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# Emergence delirium or pain after anaesthesia—how to distinguish between the two in young children: a retrospective analysis of observational studies

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## Abstract

**Background:** Early postoperative negative behaviour in preschool children after general anaesthesia is a common problem. The distinction between emergence delirium (ED) and pain is difficult, but management differs between the two. The aim of the current analysis was to identify individual observational variables that can be used to diagnose ED and allow distinction from postoperative pain.

**Methods:** This retrospective analysis of data from three previous prospective observational studies included children undergoing general anaesthesia for elective adeno-tonsillectomy, sub-umbilical surgery, and MRI scanning. Two trained observers simultaneously applied the Face, Legs, Activity, Cry, Consolability Scale; the Children's Hospital Eastern Ontario Pain Scale; the Children's and Infants' Postoperative Pain Scale or the Paediatric Anaesthesia Emergence Delirium (PAED) scale. Data from each domain of the scales were available at awakening and at five, 10, and 15 min after anaesthesia. Each patient was analysed over time, and subsequently, each evaluation was considered as a single event. The descriptive behaviour items overlapping in the assessed scales were identified as dichotomous variable ('true/false') and then were applied for each evaluation.

**Results:** Children ($n$=512) were assessed for a total of 2048 evaluations. Most children (69%) displayed at least one episode of ED and/or pain. Almost 15% of children demonstrated both ED and pain. Children with ED showed 'no eye contact' and 'no awareness of surroundings'. Children with pain displayed 'abnormal facial expression', 'crying', and 'inconsolability'.

**Conclusions:** 'No eye contact' and 'no awareness of surroundings' identifies ED. 'Abnormal facial expression', 'crying', and 'inconsolability' indicate acute pain in children in the early postoperative period.

**Key words:** acute pain; anaesthesia recovery period; child; delirium; general anaesthesia

All three observational studies analysed, received approval from the institutional ethics committee (Ospedale San Gerardo, Monza, Italy, NCT 01096797; A.O. Ospedale Civile di Legnano, Italy, number 430; and Policlinico Universitario, Catania, Italy, number 318).

Early-postoperative negative behaviour (e-PONB) is a common problem in young children undergoing general anaesthesia.[1] Recognition and management of e-PONB in recovery room is still problematic despite the availability of multiple assessment tools and treatment options.[2–4]

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**Editor's key points**

- Emergence delirium and pain are difficult to distinguish in preschool children.
- Management strategies, and consequences of, the two conditions are different.
- The authors retrospectively analysed data from three studies during which four different clinical observational scales were used.
- Features specific to emergence delirium and pain were identified.

e-PONB may cause self-injury of the child or accidental removal of i.v. catheters, drainages, or dressing and may require extra nursing care, additional time in recovery room, and supplemental sedatives or analgesic drugs.[5 6] It also reduces parental and caregivers' satisfaction.[5 7 8] Short- and long-term psychological implications of e-PONB are unclear. Children with e-PONB may have a higher risk of developing separation anxiety, apathy, and sleep and eating disorders up to 30 days after surgery.[9–11]

The two clinical components of e-PONB, emergence delirium (ED) and postoperative pain, have divergent trends over time in the early postoperative phase.[12] However, children with ED may at the same time also suffer from pain, and pain-related behaviours could be rated as ED and *vice versa*.[2 3 13] This may lead to either a pharmacological treatment of a self–limiting disturbance (ED) or to an under or delayed treatment of postoperative pain.

The Paediatric Anaesthesia Emergence Delirium (PAED) scale, the only validated scale to quantify ED, and the most commonly used behavioural pain scales during the postoperative period, generates composite scores to characterize ED and pain. Moreover, the PAED scale[14] shares some descriptors with the Faces, Legs, Activity, Cry, and Consolability (FLACC) Scale[15]; Children's and Infants' Postoperative Pain (CHIPP) scale; or Children's Hospital of Eastern Ontario Pain (CHEOP) scale.[16–18] This may produce an artificial overlap with overestimation of pain and/or ED.

