



Normal and abnormal face selectivity of the M170 response in developmental prosopagnosics

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Abstract

Developmental prosopagnosia is a lifelong impairment in face recognition despite normal low-level visual processing. Here we used magnetoencephalography (MEG) to examine the M170 response, a component occurring approximately 170 ms after stimulus onset, in a group of five developmental prosopagnosics. In normal subjects, the M170 is “face-selective”, with a consistently higher amplitude to faces than to a wide variety of other visual stimulus categories; the N170, a component recorded using event-related potentials (ERP) and thought to be analogous to the M170, also shows this “face selectivity”. Two previous ERP studies with developmental prosopagnosics have found attenuation or absence of face selectivity in the N170 response of these subjects [Bentin, S., Deouell, L. Y., & Soroker, N. (1999). Selective visual streaming in face recognition: Evidence from developmental prosopagnosia. *Neuroreport*, 10, 823–827; Kress, T., & Daum, I. (2003). Event-related potentials reflect impaired face recognition in patients with congenital prosopagnosia. *Neuroscience Letters*, 352, 133–136]. Three of our developmental prosopagnosic group showed this non-selective pattern at the M170 while the remaining two prosopagnosics were indistinguishable from normal controls. Thus, impaired face recognition is not necessarily correlated with an absence of the “face-selective” M170. Furthermore, ERP recordings collected simultaneously in the two developmental prosopagnosics with seemingly selective M170s also showed N170s within the same normal selective range, demonstrating that the face-selective signals found with MEG are not due to differences between MEG and ERP. While the presence of face selectivity at these neurophysiological markers is insufficient for predicting normal behavioral performance with faces, it could help to distinguish different classes of face recognition deficits.

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1. Introduction

Prosopagnosia, an impairment in the recognition of faces despite normal low-level visual processing, has often been cited as evidence for “special” processing of faces in the human visual system (Farah, 1996; McNeil & Warrington, 1993). Although initial reports of this impairment came from the examination of patients who had acquired it following brain damage, more recently it has become apparent that there is a sizable population of individuals for whom it is a lifelong condition (Bentin, Deouell, & Soroker, 1999; Duchaine, 2000; Duchaine & Nakayama, 2005; McConachie, 1976). These so-called “developmental” prosopagnosics usu-

ally have no history of head trauma, yet fail to develop normal face recognition capabilities. In everyday life, as well as on laboratory tests, developmental prosopagnosics show impairments in recognition of faces—sometimes even for parents, siblings, or spouses—that often lead to distressing social consequences. Although in some cases the condition may be linked to early head injury (Barton, Cherkasova, Press, Intriligator, & O’Connor, 2003; Laeng & Caviness, 2001; Michelon & Biederman, 2003), early visual problems (Le Grand, Mondloch, Maurer, & Brent, 2001), or genetic factors (De Haan, 1999; Duchaine & Nakayama, 2005), the etiology is often unknown.

One means of assessing the neural substrates of this behavioral impairment comes from neurophysiological methods such as event-related potentials (ERP) and magnetoencephalography (MEG). Due to their extremely high

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temporal resolution, these neurophysiological techniques can index even relatively early, short-latency cortical processes. In addition, they are known to measure a component related to face processing, the N170 (in ERP) or M170 (in MEG). Occurring approximately 170 ms after stimulus onset, the M170/N170 shows a higher-amplitude response to faces than to a variety of other stimuli, including houses, cars, animals, flowers, tools, and textures (Bentin, Allison, Puce, Perez, & McCarthy, 1996; Itier & Taylor, 2004; Liu, Higuchi, Marantz, & Kanwisher, 2000; Sams, Hietanen, Hari, Ilmoniemi, & Lounasmaa, 1997). This has led researchers to label this response as “face-selective”, despite the fact that, unlike a single-unit recording, the neurophysiological signal arises from the combination of a large number of neural responses. Although the spatial resolution of MEG and ERP is relatively low, some clue as to the origin of the M170/N170 comes from intracranial electrode recordings in patients (Allison, Puce, Spencer, & McCarthy, 1999), which have reported finding a negative deflection at approximately 200 ms in electrodes placed on the ventral surface in occipitotemporal cortex, particularly along the fusiform gyrus. Like the M170/N170 response, the N200 response is much greater for faces than for cars, hands, butterflies, letter strings, number strings, and phase-scrambled faces.

Previous studies of face perception in developmental prosopagnosia have examined the amplitude of the N170 response in a total of three subjects. Bentin et al. (1999) recorded ERPs from one prosopagnosic, YT, while presenting pictures of faces, cars, furniture, and phase-scrambled faces. In terms of behavioral performance, YT was severely but selectively impaired with faces, recognizing only 24 out of 670 famous faces while performing perfectly on object naming tasks. Yet he showed an N170 response for faces similar to those of normal controls, both in terms of amplitude and distribution. However, his N170 response to non-face objects was much larger than those of normal controls, resulting in a significantly lower difference between faces and objects (3.35 μV for YT versus 4.5–8.7 μV for controls in the right hemisphere).

More recently, Kress and Daum (2003) have reported on two female developmental prosopagnosics, SO and GH. Again, both performed in the normal range on simple object recognition tasks. On the face subtest of the Recognition Memory Test (RMT), SO scored more than 2 standard deviations below controls, while GH was in the normal range. Neither showed any difference in ERP amplitude to faces versus houses; again, as in prosopagnosic YT, the lack of selectivity appears to stem from a larger N170 to non-face objects rather than a reduced N170 for faces.

Yet, many questions regarding the neurophysiology of developmental prosopagnosia remain. The most obvious issue is that of the heterogeneity of the population. As indicated above, most previous studies of developmental prosopagnosia have relied on two to three subjects at most (cf. Duchaine & Nakayama, 2005). While studying individual cases is the norm for neuropsychology, it must be kept in

mind that developmental prosopagnosia is defined by sub-standard behavioral performance in laboratory tests, not by clinical etiology. As a result, the condition is likely caused by impairments to different mechanisms in different individuals. As such, it is unsurprising that functional imaging of developmental prosopagnosia has had inconsistent results. Looking at the fusiform face area (FFA), a region which shows a higher activation to faces than to objects (Kanwisher, McDermott, & Chun, 1997; McCarthy, Puce, Gore, & Allison, 1997), Hadjikhani and de Gelder (2002) found no face-selective FFA in one congenital and two acquired prosopagnosics, while Hasson, Avidan, Deouell, Bentin, and Malach (2003) reported normal FFA activation in one developmental prosopagnosic subject (YT, discussed above for his abnormal N170). These results indicate that with larger samples it may be possible to find different subsets of developmental prosopagnosics—not an unreasonable proposition, given that the causes of developmental prosopagnosia and the means by which face recognition systems can be damaged are so varied.

