



Diagram of a noradrenergic axonal terminal showing the release and re-uptake of norepinephrine

Figure 1. Diagram of a noradrenergic axonal terminal showing the release and re-uptake of norepinephrine. (a) Norepinephrine (NE) is synthesised from tyrosine – via hydroxylation to form dihydroxyphenylalanine (dopa), decarboxylation to form dopamine, and hydroxylation to form NE – and (b) stored in vesicles. (c) As a result of an appropriate stimulus (not shown), NE is released into the synaptic cleft. (d) Released NE activates the adrenergic receptors located on the postsynaptic membrane (α_1 , β_1 and β_2) and also (e) presynaptic membrane (α_2 , β_2), and causes (f) postsynaptic reactions such as protein kinase activation and protein phosphorylation. (g) The norepinephrine transporter (NET) is responsible for re-uptake of the NE in the synaptic cleft, and terminates its action. (h) After re-uptake by NET, a small portion of the NE is re-stored in vesicles [following uptake by vesicular amine transporter 2 (VMAT₂)]; (i) the rest is metabolised in the mitochondria by the enzyme monoamine oxidase (MOA), and (j) the end product dihydroxyphenylglycol (DHPG) is released into the circulation. (k) A small portion of the synaptic NE leaks into the circulation, or (l) is taken up by another system (uptake 2) and (m) metabolised to form normetanephrine (NMN). Because 70–90% of the synaptic NE is taken up by NET, a blockade of NET is likely to produce a shift towards the NMN pathway and away from the DHPG pathway. A high ratio of plasma NMN to DHPG might prove useful in measuring this blockade (**fig001drn**).