

Sex difference in the role of acute catecholamines in subsequent PTSD

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Background

A potentially traumatic event, such as a motor vehicle accident (MVA), can result in subsequent PTSD¹. When confronted with severe threat, the sympathetic adrenal medullary (SAM) system releases the catecholamines epinephrine, norepinephrine, and dopamine to trigger a hyperarousal response, commonly referred to as the fight-or-flight response²⁻⁴. However, most research has been based on men and male animals⁵⁻⁶ and little is known about how sex differences in the acute trauma response influence symptom development⁵⁻⁶. We have previously suggested that men may be more likely to develop PTSD through a hyperarousal pathway, whereas a hypoarousal pathway (characterised by low catecholamine levels, low heart rate, and possibly dissociation) may be more likely to cause PTSD in women^{5, 7}.

The present study

The purpose of the present pilot study⁸ was to examine sex differences in the acute trauma response to serious accidents and their impact on subsequent PTSD. We hypothesised that sex moderates the role of the acute stress response in the development of PTSD symptoms, with acute catecholamine levels being positively associated with PTSD symptoms in men, but negatively associated with PTSD symptoms in women.

Methods

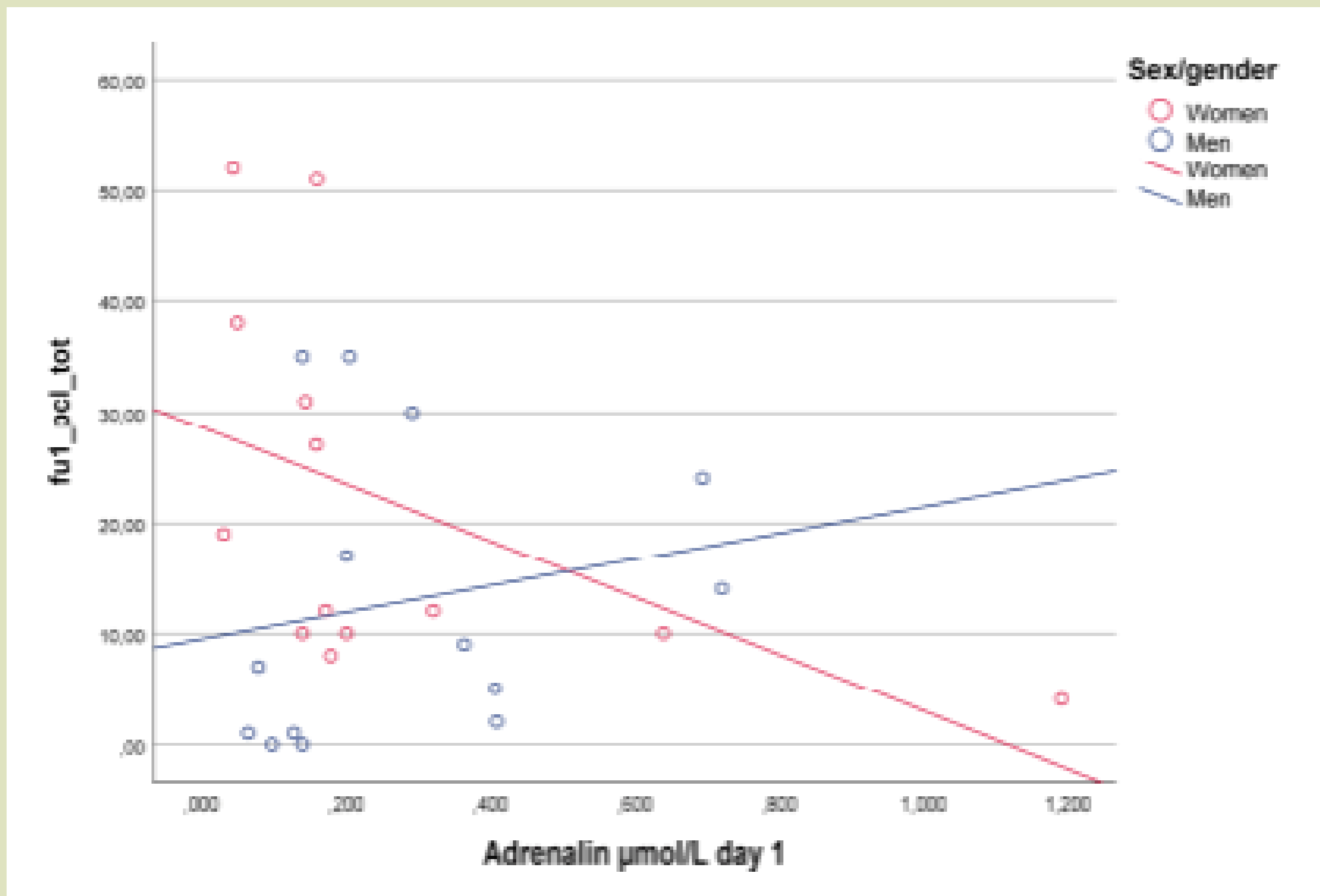
The participants had been involved in an MVA or another accident severe enough to elicit a trauma call and admission to the Hospital of South West Jutland in Denmark, a Level 2 trauma unit. Blood samples were collected at the hospital on the morning following the accident. Participants filled out questionnaires at 3 and 6 months, assessing ICD-11 and DSM-5 PTSD and CPTSD symptoms. Of 77 included participants, 33 provided PTSD data at 3 months (use QR code for flow chart). Non-parametric correlations were analysed with Spearmann's rho.



