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Evidence for the existence and development of visual inhibition in humans

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Neural inhibition forms a major mechanism by which the nervous system refines and elaborates its input[1]. Several recent experiments have demonstrated the existence of inhibition between orientation-selective cells of the primary visual cortex of the cat[2–7] and although the precise function of this inhibition is uncertain, there is evidence that it enhances orientation tuning[7] and that it is involved in pattern recognition[8]. Here we report a series of experiments which, on the basis of evoked potential responses to oriented stimuli, suggest that similar processes may exist in humans. Recordings from young infants further suggest that the machinery which mediates orientation-specific interactions may not be functional at birth, but develops only after 6–8 months.

The stimuli used in these studies were sinusoidal gratings: a test of variable contrast and a high-contrast (20%) mask of slightly different spatial frequency, oriented either orthogonal or parallel to the test. Both test and mask gratings were phase reversed at rates from 3 to 7 Hz. Visually evoked potentials (VEPs) were appropriately filtered, amplified and averaged (by computer) in synchrony with the test phase reversal. Averaging at this frequency accumulated the potentials generated by the test, but not those generated directly by the mask (which was phase reversed at a different frequency). Measurements were made on three adults, all of whom had corrected 6/6 vision, and on three infants, all of whom had normal vision (1–2-dioptre hypermetropia), over a period of 8 months.

Some of the results for the adults are presented in Fig. 1. They show the amplitude of the evoked potential as a function of test grating contrast, measured with no mask and with superimposed orthogonal or parallel masks. In the absence of any mask, the VEP modulated at twice the temporal frequency of the test, with very little modulation at the first, third or fourth harmonics. The amplitude of modulation increased monotonically (roughly logarithmically) with contrast up to a saturation point, then began to decrease (except for M.C.M.). Like Campbell and Maffei[9], we find that extrapolation of contrast response curves efficiently predicts psychophysical thresholds. Superposition of the orthogonal mask did not affect the form of the VEP (by introducing higher or lower harmonics) but significantly reduced the amplitude of second-harmonic modulation. The reduction was greater at high than at low contrasts, yielding contrast response curves of lower slope. Interestingly, the orthogonal mask had very little effect on threshold, either that measured psychophysically or the VEP estimate. The attenuation produced by the mask is multiplicative (or divisive), reducing the contrast response curve without significantly affecting contrast threshold.

To be sure that the multiplicative attenuation results from an interaction between mechanisms tuned to different orientations, we also measured the effect of a superimposed parallel mask (Fig. 1). This mask also attenuated the VEP amplitudes[10,11], but the attenuation shifted the contrast response curve to the right, without lowering its slope. Extrapolation of the curve again predicts the psychophysically measured threshold, which is much higher than that measured either with no mask or with the orthogonal mask[12,13]. As a further control, we measured VEP response with orthogonal masks of varying spatial frequency. Masks of spatial frequencies differing by more than two octaves from the test had no effect on VEP amplitude. Change of the contrast response curve is specific to masks of different orientations but with similar spatial frequencies to those of the test.

Measurements were made over a wide range of test spatial frequencies (keeping the mask at 0.8 times the frequency of the test). For all test frequencies from 0.5 to 10 cycles deg^{-1} (the range giving reliable contrast response curves), the orthogonal mask reduced the slope of the contrast response curve to a degree comparable to that shown in Fig. 1. The effect was also obtained over a range of temporal frequencies from 5 to 14 Hz.

Contrast response curves (with and without masking gratings) were also measured for three infants over an 8-month time span, to monitor the developmental course of the effect. Figure 2 shows samples of the results for one of the infants at $3\frac{1}{2}$ months, 4 months and 10 months. At $3\frac{1}{2}$ months, the three curves are virtually parallel. Those curves for the parallel mask and the orthogonal mask are superimposed, both slightly below the curve for no mask. Two weeks later, the pattern has changed. The curves are still parallel, but that with the orthogonal mask is now coincident with the no-mask curve, both of which are higher than the curve for the parallel mask. At 10 months the pattern is virtually the same as for adults, with the orthogonal noise producing a change in slope and the parallel noise a uniform depression. As the choice of spatial and temporal frequencies could be relevant, for one of the infants (T.L.B.) we measured contrast response curves with a range of spatial and temporal frequencies (0.5–2 cycles deg^{-1}; 3–7.2 Hz), at various stages. There was no evidence of multiplicative attenuation at any frequency before 6 months of age (although very low temporal frequencies were not used for technical reasons). We have also repeated the experiments with kittens[14] (where more extensive measurements were possible), and shown that the effect is not present before 40 days, regardless of the spatial or temporal

