

scribed loss of cortical glutamatergic pyramidal neurons occurs, leading to reduced excitatory input to the remaining cells. This is compounded by reduced excitatory cholinergic modulation.  $\gamma$ -Aminobutyric acid interneurons are preserved, which suggests that inhibitory tone is maintained and perhaps increased. Functional sparing of serotonergic innervation may occur and maintain a negative modulatory effect through serotonin 1A receptors. Therefore, approaches that improve the efficacy of the remaining glutamate transmission may be useful. This improvement may be achieved by action on receptors of cortical pyramidal neurons with agonists (muscarinic receptors), partial agonists (for example, D-cycloserine in the case of N-methyl-D-aspartic acid receptor complexes), or antagonists (serotonin 1A receptors). Drugs that affect transmission are an important goal, as they will be required for most patients if functional disabilities already present are to be improved or reversed. They will also be required for all patients with Alzheimer's disease during the development of prophylactic agents (1).

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#### The Progress of Science

The instrumentation issue of *Science* (25 Sept.) prompts me to the following thoughts. New machines to power scientific inquiry to higher levels of sensitivity and resolution are detailed to fascinate and excite, but in the end, this tech junkie is left with the sad reality that most of them will be unattainable. Having just completed another masochistic session on a National Institutes of Health Shared Instrument Study Section, I find the contrast between the great opportunities for inquiry afforded by the instruments discussed in *Science* and the

limited funding provided by the government to acquire these expensive tools is remarkable. There can be no doubt that technology is the engine for scientific advance. This is not to demean the importance of a good idea, but it is the quality of the scientific tools that raises the level of the questions and the efficiency of the experimental approach. The lack of a vocal constituency for shared instrument funding has made it the target of choice for removal from the appropriations request menu supplied to Congress. This results in the type of financing strategies that fund five equipment requests from 60 submissions. It should be stated that each instrument grant is usually submitted by from four to ten investigators whose individual research programs would greatly benefit from better analytical tools. Each of those investigators has postdocs and students who would learn these new approaches and then be educated to ask more sophisticated questions about their problems.

Our students and research programs will go on in the absence of such equipment, but the scientific problems we face will not become less complex because of a lack of funds or a commitment to provide the technical means to unravel them.

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