2012

The notion that new neurons are added to the adult brain has been the subject of controversy ever since the mid-1980s, when Fernando Nottebohm's lab reported that adult neurogenesis occurs in the canary brain and is functionally linked to seasonal acquisition of new song. Early debates focused on whether or not this phenomenon was restricted to birds, but then came incontrovertible evidence of adult neurogenesis in rodents, specifically in the dentate gyrus of the hippocampus and the olfactory bulbs. Now, almost 30 years later, the debate is centered on the extent to which these findings in birds and rodents generalize to non-human primates and humans, and if they do, whether there are temporal and/or spatial (brain region) limits to postnatal neurogenesis in monkeys and humans? Nottebohm himself has stayed out of the fray, maintaining that the important question is how species solve problems that are relevant to them in nature. On the other hand, Pasko Rakic has taken the viewpoint that adult neurogenesis, particularly in the hippocampus and cortex, would in principle be evolutionarily disadvantageous to humans, because as a species, it would not be a good idea to sacrifice longevity of memory in the service of plasticity. Rakic was a long-time and staunch disbeliever of any type of adult neurogenesis in non-human primates and humans, but made small concessions every now and then, like the time when he himself found adult-born neurons in the hippocampus of macaque monkeys. Rakic has been particularly critical of work by Elizabeth Gould in rodents and non-human primates, and work by Fred Gage in humans has also figured prominently into the debate. A 2001 article from The New Yorker accompanies this question; it provides a human context for the debate as it stood some 10 years ago. Please address the following questions in this ongoing controversy.

1. What is the evidence for a gradual decrease in the prevalence of *adult* neurogenesis as one moves up the phylogenetic tree from birds to rodents, to monkeys, to humans?

2. To the extent that you find evidence for *postnatal* neurogenesis in rodents, non-human primates, and humans, does postnatal neurogenesis appear to be restricted to particular brain regions or to particular stages of development? In other words, evaluate the evidence for temporal or spatial constraints on postnatal neurogenesis in rodents, non-human primates, and humans.

3. To what extent do methodological considerations influence the debate? Do you think there are legitimate reasons for differences in interpretation of results based on methodology alone? If so, is it a matter of old vs new methods for identifying adult-born neurons, or is one method sufficiently flawed so as not to be trusted?

2011

Current Controversy: Aggression and the brain: structure, function, and criminal responsibility.

Before John Hinkly tried to assassinate Ronald Regan the requirements for an insanity defense generally included an impairment in either impulse control ("impaired volition") or knowledge of right and wrong. Afterwards, most states modified their laws such that either the criteria for an insanity defense was narrowed with respect to what "impaired volition" meant, or this criterion was removed from consideration, or the insanity defense itself was eliminated. The well known neuroscientist, Robert Sapolsky, suggests that "contemporary neuroscience argues strongly against" the view that "an inability to tell right from wrong should be the sole basis of an acceptable insanity defense." He further argues that data on the brain suggests we should bring back "impaired volition" as grounds for an insanity defense. Here, you will be asked to review and evaluate some of the contemporary data on brain function in relation to aggression, and then discuss their implications with regards to some issues of social policy including the position taken by Sapolsky.

Part I

Data about brain mechanisms influencing aggressive behavior have come from two related sources, the study of brain structures involved in aggression, and the study of transmitter systems and genes associated with them. There are two alternative series of questions below. The first focuses on brain structures and pathways and the second on the gene for monoamine oxidase A (the MAOA gene) and serotonergic mechanisms. Please choose one of these and address the questions under that section. Think carefully about your choice because you will use this perspective throughout the exam. We recommend that you read the entire question first before you begin. Part I should be roughly 8 pages in length. After you have answered A or B of Part I, continue on to Part II, which should be roughly 5-7 pages. Suggested page lengths exclude references.

A. Brain structures

Our understanding of brain structures associated with aggression comes from animal experimentation as well as study of humans with brain disorders. Much attention has focused on the roles played by the amygdala and the frontal cortex.

1. Describe the neural circuitry connecting parts of the cortex and amygdala that are implicated in aggressive behavior in ***non-human*** animals, and critically evaluate the relevant data implicating this circuit(s) in aggression. Be explicit about any specific sub-regions of the cortex and amygdala that are believed to be important for aggressive behavior.

2. Critically discuss the evidence that these same brain areas are involved in aggressive behavior in ***humans.*** More specifically, describe the key findings that have come from studies of each of the following three classes of people: (a) those with brain disorders (e.g. those associated with seizures, tumors, or other kinds of damage to these areas), (b) healthy people with subclinical

antisocial personality disorder, and (c) individuals with clinically diagnosed antisocial personality disorder.

Or:

B. Monoamine oxidase A and serotonergic systems

Monoamine oxidase A (MAOA) is an enzyme that breaks down monoamine transmitters in the synaptic cleft. Animal studies have revealed that MAOA can influence aggression, and variants in the promoter region of the gene that encodes MAOA in humans have been associated with some indices of aggression. In addition, there is considerable evidence that serotonergic systems in the forebrain modulate aggression in humans as well as non-human animals.

1. Review and critically evaluate the key pharmacological and molecular evidence from ***non-human*** animal models suggesting that monoamines and serotonin are critical mediators of aggressive behavior. Discuss the extent to which you are convinced by it, and what you see as the most likely roles that monomines and serotonin play in mediating aggressive behavior. Be sure to include information on: the type of aggressive behavior being studied, the brain regions where these changes are thought to take place, genetic background of the model, and conditions under which the aggressive behaviors are studied.

2. Examine and critically evaluate the data implicating these transmitter systems in ***human*** aggressive behavior. Discuss what kinds of conclusions we can draw from these data.

Part II

There are many ethical issues associated with aggression and what to do about it, and the issue here is whether our understanding of its biology should influence the decisions we make as a society about how to deal with these problems. Two important issues regarding aggression are structured around questions of culpability and intervention. For example, should the criminal justice system take into account the structure and/or function of the frontal cortex when decisions are made about the nature of punishment for violent crimes? Should policies be the same for an individual whose frontal lobe was damaged in war and one whose frontal lobe simply did not develop normally? Should children that may be at risk for heightened aggression because of the MAOA/5-HT genetic variation be provided special early training in impulse control or receive mandatory pharmacological treatment? Choose either the issue of culpability or the issue of intervention, and identify the main ethical question and present your argument (either pro or con). Be sure to couch your answer in the context of what is and is not known about the biology involved (that you discussed in Part I). In addition, make sure that you anticipate the counterargument***s***, ***including those that have been spelled out in the literature by other scientists***, when you argue for your position.