Press release: European College of Neuropsychopharmacology (ECNP) congress, Copenhagen

Study shows 1/3 of young children admitted to intensive care for sepsis show PTSD symptoms years later

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Type of study: not peer reviewed/observational study/people

Doctors have found that children who have been in Intensive Care Units (ICUs) for sepsis have a significantly increased risk of Post-Traumatic Stress Disorder (PTSD), with around 1/3 showing PTSD symptoms. In some young people, these may persist for years following discharge. There is some evidence that these children have altered immune responses during their stay in ICU and this may be a risk factor for later PTSD symptom development, but this needs to be confirmed.

Sepsis is a potentially life-threatening condition caused by the body's immune system reacting to overwhelming to infection. It can lead to septic shock, damage to major organs, a rapid and potentially fatal blood pressure drop, and needs immediate hospital treatment.

Between 2010 and 2017, researchers from St Mary's Hospital and Imperial College in London followed up 69 young patients (all older than 3 years, average age of 4.2 years, 48% male) who had been admitted to intensive care for treatment of sepsis. When reviewed at an average follow up time of 4.6 years later, 31% of the children showed signs of PTSD. In some cases PTSD symptoms were still evident up to 7 years after discharge. The results from the study also indicated that children who had experienced rapid increases in inflammation during their stay were at higher risk. The data was controlled for potentially misleading (confounding) factors, such as length of stay in intensive care, medications, etc.

Lead researcher, Dr Georgina Corbet Burcher (Imperial College, London) said, "Young people survive critical illness at greater rates than ever before, but in some there is a high psychological price. PTSD symptoms can lead to long term effects on their mental health and wellbeing which persist in the absence of 'physical' after-effects. It appears that those who suffer from sepsis may be at particular risk for subsequent PTSD symptom development.

Recent studies indicate that PTSD affects around 7% of young people in the UK. On average, the risk is increased if a child has to spend time in an Intensive Care Unit, with around 20-30% of children overall showing symptoms at 3-12 months following discharge. This is the first study to look at the longer term endurance of symptoms after sepsis, indicating that they may persist in some children.

There's many questions still unanswered-in particular why it is that sepsis might be a risk factor for later development of PTSD symptoms, which children are at risk of longer term symptoms and the potential mechanism behind the brain's response to high levels of inflammation. We also need to bear in mind that this is a small study in a single centre, so these findings need to be confirmed in other settings".

The World Health organisation estimates that around 3 million newborns and 1.2 million children suffer from sepsis globally each year. In the general population, they estimate that 30 million suffer each year, with around 6 million deaths (<u>https://www.who.int/news-room/fact-</u>

<u>sheets/detail/sepsis</u>). In the US, around 75,000 children contract sepsis every year, while the UK's Sepsis Trust estimated that 25,000 children contract sepsis every year, although not all are admitted to ICU.

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Notes for Editors

European College of Neuropsychopharmacology (ECNP) The ECNP is an independent scientific association dedicated to the science and treatment of disorders of the brain. It is the largest non-institutional supporter of applied and translational neuroscience research and education in Europe. Website: <u>www.ecnp.eu</u>

The 31st annual ECNP Congress takes place from 7th to 10th September in Copenhagen. It is Europe's premier scientific meeting for disease-oriented brain research, annually attracting up to 6,000 neuroscientists, psychiatrists, neurologists and psychologists from around the world. Congress website: https://2019.ecnp.eu/

Conference abstract (note, some statistics have been changed since this abstract was submitted)

Post-traumatic stress disorder following childhood sepsis and associated factors

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Introduction:

Symptoms of post-traumatic stress disorder (PTSD) have been detected in approximately 30% of children following paediatric intensive care unit (PICU) admissions. They are particularly common following sepsis. Contributing factors may include illness severity and the use of psychoactive medications (as shown in adult ICU survivors), and high levels of inflammation. Furthermore, experiencing other traumas may influence symptom development. These influences have not been previously explored in a paediatric cohort.

Aims:

We investigated effects of the following factors on post-PICU PTSD symptoms:

- Illness severity
- Psychoactive medications
- Inflammatory markers
- Other trauma experiences

Methods:

This observational cohort study reviewed children admitted for sepsis between 2010 and 2018. PTSD symptoms were assessed on children aged >3 years using parental report on the Trauma and Behaviour Health Checklist. Clinical characteristics were transcribed from case notes at three times points (admission, 48 hours and 7 days).

Results:

Sixty-nine patients were included in the analysis. 48% were male and 64% were white British ethnicity. The mean age on admission was 4.1 yrs (SD 4.7yrs) and mean age on completion was 8.9 yrs (4.8yrs). 44% scored at risk of PTSD at any time since discharge. 25% scored at risk of 'chronic PTSD' through reporting enduring symptoms.

Demographic factors: Age was positively associated with PTSD score (r=0.3, p=0.02). There were no associations with social class, ethnicity, gender or time since admission for risk of PTSD. 12% reported preexisting emotional/behavioural problems. These were not associated with subsequent PTSD risk (p=0.6).

PICU factors: Higher PTSD scores were seen in patients who had longer duration of receiving benzodiazepines (r=0.3, p=0.008), morphine (r=0.3, p=0.046), and intubation and ventilation (r=0.3, p=0.03). Use of corticosteroids showed no association with PTSD symptoms (p=0.52).

Inflammatory markers: Peak CRP values on admission and at 48 hours were combined to provide a measure of increasing inflammation. This value was positively associated with PTSD symptoms (r=0.3, p=0.048). There was no significant relationship with WCC change (p=0.9).

Other traumatic events: 31% of patients reported the presence of another trauma in addition to the admission to PICU. Presence of another trauma was significantly associated with PTSD risk (p=0.005) and a trend towards chronic PTSD (p=0.07).

Conclusion:

This study reinforces the high prevalence PTSD post-PICU. It highlights novel associated factors that warrant further investigation. Chronic symptoms (>1 year) have not previously been studied in other cohorts and are detectable in a substantial proportion of patients. Analogous to adults, children at risk received greater amounts of benzodiazepines and morphine (both linked to higher rates of delirium) and longer admissions. Inflammatory mediators may drive development of psychopathology through the creation of a neurotoxic milieu after crossing the blood brain barrier. Additionally, another experience of trauma may act as a 'PTSD sensitiser' for young people, promoting presentation of a greater symptom burden following PICU admission.

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