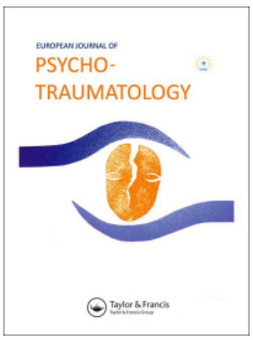

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LETTER TO THE EDITOR

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 over-estimated 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 neuronales 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. Críticamente, en comparación con los controles, se reportó un mayor volumen de materia gris en la mayoría de las regiones neuronales del TEPT canónicamente 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.

创伤后应激障碍时间缺陷神经相关性的初步证据

最近有人提出, 时间处理缺陷可能被认为是创伤后应激障碍 (PTSD) 的一个认知标志。然而, 这种PTSD认知缺陷的神经相关性仍然未知。已经考查了来自 8 名患有 PTSD 的参与者和 19 名健康对照的基于体素的形态测量和超秒感知时间处理数据。与之前调查一致, PTSD 患者高估了所显示刺激的持续时间。此外, 其时间估计比对照更具可变性。至关重要的是, 与对照组相比, 在大多数PTSD超秒感知时间严格相关的神经区域中报告了更高的灰质体积。这些数据提供了初步证据, 表明该神经网络的异常神经可塑性可能是造成 PTSD 时间体验改变的原因。

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KEYWORDS
PTSD; Perceptual timing; supra-second duration; grey matter volume

PALABRAS CLAVE
TEPT; tiempo de percepción; duración en supra segundos; volumen de materia gris

关键词
PTSD; 感知时间; 超秒持续时间; 灰质体积

HIGHLIGHTS

- We provide preliminary evidence that abnormal grey matter volume of neural regions canonically associated with supra-second perceptual timing may be responsible for the altered experience of time in PTSD.

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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Supplemental data for this article can be accessed here

ener, 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 pa-rticipants. 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. Al-ternatively, 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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