Anne Buckingham Young’s Role in Movement Disorder Research

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Dr. Anne Buckingham Young’s research on a variety of movement disorders, including Parkinson’s disease, Huntington’s disease, and tremors, has been critical in advancing the understanding of these disorders and in furthering the emphasis on research in these fields. Her extensive and dedicated research background provided her with several unique leadership opportunities in the neuroscience community; Dr. Young was hired as the first female chief of Massachusetts General Hospital and is the only person, male or female, to have been president of both the American Neurological Association and the international Society for Neuroscience. Dr. Young also established the Mass General Institute for Neurodegenerative Disease (known as MIND), providing many opportunities for research on drug development and modeling of Parkinson’s, Huntington’s, Alzheimer’s, and other diseases. Her laboratory, in which she now works full-time, focuses on disorders of the basal ganglia, specifically Parkinson’s and Huntington’s diseases. With her late husband, Dr. Young developed the most widely used model of basal ganglia function (1). Overall, Dr. Young’s dedication to research has provided a strong base for pharmacological treatment exploration of these movement disorders, both in terms of publishing solid initial research and by providing a successful research institution in which to study these problems.

Dr. Young, along with two other researchers, published a paper in 1989 that quickly became one of the most widely cited in movement disorder research (1). This paper combined data from animal models and post-mortem human subjects in an attempt to determine the specific neuron projections in the basal ganglia responsible for a variety of disorders. It is impossible to do these types of experiments while the human patients are alive, as it violates many ethical codes to perform unnecessary brain operations, so all human data must be collected after death. Researchers must collect as much symptomatic data while the patient is alive and then try to synthesize that data with the physical condition of the brain after death.

While Parkinson’s disease had been clearly linked to malfunction of the basal ganglia based on symptom reporting followed by post-mortem analysis, other movement disorders causing an excess of movement could not be conclusively linked to the area (2). By analyzing both animal and human post-mortem structural changes in the basal ganglia after gathering data on their
symptoms when alive, Dr. Young and the other researchers were able to conclusively identify sub-portions of the basal ganglia that they believed were causing the disease. Hyperkinesia, or the production of excess movement, was determined to be controlled by neurons connected to the lateral globus pallidus while hypokinetic disorders, such as Parkinson’s disease, were hypothesized to be connected to changes in several small groups of neurons that result in an overall output increase from the basal ganglia (2). This paper provided a solid foundation for the rest of the research community to begin producing drugs and treatments that specifically target these areas instead of targeting the whole basal ganglia.

After this critical set of discoveries, Dr. Young went on to supervise a variety of research projects related to Parkinson’s disease and Huntington’s disease. She also had input on papers related to other movement disorders, but her main specialty was working with these two disorders. She was especially involved after her creation of MIND, where she could oversee many research projects at once because they were all grouped in one location. A small sampling of such papers shows how broad and far-reaching Dr. Young’s influence and work can be. Her initial research in the field allowed for rapid expansion of other projects and treatment options, as well as confirming existing theories about the mechanisms behind these diseases.

For example, new therapeutic approaches for Parkinson’s and Huntington’s diseases were proposed in a 2006 paper under the supervision of Dr. Young. After locating the part of the basal ganglia that is malfunctioning in these diseases, researchers were able to identify a high percentage of misfolded proteins in the area. The accumulation of these misfolded proteins usually causes detrimental aggregations in the brain region, leading to disease symptoms. Reducing the number of size of these aggregations with a pharmacological treatment could reduce or stop symptoms altogether (3). Identifying this pharmacological goal allowed researchers to create a compound that reduces dysfunction in the proteins to begin with and also led to the discovery that the larger aggregations of proteins may be more protective than detrimental. The researchers on this project now believe that the intermediate form of the protein between individual and aggregation stages may be the most toxic and that the accumulations themselves prevent the misfolded proteins from causing too much damage (3). Another experiment that Dr. Young contributed to showed that while some proteins are more apt to misfolding, the genes for others are simply turned off the and proteins are never created in the first place (4). Abnormal neuron connectivity due to limited gene expression and protein

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production in certain brain regions is now thought to be one of the causes of the cognitive
dysfunction and cortical atrophy in Huntington’s disease (4).

Dr. Young’s influence has also expanded the field of neurodegenerative disease study into other
subsets of biology such as genetics. In a 2010 study, researchers analyzed 410 genome-wide
gene samples from patients with symptomatic Parkinson’s patients, subclinical patients, and
healthy control patients and found ten sets of genes previously unrelated to Parkinson’s. As in
the study with Huntington’s disease (4), these researchers found that certain genes were under-
expressed, leading to a lack of enzymatic production. In this case, the enzyme that typically
blocks dopaminergic neuron cell death was not produced in quantities as high as in control
patients, due to an under-expression of a particular gene set in the Parkinson’s patients (5). This
gene is now being investigated as an early intervention target in the hopes that researchers will
be able to prevent Parkinson’s disease from progressing before the patient even becomes
symptomatic.

Dr. Young’s work has also helped to improve the animal models used to study movement
disorders. It is impossible to obtain enough animals with naturally-occurring movement disorders
to perform a study, so to be efficient and cost-effective researchers must induce these diseases in
some way. The animals will not actually have Parkinson’s disease, but they will show the
associated symptoms, which can then be studied and potential treatments can be tested.
Researchers under the supervision of Dr. Young discovered that injecting thyrotropin-releasing
hormone (TRH) into the striatum of laboratory rats could induce Parkinson-like symptoms of
abnormal movement. It is thought that this disruption occurs because of the increase in dopamine
release stimulated by TRH (6).

Dr. Young has had an immense impact on the study, modeling, and treatment of
neurodegenerative diseases through her research and her implementation and leadership of
institutions dedicated to researching these issues. Her research into the brain regions underlying
movement disorders was critical to the further study of these diseases, especially Parkinson’s and
Huntington’s disease, and she has been part of the movement advocating treatment of the
biological problem rather than just treatment of the symptoms. Dr. Young has undoubtedly been
an inspiration for female neuroscience students across disciplines, and she has shown very
effectively that pursuing your passion in research can lead to many great discoveries.
References

1. A. B. Young, Anne Buckingham Young Department of Neurology Staff Page, Massachusetts General Hospital (2014).


