

DR PAUL LEE-ARCHER (Orcid ID : 0000-0001-8640-8792)

PROF BRITTA S VON UNGERN-STERMBERG (Orcid ID : 0000-0002-8043-8541)

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## **An observational study of hypoactive delirium in the post-anesthesia recovery unit of a pediatric hospital**

Paul F Lee-Archer<sup>1,2,3</sup>, Britta S von Ungern-Sternberg<sup>4,5,6</sup>, Michael C. Reade<sup>2</sup>, KC Law<sup>1</sup>,  
Deborah Long<sup>3,7</sup>

1. Department of Anesthesia, Queensland Children's Hospital, Brisbane, Australia
2. Faculty of Medicine, The University of Queensland, Brisbane, Australia
3. Pediatric Critical Care Research Group, Child Health Research Centre, The University of Queensland, Brisbane, Australia
4. Department of Anesthesia and Pain Management, Perth Children's Hospital, Perth, Australia
5. Division of Emergency Medicine, Anesthesia and Pain Medicine, Medical School, The University of Western Australia, Perth, Australia
6. Perioperative Medicine Team, Telethon Kids Institute, Perth, Australia
7. Pediatric Intensive Care Unit, Queensland Children's Hospital, Brisbane, Australia

*Corresponding Author:* Dr P. F. Lee-Archer, Department of Anesthesia, Division of Critical Care, Queensland Children's Hospital, 501 Stanley St, South Brisbane, 4101, Australia. Email: [Paul.Lee-Archer@health.qld.gov.au](mailto:Paul.Lee-Archer@health.qld.gov.au)

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## Data Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## Clinical Implications

What is already known about this topic:

- Emergence delirium is a common problem in children recovering from general anesthesia.
- Hypoactive delirium has been well-described in children in the intensive care unit but has not been widely studied in the recovery setting.

What this study adds:

- Nearly a quarter of all cases of emergence delirium in a single pediatric hospital were found to be hypoactive in nature.
- The Cornell Assessment of Pediatric Delirium (CAP-D) is a rapid, easy to use tool that is an extension of the Pediatric Assessment of Pediatric Delirium (PAED) scale. It can detect hyperactive and hypoactive delirium and may be an appropriate measure for use in recovery units.

## Abstract

**Background:** Hypoactive delirium is present when an awake child is unaware of his or her surroundings, is unable to focus attention, and appears quiet and withdrawn. This condition has been well-described in the intensive care setting but has not been extensively studied in the immediate post-anesthetic period.

**Aim:** To determine if hypoactive emergence delirium occurs in the recovery unit of a pediatric hospital, and if so, what proportion of emergence delirium is hypoactive in nature.

**Methods:** We conducted an observational study using the Cornell Assessment of Pediatric Delirium (CAP-D) in a cohort of 4424 children recovered at a tertiary pediatric hospital. The incidence of emergence delirium detected using the Pediatric Anesthetic Emergence Delirium (PAED) scale was also recorded for comparison.

**Results:** There were 74 cases of emergence delirium detected during the study period using the CAP-D (1.7%). Only 57 cases were detected using the PAED scale. The additional 17 cases detected using the CAP-D represent cases of hypoactive delirium. In this cohort of pediatric patients, 23% of all cases of emergence delirium were hypoactive in nature.

**Conclusion:** The significance of hypoactive delirium in this population is unknown, however previous studies have shown that emergence delirium can result in post-operative

behaviour changes and may affect compliance with future episodes of care. However, hypoactive delirium is often missed without active screening. The prevalence detected in this study therefore suggests hypoactive delirium warrants further investigation.

## **Introduction**

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-V), the key features of delirium are disturbances in attention and awareness. Emergence delirium is defined as a mental disturbance that occurs during the recovery from general anesthesia.<sup>1</sup> It is usually associated with combative behaviours, motor agitation, inability to recognise familiar objects and people and an inability to be consoled.<sup>2</sup> However, children who are quiet and withdrawn may also be confused and disorientated and be experiencing a subtype of delirium known as hypoactive delirium.<sup>3</sup> This condition has been well-described in the intensive care setting but is not commonly associated with the period of emergence from general anesthesia.

