Multimodal MRI in Parkinson's disease and parkinsonian syndromes

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Résumé

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The diagnosis of Parkinson's disease (PD) is mainly based on a set of clinical assessments that do not provide great accuracy. An approach measuring simultaneously MR parameters sensitive to complementary tissue characteristics (e.g. volume atrophy, iron deposition, and microstructural damage) could have great potential for investigating pathological changes in this disease. Multimodal MRI (mMRI) uses different MR parameters from T1-weighted images, R2* relaxometry and diffusion tensor imaging (DTI). T1-based volumetry allows characterizing brain atrophy. T2*- relaxometry is a sensitive and reliable technique for the quantification *in vivo* of iron levels (Péran et al., 2007, 2009). DTI provides quantitative parameters reflecting microstructural modifications, such as mean diffusivity (MD) or fractional anisotropy (FA). A first study in 2010 showed that mMRI could discriminate between PD patients and controls using combinations of three different markers i.e. relaxation rates (R2*) in the substantia nigra (SN), FA in the SN and MD in the putamen or caudate nucleus were able to distinguish PD patients from healthy controls (Péran et al., 2010). During the last decade, many works, using different iron-sensitive MRI methods, confirmed the importance of nigral iron increase in PD patients compared to controls (Guan, Xu and Zhang, 2017). Recently, quantitative susceptibility mapping (QSM) method demonstrated to be the most sensitive quantitative technique for detecting a significant increase of iron for PD (Barbosa et al., 2015). QSM is able to detect nigral iron increase even in prodromal stage of PD such as idiopathic rapid eye movement sleep behavior disorder (Sun et al., 2019). It is important to note that iron-content in the substantia nigra do not differ between PD and multiple system atrophy (MSA) patients (i.e. patient with atypical parkinsonism), and between MSA variants (Barbagallo *et al.*, 2016). Thus, iron nigral increase is not useful for differential diagnosis between PD and MSA. However, the putamina of MSA patients showed higher R2* values than those of PD patients (Barbagallo *et al.*, 2016; Péran *et al.*, 2018). Concerning the DTI markers in SN, a meta-analysis showed also that microstructural modifications measured by diffusion parameters located in SN but also in the corpus callosum, and the cingulate and temporal cortices could be useful to study PD pathophysiology and severity (Atkinson-Clement et al., 2017). Recently, new indices such as free water

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(FW) from diffusion weighted imaging showed very interesting results discriminating PD and controls (Planetta et al., 2016). Recently, Arribarat and collaborators showed a specific increase in R2* in the anterior SN concomitant with the specific increase in FW in the posterior SN suggesting different underlying pathophysiological processes (Arribarat et al., 2019). Recently, new MRI methods such as nigrosome Imaging and Neuromelanin Sensitive MRI (NMI) demonstrated to provide promising makers for parkinsonian syndromes. Even if it does not exist a standard method for NMI, previous results showed consistent differences between PD patients and controls (Pavese and Tai, 2018). High-spatial-resolution susceptibility MRI demonstrated its efficiency to detect the loss of nigrosome-1 in PD patients (Kim, Sung and Lee, 2019). Using a totally data-driven whole-brain multimodal pipeline based on support vector machine, Nemmi and colleagues showed that indexes derived from resting-state functional MRI alone could also discriminate between PD and HC (Nemmi *et al.*, 2019).

An important consideration is that MRI quantitative markers with good performances for diagnosis are not necessarily the best suited to monitor disease progression. More efforts need to be done in order to increase reliably and sensitivity of progression MRI markers of PD (Yang, Burciu and Vaillancourt, 2018). A standardized multimodal brainstem-dedicated MRI approach at high resolution able to quantify microstructural modification in brainstem nuclei would be a promising tool to detect early changes in PD.

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Mots-Clés: Imaging, MRI, Parkinson's Disease