Results

Estimated PTSD prevalence was low, especially for ICD-11 PTSD, and sex differences in PTSD severity were negligible. Men had higher norepinephrine and epinephrine levels than women on the morning following the accident, consistent with a more evident hyperarousal response in men. Epinephrine was positively correlated with subsequent PTSD symptoms in men. Though correlations were not statistically significant due to low power, effect sizes were mostly moderate. In contrast, epinephrine was strongly negatively correlated with subsequent PTSD symptoms in women. Z-tests indicated significant moderation by sex at multiple times. Norepinephrine was moderately, though not statistically associated with PTSD in both sexes. Dopamine was not associated with PTSD severity.

Figure 1: Scatterplot showing acute epinephrine levels in relation to 3-month DSM-5 PTSD symptoms



Discussion

Though preliminary, the present findings indicate that the role of acute epinephrine in PTSD symptom development is moderated by sex, with high levels in men and low levels in women being associated with PTSD symptom development. If replicated, this may indicate in accordance with prior research and theory that the fight-or-flight response is associated with PTSD development in men⁹⁻¹⁰, but not in women. The consistently negative correlations between epinephrine and subsequent PTSD symptoms in women may indicate in accordance with our hypothesis that an acute SAM hypoarousal response is more likely to become sensitised and lead to PTSD development in women⁸. Sex was not found in the present study to moderate associations between either dopamine nor norepinephrine PTSD symptoms. In fact, in spite of being positively correlated with epinephrine ($\rho=.46$), norepinephrine was negatively correlated with PTSD symptoms in both sexes.

The present findings are preliminary and need to be investigated further. Even so, these data suggest that sex may moderate several associations between biomarkers and PTSD after a potentially traumatic accident⁸.

Table 1: Correlations (Spearmann's ρ) between catecholamines and PTSD severity

	Baseline ICD-11 PTSD	3 month DSM-5 PTSD	3 month ICD-11 PTSD	3 month ICD-11 CPTSD	6 month DSM-5 PTSD	6 month ICD-11 PTSD	6 month ICD-11 CPTSD
Women							
Day 1 epinephrine	-.74 ^{3d}	-.68 ^{2d}	-.58 ^{2a}	-.53 ¹	-.49 ^b	-.64 ^{1b}	-.51 ^a
Day 1 norepinephrine	-.10	-.51 ¹	-.24	-.24	-.06	-.29	-.16
Day 1 dopamine	-.04	.11	.18	-.05	-.04	-.04	.30
Men							
Day 1 epinephrine	.34	.41	.12	.12	.49	.52	.42
Day 1 norepinephrine	-.22	-.39	-.28	-.21	-.27	-.32	-.33
Day 1 dopamine	.20	.02	-.02	-.02	.12	.03	.03

¹⁾ $p < .10$; ²⁾ $p < .05$; ³⁾ $p < .01$
2-tailed p values for Z score test indicating sex moderation: ^{a)} $p < .10$; ^{b)} $p < .05$; ^{c)} $p < .01$; ^{d)} $p < .005$