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The human brain faces a variety of computational tradeoffs, such as the flexibility/stability tradeoff. In this lecture, Dr. Cools will argue that the major ascending neuromodulatory systems originating from the midbrain are well suited to dynamically regulate these computational tradeoffs depending on our constantly changing task demands. Her working hypothesis follows from a number of general principles of chemical neuromodulation, which she will illustrate by reviewing evidence from recent pharmacological PET/fMRI studies on (cost/benefit decision making about) cognitive control. These studies also begin to elucidate the mechanisms underlying the huge variability in catecholaminergic drug effects across different individuals and behaviors.