There is a clear clinical need of a simple strategy that allows reliable identification of the two major components of e-PONB (ED and pain) during the early post-anaesthesia period. However, the weight of the internal components of the scales on determining either ED or pain has not been defined clearly.[2 12]

The aim of this retrospective analysis was to identify individual observation domains of the commonly used PAED, FLACC, CHIPP, and CHEOPS scales, which can differentiate between ED and pain. A simple and reliable differentiation between ED and pain would allow the clinician optimal management of e-PONB in young children after receiving general anaesthesia.

## Methods

A retrospective analysis of databases of three prospective observational trials involving preschool children (ages one to six yr) was performed. The complete database included the scores of postoperative observational scales of 150 consecutive children undergoing elective adenoidectomy and/or tonsillectomy; 200 consecutive children undergoing elective sub-umbilical surgery; and 162 consecutive children undergoing magnetic resonance imaging (MRI) scanning under general anaesthesia. All children received general anaesthesia without premedication, and a with all patients parents were present at induction.

In children undergoing adenoidectomy and/or tonsillectomy, anaesthesia was induced using sevoflurane (2–5%); propofol (2–7 mg $kg^{-1}$) and fentanyl (1.5–2 mcg $kg^{-1}$) administered before tracheal intubation. Anaesthesia was maintained using sevoflurane (2–3%), fentanyl was used as required, and paracetamol (15 mg $kg^{-1}$ i.v.) was given intra-operatively. Children undergoing sub-umbilical surgery received general anaesthesia with sevoflurane and effective caudal anaesthesia before incision, using a 1 ml $kg^{-1}$ of 0.2% ropivacaine. Children undergoing MRI scanning received propofol or sevoflurane anaesthesia. Induction was achieved with propofol (2–4 mg $kg^{-1}$) or sevoflurane inhalation (up to 7%). Propofol (continuous infusion of 60–100 mcg $kg^{-1}$ $min^{-1}$) or sevoflurane (1–1.5%) was used for maintenance of anaesthesia with spontaneous ventilation.

Two trained observers simultaneously and independently determined each single item of FLACC, CHEOP, CHIPP, or PAED scales every five min during the first 15 min after awakening. All children awaked in the operating theatre or in the MRI room. The evaluation time started at awakening of each child defined as 'spontaneous eyes opening'. FLACC scales are routinely used clinically in the hospitals' participants. The CHEOP and CHIPP scales were included to increase the number of validated domains of pain behaviour in young children. No medication (sedatives or analgesics) was given for 15 min after they were admitted to the recovery room.

Patients were defined as having ED (if PAED score ≥10), pain (if FLACC score ≥four), both ED and pain (if PAED score ≥10 and FLACC score ≥four), or normal behaviour (if PAED score <10 and FLACC score <four). The onset of ED, defined as the first evaluation for each patient with PAED score ≥10, and the onset of pain, defined as the first evaluation with a FLACC score ≥four, CHIPP score ≥four, or CHEOP score ≥seven, were analysed over time.

Each evaluation was analysed as a single event to characterize ED and pain. The PAED, FLACC, CHIPP, and CHEOP scales include the following common 'overlapping' descriptive items: 'abnormal facial expression' (FLACC, CHIPP, and CHEOP); 'crying' (FLACC, CHIPP, and CHEOP); 'inconsolability' (FLACC and PAED); 'purposeful actions' (FLACC, CHIPP, CHEOP, and PAED); 'abnormal leg position' (FLACC, CHEOP, and CHIP); and 'restlessness' (PAED and CHIPP). The categories 'no eye contact' and 'no awareness of surroundings' are included only in the PAED scale and are considered as the most important items for ED identification.[4 13 14]

To prevent subjectivity of the weighting of the individual descriptors, two authors (M.S. and P.M.I.) retrospectively analysed the data and applied the dichotomous definition ('true/false') of the single evaluation using the following questions:

- Is the facial expression abnormal?
- Is the child crying?
- Is the child inconsolable?
- Is the activity normal and purposeful?
- Are the legs in a normal position?
- Is the child restless?
- Does the child make eye contact with the caregiver?
- Is the child aware of surroundings?

