MULTIPLE SCLEROSIS

Can Pittsburgh compound B PET imaging quantify demyelination in MS?

Pittsburgh compound B (PIB) could be used to quantify myelin loss in patients with multiple sclerosis (MS), according to a proof-of-concept study published in *Annals of Neurology*. The quantification of demyelination in this disease could “improve our understanding of the pathophysiology of MS ... and provide a means of evaluating new promyelinating strategies in future clinical trials”, says lead investigator Bruno Stankoff, of University Pierre et Marie Curie, Paris, France.

Demyelination is one of the main features of MS and MRI can detect demyelinating lesions; however, to date, no imaging technique is able to quantify demyelination or remyelination. Research has shown that derivatives of the stain Congo Red bind to both myelin and amyloid plaques. This finding led Stankoff

and colleagues to hypothesize that PIB, which is a thioflavin T derivative that binds to amyloid- β and also displays an affinity for myelin, could be used as a myelin imaging marker.

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To assess the ability of PIB to quantify demyelination, the researchers first determined whether PIB selectively bound to myelin *in vitro*. These investigators found that in mice, PIB staining was restricted to white matter tracts, labeling deep cerebellum white matter and the corpus callosum. A similar pattern of labeling was observed in postmortem tissue from patients with MS, except that within demyelinating lesions a lack of PIB staining was evident. In fact, within one lesion, PIB fluorescence was shown to distinguish between fully demyelinated areas, partially remyelinated areas and normal-appearing white matter.

In a separate set of experiments, the researchers showed that PIB staining was associated with myelin expression. Mutant shiverer mice do not express myelin basic protein, and have much less myelin than do wild-type mice. *In vivo* experiments showed that PIB

injected systemically selectively labeled white matter in wild-type mice. In shiverer mice, PIB fluorescence was markedly reduced in comparison with PIB labeling in control animals, indicating that the level of PIB staining correlated with myelin content in white matter.

PET imaging studies provided further evidence that PIB could be a potential imaging marker of myelin. The researchers showed that in baboons, PIB selectively labeled white matter, particularly in subcortical areas. Furthermore, in two patients with relapsing–remitting MS, PIB labeled white matter, except in several MS lesions identified by MRI. Myelin loss is extremely heterogeneous between lesions, and this observation was reflected in the current study, as “the decrease in PIB uptake was less pronounced in new gadolinium-enhancing lesions, suggesting that in new lesions demyelination is not fully established,” reports Stankoff. “This work emphasizes that PIB PET could be used to detect demyelination in diseases such as MS.”

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Original article Stankoff, B. *et al.* Imaging CNS myelin by PET in multiple sclerosis using the [^{11}C]PIB. *Ann. Neurol.* doi:10.1002/ana.22320

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