Although it is generally agreed that ERP and MEG reflect roughly the same neural sources (Hämäläinen, Hari, Ilmoniemi, Knuutila, & Lounasmaa, 1993), there are some differences between the N170 and M170 responses to faces. For example, some researchers have reported that the N170 response to inverted faces shows both a longer latency and a greater amplitude than the response to upright faces (Rossion et al., 2000), whereas the M170 shows only a latency delay (Liu et al., 2000). The two components also differ in their responses to eyes presented alone: while the M170 again shows only a latency delay but no change in amplitude, the N170 is much larger to eyes alone than to whole faces. Since the superior temporal sulcus (STS) is known to be involved in the processing of eye gaze (Haxby, Hoffman, & Gobbini, 2000; Perrett et al., 1985), this has led some researchers to propose that the N170 reflects the activity of STS (Allison, Puce, & McCarthy, 2000), instead of or in addition to a ventral source lateral to the fusiform gyrus (Bentin et al., 1996). In contrast, the M170 is thought to reflect ventral generators alone, and has been localized to the posterior fusiform gyrus (Halgren, Raji, Marinkovic, Jousmäki, & Hari, 2000).

In our experiment, we sought to examine a larger group of developmental prosopagnosics than previously tested with neurophysiological techniques. Using MEG, we examined five individuals who complain of serious face recognition impairments in daily life and whose behavioral performance on face recognition tasks was out of the normal range. By examining a relatively large group of developmental prosopagnosics, we hoped not only to shed additional light on the relationship between this behavioral impairment and a neurophysiological marker of face perception, but also to determine whether differences in the response profile of the M170 exist within this population. In addition, to address the issue of differences between MEG and ERP, we also recorded MEG and EEG responses simultaneously in two of the developmental prosopagnosics.

2. Methods

2.1. Subjects

Five developmental prosopagnosic individuals who had previously contacted the Center for Prosopagnosia Research at Harvard University (<http://www.faceblind.org>) were recruited to participate in this study. All prosopagnosic subjects were right-handed individuals between the ages of 23 and 53; three were male (EB, KNL, and ML) and two were female (KL, NM). All prosopagnosics had normal vision or mild myopia, and none reported any difficulty in seeing stimuli while in the MEG setup.

All prosopagnosic subjects reported a history of face recognition problems and performed poorly on a battery of face recognition tests. None reported any neurological or psychiatric history that may have contributed to their difficulties with faces. KNL and EB have also undergone MRI, and no obvious structural abnormalities were found in either case.

Tables 1 and 2 display the results of neuropsychological testing for the five prosopagnosic subjects. Table 1 shows their performance on several tests of basic vision and object recognition, including contrast sensitivity and line drawing naming. Table 2 presents data from tests of face recognition. In the famous face identification, 16 college students served as controls for ML, and 20 adults between the ages of 35 and 45 served as controls for the other four prosopagnosics. Normal controls for the old/new face discrimination task were 17 graduate students between the ages of 24 and 40. For further details on the neuropsychological testing, readers may also wish to consult previous publications. Data from ML, KL, and NM appear in Duchaine and Nakayama (2005), and EB is discussed in Duchaine et al. (2004).

Control data for MEG and EEG were collected from subjects between the ages of 18 and 40, the majority of whom were undergraduate or graduate students attending local universities. All normal controls were right-handed, with normal or contact-corrected vision. These control subjects were initially run as part of a separate study using the same experimental procedure for MEG; eight controls participated in combined MEG/EEG recordings. Of these eight subjects, the EEG data from three were excluded due to noise or incorrect referencing. Some subjects who participated in the combined MEG/EEG recordings were not included due to noisy MEG data, particularly in initial testing of the simultaneous MEG/EEG setup, where inadequate shielding of the electrode cap created noise artifacts in the first 50 ms post-stimulus onset. (This problem was corrected by the time the developmental prosopagnosics were tested.) However, extensive post-hoc examination of the excluded subjects found no individual in which a normal but non-selective M170 was present. Instead, the M170 response was either contaminated by a large noise artifact, as described above, or difficult to find at all, due to alpha wave (associated with wakeful relaxation) or an unusual head position in the MEG setup.

Since the control group for MEG consisted mainly of undergraduate and graduate students from local universities, on the whole the controls were younger than the developmental prosopagnosics (23–53 years old; mean age = 42). However, age is unlikely to account for differences in MEG signal amplitude between the two groups. A previous study in which young (19–38 years) and older (51–81 years) subjects were tested using MEG reported no significant difference between the two groups in M170 amplitude (Nakamura et al., 2001).

Table 1
Assessment of basic visual function in five developmental prosopagnosics

ID	Sex	Age	Pelli–Robson contrast sensitivity test			Birmingham object recognition battery				Snodgrass line drawings (%)
			Left eye	Right eye	Binocular	Length	Size	Orientation	Position of gap	
EB	M	53	1.65	1.65	1.80	27/30	29/30	27/30	39/40	99
KL	F	44	1.8	1.95	1.95	27/30	29/30	25/30	36/40	–
KNL	M	50	1.8	1.8	1.95	29/30	29/30	25/30	39/40	97
ML	M	23	1.35 ^a	1.65	1.80 ^a	30/30	26/30	27/30	36/40	93
NM	F	40	1.65	1.80	1.95	27/30	24/30	26/30	32/40	97

^a Impaired.

Table 2
Assessment of face perception in five developmental prosopagnosics

ID	Famous faces (Z-score)	Old/new face discrimination 1		Old/new face discrimination 2	
		Accuracy (Z-score)	RT (Z-score)	Accuracy (Z-score)	RT (Z-score)
EB	–10.1 ^a	–3.43 ^a	3.46 ^a	–9.41 ^a	4.98 ^a
KL	–6.49 ^a	–1.46 ^b	7.03 ^a	–6.67 ^a	3.04 ^a
KNL	–3.92 ^a	–3.13 ^a	5.10 ^a	–1.56 ^b	1.5 ^b
ML	–15.3 ^a	–4.97 ^a	3.2 ^a	–7.87 ^a	4.8 ^a
NM	–3.92 ^a	–3.31 ^a	2.63 ^a	–6.09 ^a	1.24

^a Impaired.

