system can be described as agonists, partial agonists, antagonists, positive allosteric modulators, negative allosteric modulators, and inverse agonists.

Agonists and Partial Agonists

Compounds that elicit the same functional biological response as the natural ligand are referred to as agonists. The biological activity of an agonist is defined by its intrinsic activity, which is the ability of a test compound to activate a macromolecular target as a function of receptor binding and produce efficacy. Efficacy, in turn, is the ability of a population of macromolecular target molecules in a given biological system to elicit a maximum response when occupied by an adequate number of agonist molecules. For the purposes of comparing sets of test compounds, agonist activity is generally defined with multiple terms that described its ability to bind to the biological target (IC_{50}), induce a functional response (EC_{50}), and the level of response relative to the natural ligand. (Percent efficacy: The natural ligand's functional response is defined as 100% efficacy.) It is important to understand that a given agonist may not provide the same level of biological response as that observed with the natural ligand, in which case the test compound is described as a partial agonist.[9] This difference in functional activation of a biological system is independent of a compound's IC_{50} and $EC_{50.}$ Thus, it is possible for two compounds to have nearly identical IC_{50}s and EC_{50}s, but different functional impact, as their percent efficacy relative to the natural ligand is different (Figure 4.3). In some cases, partial agonists can effectively compete with the natural ligand, effectively lowering the functional response observed in a biological setting.

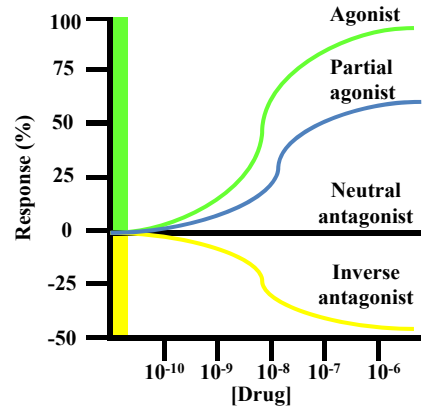

FIGURE 4.3 Full agonists (green) induce GPCR signaling equal to that of the endogenous ligand, while partial agonists (blue) activate GPCR signaling to a lesser extent. Neutral antagonists (black) do not induce GPCR activity, but will block agonist activity. Inverse agonists suppress basal activity of a constitutively active GPCR.