The observation scales considered have different numeric weighting methods. FLACC and CHIPP items with a score of zero identify normal behaviour, and items with scores of one or two points for each variable identify different grades of abnormal behaviour. PAED and CHEOP items with a score of zero or one identify normal behaviour; and items with scores of and two, three, or four points for each variable identify different grades of abnormal behaviour. Therefore, a true/false option was applied for the selected parameters as follows: each item of

FLACC and CHIPP scale was defined as 'true' when scored ≥one; variables of PAED and CHEOP scales were considered true when scored ≥two. The true/false selected parameters were applied for each single event and then analysed for each time point.

### Statistical analysis

Continuous data were analysed using ANOVA test for two groups and were presented as mean (SD) or median and interquartile range of 25–75%. The incidence of e-PONB was presented as frequency, percentage, and 95% confidence interval (95% CI) and compared using uncorrected $\chi^2$ test. Factor analysis on parameters evaluating e-PONB was performed on true/false parameters (Barlett's test of sphericity <0.05). The relative risk to manifest each parameter related to a specific behaviour was presented as risk ratio and 95% CI. Statistical significance was defined as a $P<0.05$.

Statistical analysis was performed using Microsoft Excel 97 (Microsoft Inc., Redmond, WA, USA), Epi info version 2004 (Epi info 3.2.2; Center for Disease Control and Prevention (CDC), Atlanta, GA, USA), Analyse-it (Software, Ltd., Leeds, United Kingdom), and IBM SPSS statistical program (version 22, IBM Corporation 1989, 2013).

Table 1 Description of study populations. Data are given as numbers (percentages) or means (range). The duration of anaesthesia was significantly different between the studies ($P<0.05$)

| | |
|---|---|
| Age (yr) | 3 (1–6) |
| Female/Male | 147 (29%)/365 (71%) |
| Procedure | |
| ENT surgery | 150 (29%) |
| Adeno-tonsillectomy | 103 (20%) |
| Tonsillectomy | 45 (9%) |
| Sub-umbilical surgery | 200 (39%) |
| General | 162 (81%) |
| Urology | 38 (19%) |
| MRI scan | 162 (32%) |
| Procedures duration (min) | 46 (26) |
| ENT surgery | 37 (15§) |
| Sub-umbilical surgery | 47 (36§) |
| MRI scan | 53 (14§) |
| General anaesthesia maintenance | |
| Sevoflurane | 381 (74%) |
| Propofol | 131 (26%) |

## Results

The combined databases included a total of 512 preschool children, ASA (physical status) I-II, with a total of 2048 individual evaluations. (Table 1). Three hundred and fifty-one children (69%, –95% CI 64–73) displayed e-PONB with at least one episode of ED and/or pain during the first 15 min after awakening.

Children having received sevoflurane were 11 times more likely of having e-PONB than those receiving propofol (RR 11, 95% CI 7–18%).

The incidence of ED decreased over the time: 254 children (50%, 95% CI 45–54) were judged as having ED at awakening; 216 (42%, 95% CI 38–47) had ED at five min; 161 (32%, 95% CI 28–36) had ED at 10 min and 72 children (14%, 95% CI 11–18) had ED at 15 min. The number of children with pain increased at each evaluation time point: 11 (2%, 95% CI 1–4) children were judged as having pain at awakening; 24 (5%, 95% CI 3–7) had pain at five min; 28 (6%, 95% CI 4–8) had pain at 10 min and 72 children (14%, 95% CI 11–17) had pain at 15 min. The number of children with the combination of both ED and pain was 77 (15%, 95% CI 12–19) at awakening, 53 (10% 95% CI 8–13) at five min, 76 (15%, 95% CI 12–18) at 10 min, 109 (21%, 95% CI 18–25) at 15 min.