^b Borderline impaired.

2.2. Stimuli

Stimuli in this experiment consisted of 300×300 pixel grayscale photographs of faces, houses, and miscellaneous objects, subtending $12^\circ \times 12^\circ$ of visual angle, presented on a white background. A further stimulus category of eyes alone was included in the simultaneous MEG/EEG recordings. Each stimulus was presented for 200 ms, followed by an interstimulus interval of 800 ms.

2.3. Procedure

Subjects were instructed to fixate¹ while viewing 100 randomly interleaved trials of each of the three stimulus categories above (50 exemplars each). MEG recordings were made using a 96-channel whole-head system with SQUID-based first-order gradiometer sensors (Kanazawa Institute of Technology MEG System at the KIT/MIT MEG Joint Research Lab at MIT), except for subject EB, who was tested after the system was upgraded to 157 channels. Magnetic brain activity was digitized continuously at a sampling rate of 500 Hz and was filtered with DC high-pass and 200 Hz low-pass cutoff and a 60 Hz notch.

EEG was recorded with standard electrode caps (Electro-Cap International, Inc.) using the 10–20 International Electrode Placement system, custom modified for MEG. Custom modifications include the use of leads made from carbon filament “wire”, the braiding of the individual leads as they leave the cap (to reduce electric noise on the MEG system), and the shaving of the housing of the posterior electrodes (to make the caps more comfortable, as this is a recumbent MEG system). Recordings were referenced to an electrode on the tip of the nose, and electrode impedance was kept below 5 k Ω . The digitization rates were the same as described above for MEG.

Informed consent was obtained from all subjects, and the study was approved by the Harvard Committee on the Use of Human Subjects in Research and the MIT Committee on the Use of Humans as Experimental Subjects.

2.4. Analysis

Data analysis was performed in MEG160 (Eagle Software Corporation, Japan), the proprietary software for the MEG system we used, and in MATLAB (Mathworks, Andover, MA). Average waveforms were computed for the Face and House conditions in each subject using a window of 500 ms (100 ms before and 400 ms after stimulus onset). The averaged waveforms were then baseline corrected, smoothed with a moving average (window of 17 points), and high-pass filtered (3 Hz, Hanning window).

The latency of the M170 response was obtained by examining the waveforms at all sensors in the Face condition; sensors were then selected for further study using an amplitude threshold of 30 fT. This threshold was not chosen due to any intrinsic physiological value of the threshold, but rather because it proved a simple and effective means of selecting sensors with an M170 response.

Due to the nature of the magnetic field generated by electric currents in the brain, the B field corresponding to the M170 in the right hemisphere constitutes a magnetic “sink”, which is commonly denoted by a negative sign; for our analyses, waveforms in right hemisphere sensors were multiplied by -1 to correct for this polarity difference.

3. Results

Tables 1 and 2 and Fig. 1 display the behavioral results from our developmental prosopagnosics. Table 1 shows the performance of these five subjects on various tests of basic vision and object recognition. The Pelli–Robson chart (Pelli, Robson, & Wilkins, 1988) measures contrast sensitivity in units of log contrast. The prosopagnosics’ performance is largely within the bounds previously described for normal adults in their age groups (Mäntyjärvi & Laitinen, 2001). All of the prosopagnosics perform normally on tests of basic object recognition such as the Birmingham Object Recognition Battery (BORB) and Snodgrass line drawing identifications. Thus, in these individuals, basic visual processing appears to be intact.

Table 2 and Fig. 1 indicate the performance of these individuals on tests of face recognition. In Famous Face Identification, we recorded the number of famous faces correctly identified out of a set of 25; for this test, a correct answer was counted as either the proper name or other uniquely identifying information (e.g., movie roles, political offices) of the individual being shown. The results are displayed in Fig. 1a, where the line indicates the mean number correct for the older adult controls (older adults: mean = 22.65, S.D. = 1.95; college students: mean = 23.62, S.D. = 1.41). Dashed lines represent one standard deviation above and below the mean. As can be seen, the developmental prosopagnosics are moderately (KNL, KL, NM) to severely impaired (EB, ML); however, even the least impaired prosopagnosics scored nearly 4 standard deviations below the mean. Each subject’s exposure to the faces that they did not identify was assessed after testing, and all of the prosopagnosics reported familiarity with nearly all of the celebrities they failed to identify.

On two old/new discrimination tasks with novel faces (Fig. 1b), the prosopagnosics again perform worse than the normal controls (black circles). EB and ML again show severe impairments, and KNL is moderately impaired. Note also that all of the prosopagnosics had slower reaction times than controls, often 2 standard deviations outside of the normal range (Table 2). Together with the data on famous face identification, these behavioral scores confirm that these

¹ Although attentional selection and task demands are not constrained in passive viewing, these factors have little or no effect on the N170 response to faces (Carmel & Bentin, 2002), and so are unlikely to affect our results.

