Are some medicines stealing your brain power?

It recently came to light that a wide range of popular medications—used routinely by tens of millions of Americans—have a nasty tendency to accelerate cognitive decline and set the stage for Alzheimer's disease. Some are prescription drugs, but many are available over-the-counter remedies like nighttime pain relievers (PM formulas of popular brands like Advil, Tylenol, and Excedrin and others) or common antihistamines (including Benadryl and to a lesser extent, Zyrtec, Claritin, and more).

These are so-called anticholinergic drugs, medications that block the parasympathetic nervous system. Back in medical school, in my first pharmacology class, I vividly recall what we learned these drugs can do. They dry up mucus, slow intestinal transit, and reduce bladder urgency; in patients with Parkinson's Disease, they tamp down involuntary muscle movement. But they also have serious side effects.

It's long been suspected that reliance on these drugs increases the risk for dementia. In fact, these drugs carry warnings for older people. Anticholinergics are known to cause confusion, memory loss, and worsening mental function in people who are older than 65 years. They're especially bad for those already experiencing mild cognitive impairment (MCI)—a high percentage of seniors who don't have much "cognitive reserve" and may metabolize medications more slowly due to age-related declines in liver and kidney function.

Why do anticholinergic drugs steal your brain power? Acetylcholine is a key neurotransmitter in the brain, and blocking it interferes with the chemical messages between neurons. In fact, the opposite principle is invoked by many Alzheimer's drugs that boost acetylcholine. Unfortunately, they don't work very well, and they, too, have a host of side effects.

In a new study undertaken at the University of East Anglia in the U.K., and sponsored by the Alzheimer's Society, medical records of 40,000 individuals with dementia were compared with a control group. It was discovered that those with dementia were 30% more likely to have taken certain anticholinergic bladder or Parkinson's medications. The more medications taken, the greater likelihood of cognitive decline.

This is not the first time anticholinergic drugs have been implicated in dementia. A 2015 study (ACT) arrived at a similar conclusion: *"The ACT results add to mounting evidence that anticholinergics aren't drugs to take long-term if you want to keep a clear head, and keep your head clear into old age. The body's production of acetylcholine diminishes with age, so blocking its effects can deliver a double*

whammy to older people. It's not surprising that problems with short-term memory, reasoning, and confusion lead the list of side effects of anticholinergic drugs, which also include drowsiness, dry mouth, urine retention, and constipation."

The ACT study was the first of its kind to include non-prescription anticholinergics. Here's why that's significant: Millions of Americans take over-the-counter sleep medications like Tylenol PM, Excedrin PM, Advil PM, Sominex, or Unisom. What all these medications have in common is the inclusion of sedating antihistamines like Benadryl (diphenhydramine) or chlorpheniramine (the active ingredient of the popular hay fever medication Chlor-Trimeton). These antihistamines—but to a lesser extent newer non-sedating daytime formulas like Zyrtec, Xyzal, and Claritin—are potent anticholinergics.

Many cold medications also contain brain-stealing antihistamines. NyQuil, for example, includes among its ingredients doxylamine succinate, a potent anticholinergic.

Another category of medications frequently prescribed to older Americans targets over-active bladder, or OAB. My experience is that these drugs don't help very much, if at all, and their side effects like constipation, dry mouth and sedation outweigh their benefits.

In fact, OAB wasn't even a disease until drugs were developed to treat it. You've probably seen ads for these drugs on TV. An entity called the Urology Care Foundation ("Your trusted source for urologic patient education") helpfully points out on its website that "Overactive bladder (OAB) is a common condition that affects millions of Americans." It's an example of a "patient advocacy organization" heavily subsidized by Big Pharma backers that seeks to goose sales by increasing public awareness (sometimes referred to as "disease-mongering").

In an article entitled "Does industry-sponsored education foster overdiagnosis and overtreatment of depression, osteoporosis and over¬active bladder syndrome? An Australian cohort study", it was pointed out that for these "overdiagnosed and overtreated conditions . . . primary care clinicians were often targeted, dinner was often provided and that a few companies sponsored most events. In most cases, sponsors' products are not cost-effective choices for the specified condition. This pattern highlights the need for professional education to be free of commercial sponsorship."

Bladder medications with strong anticholinergic effects include Oxytrol, Ditropan XL, Detrol and Detrol LA.

Of the Parkinson's drugs, Artane and Cogentin showed the strongest association with dementia.

Among antidepressants, Paxil, amitriptyline (Elavil) and doxepin (Sinequan) have the highest "anticholinergic burden score."

You see, despite today's emphasis on "precision medicine," there's no such thing as a "clean," side effect-free drug. Drugs are by their very nature, inherently "dirty." They have off-target effects (called pleiotropic effects) which means that they never act solely on the specific organ they were designed to regulate, e.g. your bladder. Rather than an intended laser-like focus on a single function, their chemical messengers travel like buckshot from a mediaeval blunderbuss throughout the body, creating unwanted and unforeseen impacts on other systems.

A classic example is Vioxx, an "ideal" non-steroidal anti-inflammatory drug designed

to minimize the GI bleeding side effects associated with early NSAIDS, including ibuprofen. It was enthusiastically embraced by the medical community until extensive post-marketing data showed it could cause blood clots. Before it was yanked from the marketplace, it's estimated that it may have been responsible for tens of thousands of deaths due to premature heart attacks and strokes.

Although not strictly anti-cholinergic, worthy of consideration among brain stealers are benzodiazepine drugs used to treat insomnia and anxiety. Anyone who's taken Xanax, Valium, Klonopin, Ativan, Restoril or Ambien can attest to their mind-numbing effects:

"I can't control my fingers I can't control my brain Oh no no no no no Ba-ba-bamp-ba ba-ba-ba-bamp-ba I wanna be sedated!" —The Ramones

A team of researchers from France and Canada linked benzodiazepine use to an increased risk of being diagnosed with Alzheimer's disease. People who had taken a benzodiazepine for just three consecutive months or less had about the same dementia risk as those who had never taken one. But those who had taken a benzodiazepine for three to six months had a 32% greater risk of developing Alzheimer's, and those taking one for more than six months had an 84% greater risk than those who hadn't taken one.

For a while it was asserted that long-term use of powerful acid blocking drugs (PPIs) was associated with dementia, but the latest study seems to have exonerated them. Small consolation to those who will suffer depression from PPIs, the latest side effect to be revealed in a recent study.

Finally, consider the case of statin drugs, long-suspected of being brain-stealers, by virtue of the fact that they deplete the brain of cholesterol (the brain is the body's most cholesterol-rich organ). But a 2016 study suggests the opposite—that statins exert a protective effect against dementia.

These studies have been criticized by many statin skeptics who point out that high blood levels of cholesterol have been consistently demonstrated to be correlated with lower risk of cognitive decline. A recent review shows survival and brain benefits of high cholesterol in individuals over 80: "Protection is particularly likely for successful cognitive aging—intact cognition at very old age."

Finally, here's an unexpected one: Hormonal treatment for prostate cancer is also associated with subsequent risk for dementia. Drugs like Lupron block androgens, which adversely affects the brain. Men who took these drugs for a year or more had twice the risk of cognitive decline.

These studies should remind us that we should familiarize ourselves with the potential side effects of drugs we take. This is especially true of the vulnerable elderly, who often are subject to polypharmacy. Doctors should take careful inventory of their patients' medications; if any aren't doing much good, they should be "de-prescribed." With tens of millions of Americans predicted to get Alzheimer's by mid-century, it's imperative we don't make matters worse with brain-stealers.