FINAL PROGRESS REPORT TO THE BIAL FOUNDATION

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This Progress Report summarizes the behavioral and biological data gathered on a sample of adolescents who had been classified as high- or low-reactive infants. The purpose of the research was to determine the degree of preservation of select behavioral and biological characteristics of high- and low-reactives from infancy to mid-adolescence.

We made laboratory assessments on 40 adolescents (20 females) who had been classified as low-reactive as infants and 30 (13 females) who had been classified as high-reactive. These 70 adolescents were 15-16 years old, and had been seen four to five years earlier in a roughly similar laboratory assessment. We also evaluated a larger group of 114 adolescents (47 low-reactives, 37 high-reactives, and 30 others) in a home interview. The rest of this report summarizes our results.

Laboratory Evaluation

Behavior. We coded the number of spontaneous comments and smiles displayed by each adolescent during their first 40 minutes in the laboratory before the placement of electrodes for the EEG and ERP recordings, after which the subject was instructed to be quiet and still.

Biology. We assessed the following biological variables: (1) EEG asymmetry at rest with eyes open, (2) beta power and the beta-alpha ratio at rest, (3) the event-related potentials to three blocks of valid and three blocks of invalid pictures with 20 pictures in each block (for example, a table vs. a woman with a tomato slice for a head), (4) event-related potentials to sentences whose last word rendered the sentence valid or invalid (for example, “The boy ran home” vs. “The boy ran to the happy”), and, finally, (5) resting heart rate and a spectral analysis of resting heart rate.

Home Interview

The home interview was conducted by one of two women who knew nothing of the subject’s past history nor their infant temperament. The interview, which lasted from 90-120 minutes, dealt with the adolescent’s academic interests and performance, extracurricular activities, sources of worry, anger, joy, and guilt, and their attitudes toward nature, religion, and human nature. An independent coder studied the film interviews and rated each adolescent on a four-point scale for degree of inhibition, where a rating of 1 reflected an uninhibited persona (the subject talked freely and extensively, smiled frequently, and showed no motor tension), and a rating of 4 indicating an inhibited persona (minimal elaboration, defensiveness, infrequent smiling, and high motor tension). Each adolescent was also rated on a four-point scale for frequency of smiling and talking during the entire interview. In addition, each adolescent was administered two Q-sorts dealing with sources of worry and personality traits and a series of questions asking each about their usual somatic reactions to each of nine situations.

Results

Behavior. There was no difference between the low- or high- reactives in the number of spontaneous comments made during the first 40 minutes of the laboratory session, although girls spoke more often than boys, a difference that was also found at

11 years of age. However, there was a temperamental difference in the frequency of smiling. High-reactives smiled less frequently than low-reactives (10.6 vs. 19.2; $t(68) = 2.3$, $p < .05$, effect size = 1.2); this difference was also found at 7 and 11 years of age. High-reactives are consistent in showing less spontaneous smiling in unfamiliar social situations than low-reactives.

Figure 1 illustrates the correlation between smiling during the laboratory and home interview and between smiling in the laboratory at 11 years of age and smiling in the laboratory at 15 years of age. These adolescents were relatively consistent in displaying either low or high values for smiling across the lab and the home, and there was intraindividual stability for smiling in the laboratory from 11 to 15 years of age. The stability correlations from 11 to15 years were highest for low-reactive males and high-reactive females because the variation in smiling was greater for these two groups than for low-reactive girls and high-reactive boys.

Q-sorts. Three items from the two Q-sorts (a total of 35 items from both Q-sorts) separated high- from low-reactives. The three items were: "Most of the time I'm happy", "I'm easy-going", and "I'm pretty serious". The low-reactives were more likely to endorse the first two; whereas the high-reactives were more likely to endorse the third.

Figure 2 illustrates that 30% of the low-reactives, but not one high-reactive combined an uninhibited persona during the interview (a rating of 1) with a mean rank on two Q-sort items that separated high- from low-reactives. The two items were: "I'm happy most of the time" and "I'm easy-going". The low-reactives were more likely to combine a rating of 1 on their interview behavior and values on the two Q-sort items in the top tercile of the distribution. By contrast, 33% of high-reactives, and only one low-reactive combined an inhibited persona (a rating of 3 or 4 in the interview) with a mean rank for the happy and easy-going items in the bottom two terciles (χ^2 = 28.1, p < .001).

