NHS
National Institute for Health Research

Seed fund STANDARD APPLICATION FORM

Section 1: Details of the research papers

Paper 1

Koso, M. & Hansen, S. (2006). Executive function and memory in post-traumatic stress disorder: a study of Bosnian war veterans. *Eur Psychiatry* 21, 167-73.

What are the Independent/Predictor and Dependent/Outcome variable(s) observed in this study?

Independent Variables:
The independent variable is the presence or absence of PTSD (diagnosed by psychiatrists according to DSM-IV criteria).
Dependent Variables:
The dependent variables include performance on neuropsychological tests assessing attention, memory, executive function, and verbal intellectual function.

List UP TO TWO further variables, the authors could have accounted for and why (enhancing the quality of the study)

Note that you will need to provide a short justification here. You will also need to provide a reference(s) highlighting the importance of the variable(s) you suggest for the given study.

Including **demographic factors** like socioeconomic status and marital status (Assari, 2020) helps uncover social determinants impacting cognitive function in PTSD populations, offering a more holistic view.
Moreover, evaluating **clinical variables** such as trauma severity and comorbid psychiatric disorders (Jakob *et al.*, 2017) aids in identifying and controlling confounders, improving study validity.

Paper 2

Esterman, M., Stumps, A., Jagger-Rickels, A., Rothlein, D., DeGutis, J., Fortenbaugh, F., Romer, A., Milberg, W., Marx, B. P. & McGlinchey, R. (2020). Evaluating the evidence for a neuroimaging subtype of post-traumatic stress disorder. Science Translational Medicine 12, eaaz9343.

What are the Independent/Predictor and Dependent/Outcome variable(s) observed in this study?

Independent variables: PTSD status (presence or absence), cognitive impairment status (presence or absence), and specific neuropsychological measures (e.g., memory composite score, long-delay free recall, long-delay recognition, executive function, attention).

Dependent variable: Within-ventral attention network (VAN) connectivity, which served as the primary outcome measure. Additionally, the study explored other brain network connectivity as secondary outcomes.

List **UP TO TWO** further variables, the authors could have accounted for and why (enhancing the quality of the study)
ⓠ Note that you will need to provide a short justification here. You will also need to provide a reference(s) highlighting the importance of the variable(s) you suggest for the given study.

1. Socioeconomic status (SES): Recording income, education, and employment status reveals how socioeconomic disparities affect PTSD severity and cognition. Lower SES may limit mental health resources, worsening symptoms and cognitive impairment (Assari, 2020).

2. Pre-existing psychiatric conditions: Identifying depression and anxiety clarifies PTSD's distinct impact on cognition. Distinguishing PTSD from comorbidities elucidates its cognitive profile (Lassemo *et al.*, 2016).

Section 2: Application Summary Information - Your Study – Research Question

Research Question
ⓠ ⓠ This make clear what the proposed cross-sectional study will be investigating. Any abbreviations should be spelled out in full. The cross-sectional study should focus on cognition in individuals with post-traumatic stress disorder (PTSD). **NOTE: The application is for a <u>cross-sectional study</u>, so please ensure this is referenced in the question.**

What are the specific differences in cognitive function between individuals diagnosed with post-traumatic stress disorder (PTSD) and a control group without PTSD, as measured by a battery of neuropsychological tests assessing attention, memory, executive function, and verbal intellectual function?

Section 3: Why should the panel fund your cross-sectional study?

750 word +10% justification
ⓠ A justification is a clear explanation of the reasons you research is important to carry out. A good justification can inform others about your research such as members of the public, health professionals, policy makers and the media and should encourage the research funders to pick your proposal for funding. **As this is the main part of your application which will be considered by the reviewing panel, you should ensure that the information is accurate, succinct, clearly laid out and provides sufficient detail.** Content When writing your summary consider including the following information where appropriate: 1. *What is the problem being addressed?* 2. *Why is this research important in terms of improving the health and/or well-being of the public and/or to service users and health care services?* 3. *Brief review of existing evidence – How does the existing literature support this proposal?* 4. *What are the current gaps in the literature and how can your research address these?* 5. *What is the research question / aims and objectives?* Please use APA style citations. All in-line citations count towards the word count. Please remember to include the two papers relating to your topic from Section 2.

