RESEARCH LETTER

Maternal Holding vs Oral Glucose Administration as Nonpharmacologic Analgesia in Newborns: A Functional Neuroimaging Study

Nonpharmacologic analgesia is administered in newborns using, for example, sweet solutions, breastfeeding, or maternal holding.1,2 Nonpharmacologic analgesia can decrease pain during minor procedures, such as a heel prick for blood sampling. From a neurophysiological standpoint, a previous study1 has demonstrated that, during a heel prick, oral glucose administration is associated with no significant cortical activation and therefore may interfere with the pain-associated response at the cortical level. Conversely, breastfeeding analgesia is associated with generalized cortical activation and may act by multisensory stimulation, possibly overwhelming the perception of pain.1

We aimed to study the effect of 2 nonpharmacologic analgesic methods (administration of an oral glucose solution and maternal holding) on neonatal cortical activation during a heel prick. We tested the hypothesis that analgesia associated with maternal holding would differ from that associated with oral glucose administration and would be mediated by a difference in cortical activation.

Methods | The independent committee for bioethics of the Institute for Maternal and Child Health, Trieste, Italy, approved the study. Written informed consent was obtained from the parents. We enrolled 40 healthy newborns undergoing a heel prick for metabolic screening on their third day of life. Data were collected from November 1, 2013, through March 31, 2014. Assessment of cortical activation during the heel prick procedure was performed by multichannel near-infrared spectroscopy (ETG-100; Hitachi Medical, Ltd), which continuously monitors concentration changes in cortical hemoglobin from 24 channels. Eighteen near-infrared light emitters and detectors were positioned bilaterally above the parietal, midtemporal, and posterior frontal cortex (Figure 1). Newborns were randomly assigned to receive different nonpharmacologic analgesia. Twenty newborns were given 2 mL of oral glucose solution at a concentration of 20% two minutes before the heel prick, and blood sampling was performed with the newborn lying supine on a changing table. Twenty newborns were held by their mothers, beginning 2 minutes before the heel prick and throughout the procedure. Specifically, the mothers sat comfortably on a chair, kept their dressed newborn in their arms, and were not allowed to talk to him or her. An increase in the oxyhemoglobin (HbO2) level during the heel prick was considered an estimation of pain.1 After removing physiological or movement noise by filtering the signal,3 the near-infrared spectroscopy data were analyzed, channel by channel, using a 1-tailed paired t test to compare the baseline measurement (mean variation in the HbO2 level in the 10 seconds before disinfection) and a pain-associated hemodynamic response (mean variation in the HbO2 level in the 25 seconds after the heel prick).3 Statistical analysis was performed separately in the 2 groups. We used the false discovery rate to control for statistical multiple testing (q = 0.05).

Results | Use of the oral glucose solution was associated with no significant cortical activity during the heel prick. Instead, maternal holding (Figure 2) was associated with a bilateral activation of the left (channel 5: \( t_{17} = -3.837 \ [P < .001] \), channel 7: \( t_{17} = -2.929 \ [P = .005] \) ) and right (channel 18: \( t_{16} = -3.136 \ [P = .003] \) ) somatosensory cortex and of the posteroinferior right frontal cortex (channel 22: \( t_{18} = -2.686 \ [P = .008] \) ). We found no difference in clinical pain expression between the 2 groups, as measured by the Neonatal Infant Pain Scale.4

Discussion | As previously shown,1 no significant cortical activation was observed during a heel prick using oral glucose analgesia. Thus, the hypothesis that this compound may act by interfering with the cortical processing of pain is further supported. Conversely, maternal holding during the heel prick was associated with cortical activation, particularly in areas associated with the processing of somatic sensations and, in newborns, with affective responses (frontal cortex).5 We speculate that such analgesia may be mediated by multisensory...
stimulation in the context of an emotionally significant attachment relationship between the newborn and his or her mother.\(^6\)

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Author Contributions: Drs Bembich and Demarini had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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**COMMENT & RESPONSE**

Don’t Forget Palliative Patients

To the Editor We appreciate the Viewpoint by Dr Schechter recently published in *JAMA Pediatrics* on the hazards of indiscriminate use of opioids in children.\(^1\) He has made major contributions to pain management for children and his words deserve great respect. We accept that pediatricians have insufficient data about the effectiveness of opioids for chronic

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Figure 2. Mean Variations in Oxyhemoglobin and Deoxyhemoglobin Levels in the Maternal Holding Group

Levels were measured in the 2D infants during the 25 seconds after the heel prick. Mean variation of the optical path length, reported in millimolar per millimeters of hemoglobin (SE, 0.5 mM/mm) is represented on the y-axes. Ch indicates channel; Cz, central; F3 and F4, superior frontal; P3 and P4, parietal; and T3 and T4, midtemporal.

* Indicates a channel that passed the threshold for the false discovery rate (q = 0.05).