ASX Announcement

Australian research sheds new light on "highest risk" group for Alzheimer's disease

MELBOURNE, 15 July 2013: Australian scientists are helping to unravel the links between a person's brain chemistry, genes and their risk of developing Alzheimer's disease (AD).

Their research, presented at this week's Alzheimer's Association International Conference (AAIC) in Boston, reveals the interplay between two known AD risk factors being the build-up of amyloid plaques in the brain and a common gene variation (BDNF Val66Met).

Professor Paul Maruff, Chief Scientific Officer at Melbourne-based cognition testing company Cogstate, said the research also painted a clearer picture of who is most at risk of developing AD.

"Our studies conducted in the Australian Imaging Biomarkers and Lifestyle (AIBL) cohort have confirmed both elevated brain amyloid and this common gene variation are risk factors for Alzheimer's disease, with the presence of both signalling those at highest risk and patients in whom cognitive deterioration was more rapid," said Professor Maruff, a co-author on all four papers.

"This is important because it can help to identify those with the most to gain from early drug treatment and perhaps even behavioural intervention designed to prevent AD. Both approaches to prevention are currently a major international focus of companies and research groups.

"This research will also help to identify those older people who have mild cognitive impairment (MCI) but who have a low risk of AD, meaning their impairment may have other causes such as depression or stress which are more readily treatable," Prof Maruff said.

The research - four studies in total – is based on data collected for the major AIBL study which used Cogstate's cognition testing as a highly-sensitive measure of cognitive health.

The AIBL study, which started in 2006 and involves more than 1000 people aged over 60 years, is looking for biomarkers, cognitive characteristics, and other factors contributing to AD.

Key findings of the four studies supported by AIBL include:

- Among healthy older people, and people who meet clinical criteria for mild cognitive impairment (MCI), high brain amyloid levels indicate that AD-related neuro-degeneration has begun and that memory will now decline at a constant rate.
- In healthy older people with abnormally high brain amyloid levels who also carry the BDNF Val66Met gene, memory and other aspects of cognition will decline faster than in those who do not carry this variant.
- Older people diagnosed with MCI, and who have normal brain amyloid levels, do not show decline in memory over time and therefore their cognitive impairment may be due to other more readily treatable causes such as depression or stress.
- The sensitivity of Cogstate's cognition testing was also confirmed as a "useful tool for the identification of AD-related memory impairment" in clinical settings.

Prof Maruff said a clearer picture of AD risk was emerging (see chart) with around 30% of Australians aged over 60 years known to have high brain amyloid levels.

Among this group, around one in three will also carry the BDNF Val66Met gene variation, further increasing their AD risk.
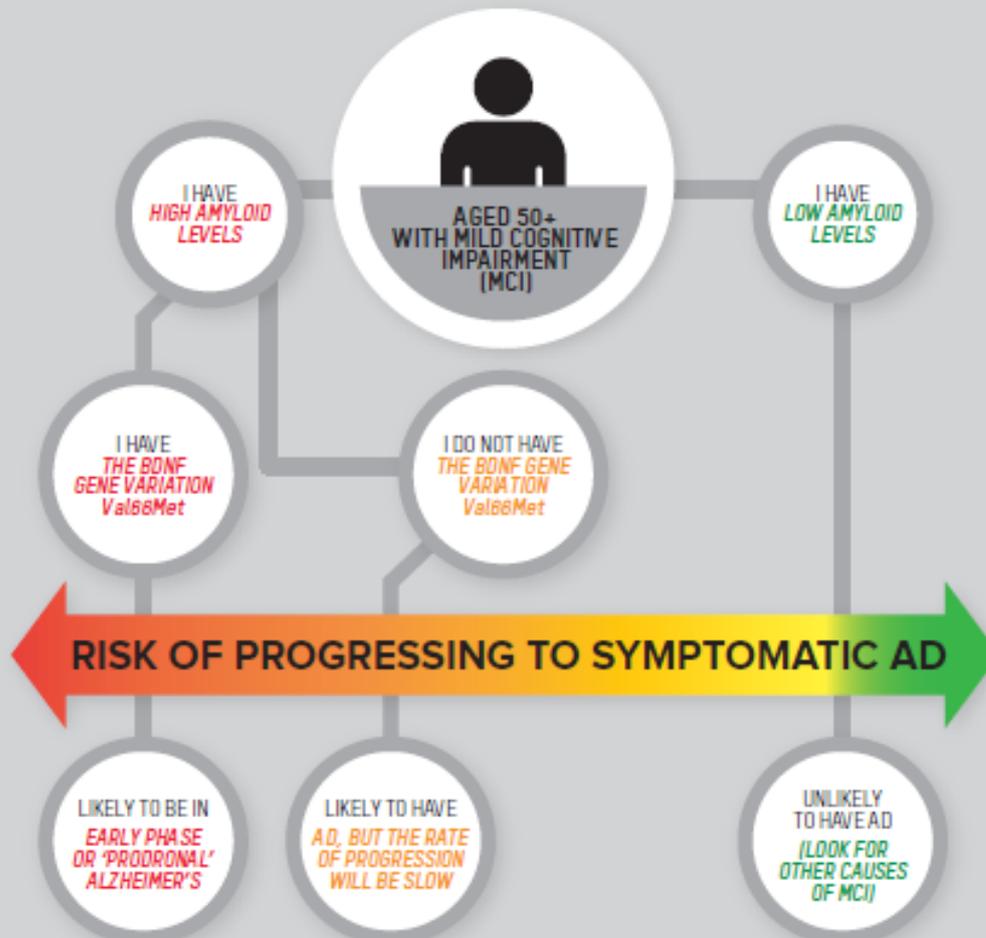
"A better understanding of these AD-related population and biological factors places us closer to developing effective AD treatments and intervention strategies," Prof Maruff said.