A child with hypoactive delirium would share some similar features to traditional emergence delirium in that they may not make eye contact with the caregiver and may not be aware of their surroundings. However, rather than being restless, agitated and making non-purposeful movements, they would make very little movement when awake, be non-communicative and not respond to social interactions. An example of how a young child or infant with hypoactive delirium would present is: not making eye contact with the nurse or even their primary carer, lying quite still in the bed without making efforts to sit or move around, not following simple commands and not interested in familiar objects such as a blanket or a soft toy.

The Cornell Assessment of Pediatric Delirium (CAP-D) was developed as an adaptation and extension of the PAED scale and is a rapid screening tool for pediatric delirium in the hospital setting (Figure 1). The additional items that are included to assess hypoactive delirium are:

- Does the child communicate needs and wants?
- Is the child underactive – very little movement while awake?
- Does it take the child a long time to respond to interactions?

The scale has been validated in the critical care setting in children ranging in age from newborns to early adolescence.<sup>3</sup> In this study we introduced the CAP-D tool into the recovery unit of a tertiary pediatric hospital and collected data about the incidence and type of emergence delirium over a three month period.

## **Aims**

The aim of this study was to determine the incidence of hypoactive delirium in post-surgical pediatric patients, using a novel measurement tool (CAP-D) for emergence delirium that has not previously been used in the recovery room setting.

## **Methods**

Ethics approval to perform this study was obtained from the Children's Health Queensland Human Research Ethics Committee (LNR/2019/QCHQ/51181). A waiver of consent was granted for study participants.

Prior to commencing the study, it was necessary to implement the new measurement tool into the recovery care plan and establish an education program to prepare the recovery staff. The CAP-D and the PAED scales were added to the recovery patient record and laminated sheets showing how to score children at various ages were placed at each bed space. The electronic record was then changed to include a section to record scores for the CAP-D and PAED scales as well as a simple "yes/no" option for emergence delirium based on the clinical judgement of the treating nurse. Severe cases of delirium that required review by the treating anesthetist were recorded. The education program for the recovery nurses consisted of a series of face-to-face teaching sessions and an online training course. A link to the online course was emailed to all recovery staff and completion was able to be tracked. Nurses were instructed to score the CAP-D at the completion of the child's stay in recovery and base their score on interactions with the child from the time of eye opening to voice until readiness for discharge to the ward.

A convenience sample of all surgical patients during a three-month period was used.

Children not recovered immediately after anesthesia, ie transferred directly to the intensive care unit, were excluded.

Data were collected on: type of surgery, gender, age, length of surgery, administration of opioids in the Post Anesthetic Care Unit (PACU) and incidence of emergence delirium. The presence of emergence delirium was recorded in three ways:

1. Based on a score of  $>8$  on the CAP-D scale
2. Based on a score of  $>8$  on the PAED scale
3. Based on clinical judgement of the recovery staff (recorded as “yes” or “no”)

In addition, if the treating nurse thought it was necessary for the anesthetist to review the child, then this was recorded.

Results were analyzed using StataSE version 14 (College Station, Texas, StataCorp Pty Ltd). Incidences are presented as proportions and compared using Chi-squared, normally distributed data are presented as means and standard deviations and compared using the Student's t-test; non-normally distributed data are presented as medians and interquartile ranges. Results were considered statistically significant if the p value was  $<0.05$ .

## Results

4424 patients were recovered in the Queensland Children's Hospital Post Anesthetic Care Unit (PACU) during the study period (1<sup>st</sup> February 2017 to the 1<sup>st</sup> May 2017). The median age was 6.2 years (range 0 to 19 years). The patient and surgical characteristics are shown in Table 1.

