Neurobiologic factors that might contribute to executive dysfunction in depression, Dr. Schwartz said. A decrease in N-acetyl aspartate, a marker or neuronal function, also may play a role. “It’s another way to look at the brain, and in depressed folks you can show that the brain is not doing what it is supposed to,” said Dr. Schwarz, director of the depression and anxiety disorders research program at the State University of New York, Syracuse.

Executive dysfunction is associated with noradrenergic, dopaminergic, and histaminergic projections to the dorsolateral prefrontal cortex. One tactic to get more norpinephrine to flow in that circuitry is to manipulate the serotonin levels, Dr. Schwartz said.

“Too much serotonin can be a bad thing in the frontal lobes. If you inhibit the inhibitor you can get more norpinephrine up there and help return executive functioning,” he added.

Pharmacologic agents that might increase norpinephrine, dopamine, and/or histamine and help improve executive function include drugs such as bupropion, atomoxetine (Strattera), and modafinil (Provigil), and drug classes such as stimulants and atypical antipsychotics, Dr. Schwartz said.

“Use of atomoxetine for executive dysfunction in depression makes biological sense and circuitry sense,” he said. “But there are no controlled studies [of atomoxetine] in executive dysfunction.”

Executive dysfunction also is associated with sleep disorders. Your brain wants you to have a homeostatic amount of sleep. If you get sleep deprived, no matter what the cause, you function poorly and make errors in omission commission, Dr. Schwartz said. Again, “there is poor metabolism in the prefrontal cortex.”

Addition of a sleep aid can have positive effects on next-day functioning. Stimulants, modafinil, or armodafinil can improve attention and concentration during the day, Dr. Schwartz said. “If you can keep people more awake during the day, and they avoid naps then they may not need a sleeping pill at night.”

Insomnia is comorbid with depression in around 85% of people (J. Clin. Psychiatry 2004;65:27-32). “That is a lot of people,” Dr. Schwartz said. Some antidepressant medications can have a direct effect on sleep, he added. For example, bupropion increases REM sleep and sleep latency, but reduces sleep continuity. Tra zodone decreases REM time and may cause daytime sedation. In contrast, nefazodone increases REM sleep time and is associated with minimal daytime sedation.

Sleep aids are a treatment op tion. Examples include zolpidem (Ambien), eszopiclone (Lunesta), and zaleplon (Sonata). “I don’t think one is better than the other, so choose based on half-life,” Dr. Schwartz suggested. Sonata has the shorter half life; Ambien is in the middle; Lunesta has the longest. “Which one can you take at 3 a.m. if you need work at 9 in the morning? Sonata.”

Modafinil is another pharmacologic option in patients with executive dysfunction and other adverse effects of impaired sleep. “This will not save one of your patients but you can try it,” Dr. Schwartz said. “It’s the only product that raises histamine that I know of, and histamine going up has good for executive function.”

Dr. Schwartz said, “Modafinil is a funny drug—does above 300 mg have any side effects. Lower doses may be better for treatment of executive dysfunction.”