Chapter 8. The Adjustment

Major Points

• The Adjustment is a method for using existing pharmaceutical drugs to tweak a person's Big Three strengths closer to optimal, mid-range values (i.e., not too strong or too weak). Doing so not only treats nearly every type of mental illness but also may improve quality of life for over 50% of the population.

• The Adjustment affects many more traits than just mood, though mood is an important trait that is affected.

• To perform The Adjustment properly in a given person, two drugs are often needed to tweak ser and nore independently, often in opposite strength directions.

• Most people, whether they suffer from a mental illness or not, have weak ser and/or strong nore.

• If the field of psychiatry were to implement The Adjustment in nearly every person seeking mental health treatment, that treatment would be vastly improved.

The Adjustment is a method whereby existing pharmaceutical drugs are used to tweak the strengths of ser and nore (and possibly dop) closer to optimal, mid-range values. The current theory hypothesizes that doing so not only treats nearly every type of overt mental illness, but also may improve quality of life, possibly dramatically, for many people (expanded dysthymics, who may constitute over 50% of the population—more on this subject in Chapter 11) who are considered normal. As we have been discussing, performing The Adjustment—a type of Big Three strength modification—affects many more traits than just mood, though mood is an important trait that is affected. An adjustment in the right direction should make people better (higher self-reported quality of life, possibly also apparent to an outside observer), and an adjustment in the wrong direction should make people worse. Adjusting dop is a secondary, less important adjustment. I don't see strong dop as pathological, unless it's so strong that it underlies mania/marked hypomania and mood cycling. However, weak dop, which may be associated with underfunctioning of the frontal lobes resulting in diminished thinking, may be pathological. As we'll discuss in the next chapter, all six categories of drugs for The Adjustment exist and are FDA approved in the United States: 1) drugs that strengthen ser, 2) drugs that weaken ser (many of which also weaken dop), 3) drugs that strengthen nore, 4) drugs that weaken nore, 5) drugs that strengthen dop, and 6) drugs that weaken dop (most of which also weaken ser).

For many people The Adjustment will involve polytherapy—which is the use of more than one drug at a time—since both ser and nore (and even dop) may have to be adjusted, possibly in opposite strength directions. In such a case, adjusting both ser and nore up or down can produce a synergistic effect that may be different not only in magnitude, but also in character, than adjusting either one alone, in that the net effect is

different than the sum of its parts, and this is not due to interactions in metabolizing the drugs.

For example, if a person has weak ser and strong nore, then, in order to perform The Adjustment, one drug will be needed to strengthen ser and another drug will be needed to weaken nore. If you think you may have bipolar disorder, definitely start the nore or ser weakening drug first, because a nore or ser strengthening drug can trigger mania or hypomania in bipolars, which is not a good thing, and it is controversial whether to use such a strengthening drug at all in bipolar disorder. Even if you don't have bipolar disorder, I don't recommend starting both drugs at the same time, mainly because it will be hard to tell which drug is doing what, including the possible side effects, or whether both drugs are even necessary. Start one first, such as the nore weakener clonidine (class of drugs: alpha 2 adrenergic agonists), assessing whether it has a positive effect on quality of life, and if so wait a month or so to let it take full effect. The dose of the drug can also be tweaked, and you should wait a month or so for full effect, though too high a dose may be unpleasant and not recommended. If, on the other hand, there is no response at all to this first drug, then try another drug from the same class, such as the nore weakener guanfacine. If the drug has a negative effect on quality of life, then perhaps that drug and that class of drugs is not recommended for you. After you and your doctor have decided what to do with the first type of drug, including whether to even take it, then the second type of drug can be added in a similar manner.

Based on people's personality traits, all forms of adjustments may be needed for real people: all combinations of weak, medium (mid-range), and strong for each of the Big Three may exist in the population, except both strong ser and strong nore. It's as if there is a practical limit to the sum of ser and nore strength in the brain. Moreover, the most common pair of strengths is weak ser and/or strong nore.

I'm not arguing that Big Three adjustments are the only neurochemical adjustments that affect quality of life, just that they are adjustments that will affect everyone or nearly everyone in principle with the existing drugs—or with potential new drugs with similar or dissimilar Big Three mechanisms. It should also be noted that the range of change of Big Three strengths that the current drugs can produce is probably much smaller than the range of genetic differences of Big Three strengths in the population, but large enough to cause a profound change in quality of life in at least some people. Similarly, the individuals with the greatest potential response to The Adjustment are probably those with the least optimal ser and nore strengths.

100% of people would respond to a Big Three strength adjustment, but at this time probably not everyone can have these strengths adjusted with the existing drugs. For example, in a given person the existing drugs may not bind properly to her particular Big Three receptors. It's also possible that some people could never have their strengths adjusted by *any* future drug, though this percentage is probably close to zero if not zero.

How could psychiatrists go about implementing The Adjustment most effectively in a given person? Well, blood levels of the Big Three, which researchers have been measuring for many years, if they indeed reflect brain strengths, would be useful in deciding how to adjust a person as well as provide monitoring of the effects of The Adjustment. Brain imaging techniques, such as PET and MRI scans, may also indicate how to adjust a given person as well as provide monitoring of the effects of The

Adjustment. And assessing Big Three personality traits, if this can be done accurately and consistently, may also be useful for implementing and monitoring The Adjustment.

The Adjustment may be the neurochemical basis for making some depressed people 'better than well', as in Peter Kramer's patients in *Listening to Prozac*—in other words, his patients had weak ser, and possibly weak dop. However, the potential benefits of the technique must be weighed against the risk of causing a 3+ year brain freeze like I accidentally suffered while The Adjustment was being performed on me (see My Case Study—Chapter 2). Other people besides myself have probably unwittingly experienced the full adjustment while being treated for psychiatric and non-psychiatric conditions simultaneously, since many of the relevant drugs have non-psychiatric uses. The Adjustment may also be a way to adjust the neural integrator, if the integrator exists (see Chapter 2).

A common misconception about antidepressants—a subset of The Adjustment drugs—is that they only deaden the emotions. When used properly, I believe they can heighten emotions, and in general improve quality of life. And maybe only drugs that weaken ser and/or nore (or only those that deactivate ser and/or nore postsynaptic receptors, such as Zyprexa) can cause the brain freeze, whereas drugs that strengthen ser and/or nore cannot. More generally, the brain freeze may occur when the strengths of ser and nore are adjusted in opposite directions—either closer to or farther away from optimal, mid-range strengths—and the magnitude of such an adjustment exceeds some limit. Nevertheless, the benefits to those who are suffering from long-term mental illness certainly make it worth their while to work with a health care professional to implement, at the very least, some component of The Adjustment.