There were 57 cases of emergence delirium detected using the PAED scale during the study period and 74 cases detected using the CAP-D scale. This difference of 17 cases represents the number of cases of hypoactive delirium detected during the study period (23% of all emergence delirium). The number of cases using each of the measurement methods is shown in Table 2.

The 74 cases of emergence delirium were analysed based on surgical specialty. Of the specialties that recorded at least one case of emergence delirium, hematology/oncology patients had the highest incidence and gastroenterology patients had the lowest incidence.

The highest incidence of hypoactive delirium was seen in radiology patients. The incidences for each specialty are shown in Table 3.

The highest incidence of emergence delirium was seen in patients aged 1, 2 and 3 and a much lower average incidence was seen in children over the age of 10. The highest incidence of hypoactive delirium was seen in children aged 2 years; 40% of all emergence delirium cases in this age group were hypoactive. The incidence of emergence delirium by age is shown in Table 4.

There was a higher rate of emergence delirium in elective cases as compared to emergency cases. During the audit period there were 9 cases of emergence delirium out of the 1055 emergency cases (0.85%) and 65 cases of emergence delirium out of the 3369 elective cases (1.93%), difference in proportions 1.08% (95% CI 0.22-1.74%,  $p=0.02$ ). Of the 9 emergency cases, 2 were hypoactive in nature (22%) and of the 65 elective cases, 15 were hypoactive (23%), difference in proportions 1% (95% CI -32.6-20.6%;  $p=0.95$ ).

There was no statistically significant difference in the incidence of emergence delirium based on gender (male: 38 cases, incidence 1.50%; female: 36 total cases, incidence 1.97%), difference in proportions 0.47% (95%CI -0.30-1.32%;  $p=0.23$ ). Of the 36 female cases, 9 were hypoactive in nature (25%) and of the 38 male cases, 6 were hypoactive (16%), difference in proportions 9% (95% CI -9.5-27.1%;  $p=0.34$ ).

Cases of emergence delirium occurred more frequently in shorter procedures. The average length of surgery in cases of emergence delirium was 53.5 minutes compared to an average of 65.4 minutes in children without emergence delirium (mean difference = 11.9 minutes, 95% CI 5.6 – 18.2 mins;  $p=0.02$ ).

Of the 74 total cases of emergence delirium detected using the CAP-D scale, 23 received opioids during their recovery stay (31.1%). In children without delirium, 670 of 4350 cases received opioids in recovery (15.4%), difference in proportions 15.7% (95%CI 6.2-27.0%;  $p=0.0002$ ).

## Discussion

This study has provided evidence that nearly a quarter of emergence delirium in this pediatric recovery unit is hypoactive in nature. The concept of hypoactive delirium in the recovery setting is novel and it will require further research to fully elucidate its significance.

Changes in the behaviour of children emerging from general anesthesia were first reported as early as 1960. Early reports described inconsolable crying and thrashing, and the terms emergence excitement or emergence agitation have often been used interchangeably with emergence delirium.<sup>4</sup> It has since emerged that inconsolability and restlessness are not reliable discriminators of emergence delirium as they can occur with pain or anxiety. Better markers of the condition are no eye contact, lack of purposeful movement and no awareness of surroundings.<sup>4</sup> Despite considerable advances in our understanding of emergence delirium over the years, there are still unanswered questions about the risk factors, causes, identification and consequences of the condition.