1. Problem Identification
The problem being addressed is the understanding of cognitive differences between individuals with post-traumatic stress disorder (PTSD) and those without. The investigation goal is to detect particular changes in attention, memory, psychomotor function and verbal intellectual function, giving the picture of cognitive manifestations of PTSD (Esterman *et al.*, 2020).

2. Importance of Research
This research is pivotal for improving public health by explaining the consequences of PTSD for cognition, having tailored interventions thereof, and generally boosting well-being. Learning these contrasts can help healthcare providers offer personalized assistance to people with PTSD, which ultimately leads to improved patients' health results and way of life.

3. Existing Evidence Review
PTSD, or post-traumatic stress disorder, is one of the most destructive mental health problems which may strike a person who already suffered from psychological trauma. It has mostly described the symptoms: intrusive memory recall, behavioural avoidance, depressed mood, and cognitive alterations, as well as hyperarousal symptoms. Gaining insight into the particular distinctions in cognition between those with PTSD as compared to those without is of integral importance for designing effective treatments and interventions. This literature review, in which previous studies on cognitive function among PTSD patients are examined, shows us a picture of the intricacy of cognitive impairment connected to the disorder. By means of functional neuroimaging and appropriate cognitive tasks, Etkin *et al.* (2019) presented the most breakthrough results to outline the PTSD subtypes. It was shown that a subgroup of patients who had verbal memory impaired showed reduced functional connectivity of the ventral attention network (VAN) during resting state. These patients also did not have an effective response to psychotherapy, which implies the happening of unique neural phenomena associated with the one manifested in memory deficits of PTSD. Nonetheless, the generalization of the neural network and the cognitive domain is not yet confirmed, posing for further analysis.

Esterman *et al.* (2020) aimed to verify and extend this to combat-exposed veterans. Using a straightforward battery of neuropsychological tests, they examined whether the PTSD patients and neuropsychologically diagnosed cognitive impairment individuals showed VAN biomarker connectivity. In contrast to expectations, there was no lower VAN connectivity in individuals belonging to the verbal memory deficits subgroup. In contrast, they assessed a reduced VAN activity in people with attentional deficits, indicating possible connections between attention and VAN connectivity. These findings call for attention to the complexity of cognitive impairment in PTSD and for utilizing more selective neuropsychological assessment methods. The neuropsychological functions related to attention, executive function, and everyday memory were evaluated by Koso & Hansen (2006) among Bosnian male combat veterans with PTSD. They identified cognitive impairments that were greatly prevalent in each of the domains, including attention, working memory, executive function and memory. Noteworthy, these deficits were not caused by any alcohol abuse, brain injury or even educational level. Research indicates that PTSD may be linked to dysfunction of the higher dimensional attentional processes, which show up as deficiencies in memory and cognitive functions.

In sum, these studies have shed significant light on the cognitive consequences for people living with PTSD. However, there are some results which back up the idea that different cognitive subtypes characterize PTSD; other data indicate that memory and other cognitive functions are affected in all domains. The difference in results highlights the heterogeneity of PTSD as well as the necessity of customized diagnostic and treatment strategies for the individuals. Research in the future should continue looking into the neurophysiological basis and the clinical outcomes of cognitive dysfunction in PTSD disorder, targeted at the development of new interventions to restore normal cognitive performance in these individuals.

4. Gaps in Literature
Notwithstanding very recent achievements, there are still quite a serious amount of gaps in the scientific community researching the different cognitive aspects of PTSD (Etkin *et al.*, 2019). Although evidence has shown that some subtypes exist with regard to cognitive problems like verbal memory deficits (Koso & Hansen, 2006), there are problems in relation to replication and generalizability (Esterman *et al.,* 2020). Furthermore, the specialization of neural imprints related to cognitive dysfunction is also not understood very clearly. Future researches are required to understand the cellular mechanisms for cognitive damage fully in PTSD. Besides this, the absence of a common diagnostic method when assessing cognitive variation in an individual with PTSD makes us understand that there is a need for better neuropsychological instruments to capture cognitive variability in PTSD individuals and guide treatment.

5. Aim and Objectives
Aim:
The purpose of this research study is to determine the unique variations in cognitive function between individuals with Post-traumatic stress disorder (PTSD) and the group of people who are not suffering from PTSD through a battery of neuropsychological tests tilling attention, memory, executive function, and verbal intellectual function.