We performed a similar analysis on the rating of frequency of smiling and talking during the interview with the mean of the two Q-sort items. As Figure 2 illustrates, more high- than low-reactives combined infrequent smiling with mean values on the two Q-sort items in the lower two terciles in the distribution; where low-reactives combined a rating of 1 for smiling with values in the top tercile for the Q-sort items. Frequency of talking in the interview was less sensitive in differentiating the low- from the high-reactives.

Although the Q-sort items for "happy" and "easy-going" separated high- from low-reactives for both genders, some items on the Q-sort separated the temperamental groups for one gender but not the other. For example, the high- and low-reactive boys were separated by four Q-sort items: "I like doing risky things", "I'm happy most of the time", "I'm shy with adults I don't know", and "I worry about terrorists", with high-reactive boys describing self as not liking risks and being less happy and confessing to being shy with strangers and worried about terrorists. The high-reactive girls differed from the low-reactives girls on two items: "I'm pretty serious" (more high- than low-reactives endorsed this item), and "I like making my friends laugh" (low-reactive girls endorsed this item more often than high-reactives).

One of the questions in the interview was: "What do you worry about?" Seventy-five percent of all the adolescents named either performance (in school, on the athletic field, or on concert stages), or unfamiliar or new situations, especially with people. They did not say they were worried about becoming ill, being harmed, losing a parent, or being attacked. These answers are the product of history which have made life safer for middle-class adolescents in the United States. The threats to the self are the possibility of incompetence, whether academic, athletic, or social, and the critical evaluation of self by others, or the individual's own superego. This is not the world of hunter-gatherers who had to fear both animal predators and enemy groups, as well as disease and the possibility of ghosts. We have reduced the threat of danger to the body but increased dramatically the threat of self-reproach or criticism by others. Put simply, failure has replaced snakes and spiders as primary sources of fear.

EEG Frontal Asymmetry and the Beta-Alpha Ratio

Although the temperamental difference in the magnitude of frontal asymmetry in the EEG at age 15 was not statistically significant, more high- than low-reactives showed right frontal activation by at least -.05 (40 vs. 8%). However, more high- than the low-reactives were right frontal active at both 11 and 15 years of age (28 vs. 5%), whereas more low-reactives were left frontal active at both ages (34 vs. 24%; $\chi^2 = 4.7$, $p < .05$). The high-reactive girls were most likely to be right frontal active at both ages.

The tendency to show left or right frontal asymmetry was stable from 11-15 years of age ($r = .43$, $p < .01$) for low-reactives and ($r = .34$, $p = .09$ for high-reactives). The stability correlation for the entire sample was .40 ($p < .01$).

Although the beta-alpha ratio at rest at age 15 did not separate the temperamental groups, this ratio was stable from 11-15 years of age ($r = .60$, $p < .01$ for low-reactives; $r = .51$, $p < .01$ for high-reactives; $r = .56$, $p < .01$ for the entire sample). Although there was no relation between frontal asymmetry and the beta-alpha ratio, high-reactives were more likely than low-reactives to combine a high beta-alpha ratio (above the median value of .90) with right frontal asymmetry; 32% of high-reactives vs. 10% of low-reactives combined a high ratio with right frontal asymmetry. The low-reactives were more likely to combine a high beta-alpha ratio with left frontal asymmetry (43 vs. 24%; $\chi^2 = 5.6$, $p < .05$; See Figure 3).

N400 to the Pictures

A repeated measures analysis of variance across all the adolescents for the six blocks of pictures revealed a significant difference in the integrated voltage from 350-450 msec. with larger values to the invalid than to the valid pictures for each valid-invalid block pair ($F\ 1/62 = 18.8$, $p < .001$). The valid and invalid blocks alternated. Although the average magnitude of the difference between values to the invalid and valid pictures (I-V difference) was not associated with temperament across all six blocks, the high- and low-reactives differed with respect to the block pair during which they showed their largest I-V difference. Over two-thirds of the adolescents showed their largest I-V difference on the first or second pair of blocks. Only 28% had their largest I-V difference on the final block pair and more high- than low-reactives were in this group (46 vs. 23%, $\chi^2 = 3.4$, $p < .05$), suggesting that the high-reactives showed a shallower habituation of the N400 to the invalid pictures.

