by 8-12 days of once daily dosing with BIIB014 in order to reach the steady state. Approximately 24 h after the last dose of BIIB014 subjects had a second [11C] SCH442416 PET scan. Studies were performed with a GE Discovery RX PET/CT and data were acquired for approximately 90 minutes. Statistical modeling of real-time receptor occupancy data was used to assist in prediction of the next dose level.

Results: Administration of 10-100 mg of BIIB014 orally over 8-12 days of dosing resulted in a range of receptor occupancies. Dose-Receptor occupancy curves were generated and full A2A site occupancy achieved at higher doses.

Conclusions: This study demonstrates for the first time that BIIB014 binds to A2a receptors in human brain. The data suggest that high occupancy of A2a brain receptors is consistently achieved at the higher dose range of BIIB014.

182

High-resolution MRI and iron-specific synchrotron X-ray analysis of the Parkinson's substantia nigra

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Objective: A powerful combination of high-field high-resolution magnetic resonance imaging (MRI) and X-ray absorption spectroscopy (XAS) is used to identify the distribution and nature of iron accumulation in the Substantia Nigra zona compacta (SNzc) in Parkinson's disease (PD) and normal elderly individuals.

Background: Regional accumulation of brain iron occurs in many neurodegenerative disorders, and provides a degree of natural contrast in MRI. Previous studies have shown statistically significant differences in relaxation parameters in the SN for PD versus controls, with differences attributed to altered iron concentrations. A combination of high-field high-resolution MRI and XAS is used to investigate the contribution of specific iron compounds to magnetic relaxation in unfixed post-mortem tissue. Cellular-level XAS will contribute to our understanding of iron mediated neurotoxicity, and correlation with MRI will allow the contribution of iron to magnetic relaxation to be determined, supporting non-invasive diagnosis and monitoring techniques.

Methods: Relaxation parameters T1, T2 and T2* are determined in unfixed tissue at a resolution of 60 μm × 60 μm × 80 μm in a Bruker 600 MHz instrument. Tissue is cryosectioned and analysed at 10 μm in-plane resolution using microfocus XAS to determine iron distribution and state.

Results: PD and control SN tissue was imaged at near-cellular resolution, with scan sequences optimised to permit calculation of the relaxation parameters within each slice. An example of an MGE sequence to obtain T2* is shown in Figure 1, with three different echo times (TE). X-ray mapping and spectroscopy analysis of cryosectioned tissue was performed at subcellular resolution, revealing local iron concentrations (Figure 2) and details of the associated iron compounds.

Conclusions: We have succeeded in obtaining high-resolution MRI and synchrotron analyses of unfixed tissues, which is necessary to avoid fixation-induced iron redistribution and phase alteration. Our approach has potential for application in a broad range of neurodegenerative disorders. The findings contribute to our understanding of altered iron storage in the PD SNzc, and to the interpretation of magnetic relaxation parameters in the SNzc of PD patients and age-matched controls (Figs. 1 and 2).

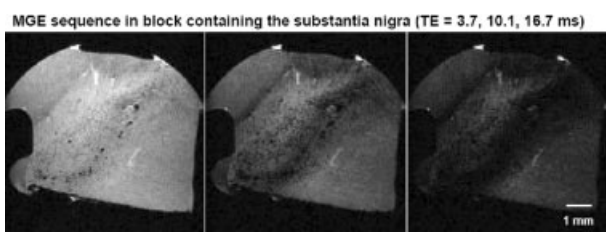

FIG. 1 (182).

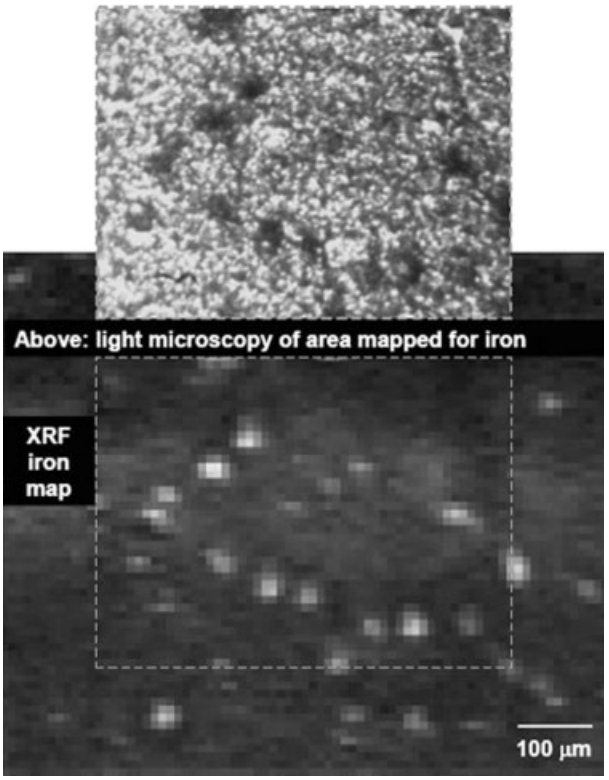

FIG. 2 (182).

183

Kansas experience with brain MRI after DBS hardware implantation

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Objective: To review the experience with and safety of brain MRI after DBS hardware implantation at the University of Kansas Medical Center.

Background: As per manufacturer guidelines the use of magnetic resonance imaging (MRI) after deep brain stimulation (DBS) hardware implantation is contraindicated in patients exposed to MRI using a full body radio-frequency (RF) coil, a receive-only head coil, or a head transmit coil that extends over the chest area. In addition, all RF pulse sequences must result in a displayed average head specific absorption rate (SAR) of less than 0.1 W/kg. In multiple centers, MRI is commonly performed after DBS hardware implantation. However, reports of permanent neurologic sequelae upon MRI scanning in a DBS patient together with dystonic-like movements in another have raised concerns regarding the use of MRI. We reviewed the safety of our past experience with brain MRI in DBS patients.

Methods: A retrospective review of records was done to identify MRI use and safety in patients with implanted DBS hardware followed at the University of Kansas Medical Center.

Results: All brain MRIs were performed using a 1.5 Tesla Siemens machine and a head send/receive coil. Two hundred and fifty six patients with implanted DBS hardware representing 399 implanted