Data mining detects signs of Lou Gehrig's disease in gene carriers long before symptoms appear

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Inspired by the use of microarray chips that look for gene combinations, psychologists are using "pattern array" software to spot movements in rats that might help them predict diseases such as Lou Gehrig's syndrome.

A report in the August issue of *Behavioral Neuroscience,* published by the American Psychological Association, describes how this novel use of data mining may enable investigators to test therapies to delay or even prevent disease, starting with hereditary forms.

The authors demonstrated their original software on mutant rats used as an animal model of amyotrophic lateral sclerosis (ALS), a progressive and fatal neurodegenerative disease that's inherited about one in 10 times. (The origins of the other cases are still under investigation.) The disease, which attacks the nerve cells that control movement, is identified with Yankee slugger Lou Gehrig, who died of ALS in 1941, two years after diagnosis.

Researchers led by Neri Kafkafi, PhD, of the Maryland Psychiatric Research Center, part of the University of Maryland's School of Medicine, mathematically analyzed about 50,000 predetermined movement patterns that resulted when rats roamed freely, one by one, in a small arena. The software created an abstract space defined by combinations of behavior such as speed, acceleration and direction of

movement. Mining the resulting behavioral data enabled researchers to test many more facets of behavior than they could analyze manually.

After videotaping the movement of two groups of rats – one type with the mutation that results in an ALS-type syndrome, the other type normal controls -- the scientists used the computer to "pan" for differences between groups and identified a unique motor pattern in mutant rats two months before disease onset (which would equate to roughly five to 10 years in humans).

Of the multitude of behavior patterns analyzed, the predefined "heavily braking while slightly turning away from the wall" showed a group difference. In two independent data sets, rats with the ALS-type mutation were significantly less likely than controls to brake and turn from the arena wall as they approached. Normal rats used that behavior for about 1.8 percent of their total movement time; the mutants for 1.2 percent.

"This is a very subtle difference but it is significant," says Kafkafi, who explains that the very subtlety underscores how hard it would be to tell the rats apart using the naked eye. "Persons with emerging ALS may also have similarly subtle symptoms."

"We can only guess why this pattern is less common in the mutants," Kafkafi adds. Losing the nerve cells that control leg muscles could result in problems with braking. The team is working with mechanical engineers to learn more about the meaning of the other movements.

Data mining to detect the subtle behavioral expression of mutations could conceivably allow investigators to test therapies aimed at preventing, slowing or stopping disease. By being able to predict more accurately which carriers may express the disease before they experience symptoms (the "premorbid" state), researchers could test medicines that

might prevent symptoms from emerging. Kafkafi says, "Such therapies could very well be effective against the non-genetic version of the disease as well."

Methods such as data mining can be therapeutically useful even before science understands how disease begins. The authors wrote, "The discovery of reliable behavioral endpoints with predictive validity, even before a good understanding of their etiology is achieved, can significantly improve intervention research."

Source: American Psychological Association