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The Brain Activity Map Project: short- and long-term prospects for Huntington's disease research

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At Risk for Huntington's Disease

HD is a genetically caused brain disorder that causes uncontrollable bodily movements and robs people's ability to walk, talk, eat, and think. The final result is a slow, ugly death. Children of parents with HD have a 50-50 chance of inheriting the disease. There is no cure or treatment.

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The Brain Activity Map Project: short- and long-term prospects for Huntington's disease research

The ambitious, recently announced national effort to map the circuitry of the brain and deepen understanding of its function could bring valuable new knowledge about what goes awry in Huntington's disease-affected brains. Still, the project likely won't have a practical impact on the search for effective treatments for years or perhaps even decades.

That's the initial assessment from three leaders in the search for HD treatments in reaction to reports that the administration of President Barack Obama will include a multi-year, public-private-academic brain mapping project in the next federal budget. The official announcement, following Obama's February 13 State of the Union remark about the importance of brain mapping, is expected this month, although political wrangling over the budget could cause a delay.

"Anything that teaches us about how the brain works will undoubtedly tell us something about how HD makes the brain dysfunction," said Simon Noble, Ph.D., the director of scientific communications for CHDI Management, Inc., the firm that furthers the goals of the CHDI Foundation, Inc., the non-profit, multi-million-dollar search for HD treatments. "At the moment, it's difficult to predict what will come out of this for HD."

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Dr. Simon Noble (photo by Gene Veritas)

Compared by the president and scientists to the $3.8 billion Human Genome Project (1990-2003), which produced a complete map of our genes, the so-called Brain Activity Map Project (BAMP) would aim to record and map the firing of the brain's 100 billion or so neurons.

Fifteen years to a mouse study

This year marks the 20th anniversary of the discovery of the HD gene, a key step in the Human Genome Project. Initially, scientists thought that discovery would lead to potential treatments just a few years later. However, the task has proved far more complex, although a number of clinical trials are in progress or in planning, including cutting-edge gene-therapy approaches made possible by the discovery of the gene.

The scientists behind the BAMP estimate that mapping a significant part of a live mouse brain would be achieved 15 years into the project. Experiments in humans necessarily would take place years later, after testing in non-human primates.

"While the Brain Activity Map is an important and worthy project, I hope it's irrelevant to Huntington's disease," Robi Blumenstein, the president of CHDI Management and a participant in an August 2012 BAMP planning session at the White House Office of Science and Technology Policy, said of the project. "Because mapping the brain is such a hard problem, the BAMP is a complex project on a long-time scale. I hope that we can deliver treatments before it becomes useful to us."

Scientists say that the large number of neurons and the complexities of the brain, a living organ, will prove far more difficult to measure and map than the much smaller amount of inanimate material in our genes. Furthermore, because HD is a genetic disease, the Genome Project in general and specifically the discovery of the HD gene have been the major, initial breakthroughs in the search for treatments.

In 1923 one scientist referred to the connections among neurons as "impenetrable jungles where many investigators have lost themselves."

Since then, little progress has occurred. In a June 2012 article, six leading scientists identified as leaders of the BAMP likened the current technology of measuring just a few neurons at a time to watching an "HDTV program by looking just at one or a few pixels on a screen."

Futuristic tools and techniques

"I think it's exciting," said George Yohrling, Ph.D., the director of medical and scientific affairs for the Huntington's Disease Society of America. "The brain is incredibly complex, as we all know. Once we know the details of how all the different neuronal pathways and networks are talking to each other in the normal and diseased states, it could help guide us to effective treatments. In theory, all of the disease areas – Parkinson's, Alzheimer's, HD – will benefit from the successful brain mapping exercise."

Dr. George Yohrling (CHDI photo)

However, Dr. Yohrling emphasized that the project's ability to furnish such information will depend on the development of new research tools. At first, such tools cost enormous sums, but come down over time, he said. The first sequencing of the genome cost billions and took more than a decade, whereas today sequencing takes three weeks and will soon cost just $1,000.

"The point of the tools is key," he explained. "We see it every day in science. You can look back 10, 15 years of how we used to do certain things in the lab and think, wow, this is so archaic!"