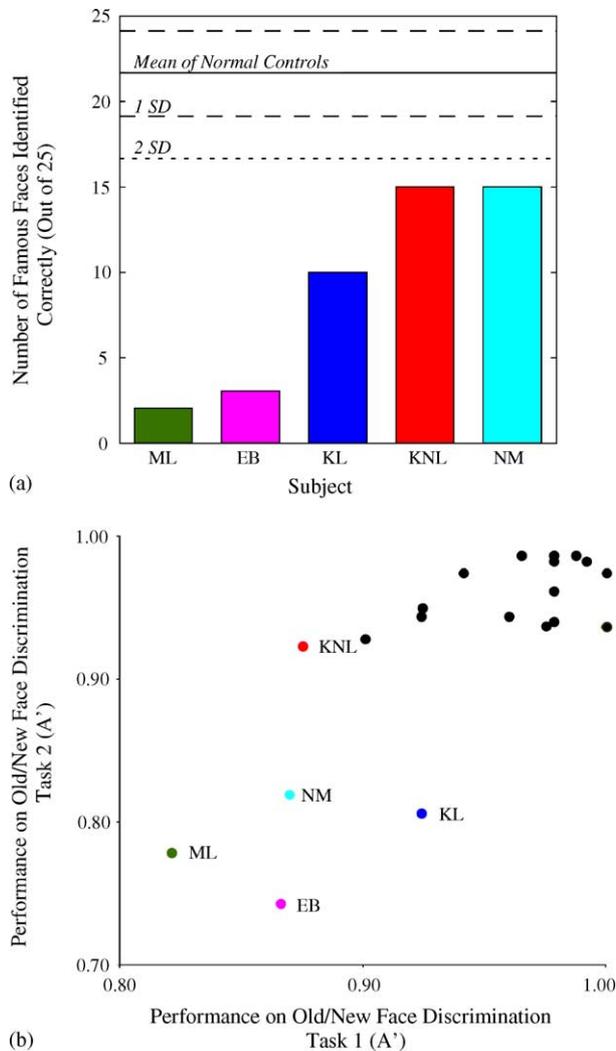


Fig. 1. Behavioral data from the five developmental prosopagnosics tested in this experiment. (a) Famous face identification task. Subjects had to name or otherwise uniquely identify a set of 25 famous faces. The line indicates the mean of normal controls, and the dashed and dotted lines represent one and two standard deviations around the mean, respectively. (b) Old/new discrimination with unfamiliar faces. Performance on two versions of this task with different face stimuli is plotted here.

subjects' self-reports of face recognition difficulties in daily life reflect an actual impairment in the processing of faces.

Fig. 2a outlines the method we used to analyze the MEG data in our subjects. In ERP studies of the N170, the sensors to be examined are usually defined a priori (often the temporal electrodes T5 and T6) due to the known properties of the N170 response and the constrained location of scalp electrodes in the International Electrode Placement system. Unlike traditional 32-channel ERP studies, our experiments utilized a 96-channel MEG SQUID electrode array (except for prosopagnosic EB; see Methods). While conferring an advantage in terms of coverage, this increase in the size of the electrode array results in greater difficulty determining which sensors to use, as there are more sensors potentially recording the M170 and the location of the head in the MEG array is

much less spatially constrained. Previous studies using this MEG system have chosen M170 "sensors of interest" by a statistical criterion of face selectivity (Liu, Harris, & Kanwisher, 2002; Liu et al., 2000), but we cannot assume that such a criterion will be met in developmental prosopagnosic subjects. To address this problem, we opted for a blind selection method based on amplitude of the M170 peak. Using the Face condition, we first located the approximate latency of the M170 peak across all sensors in each subject. In Fig. 2a, the waveforms across all sensors in one subject are displayed; the M170 is clearly visible as a major peak in the 150–200 ms time range (occurring at approximately 180 ms in this subject, indicated by the red line). Sensors were then selected for further analysis based on a threshold of a magnetic field strength of 30 fT (10^{-15} T), a liberal value that nonetheless excluded the majority of sensors without an M170 response (indicated by the blue bounding box in the figure). The right-hand panel of Fig. 2a shows the resulting M170 sensors (filled circles) on a scalp map of the MEG channels (open circles), overlaid with the absolute value of the M170 amplitude at the selected latency. At no time during this process was the selectivity of the M170 for faces versus other stimuli examined.

The grand average waveform of the M170 response across all sensors meeting our amplitude criteria in the normal controls is displayed in Fig. 2b. In this grand average, there is a clear "face-selective" M170 response, with the response to faces (black) larger than that to houses (red). (The object condition is not included because the amplitude of the response is so low across all subjects as to be non-diagnostic.) Individual grand average waveforms of the M170 response to faces versus houses for each normal control are shown in Fig. 2c. Within individual subjects, a consistent "face-selective" M170 is again apparent. We performed a repeated-measures ANOVA with hemisphere (left \times right) and condition (face \times house) as within-subject factors. As expected, it showed a significant main effect of condition ($F = 195.6$, $p \approx 0$). The main effect of hemisphere approached significance ($F = 3.45$, $p = 0.081$), with measured M170 amplitudes somewhat larger in the left hemisphere, but the interaction of condition and hemisphere was not significant ($F < 1$).

In contrast, the developmental prosopagnosics vary dramatically in the nature of their M170 responses (Fig. 2d). M170 responses in three of the prosopagnosics (EB, KNL, and NM) show little or no selectivity for faces, in keeping with previously reported ERP results. All three show equivalent amplitude for faces and houses whereas all of the control subjects show a greater peak amplitude for the response to faces. However, perhaps most surprising is the result from the remaining two prosopagnosics (KL and ML): despite their clear behavioral deficits in face recognition, their M170 responses are indistinguishable from those of normal controls. Examining the "face selectivity effect" (Bentin et al., 1999, p. 826), the difference between the M170 amplitude to faces versus houses, the normal mean is 26.9 fT (S.D. = 10 fT) over the right and 26.1 fT (S.D. = 9.6 fT) over the left hemisphere. The face selectivity effects for KL (right hemisphere = 17.3 fT, left