These findings are contained in four papers being presented at the *Alzheimer's Association International Conference (AAIC),* July 13 – 18. The titles are:

1. Cognitive consequences of high Aβ amyloid in MCI and healthy older adults: Implications for early detection of AD (ID: 38133)
2. Aβ amyloid and cognitive change: Examining the preclinical and prodromal stages of AD (ID: 38139)
3. Modulation of Aβ amyloid-related cognitive decline by brain-derived neurotrophic factor Val66Met polymorphism in preclinical AD (ID: 38143)
4. Clinical utility of the Cogstate brief battery in AD related memory impairment (ID: 38432)

FACTORS IN ALZHEIMER'S RISK

Studies using Cogstate testing have shown how a person's brain chemistry (high amyloid levels) and genetic makeup (BDNF gene variation Val66Met) determine Alzheimer's disease' risk.

AGED 50+ WITH MILD COGNITIVE IMPAIRMENT (MCI)

I HAVE *HIGH AMYLOID LEVELS*

I HAVE *LOW AMYLOID LEVELS*

I HAVE *THE BDNF GENE VARIATION Val66Met*

I DO NOT HAVE *THE BDNF GENE VARIATION Val66Met*

RISK OF PROGRESSING TO SYMPTOMATIC AD

LIKELY TO BE IN *EARLY PHASE OR 'PRODRONAL' ALZHEIMER'S*

LIKELY TO HAVE *AD, BUT THE RATE OF PROGRESSION WILL BE SLOW*

UNLIKELY TO HAVE AD *(LOOK FOR OTHER CAUSES OF MCI)*

Beta-amyloid protein forms plaques in the brain, damaging neurons and leading to Alzheimer's disease (AD). The VAL66met section of the BDNF gene has been connected with memory retention.

COGSTATE

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About Cogstate

Cogstate Ltd (ASX: CGS) is a multi-faceted cognitive assessment and training company, focused on the development and commercialisation of rapid, computerised tests of cognition (brain function). It has three distinct business units:

Clinical Trials: In the clinical drug trial market, Cogstate technology and associated services are used by pharmaceutical and biotechnology companies to quantify the effect of drugs or other interventions on human subjects participating in clinical trials. Since sales into the clinical trials market began in 2004, Cogstate has secured agreements with top pharmaceutical companies including Pfizer, AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Johnson & Johnson, Novartis, Lundbeck, Dainippon Sumitomo, Targacept, Otsuka, and Servier.

Axon Sports: The mission of Axon Sports is to "protect and train the athletic brain". Axon's focus is to research, develop and deliver cutting edge tools to assess, monitor and improve the athletic brain.

Axon has been developing sport specific training products, initially focussed on American football and baseball, and the resulting technologies have now been launched within a small number of elite US college programs. In addition, the first of Axon's consumer iPad apps was launched in 2012.

In the area of sports related concussion, Cogstate's technology has been used by a number of highly regarded institutions and sporting organisations around the world for almost 10 years. That technology is now marketed to consumers as Axon Sports. Current users of Cogstate/Axon Sports in Australia include the AFL and NRL, whilst in the USA elite programs such as the NBA, WNBA, NHL as well as college programs such as University of Notre Dame, University of Michigan and University of Connecticut all use the Axon Sports system.

Healthcare: In the primary care or general practice setting, the Cogstate's COGNIGRAM™ assesses cognition in patients and the reports generated on the basis of this assessment can allow physicians to identify subtle changes that could be indicative of the early stage of a neurodegenerative disease, such as Alzheimer's disease. Cogstate intends to develop COGNIGRAM™ to monitor changes in cognitive function following concussion or after treatment with drugs or other types of interventions. In June 2012, Cogstate entered into an agreement with Merck Canada Inc. providing it with the exclusive right to market and promote COGNIGRAM™ in Canada.