

# Method to predict Alzheimer's disease within two years of screening

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At the first signs of memory loss, most people start worrying and wonder, "What if I have Alzheimer's disease?" And yet, the disease is often diagnosed late in its development and sometimes up to ten years after the first pathological changes have affected the brain. A major goal in the treatment of Alzheimer's disease has been to provide earlier diagnosis so that patients can receive treatment as early as possible. A study by Sylvie Belleville, PhD, Director of Research at the Institut universitaire de gériatrie de Montréal, an institution affiliated with Université de Montréal, has shown a way to do just that. In their study, Sylvie Belleville and her team accurately predicted (at a rate of 90%) which of their research subjects with mild cognitive impairment would receive a clinical diagnosis of Alzheimer's disease within the following two years and which subjects would not develop this disease. The study was published in Volume 38, Issue 2 of the prestigious *Journal of Alzheimer's Disease*.

By combining brain imaging analysis with a neuropsychological assessment, Sylvie Belleville achieved remarkable sensitivity (targeting the people who will develop the disease) and specificity (eliminating false positives, that is those who would remain stable). The level of accuracy of this classification system is the major breakthrough of the study. "When used individually, neuroimaging and neuropsychology are effective but only up to a certain point. It is when combining and analyzing the results from both methods that we could achieve such an exceptional level of accuracy," explained Sylvie Belleville.



## Major benefits for Alzheimer's patients and for research

"For the moment, we can't diagnose this disease very early due to the lack of reliable protocols. Thus, there is a risk of erronously identifying the disease when trying to diagnose it too early. Identifying markers that correctly predict the subsequent onset of more severe symptoms that are sensitive and specific considerably reduces the uncertainty of early diagnosis. The innovation here is showing that two different approaches can be combined to aid in diagnosis," said Sylvie Belleville.

Researchers who work on Alzheimer's disease can build on this advance to go even further. "The clinical benefits of these extra two years are enormous. We can now evaluate the effectiveness of pharmacological and non-pharmacological therapies on the outcome of a clinical diagnosis of Alzheimer's disease in people identified with these tools. We could assess whether these treatments are more effective when administered earlier. The questions we now need to answer are whether pharmacological treatment started at the onset of early warning signs will slow the illness and whether brain plasticity could be stimulated in a more structured way to delay symptoms that cause disability."

### **Research summary**

The objective of this work was to examine the potential benefit of combining two classes of measures for the detection of incipient dementia in individuals with mild cognitive impairment (MCI). Baseline measures included MRI measures of hippocampal volume, cortical thickness and white matter hyperintensities as well as different measures of episodic memory and executive control functions. The study identified the measures that best predicted which MCI patients would progress to dementia compared to those who remained stable. The



strongest neuroimaging predictors were baseline cortical thickness in the right anterior cingulate and middle frontal gyri. For cognitive predictors, we found that deficits in both free recall and recognition episodic memory tasks were highly suggestive of progression to dementia. Cortical thinning in the right anterior cingulate gyrus, combined to controlled and familiarity-based retrieval deficits, achieved a classification accuracy of 87.5%, a specificity of 90.9% and a sensitivity of 83.3%. This predictive model including both classes of measures provided more accurate predictions than those based on neuroimaging or cognitive measures alone.

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