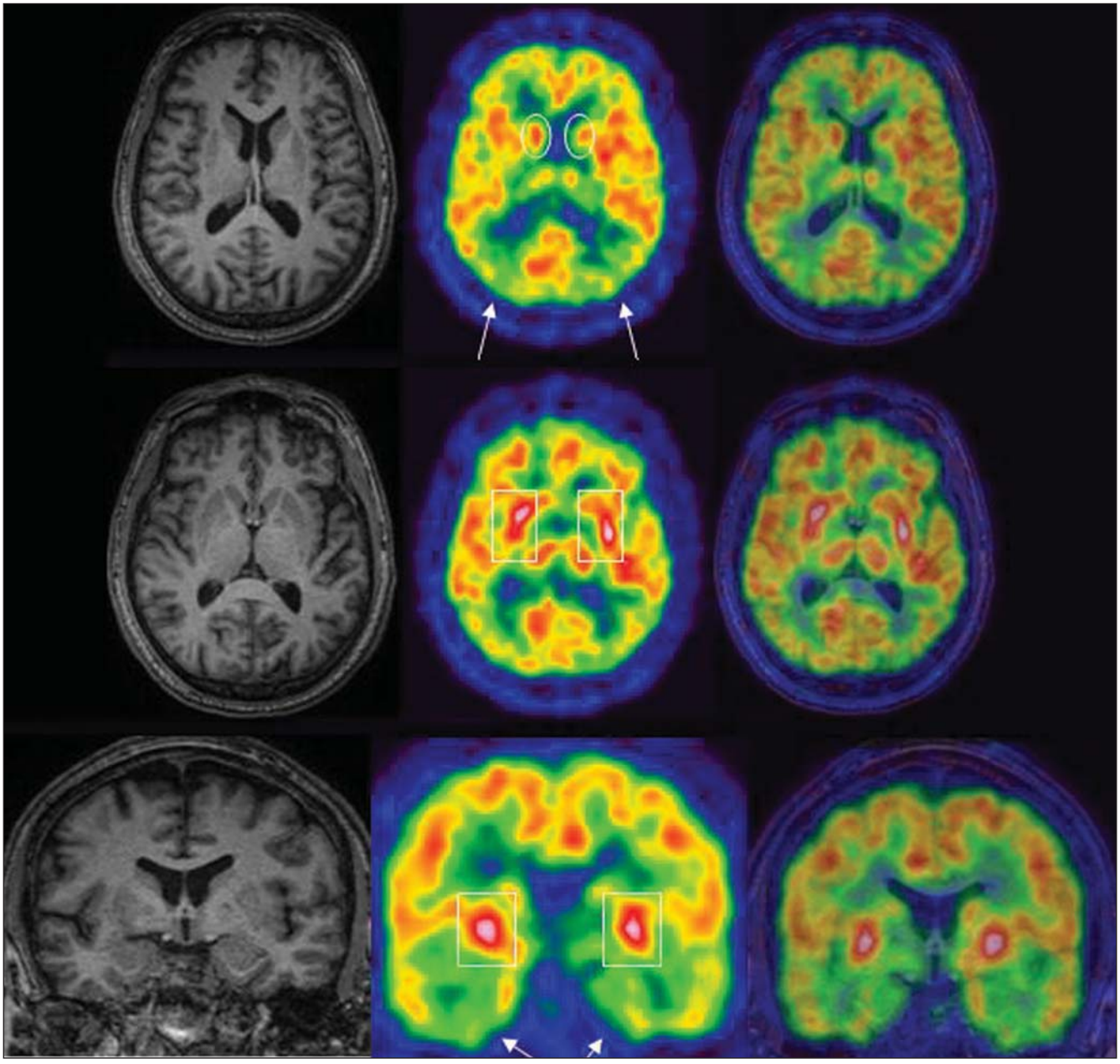

Figure 8. C.V., a 57-year-old patient with Parkinsonian syndrome. Hyper FDG uptake by the striated body can be observed (circles and rectangles) in association with temporoparietal hypo-uptake (arrows). Such findings are quite representative of Parkinson's disease. Por ser um estudo normal, a RM exclui a hipótese de outras causa de parkinsonismo, além de ajudar na localização precisa dos achados do PET.