Rope-A-Dopamine: Mystery of Muhammad Ali's Parkinson's Continues

By Krystal Alexander — June 9, 2016

Muhammad Ali has been lauded for his oratorical skill, his activism and certainly his boxing. Yet for decades it has been believed that even one of the greatest boxers was not good enough to prevent the kind of head trauma that led to the Parkinson's disease he suffered from for more than 30 years.

Yet was it really boxing that caused it? We are inching closer to learning the truth, but some questions remain.

In 1979, Ali retired but came out of retirement twice, to fight Larry Holmes and then Trevor Berbick. On December 12th, 1981, after a very poor showing in his final fight, he retired for good. Three years later, the public learned he had developed Parkinson's and speculation began; did The Greatest fight one time too many?

Parkinson’s versus CTE: How do we tell the difference?

Parkinson's disease is generally considered a clinical diagnosis -- that means doctors see symptoms first. Only then will there be tests for structural evidence. Though it is primarily in older people, it afflicts the young in rare cases as well.

According to neurologist Dr. Michael Okun, Ali was a textbook case of early onset Parkinson’s disease because he started exhibiting symptoms, the symptoms were more prominent on one side of his body, and he was responsive to the traditional dopaminergic medication. But the other
diagnosis given Ali's career would be Chronic Traumatic Encephalopathy (CTE), which is also exemplified by slurred speech, motor dysfunction, and depression. A third possible answer is that the head trauma lowered the threshold for the onset of his Parkinson’s.

CTE causes a buildup of the tau protein around the blood vessels of the brain, resulting in disruption of the normal functioning of neurons and eventual neuronal death. As CTE progresses from Stage 1 to 4, the tau deposits have so overwhelmed the brain that there is marked cortical atrophy (loss of brain mass) and resultant cognitive dysfunction with time.

Such a diagnosis was not possible in 1984, nor is it now. It can only be diagnosed by postmortem neuropathological analysis. In recent years a number of former/retired NFL players, other athletes, and their families, have graciously donated their brains to science, and in so doing have allowed for further development on CTE research.

As awareness of concussions has increased, more athletes and their families have allowed the brains of players to be analyzed. Perhaps the only answer can be found if Ali’s family does just that.

Ali lived with Parkinson's for more than three decades and billions of dollars have been spent. Why has progress been so elusive?

**The dopamine issue**

Progress has been hindered in treatment of Parkinson’s, coupled with the inability to establish a cause. Approximately 15 percent of Parkinson’s cases are attributable to a genetic mutation of either the SNCA or LRRK2 genes. A recent study [3] in *Nature Genetics* lists a third gene, TMEM230.

The TMEM230 gene produces a protein that is involved in packaging of dopamine in neurons. Dopamine is stored in this packaging, known as synaptic vesicles, and released from the membrane of one cell where it can then land on the appropriate receptors and take its effect. The scientists believe that the protein is involved in the movement of these vesicles. They suggest that regulating synaptic vesicle trafficking may be a potential therapeutic intervention.

The death of Muhammad Ali is spurring greater awareness of the disease, and that is likely to lead to more funding. While Ali used his Rope-a-dope technique in the ring with his toughest opponents, if you will allow me to be just a bit too clever, he might allow science to Rope-a-dopamine the disease.

**Rope-a-dopamine versus what?**

Ali was a fighter who was trying to fight something he couldn’t see, but that was slowly winning. As Michael J. Fox, who also has young onset Parkinson’s, stated in an interview with the NBC’s *Today show* [4], “You don’t fight it. You live it. You live with it.” There is currently no cure and the majority of treatments center around some combination of providing an exogenous form of dopamine (or its precursor) or inhibiting its breakdown. As you can imagine, that limits what a doctor can prescribe.

Yet as of 2014 [5], 37 new medicines were in development for the treatment of Parkinson’s disease. Additionally, there are 43 active U.S. clinical trials with regards to Parkinson’s, all in various
phases. Because of the renewed interest in Ali due to his death, research is likely to ramp up again.

It’s fair to say that research may not yet be where Ali could have been helped, but scientists aren’t down for the count. The fight continues.