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Sex differences in visual evoked potentials in school-age children: What is the evidence beyond the checkerboard?



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ABSTRACT

Visual evoked potentials (VEPs) are known to be influenced by several biological variables, including sex. In adult populations studies using conventional high-contrast checkerboard have shown that females display larger amplitudes and shorter latencies than males. To date, few studies have been conducted in children; the available data suggests that girls display significantly larger amplitudes than boys but the effect on latency is absent or negligible. We investigated sex-related VEP differences in 149 school-age (11.3 ± 0.6 years) children from Northern Quebec using several VEP protocols: achromatic pattern-reversal VEPs at high (95%) and low contrast (30%, 12% and 4%), as well as motion-onset VEPs and isoluminant pattern-reversal VEPs. Girls showed significantly larger amplitudes in achromatic VEPs for most of the contrast levels as well as in N2 response to motion-onset. No significant difference was found regarding the amplitude of isoluminant VEPs. In addition, girls showed shorter latencies for the achromatic N75 and a trend (p < 0.1) for the P100, regardless of the contrast level. Interestingly, this latency effect appeared mostly due to head size, not sex. No differences in latency were found for motion or isoluminant responses. Overall, these findings show that sex-related differences are present in children mostly in VEP amplitude not only for high contrast achromatic pattern-reversal but also for low contrast levels and motion-onset VEPs, suggesting that sex affects VEP responses in a general fashion.

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1. Introduction

VEPs provide information on the integrity of the visual system with the advantage of being able to isolate early (sensory) visual processing because of the high temporal resolution of the electrophysiological technique. It is well known that several biological variables, such as age and, to a lesser extent, sex, can influence VEP measurements. Regarding sex, there is considerable evidence of shorter latency in adult females compared to adult males (Allison et al., 1983; Celesia et al., 1987; Chu, 1987; Emmerson-Hanover et al., 1994; Gregori et al.,

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Earlier studies examining age and/or sex effects on VEPs have focused on latency, often ignoring amplitude because of its putative greater variability between subjects. However, the few studies that have looked at sex differences in amplitude have found significant effects, with females having larger amplitudes than males, not only in adults but also in children (Chu, 1987; Cohn et al., 1985b; Emmerson-Hanover et al., 1994; La Marche et al., 1986; Mitchell et al., 1987; Snyder et al., 1981). Interestingly, amplitude tends to decrease from childhood to puberty for both sexes, whereas during adulthood, amplitude generally increases with age only in women and stabilizes in men (Emmerson-Hanover et al., 1994; La Marche et al., 1986). As a result, one might expect this sex difference to increase with age, but the few studies that have addressed this question have failed to find significant differences in older individual groups (Mitchell et al., 1987; Snyder et al., 1981).

Variability across VEP studies in both latency and amplitude findings can be attributed to a wide range of factors, including sample size,

Abbreviations: ANCOVA, analysis of covariance; DHA, docosahexaenoic acid; ERPs, event-related potentials; fMRI, functional magnetic resonance imaging; PCB, polychlorinated biphenyl; VEPs, visual evoked potentials.

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confounding variables, statistical tests, and, more critically, age. In fact, the effect of sex on VEPs in the literature was often assessed as a secondary objective. This is manifest in several studies that aimed at evaluating how age affects VEPs. In these studies, researchers used relatively large sample sizes that included children, adults and elderly individuals to reveal age-related effects in a lifespan perspective (Allison et al., 1983; Chu, 1987; Emmerson-Hanover et al., 1994; Snyder et al., 1981). However, when assessing sex differences within a given subgroup (e.g. in children), the number of subjects dropped, decreasing the statistical power to detect significant effects.

The aim of this study was twofold. First, sex differences were assessed in school-age children just before the onset of puberty in a large, demographically homogenous sample with a relatively narrow age range (between 10 and 13 years old), which enabled us to control for the potential confounding effect of age on sex-related VEP differences. Second, we examined whether sex differences are present not only for achromatic pattern-reversal stimulation, as reported by previous studies, but also for isoluminant pattern-reversal and motion-onset VEPs (Figs. 1 and 2). To our knowledge, sex differences in VEPs have been examined in very few studies for visual stimuli other than with high contrast checkerboards (Cohn et al., 1985a; Kuba et al., 2012).

2. Material and methods

The data for this study came from the 11-year follow-up of a longitudinal study of Inuit children from Arctic Quebec in Canada (a region called Nunavik), which was designed to assess the impact of exposure to environmental contaminants on child development (Jacobson et al., 2008; Muckle et al., 2001). The study provided a unique opportunity to examine sex differences in VEP in children because a broad range of demographic and other potential confounding variables were documented (environmental contaminant exposure, fish nutrients, anthropomorphic measurements, socioeconomic status, etc.) and three different types of VEPs were collected (Ethier et al., 2012; Jacques et al., 2011).

2.1. Participants

VEP measurements were obtained from 169 children in this cohort (age: mean + SD = 11.3 \pm 0.6 years; range = 10.0–13.0). The following inclusion criteria were used: no known ophthalmic, neurological or developmental disorder, no medication, birth weight \geq 2500 g and gestation duration \geq 37 weeks. Although the gestation duration was slightly lower than 37 weeks for four children (two were born between 36 and 37 weeks and two between 35 and 36 weeks), their VEP responses did not differ significantly from the others (all *ps* > 0.15). The sample was characterized by the same proportion of girls and boys (51% females).

2.2. Procedures

Visual screening assessments for color, depth and acuity were performed using the Ishihara Test for Color Blindness®, the Titmus Stereotest and the Snellen E-chart. Visual acuity was considered normal when scores ranged from 20/20 to 20/30 given that the testing conditions were not as optimal as in a clinical setting. The research procedures were approved by the Sainte-Justine Hospital, Laval University, and Wayne State University research ethics committees. A written informed consent was obtained from a parent of each participant as well as a written assent from the child.

2.3. Visual evoked potentials

Subjects viewed the stimuli binocularly from a distance of 57 cm in a dimly lit room (meso-to-photopic condition) to ensure that no other light source affects the contrast of the visual stimulation. They



Fig. 1. VEP grand mean average of boys and girls for achromatic pattern-reversal VEPs. VEP responses typically show three major components: N75, P100 and N150. Latencies and amplitudes were measured for each component at four contrast levels, 95%, 30%, 12% and 4%.

were instructed to fixate a small red dot located in the center of the screen (VP171b LCD ViewSonic monitor; 1024×768 pixels, 75 Hz). All stimuli were generated with Matlab and presented with Presentation® software (Neurobehavioral Systems, Inc.). Whenever the reflection of the stimulus was not centered over the pupil, the examiner who sat beside the child interrupted the electrophysiological recordings to readjust the child's gaze.

VEPs were recorded from the scalp over the visual cortex according to the International 10–20 system from an Ag–AgCl electrode using an INSTEP computer system. Active electrode was located at Oz site for achromatic and isoluminant pattern-reversal VEPs with the reference electrode at Fz. T5 and T6 derivations were used for motion-onset VEPs with the reference on the linked ear lobes. The ground electrode

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