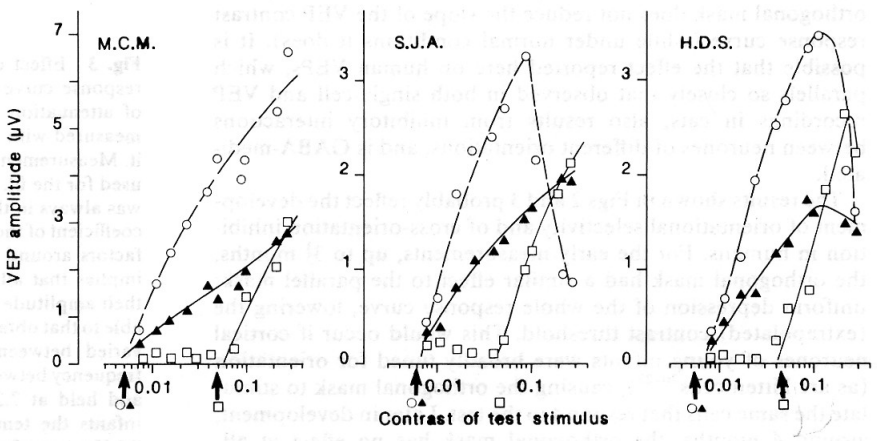

Fig. 1 Amplitude of the second harmonic of VEP modulation as a function of grating contrast. The test was a sinusoidal grating of 1 cycle deg^{-1} measured with no mask (○) and with masks of 0.8 cycles deg^{-1} orthogonal (▲) or parallel (□) to the test grating. The temporal frequency of the test was chosen to be just high enough to give a clear second-harmonic response for each observer, with no significant modulation at the higher harmonics (M.C.M., 7.2 Hz; S.J.A., 10 Hz; H.D.S., 7.2 Hz). The mask was modulated at 0.8 times this frequency. The arrows indicate the psychophysical detection thresholds, measured for the three conditions using the method of adjustment (average of five settings). The screen subtended a 30-cm square and had a mean luminance of 40 cd m^{-2}. Evoked potentials were differentially recorded with electrodes on the vertex and 2.5 cm above the inion, with a third electrode on the forehead serving as earth. The average multiplicative factors by which the slope of the contrast response curve was attenuated by the orthogonal mask were 0.38 ± 0.04 for M.C.M., 0.39 for S.J.A. and 0.33 ± 0.03 for H.D.S.

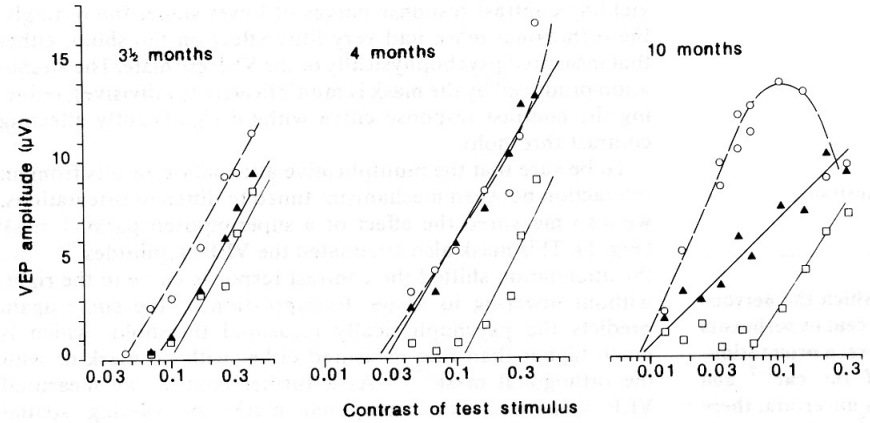

Fig. 2 Representative contrast response curves for one of the infants (T.L.B.) at $3\frac{1}{2}$, 4 and 10 months: ○, no mask; ▲, orthogonal mask; □, parallel mask (see Fig. 1 legend for experimental details). Spatial and temporal frequencies were 0.8 cycles deg^{-1}, 5 Hz at $3\frac{1}{2}$ months, and 1 cycle deg^{-1}, 7.2 Hz for the other curves. The recording electrodes were positioned on the vertex and 1.5 cm above the inion, with the earth electrode on the forehead.

frequency of the stimulus (0.05–0.8 cycles deg^{-1}; 0.8–7 Hz).

An estimate of the average multiplicative factor by which the orthogonal mask attenuated the VEP amplitude was obtained by plotting the VEP amplitudes measured with the orthogonal mask against those measured with no mask, and calculating the best linear estimate of the relationship (by least-squares fit). The slope of the equation of linear fit provides an estimate of the multiplicative factor of attenuation, with its associated error. Figure 3 plots the multiplication factor for the three infants as a function of age. Up to about 6 months the factor is ~1, indicating that the orthogonal mask had no effect on the slope of the contrast response curves. After this, the multiplication factor begins to decrease rapidly, reaching adult values at about 8 months.

