



When What You Don't Know *Can* Hurt You

Is ignorance bliss? Probably not, say anosognosia researchers. Its manifestation in Alzheimer's patients poses unique challenges.

I was aghast. While discussing famous television and movie comedy scenes with a group of friends, I discovered that a younger acquaintance was utterly unaware of the quirky brilliance of BBC-TV's 1969-74 series *Monty Python's Flying Circus* and the movies that followed from it. While I admit that both the TV episodes and the films suffer from a fair proportion of comedic bits that don't resonate on the American palate, the creative minds behind *Monty Python* are responsible for some of the most sublimely funny sketches I have ever seen. Unswayed by our enthusiastic tales of classics like "Nobody Expects the Spanish Inquisition," "Fish-Slapping Dance" and "Philosophers' Football," he stuck unrepentant to what he had heard from the less enlightened and refused to consider Python as anything other than "some weird old British show." How sad. How misguided. He simply didn't know what he was missing.

And Now for Something Completely Different

Many people with AD also don't know what they're missing. In fact, more than half of AD patients have been classified as having at least partial unawareness of their deficits.^{1,2} Caregivers often attribute a patient's apparent inability to recognize their shortcomings to a conscious act of denial, *i.e.*, an unwillingness to accept the problem. In contrast, the data support the idea that the problem is true *anosognosia* or organic lack of awareness. Acknowledging that it is an oversimplification from the perspective of cognitive psychology, it appears that AD patients actually forget that they forget.

Anosognosia is one of those classically arcane syndromes for which behavioral

neurology is famous. The term was coined by Babinski in 1914 to describe the observation of unawareness of hemiparesis in patients with right hemisphere strokes. The phenomenon has remained closely aligned with neurological neglect syndrome ever since. It even reached a degree of popular recognition after Oliver Sacks described a particularly florid case in *The Man Who Mistook His Wife for a Hat*. In that compilation of behavioral neurology oddities, Dr. Sacks told the story of a man who awakened to find what he thought was a severed human leg in his bed. Terrified, the man threw the gruesome thing out of the bed and was astonished to find that he was compelled to follow after it—because it was attached to him! In a fit of rage he proceeded to pummel the strange limb and try to remove it from his body. When asked where his own left leg might have been during the ordeal, the man replied, "I don't know. ... I have no idea. It's disappeared. It's gone. It's nowhere to be found."³

This is obviously something more complicated than a simple somatosensory deficit after stroke, but the exact localization of lesions causing anosognosia remains an enigma. It seems that damage almost anywhere—frontal, temporal or parietal lobes, and even subcortical lesions—can be sufficient to cause unawareness for hemiparesis. Nonetheless, the likelihood of anosognosia is highest when frontal and parietal structures are both damaged.⁴ Since people with AD develop heavy neurofibrillary tangle burden in the temporal and parietal regions, as well as prominent amyloid deposition in the frontal lobes, I guess we shouldn't be surprised that they have a high rate of unawareness for cognitive and behavioral deficits. That assumption must be tempered, however, because

not everyone with AD is unaware of their problem.

The Argument Clinic

If you're confused about what's going on to cause anosognosia at this point, don't worry. You're not alone: investigators still can't agree on a gold standard to measure the presence, severity or impact of the problem.^{5,6}

Most studies suggest an increase in the degree of anosognosia with greater dementia severity, but there are hints that people with AD may be unaware of different things at varying stages of the disease.⁶ For instance, complaints of memory loss are very common in the course of healthy aging, and many people with AD will indeed acknowledge forgetfulness (though they may discount its importance relative to their peers). Intriguingly, in one study patients with MCI showed *more* awareness of their own memory problems than did their family members, while those with mild AD (MMSE ≥ 24) were less aware of the problem than the families.¹

This leads to an interesting paradox. It suggests that the person who complains most about his or her forgetfulness is actually less likely to have AD. In contrast, the same phenomenon also means we need to keep up our guard, because that same person is at ominously high risk for developing AD over the next few years. This close attention to self-reported complaints is endorsed in the American Academy of Neurology practice guidelines for mild cognitive impairment. Close scrutiny of emerging memory complaints will probably be even more important in the future as we look toward starting disease-modifying treatments at the earliest possible point in the course of AD.