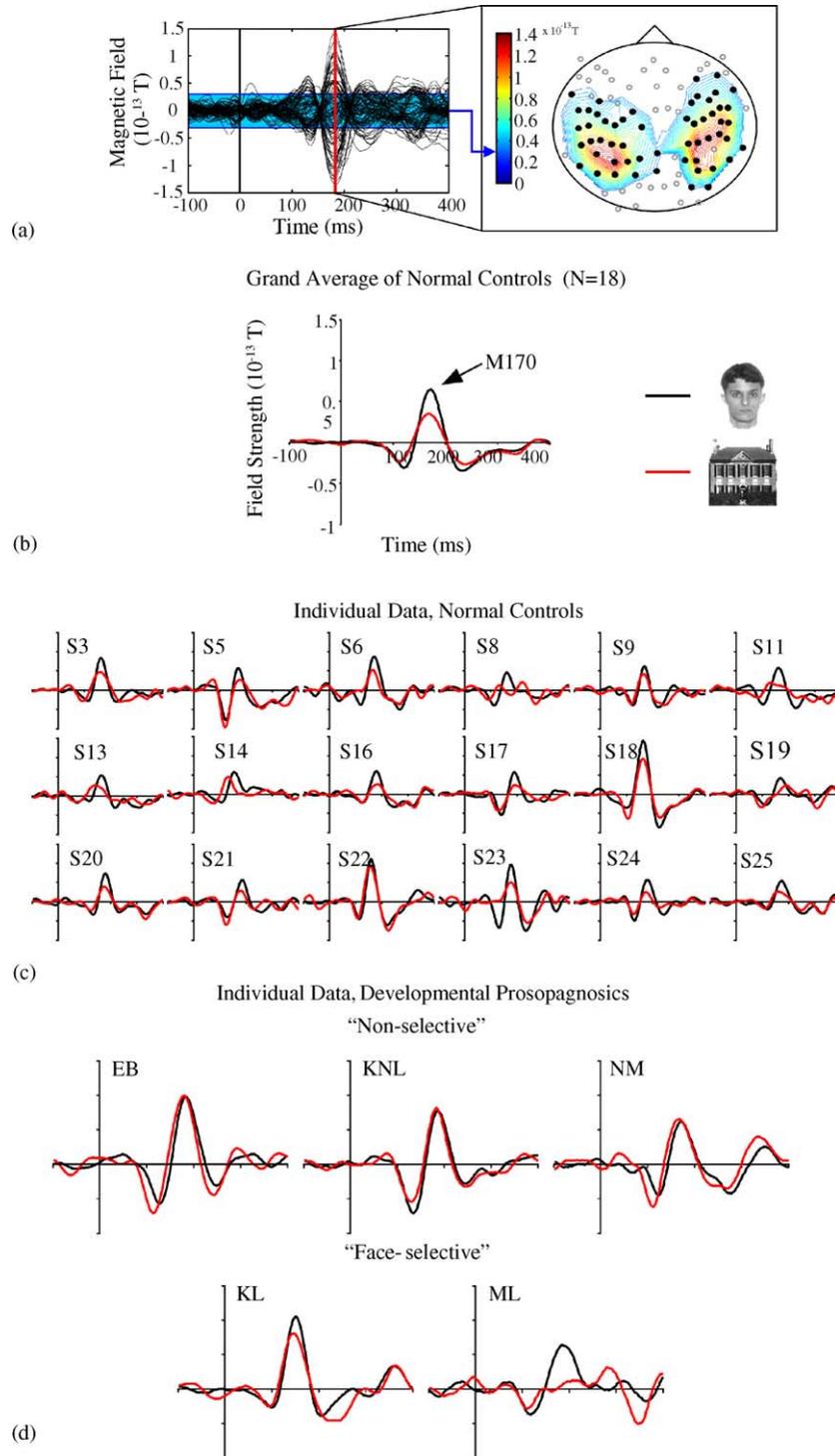


Fig. 2. MEG results. (a) M170 sensor selection process. The latency of the M170 in each subject was first determined by inspecting the waveforms across all sensors in the 130–200 ms time range. Those occipitotemporal sensors meeting an amplitude threshold of 30 fT (blue bounding box) at the peak M170 latency (red line) were then selected as M170 sensors. On the contour plot at right, the sensor array is designated by open gray circles; filled black circles indicate the sensors above the amplitude threshold for the M170 response. (b) The grand average waveform across all M170 sensors in both hemispheres for faces (black) and houses (red), averaged across 18 normal controls. This grand average M170 response is “face-selective”, showing a much larger response to faces than to houses. (c) Grand average waveforms across M170 sensors and hemispheres for faces and houses within individual controls. All of the control subjects show a greater M170 response to faces than to houses. (d) Grand average waveforms for developmental prosopagnosics. The waveforms from the developmental prosopagnosic subjects are clearly divided between “non-selective” and “face-selective” M170 responses.

hemisphere = 26.9 fT) and ML (right hemisphere = 57.6 fT, left hemisphere = 35.6 fT) are obviously within (or, in the case of ML's right hemisphere M170, above) the normal range.

However, the division between “non-selective” and “face-selective” M170 responses in our prosopagnosic subjects is based on averages computed across multiple sensors. Given that sensors vary from one another in both the amplitude and latency of the M170 response, it is possible that the “non-selective” response seen in some developmental prosopagnosics results from averaging alone. In the case of our prosopagnosics with non-selective M170 responses, for example, sensors which record an extremely high M170 response to houses or an extremely low M170 response to faces could skew the average waveform towards “non-selectivity”. Similarly, a “non-selective” grand average waveform could result from combining several M170 responses which are “face-selective” but highly variable in latency.

To ascertain whether the null result reported here truly reflects the signal recorded at the majority of sensors, rather than some artifact of averaging, we undertook a sensor-by-sensor analysis of the M170 response. In every subject, we found the peak amplitude of the M170 response to faces and houses for each sensor; the results are plotted in Fig. 3. The diagonal line in each plot represents unity, the case in which the amplitude of the M170 is equal for faces and houses. Sensors falling above the line are those in which the M170 response recorded is “face-selective”, having a higher amplitude to faces than to houses. Likewise, sensors plotted below the unity line are “house-selective”, for lack of a better term.

The averaged data across all sensors for each subject is shown in Fig. 3a. In keeping with the grand average waveform presented in Fig. 2b, all of the normal subjects (black circles) show “face-selectivity” on average, with a greater M170 response to faces than to houses. Again, three of the prosopagnosics show “non-selective” M170 responses, while the other two are indistinguishable from controls.

Of greater interest, given our concerns about averaging, are the individual data plots shown in parts (b) and (c) of Fig. 3. These results strongly support the conclusions drawn from the average waveforms; yet, because they take the response of each sensor individually, they also show the consistency of the response within any given subject, ruling out any notion of averaging artifacts. Consider the responses for the 18 normal observers (Fig. 3b). In each subject, all but a tiny fraction of sensors yield larger responses to faces than to houses. The results for the prosopagnosics are plotted in Fig. 3c. In two prosopagnosic subjects, KL and ML, sensors show the same preference for faces as those in normal controls. In contrast, sensor recordings in prosopagnosics EB, KNL, and NM show no face selectivity, straddling the line of unity.

We also examined the M170 response in normal and prosopagnosic subjects using a more conservative threshold based on a statistical criterion. The majority of studies of the M170/N170 response have argued that this component is “face-selective” on the basis of statistical tests which show a

significantly higher response to faces compared to other stimuli. This question is especially interesting with regards to our prosopagnosics showing “face-selective” M170 responses. With a more stringent, statistically defined threshold, these subjects may form a subset distinct from the controls.