Fifty-one percent of low-reactives, but only 23% of high-reactives, showed a linear decrease in the magnitude of the N400 across blocks; whereas 37% of high-reactives and only 16% of low-reactives showed a linear increase in the I-V difference across blocks ($\chi^2 = 3.1$, $p < .10$). The high-reactives had larger I-V differences on the final block pair.

Although there was no significant correlation between the absolute magnitude of the N400 and the I-V difference across all subjects, the low-reactives with large N400 values had small I-V differences on blocks 5-6. By contrast, the high-reactives with large N400 values had large I-V differences on the final block pair ($\chi^2 = 4.6$, $p < .05$) (See Figure 4).

Asymmetry and the magnitude of the N400

The larger the I-V difference, the larger the values at F4 (right frontal area) than at at F3 (left frontal area). Among 17 adolescents whose largest I-V difference was ≥ 7 microvolts, 11 had larger values at F4 than at F3 (by one microvolt). By contrast, of the 20 subjects whose largest I-V difference was less than 7 microvolts, only 5 had larger values at F4 and the remaining 15 had larger values at F3 ($\chi^2 = 6.2$, $p < .01$).

The same result was found on a larger sample of over 150 preadolescents from this population evaluated at 11 years of age. This group of high- and low-reactives saw two series of pictures presented in an oddball paradigm. Fifteen percent of the pictures in the first series of 169 scenes were unique but valid; 15% in the second series of 169 pictures were also unique but each illustrated an invalid scene.

As expected, the invalid pictures produced larger N400s than the valid ones. Among those whose N400 values were larger to the valid than to the invalid scenes, the voltages at F3 were larger than those at F4. There was almost a linear relation between the magnitude of the I-V difference and the F3-F4 difference between valid and invalid scenes. When the values to the valid pictures were larger than those to the invalid ones (by 2000 microvolts), adolescents were likely to show larger values at F3 than at F4. When the invalid-valid difference favored a larger response to the invalid scenes (by

2000 microvolts), more subjects had larger values at F4 than at F3 (see Figure 5 which illustrates the ratio of the number of subjects with larger values at F3 over those with larger values at F4 (by at least 1000 microvolts) for the valid-invalid scenes at 11 years of age). Figure 5 reveals that the larger the I-V difference, the more likely F4 values were larger than those at F3.

N100 to the Pictures

Recent research suggests that individuals can detect some of the gross features of visual stimuli by 100 msec. Most subjects showed a prominent negative waveform between 110 and 180 msec., usually larger at F4 than at F3. This bias for the right frontal area was not true of the N400 to the pictures. We computed the integrated values for this waveform from 100 to 180 msec. Figure 6 illustrates the median values for the valid and invalid pictures at F4 across each of the six blocks. As with the N400, the high-reactives showed shallower habituation of the N100- 180 waveform to the invalid pictures.

We examined each subject's N100 values to the invalid pictures (blocks 2, 4, and 6) to determine which adolescents showed a linear decrease across the three blocks, compared with no change or an increase in voltage across blocks. Thirty-seven percent of low-reactives, but only 18% of high-reactives, showed a linear decrease in the magnitude of the N100. By contrast, 16% of low-reactives but 52% of high-reactives showed no change or an increase in voltage over the three blocks ($\chi^2 = 7.6$, $p < .01$). Moreover, 51% of the high-reactives, but only 23% of low-reactives, had an I-V difference on blocks 5-6 greater than 1 microvolt ($\chi^2 = 6.8$, $p < .05$). By contrast, 36% of low-reactives, and 22% of high-reactives, had a difference in which the N100 to the valid pictures was larger than that to the invalid pictures for both the N100 and the N400 on the final block pair. Thirteen of 19 high-reactives had an I-V difference greater than 1 microvolt on the final block pair for both the N100 and N400, compared with only 9 of 23 low-reactives. By contrast, 14 of 23 low-reactives had their largest values on blocks 5-6 to the valid rather than the invalid pictures for both the N100 and N400, compared with only six high-reactives ($\chi^2 = 3.5$, $p < .05$). Thus, high-reactives showed a shallower habituation to the invalid pictures for both the N100 and N400 waveforms.

