Question 1: Why and where do benzodiazepines reduce anxiety?

Answer: The proper action of GABAergic interneurons is critical to the proper functioning of the brain. $GABA_A$ receptors are GABA-gated chloride channels that mediate fast IPSPs. In addition to its GABA binding site, the $GABA_A$ receptor contains sites where chemicals can act to powerfully modulate its chloride ion channel function. Benzodiazepines bind to one of these sites and act to make GABA highly effective in opening the channel and producing inhibition. A study of patients with panic disorder using PET imaging demonstrated a reduced number of benzodiazepine binding in regions of frontal cortex that show hyperactive responsiveness during anxiety. Therefore, the calming actions of benzodiazepines may be due to the suppression of activity in the brain circuits used in the stress response.

Question 2: Depression is often accompanied by bulimia nervosa, which is characterized by frequent eating binges followed by purging. Where does the regulation of mood and appetite converge in the brain?

Answer: In severely depressed patients, the HPA axis is hyperactive. Blood cortisol levels are elevated as is the concentration of CRH in the CSF. The activation of the hippocampal glucocorticoid receptors by cortisol leads to feedback inhibition of the HPA axis. In depressed patients, this feedback is disrupted, explaining why HPA function is hyperactive. In addition, the regulation of mood and appetite converge at the hypothalamic-pituitary-adrenal (HPA) axis. Therefore, hyperactivity of the HPA axis may also be responsible for the disruption in feeding behavior termed as bulimia nervosa.

Question 3: Snuggling with your mom as a baby might help you cope with stress better as an adult. Why?

Answer: Tactile stimulation activates the ascending serotonergic inputs to the hippocampus, and the serotonin triggers a long-lasting increase in the expression of the glucocorticoid receptor gene. More glucocorticoid receptors equip the organism to respond to stressors as adults. The beneficial effect of tactile stimulation is limited to a critical period of early postnatal life. Stimulation in adults does not have the same effect.

Question 4: What three types of drugs are used to treat depression? What do they have in common?

Answer: The most popular antidepressant drugs include:

(1) Tricyclic compounds, such as imipramine, which block the reuptake of both norepinephrine and serotonin by transporters.

(2) SSRIs, such as fluoxetine, which act only on serotonin terminals.

(3) NE-selective reuptake inhibitors, such as reboxetine, and

(4) MAO inhibitors, such as phenelzine, which reduce the enzymatic degradation of serotonin and norepinephrine.

All of these drugs elevate the levels of monoamine neurotransmitters in the brain, but their therapeutic actions take weeks to develop.

Question 5: Psychiatrists often refer to the dopamine theory of schizophrenia. Why do they believe dopamine is linked to schizophrenia? Why must we be cautious in accepting a simple correlation between schizophrenia and too much dopamine?

Answer: According to the dopamine hypothesis of schizophrenia, psychotic episodes in schizophrenia are triggered specifically by the activation of dopamine receptors. A link between the mesocorticolimbic dopamine system and schizophrenia has been made on the basis of two main observations. The first relates to the effects of amphetamine in otherwise healthy people. Amphetamine enhances neurotransmission at catecholamine-utilizing synapses and causes the release of dopamine. An overdose may lead to a psychotic episode with positive symptoms that are virtually indistinguishable from those of schizophrenia. The second reason to associate dopamine with schizophrenia relates to the CNS effects of drugs that are effective in reducing the positive symptoms of the disorder. The neuroleptic dosages effective in controlling schizophrenia correlate well with the binding affinities of the drugs for D2 receptors. Therefore, we must be cautious in accepting a simple correlation between schizophrenia and too much dopamine. There seems to be more to the disorder than an overactive dopamine system. One indication is that newly developed antipsychotic drugs, like clozapine, have little effect on D2 receptors. Another indication is that there is more to schizophrenia than dopamine comes from the behavioral effects of phencyclidine (PCP). PCP intoxication is typically accompanied by many symptoms of schizophrenia, both positive and negative. However, PCP has no effect on dopaminergic transmission.