Previous studies have shown that the VEP response to modulated stimuli can be modified by addition of superimposed[10,11,15,16] or adjacent[17,18] masks modulated at different temporal frequencies. These results have been explained by rectifying[16] or multiplicative[18] nonlinearities in the neural mechanisms that generate the VEP. Here we extend these studies by showing that the VEP contrast response curves are modified by parallel and orthogonal masks in a different way, implying an orientation-specific interaction: the orthogonal mask lowers the slope of the curve, while the parallel mask does not. Attenuation of contrast response slope, without a significant accompanying change in threshold, is similar to results found in cells in the cat primary visual cortex when a stimulus orthogonal to the cell's preferred orientation is introduced[4]. It is likely that the multiplicative attenuation of single cortical cell response is mediated by inhibitory processes and that γ-aminobutyric acid (GABA) is the transmitter of the inhibition[5–7]. Recent experiments in our laboratory provide similar evidence that the attenuation of VEPs (in cat) by orthogonal stimuli is also GABA-mediated[19]. When bicuculline (a GABA blocker) is applied to the cortex (either topically or iontophoretically), an orthogonal mask does not reduce the slope of the VEP contrast response curve (while under normal conditions it does). It is possible that the effect reported here on human VEPs, which parallels so closely that observed in both single-cell and VEP recordings in cats, also results from inhibitory interactions between neurones of different orientations, and is GABA-mediated.

The results shown in Figs 2 and 3 probably reflect the development of orientational selectivity and of cross-orientation inhibition in humans. For the early measurements, up to $3\frac{1}{2}$ months, the orthogonal mask had a similar effect to the parallel mask: uniform depression of the whole response curve, lowering the (extrapolated) contrast threshold. This would occur if cortical neurones of young infants were broadly tuned for orientation (as are kitten cells[20–22]), causing the orthogonal mask to stimulate the same cells that respond to the test. Later in development, around 4 months, the orthogonal mask has no effect at all, suggesting that at this age the cells have some selectivity for orientation, but that inhibitory mechanisms which change the slope of the curve are not yet in place. These mechanisms do not appear until about 6 months, whereupon they mature rapidly.

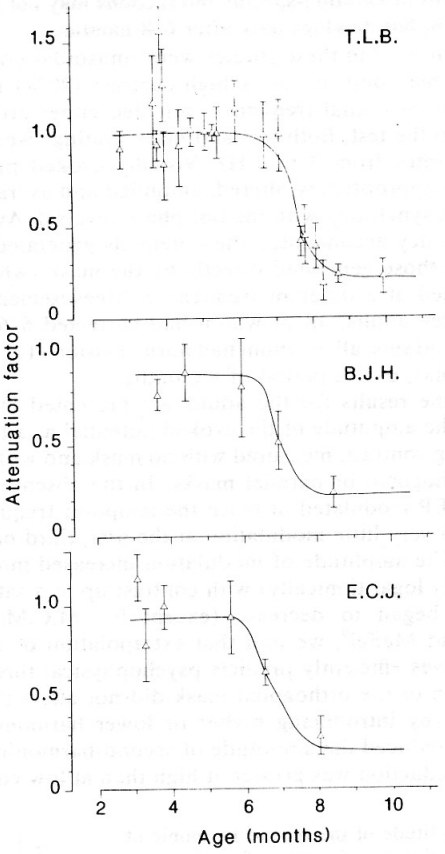

Fig. 3 Effect of orthogonal masks on the slope of the contrast response curve as a function of age for three infants. The index of attenuation is calculated by linear fit of the VEP amplitudes measured with the orthogonal mask with those measured without it. Measurements of all contrasts up to the point of saturation were used for the fit. The correlation between the linear fit and the data was always in the range of 0.75–0.95. The ordinate plots the linear coefficient of the fit, and the bars the associated error. Multiplicative factors around 1 imply no multiplicative attenuation, while 0.25 implies that all VEP amplitudes were reduced to one-quarter of their amplitude. The value of 0.25, found after 8 months, is comparable to that obtained with adults. For T.L.B. the temporal frequency varied between 3 and 7.2 Hz (between sessions) and spatial frequency between 0.2 and 2 cycles deg^{-1} up to the age of 5 months, and held at 7.2 Hz and 1 cycle deg^{-1} thereafter. For the other infants the temporal frequency was 5 Hz up to 5 months, and 7.2 Hz thereafter, with spatial frequency always 1 cycle deg^{-1}. The variation in temporal and spatial frequencies did not affect the multiplicative factor.

There is strong evidence that acuity and contrast sensitivity of infant vision improve steadily with age[23–29], with most of the development occurring within the first 6 months[30]. Fine- resolution tasks such as stereopsis are also adult-like by 6 months of age[30]. However, it is not until 6 months of age that we find evidence for cross-orientation inhibition. This result is interesting, as several physiological[31,32] and anatomical[33] studies have shown that in the cat, inhibition develops after most of the functions associated with excitation have matured.

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