Title: **BIS-awake in Children Using the Paediatric Quattro Sensor**

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ABSTRACT BODY:

Introduction: The Bispectral Index (BIS) is derived from the EEG. It is known that EEG changes with maturation; therefore BIS needs evaluation in children. There is strong evidence that BIS has poor performance in children less than one year of age; while in older children several studies have suggested that BIS may have similar performance to adults. However the studies in older children are frequently of questionable relevance due to use of outdated sensors and algorithms, not adjusting for multiple comparisons, including broad age groups or using clinically inappropriate outcome measures or methods of analysis. Depth monitors such as BIS are difficult to validate, as "depth of anaesthesia" is an abstract concept that is difficult to define. However a central aim of a depth monitor is to reliably detect wakefulness. If a depth monitor is regarded as a test for wakefulness then the most appropriate way to assess the performance of that monitor is to assess the specificity and sensitivity in detecting wakefulness against a gold standard measure of wakefulness. The aim of this study was to compare the performance of BIS in correctly identifying presence of wakefulness over different age groups. This study uses the newest BIS Quattro sensor, which has recently been advocated for paediatric use.

Methods: The study population was 170 children aged between 1 and 13 years recovering from anaesthesia for procedures that required no opioids, no muscle relaxation and was not expected to involve any residual pain. The choice of anaesthetic and doses were at the discretion of the anaesthetist. In each child wakefulness was assessed at one predetermined time point. A child was determined to be awake if they were phonating, obeying command, eye-opening or had continual purposeful movement. If the child was not obviously awake the child's name was called, they were told to open their eyes and the shoulder gently rubbed twice. If the responded to the stimulus within 10 seconds with opening their eyes, phonating or crying then they were classified as awake. The BIS was recorded 45 seconds later. The assessor of consciousness was blinded to the BIS. Children were divided into three groups (1-3, 3-6, 6-9 and 9-12 years). For each age group a receiver operating characteristic (ROC) curve was generated and areas under the curve compared across ages with ANOVA.

Results: Of the 170 children, 4 children were excluded for protocol violations (opioids or other sedatives given) and another 5 because the signal quality index for BIS was poor. The areas under the curves for each age group are listed in table 1. The area was least in the youngest age group and greatest in the oldest age group, but there was no evidence for a difference when tested with ANOVA (P=0.26). For all age groups combined, a BIS of 50 provided 100% sensitivity to detect wakefulness.

Table 1.

Age Groups	ROC area	Std. Err.	95% conf. interval
1-3 yrs	0.80	0.08	0.64 – 0.95
3-6 yrs	0.88	0.06	0.76 – 1.00
6-9 yrs	0.85	0.05	0.74 – 0.95
9-13 yrs	0.95	0.04	0.87 – 1.00

Discussion: This study found that during emergence from volatile anaesthesia in children, the new BIS Quattro sensor is least accurate in measuring wakefulness in the youngest age group and most accurate in measuring wakefulness in the oldest age group, though this study found no evidence for any substantial difference across all age groups. The sensitivity of the instrument is of paramount importance for preventing awareness. Therefore if BIS is to be used in children aged between 1 and 12 years of age to prevent episodes of wakefulness occurring with lightening of anaesthesia then the results from this study suggest the BIS should be maintained below 50.