Regardless of their insight regarding memory impairment, it is pretty clear that people with AD are often less aware of losses in functional skills, like driving. It may be more proper to think of poor prediction rather than awareness when it comes to functional ability, since many patients will recognize failures when they occur and be quite frustrated by them. AD patients differ from healthy folks in that they are poor at predicting those failures.⁵ It shouldn't be a surprise to find that anosognosia tends to correlate well with executive dysfunction, since planning, self-monitoring and self-awareness are key elements in most conceptual models of executive function.

Interestingly, the literature suggests that unawareness is inversely correlated with depressive complaints in AD. Perhaps ignorance really is bliss? One recent study suggests we probably shouldn't jump to that conclusion.² Professor Sergio Starkstein—who has been one of the leading thinkers in dementia-related anosognosia for over a decade—and his colleagues reported earlier this year that poor insight is a risk factor for dangerous behaviors in patients with AD. They found that in the month prior to assessment, 16 percent of 278 consecutive AD patients carried out some dangerous act that seemed likely (in a caregiver's eyes) to put them at risk for physical harm. The presence of these dangerous acts didn't correlate with age, education, depression or dementia severity, but the risky behaviors were associated with anosognosia. That relationship wasn't subtle, either. Unawareness nearly tripled the risk for dangerous acts compared to AD patients with more preserved recognition of their problems. Furthermore, almost 85 percent of patients with dangerous behaviors explicitly denied them.

It is important to note that most anosognosic patients had not committed dangerous acts; it appears that a combustible mixture of disinhibition and unawareness is generally required to trigger the problem. So rather than ignorance being bliss, it appears that what you don't

know *can* hurt you.

The Monty Python troupe predicted this relationship between disinhibition, anosognosia and dangerous behaviors very nicely in their 1975 film, *Monty Python and the Holy Grail*. Python aficionados—but probably not my misinformed younger friend—will remember the odd blend of slapstick and dark comedy in the scenes that involved the Black Knight at the bridge. After rather messily losing both arms to King Arthur's sword, the Black Knight proclaimed that the injuries were “just a flesh wound.” Moreover, he continued to fight despite Arthur's dismay and the obvious impediment of not having a sword hand. OK, I acknowledge that the Black Knight's refusal to yield is a bit of a stretch for anosognosia, but I rarely miss the chance to recount a favorite Python skit. As an aside, John Cleese (who wrote the sketch and played the Knight) has reportedly acknowledged that the scene could have been construed as heartless and sadistic, but felt that the Black Knight's staunch refusal to give up the fight despite

overwhelming evidence against his position contributed to a satiric rather than a mean-spirited tone.

So, while most of us are unlikely to encounter an anosognosic man-at-arms in our practices, we probably should be looking carefully at low self-awareness of deficits and misplaced confidence as an ongoing source of risk in our patients with AD. **PN**

1. Kalbe E, Salma E, Perani D, et al. Anosognosia in very mild Alzheimer's disease but not mild cognitive impairment. *Dement Geriatr Cogn Disord* 2005;19:349-56.

2. Starkstein SE, Jorge R, Mizrahi R, et al. Insight and danger in Alzheimer's disease. *Eur J Neurology* 2007;14:455-60.

3. Sacks O. *The Man Who Mistook His Wife for a Hat and Other Clinical Tales*. New York, Simon & Schuster (Summit), 1985

4. Pia L, Neppi-Modona M., Ricci R., Berti A. The anatomy of anosognosia for hemiplegia: a metanalysis. *Cortex* 2004;40:367-77.

5. Smyth KA, Neundorfer MM, Koss E, et al. Quality of Life and Deficit Identification in Dementia. *Dementia* 2002;1:345-58.

6. Starkstein SE, Jorge R, Mizrahi R, Robinson RG. A diagnostic formulation for anosognosia in Alzheimer's disease. *J. Neurol. Neurosurg. Psychiatry* 2006;77:719-25.



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