Finally, significantly more high- than low-reactives had large I-V differences (≥ 4 microvolts) at F3 on the final block pair for both the N100 and the N400 waveforms ($\chi^2 = 5.9$, $p < .01$). We believe this result occurred because high-reactives were more likely than low-reactives to try to name the invalid pictures.

Correlates of N400 to the Invalid Pictures

The high-reactive boys with larger I-V differences had a special behavioral profile. They were more fearful to unfamiliar events in the laboratory at 21 months of age, had larger N400 values to a set of invalid pictures presented when they were 11 years old, and were more subdued both in the home interview and in the laboratory. On the Q-sort, the high-reactives with shallower habituation to the invalid pictures were more likely to endorse the item, "I'm shy with adults I don't know" ($t(24) = 2.80$, $p = .01$), and during the home interview, 8 of the 13 were given a rating of 3 or 4, reflecting behavioral inhibition, compared with only 4 of the remaining 14 high-reactives.

We classified each adolescent as clearly uninhibited (N=35) or not (N=27) based on their behavior during both the laboratory and the home interview. The adolescents in the latter group (combining both low- and high-reactives) were more likely to have large I-V differences on the final block pair ($N \geq 6$ microvolts; 51 vs. 22%, $\chi^2 = 4.0$, $p < .05$).

We compared the interview and Q-sort replies for those adolescents whose largest I-V difference was greater than 6 microvolts with those whose largest I-V difference was less than 6 microvolts. We noted earlier that performance in school and extra academic activities were a primary source of worry for most adolescents as revealed by the interview and the Q-sorts. However, excluding low-reactive girls, the adolescents in the other three groups with large I-V differences were more likely to reveal in the interview and the Q-sort that unfamiliar social situations, social rejection, and being alone were more serious sources of worry than performance.

A poor performance is both less ambiguous and under greater individual control than the anticipation of awkward social interactions because the person cannot predict what others might do in that interaction. We examined the relation between the largest I-V difference on the N400 to the pictures with the tendency to be more concerned with performance (on academic or extracurricular activities) or more concerned with social relationships. Low-reactives with large I-V differences (≥ 6 microvolts) were more concerned with their performance than with social relationships (14 of 20). Low-reactives with smaller I-V differences were more concerned with their social relationships (9 of 14). Among high-reactives, exactly the opposite result emerged. If the I-V difference was ≥ 6 microvolts, 7 of 14 were more concerned with social relationships whereas those with a smaller I-V difference were more concerned with performance (9 out of 10). Thus, low-reactives who are very concerned with the quality of their performance had large I-V differences; high-reactives who were very concerned with their social relationships had large I-V differences. It appears that it is the intensity of the worry, and not its content, that best predicts the magnitude of the I-V difference.

N400 to the Incongruous Sentences

A total of 53 adolescents had valid data on this episode (25 high-reactives and 28 low-reactives). The difference between high- and low-reactives across all 80 sentences (40 valid and 40 invalid) was only significant for boys. Eleven of 13 high-reactive boys, but only 6 of 15 low-reactive boys, had an I-V difference greater than 1 microvolt ($\chi^2 = 5.4$, $p < .05$). However, when we examined the N400 to the sentences for the first and second halves of the procedure, we found results similar to those reported for the pictures. The low-reactives showed habituation of the N400 from the first to the second half of the procedure (4.2 vs. 3.2 microvolts), whereas the high-reactives did not (4.5 microvolts on the first half and 4.8 on the second half). Fifty percent of the high-reactives had an I-V difference on the second half greater than 2 microvolts, compared with 27% of the low-reactives ($\chi^2 = 3.1$, $p < .10$). The proportion of adolescents with an I-V difference greater than 2 microvolts, on either the first or the second half, was 75% for high-reactives and only 50% for low-reactives ($\chi^2 = 3.6$, $p < .10$).

Further, more high- than low-reactives had large I-V differences to both the invalid pictures and the incongruous sentences. The 13 high-reactives with an I-V difference to the pictures (for both the N100 and N400) greater than 1 microvolt on the final block pair, compared with the other 14 high-reactives, had an I-V difference to the sentences greater than 1 microvolt (77 vs. 35%, $\chi^2 = 4.6$, $p < .05$). In addition, 5 of these 13 high-reactives combined infrequent smiling in the laboratory with a high fear score at 21 months, compared with only 1 of 14 of the remaining high-reactives. Thus, the high-reactives who showed relatively shallow habituation of both the N100 and the N400 to the invalid pictures and larger I-V differences to the sentences were more subdued in the laboratory and more fearful in the second year of life.