Using a point-to-point *t*-test for the face versus house conditions, we created a map of *t*-values at each sensor over all time points; the previously selected sensors which also met the criterion of $p \leq 0.05$ ($t(99) = 1.96$) at the latency of the M170 were then labeled as having “face-selective” M170 responses. In Fig. 4, a plot of selectivity versus total number of M170 sensors, the distinction between the developmental prosopagnosics with non-selective and face-selective M170 responses can clearly be seen. The three subjects with “non-selective” M170 responses (EB, KNL, and NM) again are easily distinguishable from the normal controls. However, the two subjects with “face-selective” M170 responses (KL and ML) are within the normal range, though at its lower end. Thus, in all of our analyses, we have found their M170 responses to be normally “face-selective”.

In two of our prosopagnosic subjects, we had the opportunity to record MEG and EEG simultaneously. Fortunately, these two prosopagnosics happened to both show normal M170 “face-selectivity”, so we can address the question of the relationship between M170 and N170 selectivity. As discussed in the Introduction section, there are minor but well-known differences between the M170 and N170 responses in terms of their sensitivity to face stimulus manipulations such as inversion and presenting features, particularly the eyes, in isolation. These discrepancies have been interpreted by some researchers as resulting from differences in the neural generators underlying each response (Allison et al., 2000; Bentin et al., 1996; Halgren et al., 2000). Since previous studies of developmental prosopagnosics which reported no selectivity for faces utilized ERP rather than MEG, it is possible (albeit unlikely) that the “face-selectivity” we report is due to these measurement considerations alone. Thus it was a question of interest whether the prosopagnosics with “face-selective” M170 responses would have “face-selective” N170 responses as well.

Fig. 5 displays the N170 responses for both prosopagnosics and five normal controls to faces, houses, and eyes and eyes alone. In Fig. 5a, the MEG and ERP waveforms averaged from five normal subjects are displayed side-by-side. The two are highly similar, even for eyes alone, which have been reported to elicit a larger N170 response than full faces (Bentin et al., 1996). However, given the small set size, the lack of a larger response for eyes alone is probably not meaningful. The comparison of true interest is that between face and house, and here the N170 shows the same “face-selectivity” as the M170 response.

Parts (b) and (c) of Fig. 5 display the individual ERP results for the five normal controls and two prosopagnosics, respectively. Prosopagnosic ML shows a clear “face-selective” N170 response, mirroring the result found with MEG. This is quite remarkable, considering his severe behavioral impair-

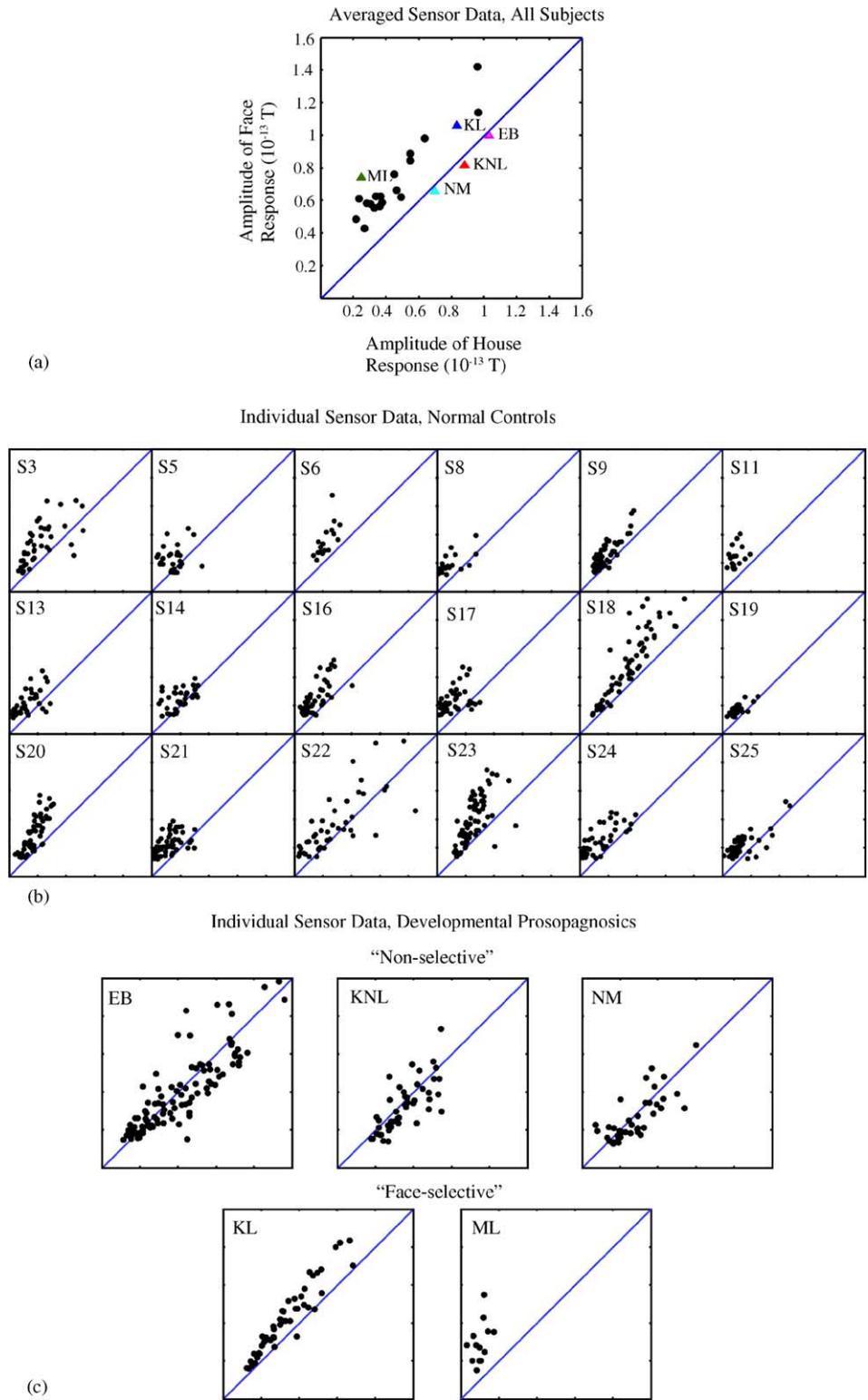


Fig. 3. Individual sensor analysis for each subject. To determine whether the averaged waveforms truly reflect the M170 response recorded by individual sensors, we analyzed the M170 response to faces versus houses for each sensor in each subject. (a) The average amplitude of the M170 response to faces versus houses for each subject. The blue line represents unity, the case in which faces and houses elicit equivalent M170 responses. Again, while all controls show “face-selective” M170 responses, the prosopagnosics’ M170 responses are either “face-selective” or “non-selective”. (b) Individual data plots of the amplitude of the M170 response to faces and houses in control subjects. The maximum value on the x - and y -axes for each individual plot is 2.5×10^{-13} T. All of the normal controls show “face-selectivity”, with greater amplitude of M170 responses for faces than for houses, at a majority of individual sensors. (c) Individual data plots for the developmental prosopagnosics. Again, the two prosopagnosics with “face-selective” M170 responses show the same pattern as normal controls. Only the M170 responses of the three “non-selective” prosopagnosics differ, straddling the line of unity.