A number of scales are available to diagnose emergence delirium, including the Pediatric Anesthesia Emergence Delirium (PAED) scale,<sup>1</sup> the Watcha Scale<sup>5</sup> and the Cravero Scale.<sup>6</sup> A comparison of these three scales found that they correlated well with each other, but none of these scales are designed to detect hypoactive delirium.<sup>7</sup> It could be argued that it is not necessary to detect hypoactive delirium as a quiet and withdrawn child is easy to care for and poses no risk of physically harming themselves. However, it is known that there is an association between hyperactive emergence delirium and PHBC,<sup>8</sup> so it is important we are able to detect all subtypes of delirium for risk stratification and to measure the effectiveness of preventative therapies. Just as hypoactive delirium in the elderly is associated with worse outcomes,<sup>9</sup> it is possible that this may also be true in children. In fact, there are parallels with delirium in the elderly and in children. At the extremes of age there is less neurocognitive reserve and therefore these groups may be more susceptible to developing delirium when exposed to insults such as stress, pain, inflammation and medications. Elderly people have less brain volume, fewer neurons and decreased levels of neurotransmitters such as noradrenaline, acetylcholine, dopamine and gamma-aminobutyric acid.<sup>10</sup> The developing brains of young children are similar, however they have the advantage of being more plastic and more likely to recover after insults. Interestingly, it has been shown that



children with developmental delay or a structurally abnormal brain are at a higher risk of developing delirium, as are elderly people with dementia.<sup>11</sup> This is in keeping with the theory of neurocognitive reserve, and those with less reserve are at higher risk of delirium when exposed to neurological stress.

The neurophysiological mechanism for delirium is not fully elucidated, however it is thought that the symptoms of delirium could result from loss of connectivity between regions of the brain.<sup>12,13</sup> There is evidence from the use of electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) that supports this theory. For example, it has been shown that a breakdown in connectivity between the dorsolateral prefrontal cortex and posterior cingulate results in inattention.<sup>12</sup> This loss of connectivity may be caused by a neurological insult in susceptible individuals, and in the case of emergence delirium the insult is general anesthesia. For most children their neuroplasticity means that symptoms of delirium are short-lived, however there is a possibility that emergence delirium results in long-term consequences and it is not known if there are worse outcomes for children who have repeat exposures.

Most of the evidence regarding neurophysiological mechanisms for delirium after anesthesia comes from studies involving adults. It is possible that the same pathways are involved in pediatric delirium, however further research is needed to confirm this. The breakdown in connectivity between brain regions could explain the symptoms of both active and hypoactive pediatric emergence delirium, with the difference in psychomotor symptoms related to involvement of different neural networks. Another possible theory is that active and hypoactive delirium share a common pathway and that the manifestation of symptoms is related to whether a child has predominantly internalising or externalising behaviours.

Pediatric delirium in various settings has been the focus of increasing interest since the beginning of this century, when studies emerged following the work done in adults and the elderly. In 2003, Turkel and Tavaré reported on 84 children in intensive care with delirium. They found that the most common symptoms were impaired attention, sleep disturbance, confusion and impaired concentration. Interestingly, in their study, there were equal

numbers of children with agitation and apathy.<sup>14</sup> In 2012, the CAP-D was described as a feasible, rapid screening tool for pediatric delirium in critically ill children.<sup>15</sup> The authors found that there was 97% concordance between the CAP-D and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for diagnosing delirium. The CAP-D has a number of advantages over other measurement tools. It is easy to use, it has been validated across the entire pediatric age range, it can be used in children with developmental delay and it can discriminate between delirium and other physical and mental health issues.<sup>16</sup> Importantly, it has the ability to detect hypoactive delirium, a state of confusion or disorientation associated with withdrawal and apathy. A recent study found that 17% of children experienced delirium in the intensive care unit, and of those 46% were hypoactive in nature based on the CAP-D scale.<sup>17</sup>

In this study, the overall incidence of emergence delirium based on the CAP-D score is lower than other reported incidences in the literature. A possible explanation for the low overall incidence of emergence delirium is that our institution has a dedicated preoperative anxiety service. The aim of the service is to identify children at high risk for anxiety and provide a range of strategies to improve the perioperative experience for the child. Some of the interventions include preoperative visits to theatre to familiarise children with the environment, involvement of occupational therapists and psychologists and, if necessary, pharmacological management. There is also the possibility of misdiagnosis or misuse of the scoring instrument by the recovery staff. The education and preparation were comprehensive, however there was no requirement to achieve a predefined level of inter-rater reliability which is a limitation of the study.

