Basic catecholamine structure and its relationship to their function

The Catechol Ring

The catechol ring is a mere 6-carbon phenyl ring. 3,4-dihydroxybenzene, to be nerdishly precise. What makes it catechol is the presence of the exciting hydroxyl groups at the 3 and 4 position. Otherwise, its just boring old phenol.

These two hydroxyl groups are what enables the catechol ring to be effective at the beta and alpha catecholamine receptors.

β- Phenylethylamine, he who begat all catecholamines and their ilk

Mighty phenylethylamine is the grandfather of all these sympathomimetic drugs, ranging from inotropes to antidepressants bronchodilators and party pills. This basic backbone is what its all about.

The absence of hydroxyl groups permits phenylethylamine to penetrate the blood brain barrier.

β- carbon atom
Hanging an extra hydroxyl group here tends to decrease lipid solubility, and thus decrease CNS penetration
ANY additional group here GREATLY increases alpha and beta receptor agonist activity.

Alpha- carbon atom
Any additional groups here block the action of MAO, and thus increase the half life. Drugs with this structure dwell longer at the synapse, and act as indirect sympathomimetics

Amine group
A methyl group here confers alpha selectivity.
The smaller the group, the more alpha effect there is.
Increase of the alkyl substituent on the amine group increases the molecules preference for beta receptors instead of alpha.
The bigger the alkyl substituent, the more beta effect there is.

The Aromatic Ring and Catechol hydroxyl groups
It all depends where you substitute the extra groups.
You need two to have the maximum receptor affinity.

However, having two polar hydroxyl groups decreases lipid solubility and keeps you out of the brain. Having no groups like phenylethylamine results in good CNS penetration.
Positions 3 and 5 = beta-2 selectivity in compounds with large amino substituents.

From Peck and Hill “Pharmacology for Anaesthesia and Intensive care” as well as the mighty “Handbook of Pharmacology and Physiology in Anaesthetic Practice” by Stoelting and Hillier. A