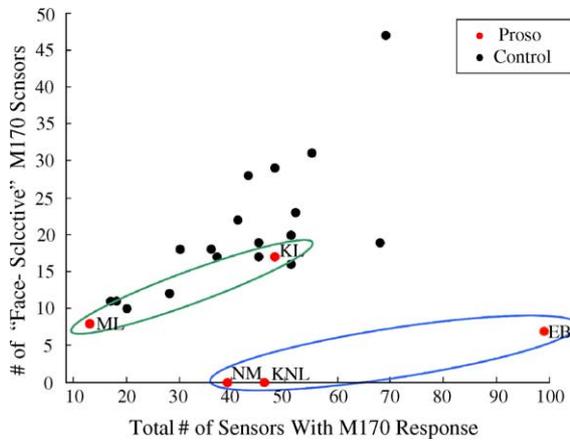


Fig. 4. The proportion of sensors displaying a M170 component for which that component showed a significantly greater amplitude for faces than houses (point-by-point t -test, $p=0.05$) in normal (black) and prosopagnosic (red) subjects. Again, the prosopagnosics are clearly divisible into two groups, one showing no selectivity at the M170 and the other indistinguishable from normal. One prosopagnosic (far right) was run after the MEG machine was upgraded from 93 to 157 channels, hence the larger number of M170 sensors in his data.

ment, and suggests that his deficits in face recognition arise at a later stage of processing than that indexed by these neurophysiological components. While KL's data shows a larger response to faces than to houses, the difference between the two conditions does not reach statistical significance. However, two of the five normal subjects (S5 and S8) tested with simultaneous MEG and ERP also show no significant difference between face and house N170 responses, so it is uncertain whether KL's "non-selective" N170 measured here truly reflects a lack of neural selectivity. Nevertheless, the presence of a normal N170 response in ML indicates that his "face-selective" M170 truly reflects an underlying "face-selective" neural generator, rather than some quirk of MEG—a point which presumably applies to other developmental prosopagnosics with "face-selective" M170 responses as well.

4. Discussion

In this experiment, we have documented profound differences in a "face-selective" neurophysiological response between developmental prosopagnosics. While three of our prosopagnosic subjects showed an M170 with no selectivity for faces, the remainder were indistinguishable from normal controls. This result stands in contrast with two previous studies (Bentin et al., 1999; Kress & Daum, 2003), and it indicates that severe face recognition impairments can be accompanied by a "face-selective" M170 response. In agreement with this latter point, Bobes et al. (2004) recently reported a normal face-selective N170 in a prosopagnosic with extensive damage to the ventral occipitotemporal cortex. Our result also parallels recent findings with fMRI showing that face-selective areas are sometimes normally activated in prosopagnosic subjects (Hasson et al., 2003).

We had the opportunity to record EEG and MEG simultaneously in two out of the five prosopagnosics we tested. In both cases, the M170 measured with MEG and the N170 measured with ERP were similar to one another and to the M170 and N170 responses seen in normal controls. This result is consistent with the idea that the M170 and N170 responses index largely the same neural processes, though further analyses are clearly necessary. In addition, it demonstrates that the normal M170 response we found in these developmental prosopagnosics is not due to technical differences between these methods.

Obviously, a major unanswered question is whether and how the selectivity differences in developmental prosopagnosia correspond to behavioral impairment. Unfortunately, we have found no correlation between M170 selectivity and the extent or type of behavioral deficits in our prosopagnosic subjects. We first looked at the relationship between the number of sensors registering a "face-selective" M170 response and the severity of face recognition impairments. Fig. 6 revisits the graph of old/new face discrimination from Fig. 1b, with circles indicating the subjects having "non-selective" (blue) versus "face-selective" (green) M170 responses. Clearly, behavioral performance as measured by old/new discrimination is not correlated with the selectivity of the M170 response. In fact, the Pearson correlation between number of "face-selective" M170 responses and old/new discrimination performance was -0.5 ; the correlation between neurophysiology and famous face performance was even lower (-0.71). Spearman rank-order correlations produced even greater negative correlations. While this is no doubt due in part to the small number of subjects, examination of individual data reveals little correspondence between behavioral performance and neurophysiology. For example, despite profound impairments on behavioral tests of face recognition, prosopagnosic ML shows clear, face-selective M170 and N170 responses. On the other hand, KNL, who is barely below the normal range on some measures, lacks a face-selective M170 response.

However, this lack of coherence is perhaps not surprising, given that the behavioral tests we have used have all involved memory (famous face identification, old/new discrimination). Failures in performance on memory tests can stem from an inadequate representation either at the level of perceptual encoding or those of memory encoding or retrieval. Since the M170 is thought to reflect perceptual "structural encoding" of faces (Eimer, 2000), rather than later mnemonic stages, it will be necessary to test whether the distinction in M170 selectivity among prosopagnosics we have seen corresponds to performance on strictly perceptual tasks such as detection of faces in noise, matching to sample, and part/configuration judgments. Regardless, in a more general sense, our results indicate some connection between the M170 response and behavioral performance: three confirmed developmental prosopagnosics also failed to show a "face-selective" M170.

