

PREDICTORS OF HD

By Lisa J. Bain – January 2008

As the search intensifies for treatments that might delay the onset or slow the progression of Huntington's disease (HD), identifying the disease early has also become more important than ever. Currently, a person is diagnosed with HD when he or she shows unmistakable motor signs, such as [chorea](#). However, recent research has demonstrated that the brain is affected many years before symptoms appear. In a study published in the journal *Neurology* (May 2007; volume 68, pp. 1710-1717), researchers investigated whether other clinical tests could identify HD earlier, before the disease has caused significant brain damage.

Who took part in this study?

The "participants" in this study were 226 individuals who were at risk for HD by virtue of having an affected family member; and who had been evaluated at Huntington Study Group (HSG) study sites in North America, Australia, and Europe between 1990 and 1999. In other words, participants were not enrolled specifically to take part in this study. During their participation in other HSG clinical or research studies, these individuals had agreed that the data collected during their examinations could be used in future research studies, as long as their identities were protected. Some of the participants had undergone genetic testing and knew they carried the gene mutation, but most had not been tested.

In order for their data to be included in this study, participants had to have been examined at least twice by clinicians at the HSG sites. Some participants had as many as 9 examinations, which allowed the investigators to track any progression of disease more accurately. All of the information collected about these participants was stored in a clinical database, from which Dr. Jane Paulsen and Dr. Douglas Langbehn from the University of Iowa retrieved data to search for early signs of HD.

What did the researchers do?

The main diagnostic tool that the HSG clinicians used to evaluate participants, the UHDRS (Unified Huntington's Disease Rating Scale), includes 15 motor items and 3 tests of cognitive function. After these tests have been completed, the neurologist gives an overall "diagnostic confidence" rating, ranging from 0 (normal) to 3 (definite HD). Drs. Paulsen and Langbehn considered all of these different specific clinical measures, as well as the participants' own sense of whether they have experienced symptoms of HD, to determine which of these items best predicted whether a person would be diagnosed with HD. Since they were looking for early signs of the disease, they only included participants who initially had a diagnostic confidence rating of 0 (no signs of HD) or 1 ("soft" signs of HD, which are also described as nonspecific motor abnormalities).

What did they learn?

As expected, the clinician's diagnostic confidence rating was a strong predictor of the likelihood that a participant would progress to a diagnosis of HD. In other words, those

with a rating of 1 were more likely to progress than those with a rating of 0. The total motor score and scores on the cognitive tests, combined with the global rating, added to the ability to predict whether an individual would progress, suggesting that the clinician's global rating alone was not picking up all the early signs of the disease.

The participants' sense of whether they were experiencing symptoms of HD also proved to be a strong predictor, which was a surprise to the researchers. "I had anticipated that there would be subtle preclinical findings in all areas, but what was especially interesting was that the subjective symptoms reported by the participants were so meaningful," said Dr. Paulsen.

Why is this study important?

One of the important outcomes of this study, according to Dr. Langbehn, was that it showed that neither the motor and cognitive scores nor the global clinical impression used to diagnose the disease were capturing all of the important information. This was a major motivator, he said, for developing even more detailed and sensitive tests that could be used in the [PREDICT-HD study](#), which began to collect data from at-risk participants in 2002.

This study also documented the importance of listening to what patients say about their illnesses. Dr. Paulsen said participants' assessments have been underappreciated in research, but that participants make a unique contribution to the overall assessment. "It's something we aren't capturing," she said.

What's next?

The ongoing PREDICT study is already providing information that confirms and extends the results of this study. In the meantime, said Dr. Langbehn, "I hope that clinicians will pay more attention to these other areas that we assessed, especially the subjective symptoms that patients report."

"We want to intervene while patients are still high functioning, when people first begin noticing something is wrong even when no one else does," added Dr. Paulsen. This study and the PREDICT study are paving the way so that when treatments do become available, clinicians will be able to identify who will benefit from them.

Chorea – The involuntary writhing movements that are a common and disabling symptoms of HD.