ED started almost exclusively during awakening. Only two children had an onset of ED at 10 or 15 min. No child had ED in two separate episodes, and ED did not recur in the same child. In contrast, a positive pain assessment could occur throughout all observation periods. (Table 2).

An unchanged e-PONB behaviour throughout the entire observation period was seen in 151 children (43%, 95% CI 38–49): ED alone in101 children (29%, 95% CI 24–34), pain alone in15 children (4%, 95% CI 3–7), and both ED and pain in 35 children (10%, 95% CI 7–14). One hundred and fifty-seven children (45%, 95% CI 12–46) with ED as the first e-PONB presentation were considered to be in pain in the following evaluation (31% presented both ED and pain; 14% presented only pain when ED had resolved). No child who had only pain as first e-PONB behaviour developed also ED at a later stage.

ED occurred as a single event in 704 observations (34%, 95% CI 32–37), pain in 136 observations (7%, 95% CI 6–8) both ED and pain as combined events occurred in 315 observations (15%, 95% CI 14–17), and normal behaviour in 893 (44%, 95% CI 41–46) evaluations.

Table 2 Onset times of ED and pain. The onset time of ED is defined as the first evaluation with PAED score ≥10 for each child; the onset of Pain is defined as the first evaluation with FLACC score ≥four, CHIPP score ≥four or CHEOP score ≥seven for each child. Data are number of children (percentage) and CI 95%

| | Awakening | 5 min | 10 min | 15 min |
|---|---|---|---|---|
| ED onset | | | | |
| PAED score ≥10 | 331 (98%) | 3 (0.9%) | 2 (0.6%) | 2 (0.6%) |
| | 96–99 | 0.2–2.8 | 0.1–2.4 | 0.1–2.4 |
| PAIN onset | | | | |
| FLACC score ≥4 | 114 (42%) | 27 (10%) | 46 (17%) | 86 (32%) |
| | 27–39 | 7–14 | 13–22 | 26–37 |
| CHIPP score ≥4 | 88 (37%) | 20 (8%) | 41 (17%) | 91 (38%) |
| | 31–43 | 5–13 | 13–23 | 32–44 |
| CHEOP score ≥7 | 156 (50%) | 36 (12%) | 41 (13%) | 81 (26%) |
| | 44–56 | 8–16 | 10–17 | 21–31 |

The factor analysis using the true/false parameters demonstrated that e-PONB had two different components (component one: 60% of variance; component two: 23%). 'No eye contact' and 'no awareness of surrounding' described the first component. In contrast, of all other items considered, particularly abnormal facial expression, crying, and inconsolability comprised the second component (Fig. 1).

All children with ED had no eye contact (704; 100%) and no awareness of surroundings (703; 100%, 95% CI 99–100). Less than 10% of children with ED showed abnormal facial expression (61; 10%, 95% CI 8–12), crying (22; 3%, 95% CI 2–5), inconsolability (41; 6%, 95% CI 4–8), purposeful actions (61; 10%, 95% CI 8–12), abnormal leg position (31; 4%, 95% CI 3–6), and restlessness (54; 8%, 95% CI 6–10).

Abnormal facial expression (131; 97%, 95% CI 92–99), crying (129; 95%, 95% CI 90–98), and inconsolability (135; 99%, 95% CI 96–100) were more prevalent in children with pain than in those with ED. Purposeful actions (123; 90%, 95% CI 84–95), abnormal leg position (117; 86%, 95% CI 79–91), and restlessness (111; 82%, 95% CI 74–88) were also observed frequently in children with pain. Less than 40% of children with pain showed no eye contact (51; 38%, 95% CI 30–46) and no awareness of surroundings (56; 41%, 95% CI 33–50).

A combination of all criteria was prevalent in children who were judged to have both ED and pain [abnormal facial expression (292; 93%, 95% CI 89–95], crying (129; 95%, 95% CI 90–98), inconsolability (296; 94%, 95% CI 91–96), purposeful actions (309; 98%, 95% CI 96–99), abnormal leg position (302; 96%, 95% CI 93–98), restlessness (293; 93%, 95% CI 90–96), no eye contact (310; 98%, 95% CI 96–99), and no awareness of surroundings (309; 98%, 95% CI 96–99)] (Table 3).

