Agonistic and Antagonistic Drug Action

Abstract

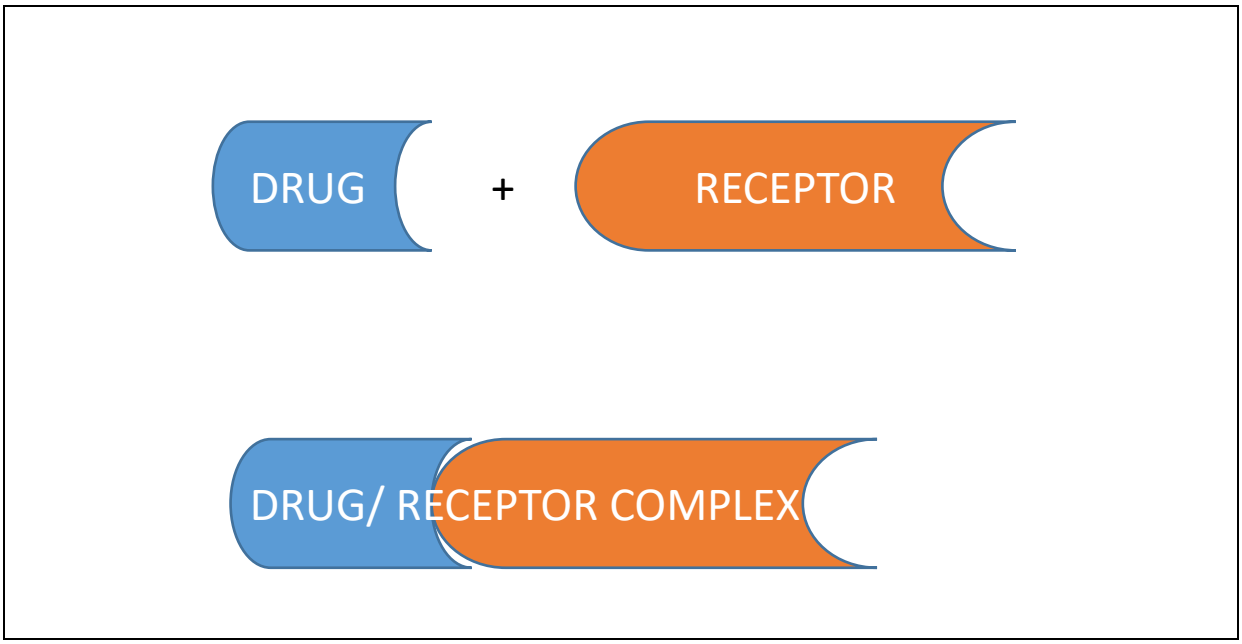
In this article in the series of 'bite sized' pharmacology, we will look at the concepts of agonism and antagonism with regards to drug action. These pharmacodynamic actions affect how a drug acts at its target site and the ensuing response to the drug.

Knowledge of agonism and antagonism can assist the prescriber in drug choice. Knowing where a drug works, whether it is an agonist or antagonist and whether any other drugs have the same or opposing actions at that site of action is a crucial part of safe prescribing practice. It also helps the prescriber understand why some drugs cannot be prescribed in combination.

Drug Action

In the most simple terms drugs can either be agonists or antagonists at their target sites. The target sites can be either receptors, ion channels, enzymes or transport systems. These were discussed in detail in 'Introduction to Pharmacodynamics' (Nurse Prescribing 2017 Volume 15 No4). These concepts of agonism and antagonism are only properly applicable using receptors as an example of a site of action (see Figure 1). When drugs bind to receptors they are said to occupy the receptor site. Agonists bind to the site and cause an effect. The amount of an agonist drug occupying the receptor site relates to the magnitude of response to the drug itself. In simple terms the more of a drug occupying a receptor, the greater the response. Antagonists bind to receptor sites but do not cause an effect. More often than not they bind and prevent the receptors normal agonist form occupying the site. When we have drugs binding to other sites, such as enzymes, ion channels and transport systems we refer to them as inducers and inhibitors rather than agonists and antagonists.

Figure 1 Basic receptor theory



Exercise

Using pharmacologically available resources such as textbooks, the BNF or online electronic medicines compendium, find out, for a drug from your area of practice where its site of action is AND whether the drug is an agonist (inducer) or antagonist (inhibitor) at the site of action.

Agonism and Agonists

Agonists are chemical mediators that bind to their targets and form a chemical-receptor complex. This is called receptor occupancy. Agonists activate the receptors to produce a response. A full agonist will activate a full response (positive efficacy) and a partial agonist will activate a partial response (partial efficacy). Inverse agonists are drugs that bind to the same receptor site as agonists but produce an opposing effect (negative efficacy). See figure 2 for diagrammatic representation of the responses. Agonists can be termed as follows

- Endogenous- coming from inside the human body such as neurotransmitters or hormones and are naturally produced by the body. An example is insulin.
- Exogenous- coming from outside the human body such as drugs and medicines or drugs given to mimic the body's normally produced agonists. An example can be any synthetic drug or synthetic insulin as a mimic.

Potency

This is a term used to describe the amount of a drug agonist required to produce a biological response at the receptor. The more potent the drug is, the less of it will be required to occupy the receptors to produce its maximum effect. Some drugs from the same class of drug family have similar efficacy but different potency. Statins are a good example. Simvastatin and atorvastatin have similar efficacy but atorvastatin has a greater potency. This is why the doses of the two drugs required to elicit maximum response is different.