The need for an anesthetist to review the patient due to emergence delirium was low overall, however this represented approximately one third of the cases of emergence delirium detected by the CAP-D scale. This relatively high rate of needing an anesthetic review may indicate that only the most severe cases of emergence delirium were being detected using the CAP-D instrument and that further education may be needed or that the cut-off score may need to be adjusted for the recovery room setting.

There was a significant difference in the use of opioids in recovery between children with and without delirium. There are a number of ways to interpret this finding. It is possible that emergence delirium was incorrectly diagnosed as pain and therefore treated with opioids or it may be that opioids were used as a primary treatment for emergence delirium. Another possibility is that higher opiate use is associated with an increased risk of emergence delirium, however there is evidence fentanyl given before emergence reduces the incidence of emergence agitation.<sup>20</sup> It is not possible to determine from the data the timing of administration and whether the opioids were given prior to, or in response to, the diagnosis of emergence delirium.

There was a higher incidence of emergence delirium in younger children, and the highest incidence was seen in the 0 to 2-year age group. This is consistent with previous studies on emergence delirium.<sup>21</sup> A high incidence was also observed in oncology patients which is also consistent with published work on this cohort of patients.<sup>22</sup> Children with cancer require multiple painful and distressing procedures and often need multiple general anesthetics. There is a high level of anxiety surrounding these interventions and anxiety is known to predispose to emergence delirium.<sup>18</sup> Another risk factor for emergence delirium is a short waking time after general anesthesia.<sup>4</sup> This is consistent with the results of this study which found shorter procedures, where the wake up is usually quicker, were associated with a higher incidence of emergence delirium. However, the difference in surgical time found in this study, whilst statistically significant, may not represent a clinically relevant difference.

The strengths of this study are that it involved a large sample of pediatric patients and it examines a condition that has not been studied extensively in the recovery room setting. However, there are also several limitations. It is a single-centre study and so results may not be applicable to all pediatric populations. The presence of pre-existing behavioural or developmental conditions was not recorded which would have provided useful data relating to delirium. The study relied on accurate data entry by the treating recovery nurse and the overall incidence of emergence delirium is very low. This may represent good institutional practices in the area of peri-operative anxiety management, however the possibility of under reporting or misuse of use of the measurement tools cannot be ruled out.

This study provides an indication that there may be a significant, but small, proportion of children who experience hypoactive delirium after general anesthesia. Further research is required to confirm this finding and explore its significance. This would require well-designed, prospective, studies that follow up children to determine the true incidence of hypoactive delirium, and if it is associated with negative behaviour changes in the days and weeks after surgery, whether this has a negative impact on the overall quality of recovery and whether this causes problems with future episodes of health care.

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<b>Number of cases</b>	4424
<b>Median age - years (IQR, range)</b>	6.2 (8.5, 19.4)
<b>Male</b>	2599 (58.7%)
<b>Female</b>	1825 (41.3%)
<b>Type of surgery</b>	
General	904 (20.4%)
ENT	777 (17.6%)
Orthopedics	723 (16.3%)
Radiology	467 (10.6%)
Plastics	384 (8.7%)
Gastroenterology	329 (7.4%)
Ophthalmology	204 (4.6%)
Dental	117 (2.6%)
Respiratory	106 (2.4%)
Hematology/Oncology	87 (2.0%)
Neurosurgery	78 (1.8%)
Cardiology	69 (1.6%)
General Medicine	38 (0.9%)
Rehabilitation Medicine	32 (0.7%)
Rheumatology	30 (0.7%)
Dermatology	26 (0.6%)
Cardiothoracic surgery	21 (0.5%)
Neurology	15 (0.3%)
Spinal surgery	10 (0.2%)
Anesthetic	7 (0.2%)

<b>Elective</b>	3369 (76%)
<b>Emergency</b>	1055 (24%)
<b>Surgery duration - mins [mean (SD)]</b>	65.4 (49.5)

Table 1. Patient and surgical characteristics (IQR = interquartile range; SD = standard deviation)

<b>Method</b>	<b>Number (%)</b>
"Yes" recorded by recovery staff	299 (6.8%)
PAED score >8	57 (1.3%)
CAP-D score >8	74 (1.7%)
Anesthetist review required	23 (0.5%)

Table 2. Incidence of emergence delirium during the audit period.

