Preliminary evidence on the neural correlates of timing deficit in post-traumatic stress disorder

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ABSTRACT
It has recently been suggested that a deficit in time processing may be considered a cognitive marker of Post-Traumatic Stress Disorder (PTSD). However, the neural correlates of this cognitive deficit in PTSD remain unknown. Voxel-based morphometry and supra-second perceptual time processing data from 8 participants with PTSD and 19 healthy controls have been examined. In line with previous investigations, PTSD patients overestimated the duration of the displayed stimuli. Moreover, their time estimation was more variable than that of controls. Critically, compared to controls, a higher grey matter volume was reported in most of neural regions of PTSD canonically associated with supra-second perceptual timing. These data provide preliminary evidence that the abnormal neuroplasticity of this neural network may be responsible for the altered experience of time in PTSD.

Evidencia preliminar sobre los correlatos neurales del déficit de tiempo en el trastorno de estrés postraumático
Recientemente se ha sugerido que un déficit en el procesamiento del tiempo puede considerarse un marcador cognitivo del trastorno de estrés postraumático (TEPT). Sin embargo, los correlatos neurales de este déficit cognitivo en el TEPT siguen siendo desconocidos. Se ha examinado la morfometría basada en vóxeles y los datos de procesamiento del tiempo de percepción en supra-segundos de 8 participantes con TEPT y 19 controles sanos. De acuerdo con investigaciones anteriores, los pacientes con TEPT sobrestimaron la duración de los estímulos mostrados. Además, su estimación del tiempo fue más variable que la de los controles. Criticamente, en comparación con los controles, se reportó un mayor volumen de materia gris en la mayoría de las regiones neurales del TEPT canonicamente asociado con el tiempo perceptual en supra-segundos. Estos datos proporcionan evidencia preliminar de que la neuroplasticidad anormal de esta red neuronal puede ser responsable de la experiencia alterada del tiempo en el TEPT.

A growing literature documents altered experience of time (e.g. time overestimation and higher estimation variability) in posttraumatic stress disorder (PTSD) (Bar-Haim, Kerem, Lamy, & Zakay, 2010; Brewin, Kleiner, Vasterling, & Field, 2007; Frewen & Lanius, 2014; Vicario & Felmingham, 2018). This suggests that a dysfunctional time representation can be a cognitive marker of PTSD, which may originate from brain alterations associated with this clinical condition, as well as from the related attention and memory deficits (Vasterling, Brailey, Cons-tans, & Sutker, 1998).

We provide a new contribution to the field by exploring the neural correlates of time processing deficits in PTSD in a pilot study. We used data from the Brain Resource International Database to study the relationship between supra-second timing alteration in PTSD and the grey matter volume (GMV) of cortical and subcortical neural regions which are known to be directly involved in the processing of supra-second perceptual timing (Wi-

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er, Turkeltaub, & Coslett, 2010). Accordingly, our regions of interest (ROI) were the right inferior frontal gyrus (IFG), the Supplemental Motor Area (SMA), and left putamen, the right middle temporal gyrus (MTG), thalamus, insula, and supramarginal gyrus (SMG).

Eight participants with PTSD (2 males, age 39.6 ± 12.9) and nineteen healthy controls (8 males, age 39.9 ± 11.5) were examined with a supra-second perceptual time estimation task of neutral visual stimuli used in a previous investigation (Vicario & Felmingham, 2018). Details about participants, paradigm and MRI data are provided in the supplemental materials. Participants’ task performance was evaluated by considering the proportional bias (PB) score, which provides a measure of the estimation accuracy; the estimation bias variability (EBV) score, which represents the standard deviation average of the proportional bias (see supplemental materials for details).

The established statistical significance criterion (p-level) was ≤0.05. In terms of behavioural performance, we confirmed previous investigations documenting time overestimation (PB. PTSD: M = 0.123 vs. Controls: M = −0.048, t = 2.147, p = .041) and higher variability (EBV. PTSD: M = 0.337 vs. Controls: M = 0.117, t = 2.971, p = .006) in PTSD compared to controls.

In terms of neural patterns, higher GMV were found in the left (PTSD: M = 0.456, Controls, M = 0.397, t = 2.069, p = .048) putamen; in the right MTG (PTSD: M = 0.537, Controls, M = 0.490, t = 2.468, p = .020), in the right insula (PTSD: M = 0.671, Controls, M = 0.603, t = 2.834, p = .008), and in the left (PTSD: M = 0.363, Controls, M = 0.287, t = 2.913, p = .007), and the right (PTSD: M = 0.405, Controls, M = 0.310, t = 3.592, p < .001) thalamus of PTSD compared to control participants. No further significant results were found (p < .05).

Further analyses exploring the association between task performance (PB and EBV scores) and ROI GMV documented a significant negative correlation, for the control group, between PB score and the GMV of the right IFG (r = −0.494, p = .031). Moreover, a no significant negative correlation trend was found between PB score and the GMV of the right MTG (r = −0.447, p = .054). On the other hand, no correlations were reported for the PTSD sample (see supplemental material for details). These results provide the first preliminary evidence on the neural bases of abnormal supra-second perceptual timing in PTSD. The greater GMV in the left putamen, middle temporal gyrus, insula and thalamus in PTSD suggests that the abnormal timing pattern of this clinical population may be related to the atypical volume of these brain regions, which are also known to be involved in the expression of classical PTSD symptoms (Mickleborough et al., 2011; van Rooij et al., 2014), including dissociative flashbacks, which have been described as trauma-related altered states of consciousness of a person’s sense of time-memory (Frewen & Lanius, 2014).

The absence of correlations between the GMV of the ROI and the respective timing performance in the PTSD, unlike what reported on healthy controls, could reflect the low numerosity of the clinical sample. Alternatively, it may indicate inefficient involvement of these brain regions when performing the current timing task. However, given the non-neuro-functional nature of the current data, further investigations involving functional neuroimaging methods with a larger clinical sample are needed.

Data availability statement
The data are deposited at the Brain Resource International Database located in Sydney, Australia (BRID, http://www.brainnet.net/about/governance-and-management/). Data can be obtained by contacting the BRAINnet Foundation administrator at michelle.wang@brainnet.net.

Disclosure statement
No potential conflict of interest was reported by the author(s).

Ethics statement
The study was approved by the Tasmanian health and Medical Research Ethics committee and at the University of Tasmania (Ref N. H0016534). All methods were performed in accordance with the relevant guidelines and regulations from our Institution and the Tasmanian health and Medical Research Ethics committee.

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