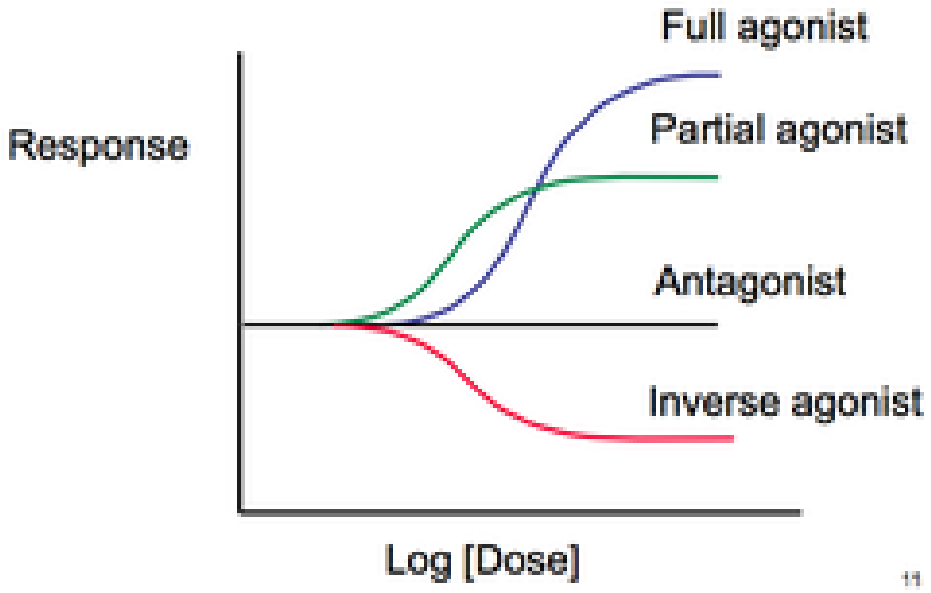


Figure 2 Log dose response curves CAN WE COVER UP THE SMALL 11 ON THE PICTURE?

Antagonism and Antagonists

Antagonists are drugs that bind to their targets and form a drug receptor complex, but without causing activation or response. They can block the receptor to its endogenous activator, thereby blocking normal function (zero efficacy). See figure 2 for diagrammatic representation of the responses.

Receptor occupancy by antagonists is important if the drug is a competitive antagonist -i.e. it competes for occupancy with another drug or with the receptor's normal mediator. The amount of drug occupying will determine any response.

Antagonists can be termed as follows

- Competitive antagonists: drugs that bind in a reversible manner to their chemical targets and prevent activation by the normal target agent by competing with the agonist for receptor occupancy. The order of binding of the agonist or antagonist is governed by their affinity for the receptor. The drug with the higher affinity (agonist or antagonist) will bind preferentially. This preference can be overcome by increasing the dose of one of the ligands.
- Non-competitive antagonists: drugs that do not necessarily bind to the chemical target but can bind at a point in the chain of events block target activation. This is known as allosteric modulation. It is non-competitive because their effects cannot be reduced or rendered zero by increasing the dose of agonist.

It is important to be aware of whether your drugs are agonists or antagonists where this is known, for example

The commonly used asthma and COPD drug salbutamol is termed as a beta adrenoceptor agonist.

The antihypertensive class of drugs that includes propranolol are termed as a beta adrenoceptor antagonist.

If these drugs were given concomitantly we could see an interaction effect that may reduce the efficacy of one drug over the other. This does however depend on specificity and we shall look at that in more detail below.

Exercise

Using pharmacologically available resources such as textbooks, the BNF or online electronic medicines compendium, find out, for a drug from your area of practice if the drug is an agonist or antagonist at the site of action and see if there are any other drugs that have the opposite effect at the site of action that you need to be aware of. You may find the interactions section (called appendix 1) of the BNF can help you with this exercise by highlighting types of interaction.

Drug Specificity

Very few drugs are specific for their intended targets within the body. A prescriber will give a drug with a specific action in mind, for example salbutamol. Salbutamol is a beta2 adrenoceptor agonist. This means it has its main action at beta2 adrenoceptors in the bronchi. This gives us its desired effect as a bronchodilator which eases breathing in asthma. However the action of salbutamol is not that specific and can act on other beta2 adrenoceptors in the

body as well as on other beta adrenoceptors (including beta1), especially if given in higher doses leading to increased receptor occupancy. This is the reason that some of the side-effects of drugs can be seen. In the case of salbutamol, action at other beta adrenoceptors can lead to palpitations and increased occupancy at non-bronchial beta adrenoceptors can cause tremor. Propranolol is a beta1 adrenoceptor antagonist. This means it has its main action at beta1 receptors in the vascular smooth muscle. This gives us its desired effect of reducing blood pressure. However the action of propranolol is not that specific and it can act on other beta1 adrenoceptors in the body and at other beta adrenoceptors (including beta2), especially in higher doses. This can lead to side effects such as bronchoconstriction and wheeze.

Exercise

Using pharmacologically available resources such as textbooks, the BNF or online electronic medicines compendium, find out, for a drug from your area of practice if the drug is specific for its target site.

This has been a brief introduction to the concepts of agonism and antagonism. In future articles in this series we will explore other aspects of pharmacology in more detail, looking at drug disposition, bioavailability and efficacy.

CAN WE PUT IN A PICTURE TO MAKE THIS MORE APPEALING IF WE HAVE SPACE? I SUGGEST A FRONT COVER BNF NEAR ONE OF THE EXERCISES?

References & Further Reading

Barber and Robertson (2015) Essentials of Pharmacology for Nurses 3rd Edition McGraw Hill London

BNF Online https://www.bnf.org/products/bnf-online/

Electronic Medicines Compendium https://www.medicines.org.uk/emc/

Robertson, D. (2017) Introduction to Pharmacodynamics. Nurse Prescribing 15:4