

Brainrobbers: Medicines that steal your brain power (Revisited!)



Paging through the archives of *Intelligent Medicine*, I came across the following article which I first published in 2018. It foretells a problem which is highlighted in a brand new research paper published in the September 2 edition of *Neurology*. It found that use of anticholinergic medication dramatically increased the incidence of mild cognitive impairment (MCI) when normal older adults used them regularly for up to ten years.

The new study focused on US seniors, average age 74, and tracked their drug usage for a decade. The novel element was that they were assessed for the presence of a key Alzheimer's gene—ApoE4—as a marker of heightened vulnerability to the brain-robbing effects of commonly used drugs, as well as for tau protein in their spinal fluid, a harbinger of susceptibility to amyloid plaque that causes fibrillary tangles in the brains of Alzheimer's patients.

There are about 100 of these anticholinergic drugs, as I detail below. Some are available only by prescription; others are readily available over-the-counter. They are commonly taken by seniors for problems like dizziness, allergy, insomnia, high blood pressure, depression, urinary problems and Parkinson's Disease.

One-third of the participants were taking anticholinergic drugs, with an average of

4.7 anticholinergic drugs taken per person! Metoprolol (Lopressor, Toprol), atenolol (Tenormin), loratadine (Claritin) and bupropion (Wellbutrin) were the most common.

Individuals taking at least one anticholinergic drug had a 47% increased risk for developing mild cognitive impairment. Furthermore, those with higher overall exposure to anticholinergic drugs had additional increased risk.

Those with evidence of Alzheimer's susceptibility at the study's outset fared even worse after ten years: those with tell-tale tau protein had a *four-fold* greater risk of MCI with frequent anticholinergic dosing; those with the ApoE4 gene experienced a *two and a half* greater risk of MCI.

Here's my article highlighting this risk back in 2018:

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.

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? It turns out acetylcholine is a key neurotransmitter in the brain. 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 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 more 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) and chlorpheniramine (the active ingredient of the popular hay fever medication Chlor-Trimeton). These antihistamines—but to a lesser extent the daytime formulas like Zyrtec, Xyzal, and Claritin—are potent anticholinergics.

Many cold medications 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 modest benefits.

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

You see, 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 specific function, their chemical messengers travel like buckshot from a medieval blunderbuss throughout the body, creating unwanted and unforeseen impacts on other systems.

These studies should remind us that we should be mindful of 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 the medications their patients are taking; 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 brainrobbers.

Calculate your "anticholinergic cognitive burden score" with this handy guide.