# T1 weighted basal ganglia hyperintensities due to gadolinium deposition – a cautionary note

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Gadolinium-based contrast agents (GBCAs) have been widely used in clinical MR imaging since the late 1980ies. Overall, they were considered safe, apart from the well-known risk of nephrogenic systemic fibrosis, which could be counteracted by limitation of their use in patients with renal insufficiency.
Now however, there have been a number of publications describing the dose-dependent deposition of Gadolinium in the brain, manifesting as high signal intensities on non-enhanced T1-weighted images particularly in the dentate nucleus and globus pallidus, but also in the thalamus and the pons.[1-3]

Gadolinium is a rare-earth metal. GBCAs encompass two structurally distinct groups: linear and macrocyclic. Some studies suggest that the deposition occurs with linear rather than with macrocyclic compounds, and it is thought that linear agents are less stable, leading to dissociation of the contrast agent into free gadolinium. [3]
It appears that Gadolinium deposition is independent of age, sex, renal function and interval between applications, but happens also with intact blood brain barrier and correlates strongly with the dose applied.

Pathological evidence comes from several studies showing Gadolinium deposition in the brain.[1,2] Gadolinium was prominently clustered within the endothelial wall, but had also crossed the blood brain barrier and accumulated in the neuronal tissue interstitium. There were, however, no apparent histologic changes between contrast and control groups in hematoxylin-eosin–stained tissues samples with visual light microscopy.

The gravity of this issue is indicated by the fact that both the Food and Drug Administration (FDA) and the European Medicines agency are currently investigating the risk of GBCAs. The communications issued by the FDA and the National Institutes of Health (NIH) involve careful consideration of the indication of GBCAs, and preferential use of macrocyclic agents.[4]

This observation is potentially significant for movement disorder neurologists and practitioners for the following reasons: Firstly, T1-weighted hyperintensities within the dentate nucleus and the globus pallidus would typically evoke a differential diagnosis of manganese, calcium or copper deposition due to manganese transporter mutations or hemodialysis, Fahr´s syndrome or Wilson´s disease. Gadolinium deposition has now to be added to this list, particularly in patients who also have a past history of multiple contrast-enhanced MRI scans. If such patients newly develop a movement disorder, the MRI appearance can be a red herring.
Secondly, so far it is unknown that the Gadolinium deposition has a clinical correlate or leads to adverse effects. To date, there are no reports indicating that GBCA exposure might have caused movement disorders. However, such symptoms might have been unrecognised or attributed to the disease which lead to MR investigations with multiple doses of GBCAs in the first place, e.g. multiple sclerosis.
There is one study evaluating the incidence of parkinsonism in patients who underwent MR imaging with and without GBCAs.[5] The authors did not find a significant difference, but there are some limitations to this study such as the fact that patients were not systematically assessed, that the majority of patients had a single GBCA administration only, that they type of GBCA was not specified and that actual Gadolinium deposition was not ascertained.
Other symptoms associated with lesions of the globus pallidus or the dentate nucleus, such as dystonia, abulia or cerebellar signs have not been investigated as yet.
In contrast, a gadolinium toxicity support group published a survey, in which half of the participants reported balance problems, and all participants complained about chronic, mostly neuropathic, pain. Although no scientific conclusion can be drawn from this, it underlines the necessity to systematically approach this matter as it has manifold medical and legal implications.

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