'No eye contact' and 'No awareness of surroundings' were strongly correlated (RR 442; 95% CI 62–3136, $P<0.0001$) with ED. This association had 99% sensitivity and 63% specificity to identify ED. On the contrary, the association had very low sensitivity (32%) and specificity (39%) for pain detection in the early postoperative period. The simultaneous presence of 'abnormal facial expression', 'crying', and 'inconsolability' was strongly correlated (RR 11; 95% CI 6–20, $P<0.0001$) with pain. This association had 93% sensitivity and 82% specificity to detect pain. On the contrary, it had 2% sensitivity and 66% specificity to detect ED.

The analysis of the true/false items over time showed that abnormal facial expression, crying, inconsolability, purposeful actions, abnormal leg position, and restlessness increased during the first 15 min after awakening. Items specific to PAED (no eye contact or no awareness of surroundings) decreased over time (Fig. 2).

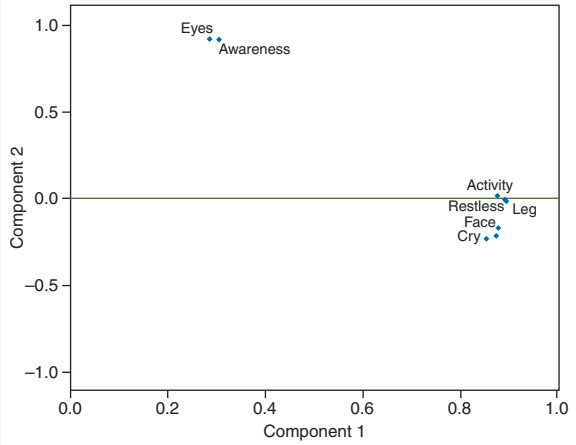


Fig 1 Component analysis of e-PONB. 'No eye contact' and 'No awareness of surrounding' better are correlated with the component one, in contrast all other items considered, particularly by 'Abnormal facial expression', 'Crying', and 'Inconsolability' are correlated to the second one.

## Discussion

The current analysis of a large database of e-PONB behaviour scales allows quantitative description of this phenomenon in preschool children undergoing general anaesthesia during elective procedures. 'No eye contact' and 'no awareness of surroundings' are distinctive characteristics of ED, and the association of the criteria of these two descriptors positively identifies ED episodes in the early postoperative period. The characterization of pain behaviours is more complicated, but the association of 'abnormal facial expression', 'crying', and 'inconsolability' demonstrated high sensitivity and specificity to detect pain in young children during the first 15 min after awakening.

It is acknowledged that the variability in clinical presentations of e-PONB makes the identification and the management of ED or pain in young children difficult.[2 4] ED is an early diagnosis and a self-limiting behaviour.[1 4 12 18 19] The current analysis showed that ED begins almost always at the awakening, resolved within 15 min, and did not recur even without pharmacological treatment. No children complaining of pain as first behaviour after awakening manifested a later onset of ED.

Almost 45% of children with ED will also present with pain behaviour during the early awakening period. Previous studies

Table 3 The weight of 'true/false' selected parameters on ED and pain. Each single event is defined as follows: Emergence Delirium (ED) if PAED score score ≥10, pain if FLACC score ≥four, and both pain and ED if PAED score ≥10 and FLACC score ≥four. Data are Risk Ratio and CI 95% for the presence of each variable in patients with ED, pain or Both pain and ED. (*) $P<0.01$

