FIGURE 435-3 [^{11}C]Dihydrotetrabenazine positron emission tomography (a marker of VMAT2) in healthy control (*A*) and Parkinson's disease (*B*) patient. Note the reduced striatal uptake of tracer, which is most pronounced in the posterior putamen and tends to be asymmetric. *(Courtesy of Dr. Jon Stoessl.)*

Genetic testing can be helpful for establishing a diagnosis but is not routinely employed as monogenic forms of PD are relatively rare and likely account for no more than 10% of cases (see discussion below). A genetic form of PD should be considered in patients with a strong positive family history, early age of onset (<40 years), a particular ethnic background (see below), and in research studies. Genetic variants of the glucocerebrosidase gene (*GBA*) are the most common genetic association with PD. They are present in 5–15% of PD patients, and in 25% of Ashkenazi PD patients. However, only about 30% of people with *GBA* variants will develop PD by age 80 years. Genetic variants of the *LRRK2* gene have also attracted particular interest as they are responsible for ~1% of typical sporadic cases of the disease. LRRK2 mutations are a particularly common cause of PD (~25%) in Ashkenazi Jews and North African Berber Arabs; however, there is considerable variability in penetrance and many carriers never develop clinical features of PD. Genetic testing is of particular interest for identifying at-risk individuals in a research setting and for defining enriched populations for clinical trials of therapies directed at a particular mutation.

Atypical, Secondary, and Other Forms of Parkinsonism Atypical parkinsonism refers to a group of neurodegenerative conditions that are usually associated with more widespread pathology than found in PD (e.g., degeneration of striatum, globus pallidus, cerebellum, and brainstem, as well as the SNc). These conditions include multiple system atrophy (MSA; **Chap. 440**), progressive supranuclear palsy (PSP; **Chap. 432**), and corticobasal syndrome (CBS; **Chap. 432**). As a group, they tend to present with parkinsonism (rigidity and bradykinesia) but manifest clinical differences from PD reflecting their more widespread pathology. These include early involvement of speech and gait, absence of rest tremor, lack of motor asymmetry, poor or no response to levodopa, and a more aggressive clinical course. In the early stages, some