<b>Specialty</b>	<b>Total cases of emergence delirium</b>	<b>Emergence delirium detected by PAED or CAP-D</b>	<b>Emergence delirium detected only by CAP-D (ie hypoactive delirium)</b>
Oncology	4 (4.6%)	4 (4.6%)	0 (0%)
ENT	22 (2.8%)	19 (2.4%)	3 (0.4%)
Radiology	13 (2.8%)	8 (1.7%)	5 (1.1%)
Dental	3 (2.6%)	3 (2.6%)	0 (0%)
General	18 (2.0%)	15 (1.6%)	3 (0.3%)
Ophthalmology	4 (2.0%)	3 (1.5%)	1 (0.5%)
Plastics	5 (1.3%)	3 (0.8%)	2 (0.5%)
Respiratory	1 (0.9%)	0 (0%)	1 (0.9%)
Orthopedics	3 (0.4%)	2 (0.3%)	1 (0.1%)
Gastroenterology	1 (0.3%)	0 (0%)	1 (0.3%)
<b>All Specialties</b>	<b>74 (1.7%)</b>	<b>57 (1.3%)</b>	<b>17 (0.4%)</b>

Table 3. Incidence of emergence delirium by speciality

Age (years)	Total cases of emergence delirium	Emergence delirium detected by PAED or CAP-D	Emergence delirium detected only by CAP-D (ie hypoactive delirium)
<1	7 (1.9%)	5 (1.4%)	2 (0.5%)
1	13 (2.7%)	12 (2.5%)	1 (0.2%)
2	10 (3.1%)	6 (1.9%)	4 (1.2%)
3	11 (3.3%)	10 (3.0%)	1 (0.3%)
4	5 (1.4%)	5 (1.4%)	0 (0%)
5	4 (1.5%)	3 (1.1%)	1 (0.4%)
6	5 (2.0%)	3 (1.2%)	2 (0.8%)
7	2 (0.9%)	2 (0.9%)	0 (0%)
8	3 (1.3%)	2 (0.8%)	1 (0.5%)
9	5 (2.2%)	4 (1.8%)	1 (0.4%)
10	3 (1.5%)	2 (1.0%)	1 (0.5%)
11	2 (0.9%)	1 (0.5%)	1 (0.5%)
12	1 (0.5%)	0 (0%)	1 (0.5%)
13	0 (0%)	0 (0%)	0 (0%)
14	2 (1%)	1 (0.5%)	1 (0.5%)
15	0 (0%)	0 (0%)	0 (0%)
16	1 (1.2%)	1 (1.2%)	0 (0%)
<b>All ages</b>	<b>74 (1.7%)</b>	<b>57 (1.3%)</b>	<b>17 (0.4%)</b>

Table 4. Incidence of emergence delirium by age.



Cornell Assessment of Pediatric Delirium (CAPD) revised						
RASS Score___(if -4 or -5 do not proceed)						
Please answer the following questions based on your interactions with the patient over the course of your shift:						
	Never 4	Rarely 3	Sometimes 2	Often 1	Always 0	Score
1. Does the child make eye contact with the caregiver?						
2. Are the child's actions purposeful?						
3. Is the child aware of his/her surroundings?						
4. Does the child communicate needs and wants?						
	Never 0	Rarely 1	Sometimes 2	Often 3	Always 4	
5. Is the child restless?						
6. Is the child inconsolable?						
7. Is the child underactive—very little movement while awake?						
8. Does it take the child a long time to respond to interactions?						
TOTAL						

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**Author/s:**

Lee-Archer, PF;von Ungern-Sternberg, BS;Reade, MC;Law, KC;Long, D

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