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Original article

Evaluation of auditory perception development in neonates by event-related potential technique

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Abstract

Objective: To investigate auditory perception development in neonates and correlate it with days after birth, left and right hemisphere development and sex using event-related potential (ERP) technique.

Methods: Sixty full-term neonates, consisting of 32 males and 28 females, aged 2–28 days were included in this study. An auditory oddball paradigm was used to elicit ERPs. N2 wave latencies and areas were recorded at different days after birth, to study on relationship between auditory perception and age, and comparison of left and right hemispheres, and males and females.

Results: Average wave forms of ERPs in neonates started from relatively irregular flat-bottomed troughs to relatively regular steep-sided ripples. A good linear relationship between ERPs and days after birth in neonates was observed. As days after birth increased, N2 latencies gradually and significantly shortened, and N2 areas gradually and significantly increased (both $P < 0.01$). N2 areas in the central part of the brain were significantly greater, and N2 latencies in the central part were significantly shorter in the left hemisphere compared with the right, indicative of left hemisphere dominance (both $P < 0.05$). N2 areas were greater and N2 latencies shorter in female neonates compared with males.

Conclusion: The neonatal period is one of rapid auditory perception development. In the days following birth, the auditory perception ability of neonates gradually increases. This occurs predominantly in the left hemisphere, with auditory perception ability appearing to develop earlier in female neonates than in males. ERP can be used as an objective index used to evaluate auditory perception development in neonates.

Keywords: Event-related potential; Neonates; Auditory perception; Development

1. Introduction

The neonatal period is a critical period of cognitive function development [1]. Proper neonatal cognitive development lays a solid foundation for future study, work, and life. However, the brain volume at birth is only 50% of an adult-sized brain. Diseases and experimental factors that disrupt normal cognitive developmental processes, such as an increase in number of synapses or dendrites, myelinization, or glial cell proliferation, potentiate cognitive impairments that pose a heavy burden on families and societies. Therefore, characterization of cognitive development in neonates has become an increasing area of interest.

Neonate cognition was previously considered to involve simple perception, passive stimulation, and simple reflex action. Evidence suggests that an infant

Abbreviations: aERP, auditory event-related potential; EEG, electroencephalogram; ERP, event-related potential; NBNA, neonatal behavioral neurological assessment

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born at 27 weeks of gestation can hear and distinguish pure tone at different frequencies [2]. Thus, a primary auditory orientation exists, whereby neonatal auditory perception is gradually strengthened. In addition, infants can proactively identify and retain sensory stimuli, and exhibit preliminary complex cognitive abilities such as learning and memory [3]. Nevertheless, while all of these mechanisms are likely a part of cognitive function development in neonates, many uncertainties remain to be explored.

Behavioral methods generally used for cognitive research are unsuitable for neonates, as they cannot express themselves using language and their motor skills are limited. Therefore, scholars deduce their conception through behaviors such as sucking, head turning, eye blinking, and eye gazing. While some valuable outcomes have been acquired from such studies, neither the time characteristics of cognitive mechanisms nor characteristics of cognitive function development are easily examined.

An event-related potential (ERP) can reflect brain cognitive function by stimulating locked neuroelectrophysiological changes within the brain, providing a scientific approach to studying cognitive development in neonates. An auditory ERP (aERP) detects the brain's attention to processing and resolution of sound stimuli. As auditory perception develops very early (an infant has hearing during the last 3 months of gestation), aERPs provide an objective, quantitative, and noninvasive tool for detection of cognitive function during early life that can be used to test neonatal cognitive ability [4–5]. N2 waves, an endogenous component of ERP relating to higher brain functions including template matching, alertness, judgment, behavior, conflict monitoring or cognitive control, primarily reflect the psychological process to identify target stimuli and are closely related to cognitive processes [6–7].

ERP is widely used in cognitive function research in adult and relatively older pediatric patients with mental disorders, but few reports describe ERP detection for studying cognitive in neonates because (1) any operation or research in neonates imparts a certain risk; (2) pediatric and adult paradigms are not suitable for neonates; (3) neonates generally do not cooperate with ERP detection without use of tranquillizers to maintain sedative and awake states. To the best of our knowledge, previous reports of ERP detection in neonates include findings from Sun et al. [8] and Cheng et al. [9] showing neonates can distinguish different emotions, as evidenced by generation of a mismatch response to stimuli with different emotional speeches. In addition, Wanrooi et al. [10] reported generation of a mismatch response in an infant 2–3 months after rapidly distinguishing similar emotional tones. In an aERP study involving infants at 2 months of age, Mai et al. [11] identified a positive slow wave in the right temporal lobe, which they considered evident of the 2-month-old infant having the ability to encode new stimuli signals. Geng et al. [12] proposed that ERP detection in a 2-month-old infant with an umbilical cord blood lead level of $\geq$2.0 μg/dL showed obvious decreases in P2, P750 and late slow waves after various speech stimuli compared with healthy controls, indicating abnormal hearing and memory. There have been no systematic reports on ERP in neonatal cognition and little has been reported on cognitive development in neonates aged less than 28 days. In this study, we used an ERP technique to clarify auditory perception and information processing in neonates, and investigate neurological mechanisms underlying neonatal auditory perception development.

2. Subjects and methods

2.1. Subjects

Full-term neonates born between December 2013 and May 2016 in the Department of Newborns, Changzhou Children's Hospital (affiliated with Nantong University, China) were included in this study. Three-month preliminary experiments were performed with the purposes of designing an auditory oddball paradigm device and exploring experimental conditions and experimental neonatal compliance. Sixty-two neonates with 39 and 40 week's gestation age (two of them rejected for crying), consisting of 32 males and 28 females, aged 2–28 days were randomly selected. Included neonates were assigned to three groups as per age: 1–10 days after birth (group A, $n = 18$), 11–20 days after birth (group B, $n = 20$) and 21–28 days after birth (group C, $n = 22$).

As suggested by professionals in the Department of Newborns, inclusion criteria included the absence of brain injury during the perinatal period, neonatal behavioral neurological assessment (NBNA) score >37 points, both ears passing a hearing screening, stable vital signs, and no obvious organic diseases. In addition, infants with one or more of the following conditions were excluded: neonatal encephalopathy, intracranial hemorrhage, severe hyperbilirubinemia, craniofacial malformation, congenital brain abnormalities, or genetic or metabolic diseases.

Experimental ERP detection is a noninvasive test whose application was approved by the ethics committee of Changzhou Children's Hospital. Written informed consent regarding ERP detection was obtained from the guardians of each neonate.

2.2. ERP recording

The digital 32-channel electroencephalogram (EEG) recording apparatus employed was from Stellate Systems Inc., Quebec, Canada. According to the International 10–20 system, recording electrodes were located