## Speaker: Sharon Naismith

## Optimising cognition in at-risk older people: A journey of discovery, clinical research and health translation.

10:15 - 11:15am
Friday, 3rd February, 2023
Pacific Ballroom E

Abstract:
Modifiable dementia risk factors such as depression, cardiovascular disease and physical and cognitive activity account for 40-50% of dementia risk and their association with neuropsychological performance is evident in both preclinical and prodromal dementia stages. Over the course of her career, Professor Naismith has examined how modifiable risk factors relate to various aspects of cognition and brain degeneration and how best to treat them. She has led the development of cognitive training programs and clinical trials targeting these risk factors. She has authored more than 350 papers across a range of fields largely focused on cognition but also utilising neuroimaging, genetics, e-health, data syntheses, as well as clinical trials and health services. Her most recent work focuses on how sleep and circadian disturbance is linked to cognitive decline, how best to treat sleep disturbance in older people and how to utilise new digital sleep technologies to derive maximal reach and scale within the rapidly rising ageing population.
In this presentation, the evolution of her program of work over time will be considered with respect to core discipline-specific foundations but also amidst the changing research landscape, research challenges and the need to optimise health impact. The importance of multidisciplinarity, career mentors and partners, capacity building, and engaging with government and policy makers will be discussed as well as other factors considered to be key to mid-career research success.

## Poster Session 06: Memory | Movement Disorders | Neurodegenerative Disorders | Demyelinating Disorders | Sleep Disorders

10:15 - 11:30am
Friday, 3rd February, 2023
Town & Country Foyer

### 1 The Impact of *APOε4* and *BDNF* val66met on Executive Function in Older Veterans with Post-traumatic Stress Disorder

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**Objective:** Both *Apolipoprotein* ε4 (*APO*ε4) and *Brain-Derived Neurotropic Factor* val66met (*BDNF*-met) have been implicated as cognitive risk polymorphisms and may signal a more rapid trajectory of cognitive decline (Boots et al., 2017; Lim et al., 2015). The presence of both risk alleles may additively result in greater cognitive difficulties (Cechova et al., 2020), specifically executive functioning (Sapkota et al., 2017). As executive functioning difficulties can be associated with Posttraumatic Stress Disorder (PTSD; Woon et al., 2017), individuals with PTSD who carry these polymorphisms may be at higher risk for decline in executive functioning. In this study, we examined the cross-sectional and longitudinal impact of these alleles on executive functioning performance in Veterans with PTSD.
**Participants and Methods:** Seventy community-dwelling male Veterans were enrolled as part of a larger study at VAPAHCS and consented to genetic analysis. A current or lifetime history of PTSD (score ≥ 40 on the CAPS-IV; Blake et al., 1995) was required for study participation. Trail Making Test B (TMT-B; Army Individual Test Battery, 1994) was used to assess executive functioning. TMT-B was part of a comprehensive neuropsychological battery administered at baseline and yearly over the following three years. Mean age and education were 61 years old (SD = 4.5; range = 55-78) and 14 years (SD = 2.3; range = 8-20), respectively.

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The majority of the sample was White (71%) and were from the Korean and Vietnam War eras.
**Results:** *APOε4* and *BDNF*-met were present in 29% and 27% of the sample, respectively; both were present in six participants. Regression models were fitted separately for TMT-B raw time-to-complete and number of errors, both cross-sectionally at screening and then longitudinally. The presence of *BDNF*-met was a significant predictor of TMT-B time and number of errors in both models (Time: $\beta$ = 0.09, p = 0.03 and $\beta$ = 0.11, p < 0.01; Errors: IRR = 2.4, p = 0.01 and IRR = 1.9, p = 0.01), while *APOε4* only predicted errors longitudinally (IRR = 1.8, p = 0.03). There was no significant allelic interaction; however, the presence of both alleles additively multiplied TMT-B errors by approximately 3.7 times at screening (IRR = 3.7; p = 0.01) and 3.3 times longitudinally (IRR = 3.3; p < 0.01).
**Conclusions:** Altogether, these results are suggestive of an adverse, additive, effect of the *APOε4* and *BDNF*-met polymorphisms on executive functioning, in particular error-proneness, with their combined presence tripling the errors made on TMT-B cross-sectionally and longitudinally. Consistent with previous research, the TMT-B error analysis increases detection of cognitive impairment, similar to other clinical samples (Varjacic et al., 2018). While TMT-B errors are typically interpreted qualitatively, the strong effect of these established risk alleles on error rates further support this metric as a clinically useful indicator of executive dysfunction in a PTSD population. In keeping with the Boston Process approach, these findings support the importance of error analysis in clinical interpretation of neuropsychological performance.

**Categories:** Genetics/Genetic Disorders
**Keyword 1:** apolipoprotein E
**Keyword 2:** executive functions

## 2 The Role of Causality in Understanding How Prior Event Knowledge Impacts New Learning

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**Objective:** The influence of prior knowledge on new learning is well established. However, there has been less research dedicated to teasing apart the key components of prior knowledge's structure that contribute to memory enhancement. In the current study, we focused on event structures, which include various relations, such as associative, causal, and temporal. Given that events possess attributes relevant to numerous cognitive memory processes, we were most interested in exploring how event structures that possess causal relations enhance new memory formation. Specifically, we examined whether events that exhibit causal associative relations provide an additional boost to new learning compared to event structures with non-causal associative relations.
**Participants and Methods:** Forty-six undergraduate students took part in the study. Participants' learning of the content of image pairs that exhibit everyday, real-world events were measured using a cued recall paradigm. The stimuli consisted of 60 image pairs that illustrated two events that were related causally and associatively (i.e., causal pairs); related only associatively (i.e., non-causal pairs); or not related at all (i.e., unrelated pairs). During an encoding phase, image pairs were presented one at a time, and after the presentation of each image pair, participants answered an encoding question that focused on the relationship between the two images. After the encoding phase and a short filler task, participants were shown a cue image (always the first picture from the pair) and were asked to provide a brief written description of the content of the second presented image from each pair. Also, as a manipulation check, we asked subjects to rate each image pair on causal direction and association strength after completion of the cued recall memory task.
**Results:** We found that, relative to unrelated pairs, events that possess associative relations (i.e., both causal and non-causal items) benefit learning of new information. In addition, causal relations provided an additional boost to new learning. Specifically, cued recall performance is best for causal pairs, followed by non-causal pairs and unrelated pairs. Moreover, causal direction ratings significantly predict overall item-level accuracy above and beyond general associative relations that exist in events. We also examined recall accuracy for specific content information within each event (i.e., agent, action, object) and found that causal

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