

Title: Dopamine Beta-Hydroxylase Deficiency *GeneReview* – Diagnosis: Additional Tests/Findings

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Physiologic Tests of Autonomic Function

- Muscle sympathetic nerve activity measured by microneurography is normal.
- Spectral analysis of beat-to-beat values of R–R interval and blood pressure indicates that individuals with DBH deficiency have greatly reduced supine resting blood pressure variability in the low-frequency component, a marker of sympathetic tone, but a relatively normal high-frequency component of heart rate variability, a marker of cardiac vagal tone [Okamoto et al 2012].

Pharmacologic Findings

There is a several-fold hypersensitivity to α 1-adrenoceptor agonists and β -adrenoceptor agonists:

- Propranolol, a β -adrenergic antagonist, does not lower heart rate.
- Intravenous atropine raises heart rate by 40-60 beats per minute.
- Pindolol, a β -adrenergic antagonist with some sympathomimetic activity, raises heart rate.
- Clonidine, a partial agonist of α 2-adrenoceptors that acts centrally to reduce sympathetic outflow and lower blood pressure in normal individuals, can also exert peripheral pressor effects by stimulation of vascular α 2-adrenoceptors. Individuals with DBH deficiency have no drop in seated mean arterial pressure following the administration of clonidine. On the contrary, significant increases in blood pressure are seen with higher doses of this agent.

Plasma DBH Enzymatic Assay

In addition to catalysis of DA, DBH catalyzes the hydroxylation of tyramine and other phenylethylamine derivatives. DBH is released into the synaptic cleft during vesicular exocytosis. A fraction of the DBH released into the synaptic cleft spills over into the blood, where it can be detected.

- Plasma levels of DBH enzyme activity vary over a wide range in different individuals, and most individuals with reduced plasma DBH enzyme activity do not have DBH deficiency.

- DBH enzyme activity is undetectable in the blood of individuals with DBH deficiency [Robertson et al 1986, Man in 't Veld et al 1987].

Assays for DBH enzymatic assay:

- A spectrophotometric procedure based on the enzymatic conversion of the substrate tyramine into the product octopamine in the presence of excess ascorbate, sodium fumarate, catalase, N-ethylmaleimide, and pargyline. The octopamine is then oxidized to *p*-hydroxybenzaldehyde.
- A two-step enzyme radioassay that incorporates conversion of phenylethylamine to phenylethanolamine by DBH, then metabolism of phenylethanolamine to N-methylphenylethanolamine by phenylethanolamine N-methyltransferase (PNMT) and radioactive S-adenosylmethionine.
- High-performance liquid chromatographic (HPLC) procedures.

References

Man in 't Veld AJ, Boomsma F, Moleman P, Schalekamp MA. Congenital dopamine-beta-hydroxylase deficiency. A novel orthostatic syndrome. *Lancet*. 1987;1:183-8.

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