| | ED ($n$=704) | Pain ($n$=136) | Both ED and pain ($n$=315) |
|---|---|---|---|
| Abnormal facial expression | 0.64 (0.62–0.68) | 20.2* (8.6–47.9) | 11 (7.5–16.5) |
| Crying | 0.6 (0.58–0.64) | 14.9* (7.3–30.8) | 10.2 (7–14.7) |
| Inconsolability | 0.62 (0.59–0.65) | 103.2* (14.6–727.6) | 13.7 (8.8–21.2) |
| Purposeful actions | 0.72 (0.68–0.75) | 5 (3.4–7.5) | 39* (18.7–81.2) |
| Abnormal leg position | 0.72 (0.68–0.74) | 4.7 (3.2–6–7) | 11* (7.6–15.8) |
| Restlessness | 0.73 (0.7–0.76) | 4.4 (3.1–6.2) | 12.7* (8.5–19) |
| No eye contact | Unlimited* | 0.58 (0.5–0.67) | 28.2 (11.8–67.4) |
| No awareness of surroundings | 417* (58.9–1961) | 0.64 (0.55–0.74) | 23.9 (10.8–53.1) |

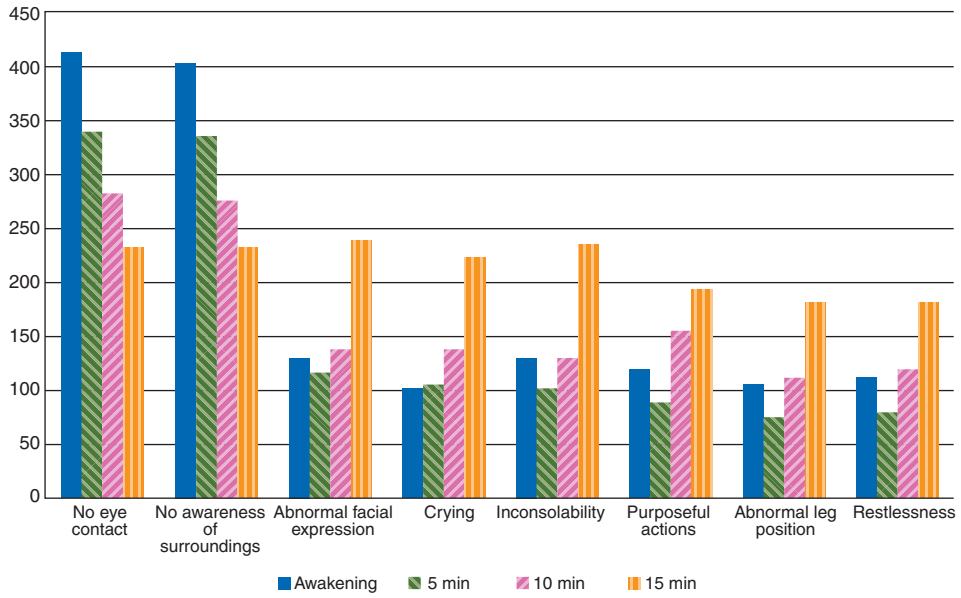


Fig 2 The trend of the 'true/false' items during the 15 min after awakening. Data are number of children at each evaluation time.

postulated a cause-effect association between pain and emergence agitation during the early phases of the postoperative period.[6 7 20 21] The cause-effect association between pain and ED was much less supported by clinical data.[19] Our data suggested that ED and pain are independent of each other and have a different trend over time.

Children undergoing general anaesthesia with sevoflurane are more likely to show e-PONB compared with children receiving propofol. Our results are consistent with a recent review, which concludes that propofol anaesthesia is associated with a reduced incidence of ED.[22]

The available observational scales assessing ED and pain are critical in identifying the major components of e-PONB because of the following main reasons. First, there are no behavioural indices clearly specific to pain or distress or agitation or ED. Second, the same observational variables are used to assess different behaviours. Third, these scales are open to subjectivity in scoring with suboptimal interobserver reliability.[2 23 24] Our results suggested that ED and pain could be assessed independently using five simple, observational, dichotomous (true/false) criteria in preschool-aged children after receiving general anaesthesia.