Indeed, the BAMP scientists' article pointed out that the project – with the gargantuan goal of imaging "every spike from every neuron" – will require an entirely new set of futuristic tools and techniques resulting from the "convergence of biotechnology and nanotechnology." They envision such innovations as three-dimensional imaging, biologically inspired computational devices, nanoprobes, DNA molecules acting as sensors, and "small wireless microcircuits, untethered in living brains, for direct monitoring of neural activity."

Whether nanoscience can shed light on the HD disease process is a "bit of a black box at the moment," Dr. Noble observed. "A lot of these things will be done in mice first. Working in a human brain is extremely difficult, if not impossible. We'll have to rely on other systems and post-mortem brains."

If such technology becomes feasible, it might help "identify early biomarkers (signs)" of HD, Dr. Yorhling said. Biomarkers are crucial for conducting clinical trials of potential treatments.

Keeping HD in the loop

Despite the likely minimal impact of the BAMP on HD research in the short run, both CHDI and HDSA plan to carefully track its progress and seek opportunities to apply its findings and even potential inclusion in some facet of the project.

"CHDI is keeping a close eye on how these grand projects develop and always considering ways that we might be involved," said Dr. Noble, referring to the BAMP and also a new brain-research initiative co-founded by former Rep. Patrick Kennedy known as One Mind for Research.

As Dr. Noble noted, the idea of brain mapping intersects with CHDI's new emphasis on systems biology.

"The brain is a system, just as the body is a system," he said. "Brain mapping is a really difficult problem, but one that's well worth pursuing. The brain is the final frontier. It's the least understood system in the human."

If the BAMP came to include disease-specific mapping, HDSA would advocate for the inclusion of HD, Dr. Yohrling said. He also held out the possibility of the HD research community someday teaming with patients to carry out an HD-specific brain-mapping project, which could become feasible as the techniques advance and become accessible to more researchers.

Posted by Gene Veritas at 12:32 PM

Labels: biomarker , biotechnology , brain , Brain Activity Map Project , CHDI Foundation , clinical trial , DNA , genetic , genome , Huntington's disease , nanoprobe , nanotechnology , neuron , researcher , systems biology

2 comments:

Larry Holler DVM, PhD said...

I am relatively new to the HD community and I must admit I have been confused by all the players in the field, many who you mention in this blog, and what their true motivations really are. My story with HD started when the Sipione research group in Alberta, Canada published data on GM1 ganglioside in mouse models of HD. GM1 was pioneered by an Italian Pharma company many years ago. The molecule was purified from Cow brain. Whe Mad Cow disease came along, the company could not find a verified source of raw material to produce GM1 so the clinical trials that were ongoing for Parkinson's and Spinal cord injury, sort of limp to their conclusion and the company went out of business. GM1 was shown to have disease modifying effects on Parkinson's disease and positive treatment effects on certain spinal cord injuries, but the research died

because there was no longer any source of pharmaceutical quantities of GM1 in the world. We have worked for almost 20 years developing a safe, and verified source to replace unknown cattle brains in the producion process. We have a flock of sheep that are carriers for a genetic disease, that results in massive accumulation of GM1 ganglioside in their brain and other tissues. We have sold our GM1 through a company called Avanti Polar Lipids for research use for many years. In order to meet the demand for Huntington's patients, all we have to do is raise more sheep. There is no other source that will satify the FDA for a natural product. We tried to offer this material to the folks in Canada, and we where politely dismissed. Evidently they have signed on with a company that is trying to make a semisynthetic GM1 that to my knowledge and everyone else who should know, has never been done in any quantity. CHDI is somehow also involved and when at the encouragement of HDSA, I contacted them, I was also politely rejected in a form letter.

Further inquiries in CHDI resulted in 2nd hand accusations that we were only "in it for the money". Later I find out that they are doing GM1 studies, apparently with the group in Canada, but still won't take the time to contact us. The word from HDSA is that CHDI will contact us if their other approach doesn't work out. Really? We believe that hese sheep were created by God for this purpose and even though we continue to hit roadblocks, we won't give up. We have 30,000 HD patients to treat, and then we have to start working on Parkinson's. Larry Holler DVM, PhD Glycoscienceresearch.com

8:59 AM, March 22, 2013

Tara said...

Larry, Keep up the work .. We support you

9:23 AM, September 12, 2014

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