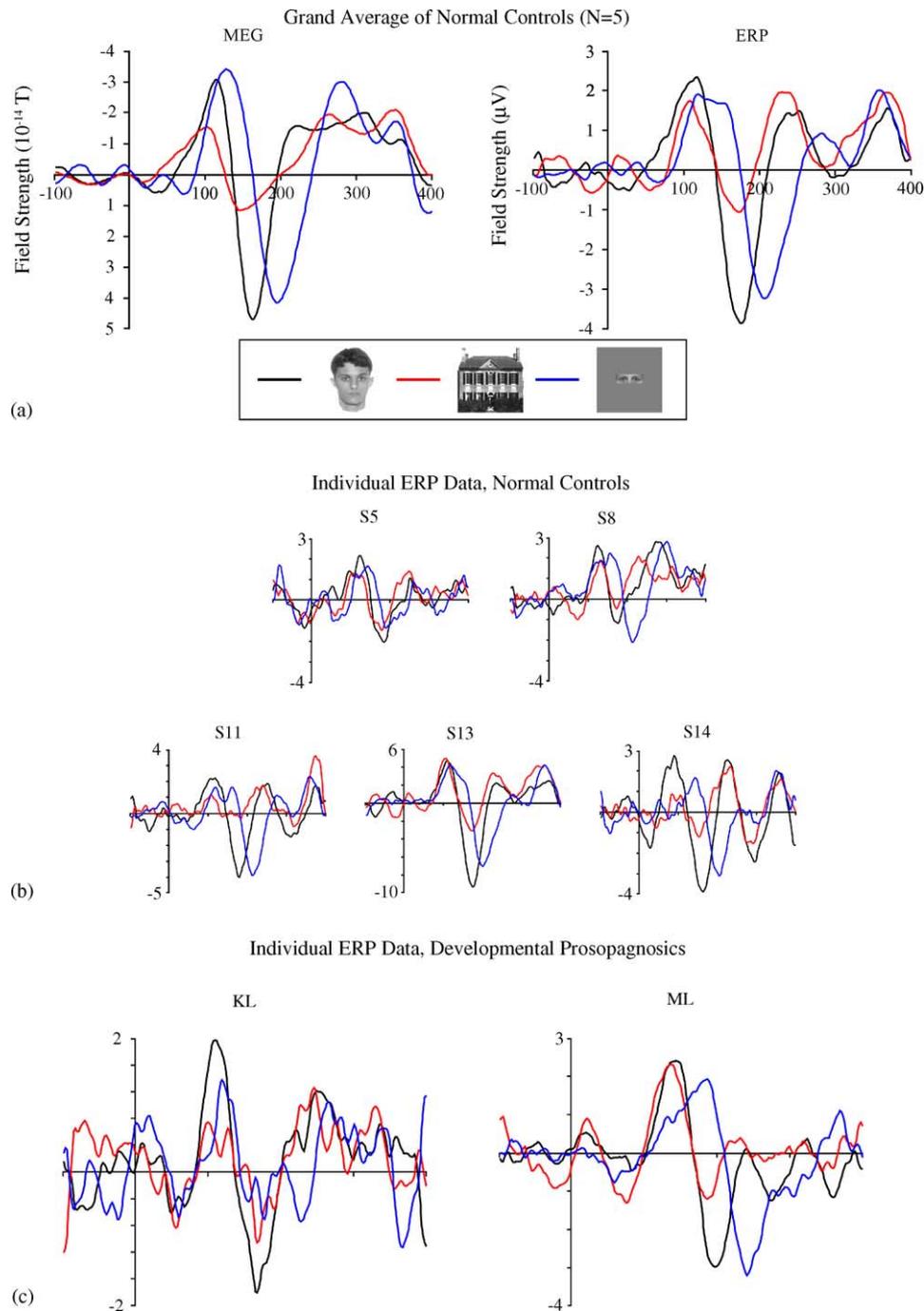


Fig. 5. ERP results. Note that the scale has not been normalized due to the wide range in amplitude between subjects. (a) The M170 (left) and N170 (right) averaged from simultaneous recordings in five normal subjects. The M170 has been inverted for comparison to the N170, which is averaged from electrodes T5 and T6 (left and right temporal sites). (b) N170 responses from simultaneous MEG/EEG recordings in five normal subjects. (c) N170 responses in the two developmental prosopagnosics with normally “face-selective” M170 responses. N170 responses in both also show a trend towards face-selectivity (not significant in KL), suggesting that the M170 and N170 responses reflect largely the same neural generators.

Thus, although the M170 response is not sufficient for normal behavioral performance with faces, it may nonetheless provide a useful means of partitioning developmental prosopagnosia. As mentioned above, there are multiple developmental courses that can lead to impaired behavioral performance and there appear to be different types of

developmental prosopagnosia (De Haan & Campbell, 1991; Duchaine, 2000). Currently it is unclear how to best characterize these types, but there are a number of possibilities that we will be investigating with this group. The perceptual/mnemonic distinction is one classic, and arguably effective, division that we will consider (Farah, 1990; Lissauer, 1890), but regard-

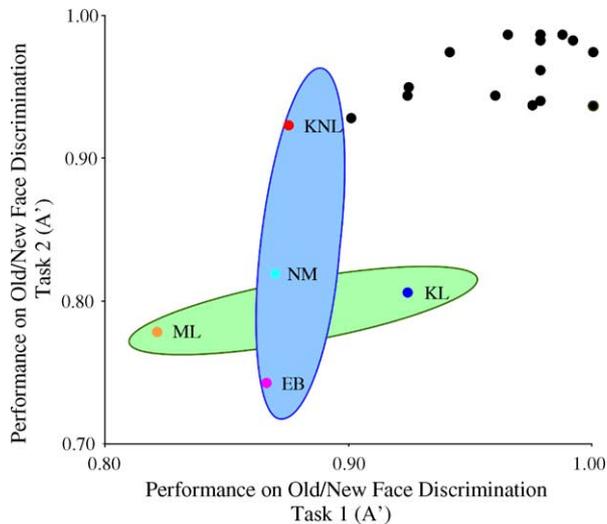


Fig. 6. Behavioral data, grouped by selectivity of M170 response (blue = “non-selective”, green = “face-selective”). No correlation between behavioral performance and neurophysiology is visible.

less of the nature of this division, the “face-selectivity” of the M170 holds promise as a neurophysiological index of a face processing stage that is impaired in developmental prosopagnosia. Developing such an understanding should clarify the role that this marker and its neural source play in normal face recognition.

5. Conclusions

Using MEG, we have examined “face-selectivity” of the M170 response in five developmental prosopagnosics. While three of the subjects showed no selectivity of the M170 response, in keeping with their behavioral impairments, the remaining two were indistinguishable from normal controls. Simultaneous recording of ERP in these two prosopagnosics revealed N170 responses also within the normal range, suggesting that differences between the two methods are not responsible for the distinction between non-selective and selective neurophysiological responses in this group. Further behavioral testing will be required to determine whether a correlation exists between this neurophysiological marker and behavioral performance on face perception.

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