In agreement with recent studies, both 'no eye contact' and 'no awareness of surroundings' represent the two key characteristics of ED.[2 4 12]

Abnormal facial expression and crying are part of all observational scales that assess pain. The results of the current study confirm their relationship with pain, during the early postoperative period. A recent trial suggested that crying is a nonspecific symptom of ED and could occur equally in other situations of distress, such as pain, hunger, or parental separation.[3] In our study, inconsolability is the most important indicator of pain behaviour in children. Moreover, in our study, the combination of abnormal facial expression, crying, and inconsolability demonstrates high sensitivity and specificity to detect pain behaviour but not ED. Only less than 6% of children with ED also demonstrated these three characteristics.

The simultaneous application of the PAED and FLACC scales in a single time point does not allow the discrimination between ED and pain in approximately 15% of children. This is probably a result of a real overlap of the two behaviours. The association of no eye contact and no awareness of surroundings in children presenting both pain and ED decreased significantly every five min. These findings indicate that if a child presents an unclear aetiology of e-PONB, clinicians should observe the child for a period of five min. It is possible that this decision time may be reduced further, but this may need to be confirmed in a future study. If e-PONB persists, clinicians should consider pain treatment as the primary option. A simple assessment chart is proposed in Fig. 3.

The main limitation of this study is that this is a retrospective database analysis of three different prospective observational trials. Even if this permitted analysis of more than 2000 observations, we are unable to describe the risk factors of ED and analyse the influence of different forms of anaesthesia on e-PONB. In the study population, the number of children with pain behaviour was smaller than reported previously. The lack of treatment and data on management of e-PONB after 15 min is also another limitation of this analysis. A survey of common current treatment practices of e-PONB is needed.[25] A subsequent prospective clinical trial based on the current analysis is required to confirm these findings. Moreover, a prospective study should clarify the use of the dichotomous criteria and their feasibility in realistic clinical settings.

In conclusion, the pooled analysis of observational e-PONB in children suggested that five dichotomous criteria allow the distinction between ED and pain in the early awakening phases after general anaesthesia. Almost all children with ED demonstrated 'no eye contact' and 'no awareness of surroundings'. The association of these two characteristics had a high sensitivity to identify ED during the first 15 min after awakening. The combination of 'abnormal facial expression', 'crying', and 'inconsolability' has a high sensitivity and specificity to detect pain in

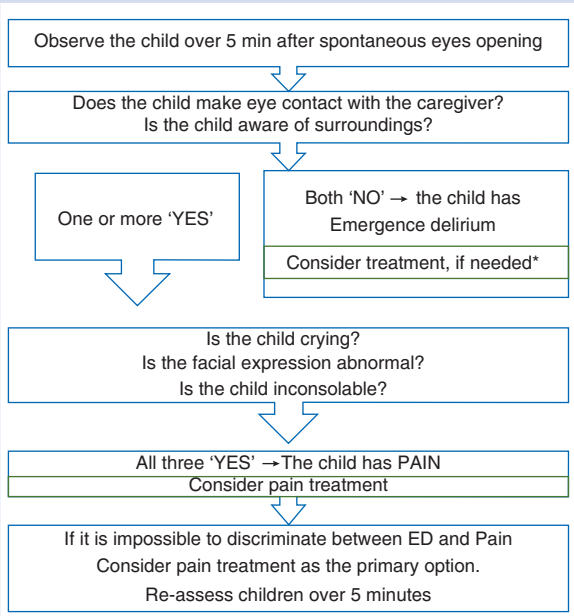


Fig 3 Simplified ('true'/'false') approach to identify emergence delirium and distinguish from pain. * Treatment of ED should be considered to protect the child from self-injury and/or provide a quiet setting where the child can recover.

the early postoperative period. In case of an unclear aetiology for e-PONB, an observation period of five min may be useful to distinguish between ED and pain, potentially allowing the identification of children requiring treatment.

## Authors' contributions

Study design/planning: M.S., P.M.I.
Study conduct: M.S., P.M.I.
Data analysis: M.S., P.M.I., T.E.
Writing paper: M.S., P.M.I.
Revising paper: all authors

## Declaration of interest

None declared.

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