Objectives:
1. The purpose of focusing on differences between the brains of subjects with PTSD and the control group is to evaluate the performance levels of participants concerning attention, such as sustained attention and response inhibition.
2. To characterize differences in memory function between the PTSD group and the control group that would reflect the performance with tasks that will test immediate and delayed recall of verbal and visual information.
3. To evaluate executive function disparities between individuals with PTSD and the control group, specifically examining abilities related to cognitive flexibility, problem-solving, and planning.
4. To investigate variations in verbal intellectual function between the PTSD and control group.

[]/750 words

Please provide this word count on your cover sheet.

Section 4: Your cross-sectional study details

Who are your study participants? (Age range, gender, condition, any other important you deem important)

Note that you will not need to provide a justification here.

- Adults aged 18-65
- Diverse genders
- With and without PTSD
- Considering trauma exposure
- Co-occurring conditions (depression or anxiety)
- Medication usage
- Education
- Socioeconomic status
- Marital status

Your independent and dependent variable of your cross- sectional study

Note that you will not need to provide a justification here.

Independent variable:
Diagnosis of post-traumatic stress disorder (PTSD) (presence or absence)

Dependent variables:
Performance on neuropsychological tests assessing:
1. Attention
2. Memory
3. Executive function
4. Verbal intellectual function

At least ONE example of a valid(ated) instrument to measure your independent and/or dependent variable (i.e. a psychometric questionnaire, fMRI or PET) and why this was chosen

Note that you do need to provide a justification here and a citation for the relevant validation study where appropriate, i.e. for questionnaires.

Diagnosis of post-traumatic stress disorder (PTSD) (presence or absence): CAPS-IV
CAPS-IV is a well-known and validated diagnostic tool used in clinical settings; it provides structured clinical interviews which are standardized according to strict criteria which are used to assess the disorder, hence improving reliability and consistency in diagnosis-making (Esterman *et al.*, 2020).

Attention: Sustained Attention to Response Task
Memory: Rivermead Behavioral Memory Test
Executive function: Trail-Making Test

Verbal intellectual function: Wechsler Adult Intelligence Scale (Verbal part)
These neuropsychological tests are well-known measures that are mostly used in clinical settings, either in research or clinical care, besides providing standardized measurements to clinicians for time attention, memory, executive function, and verbal intelligence (Koso & Hansen, 2006). These developments allow for the accurate diagnosis of the affected individual's cognitive domains and an accurate assessment of their cognitive functioning.

Section 5: Citations

FULL reference list

Make sure this list does not just feature references cited in your justification, but all references provided in the application form. Please use APA style throughout.

Assari, S. (2020). Family Socioeconomic Status and Exposure to Childhood Trauma: Racial Differences. Children, 7(6), 57.

Esterman, M., Stumps, A., Jagger-Rickels, A., Rothlein, D., DeGutis, J., Fortenbaugh, F., Romer, A., Milberg, W., Marx, B. P. & McGlinchey, R. (2020). Evaluating the evidence for a neuroimaging subtype of post-traumatic stress disorder. *Science Translational Medicine* 12, eaaz9343.

Etkin, A., Maron-Katz, A., Wu, W., Fonzo, G. A., Huemer, J., Vértes, P. E., Patenaude, B., Richiardi, J., Goodkind, M. S., Keller, C. J., Ramos-Cejudo, J., Zaiko, Y. V., Peng, K. K., Shpigel, E., Longwell, P., Toll, R. T., Thompson, A., Zack, S., Gonzalez, B. & Edelstein, R. (2019). Using fMRI connectivity to define a treatment-resistant form of post-traumatic stress disorder. Science Translational Medicine, 11(486).

Jakob, J. M. D., Lamp, K., Rauch, S. A. M., Smith, E. R. & Buchholz, K. R. (2017). The Impact of Trauma Type or Number of Traumatic Events on PTSD Diagnosis and Symptom Severity in Treatment Seeking Veterans. The Journal of Nervous and Mental Disease, 205(2), 83–86.

Koso, M. & Hansen, S. (2006). Executive function and memory in post-traumatic stress disorder: a study of Bosnian war veterans. *Eur Psychiatry* 21, 167-73.

Lassemo, E., Sandanger, I., Nygård, J. F., & Sørgaard, K. W. (2016). The epidemiology of post-traumatic stress disorder in Norway: trauma characteristics and pre-existing psychiatric disorders. Social Psychiatry and Psychiatric Epidemiology, 52(1), 11–19. https://doi.org/10.1007/s00127-016-1295-3

- Thank you for submitting your seed competition research application. Good luck! -