At both 11 and 15 years of age, the invalid events (the pictures at age 11 and 15 and the sentences at age 15) produced larger values at F4 for low-reactives, but larger values at F3 for the high-reactives. This fact suggests that the high-reactives were more often trying to interpret the invalid events by activating semantic networks. The high-reactives appeared to be cognitively active; the low-reactives appeared to be more passive. In addition, boys were more likely than girls to show larger values at F3 than at F4 to the invalid pictures, suggesting a cognitively active mental set.

We examined the F3-F4 asymmetry to valid-invalid comparisons separately for the pictures and sentences. When the larger asymmetry favored F3 over F4 (by 1 microvolt) for both pictures and sentences, the values were larger to the valid stimuli. When the larger asymmetry favored F4 over F3, most subjects had larger values to the invalid than to the valid stimuli. The valid pictures and sentences had some surprise value for each was unique, but because the stimuli were meaningful, semantic networks were evoked and, therefore, F3 values were larger than those at F4. The invalid pictures and sentences, which were also surprising, were less easily interpreted and larger asymmetries appeared at F4 than at F3, especially, for the low-reactives. It is important to note that there was no relation between the F3-F4 difference to the pictures or sentences and resting EEG asymmetry gathered earlier in the session.

In sum, for both pictures and sentences, when F4 was greater than F3, the stimuli were more often invalid; when F3 was larger than F4, the stimuli were usually valid.

The ratio of the number of subjects with F3 values larger than F4 to the valid and invalid sentences was 3.0 for high-reactives but 0.2 for low-reactives ($\chi^2 = 8.8$, $p < .05$).

Cardiovascular Reactions

We assessed heart rate at rest and performed a spectral analysis on the supine heart rate. The spectral analysis revealed that low-reactive boys were most likely to be vagal (7 of 16), a fact that was also true at age 11. By contrast, only 2 of 10 high-reactive boys were vagal in the spectral analysis. The ratio of low over high power in the spectral analysis (high power reflects vagal influence) was stable from 11 to 15 for boys ($r = .60$) but not for girls ($r = -.10$).

More high- than low-reative boys had high resting heart rates at both 11 and 15 years of age ($r = .36$, $p < .05$). Resting heart rate was stable for girls ($r = .53$), but there were no temperamental differences. Only among boys did more low- than high-reactives have low heart rates at both 11 and 15 years of age ($\chi^2 = 4.5$, $p < .05$). Further, among boys, more low- than high-reactives combined high vagal tone on the spectral analysis with a low resting heart rate; whereas more high-reactives combined sympathetic tone with a high resting heart rate. The fact that this was not true for the girls suggests that the relation between temperament and the cardiovascular system differs for the sexes.

Reports of Somatic Reactions

Each adolescent reported his or her usual somatic reactions to nine situations. The somatic reactions they could select were: sweating of the palms, increase in heart rate, muscle tension, stomach tension, breathing difficulty, face flushing, or none of the above. Most subjects reported somatic reactions to the four situations in which they were being evaluated by another (when they met a stranger, had to speak in front of the class, and when a teacher or parent criticized them). Very few reported somatic reactions to the other five situations that did not involve evaluation (insects, storms, being alone at home, being snubbed by a peer, or seeing a large amount of blood). Hence, we computed the mean number of somatic reactions to the four evaluative contexts (mean = 1.5).

There were no significant temperamental differences in this variable, even though low-reactive girls had the largest number of somatic reports. Surprisingly, those with many somatic reports failed to show larger reactions for heart rate, EEG asymmetry, or other biological variables one might expect to be correlated with frequent somatic reactions. These data suggest that verbal reports of usual somatic reactions to evaluative situations are, in part, psychological constructions influenced by the subject's receptivity to bodily experience. Some individuals detect bodily change more readily than others, but that does not mean that they are more tense or anxious than others. Indeed, among low-reactive girls, there was a positive relation between the number of somatic reports and a self-description on the Q-sort indicating that the subjects regarded themselves as "easy-going" ($r = .47$, $p < .05$). There was no comparable relation for the other groups. These data suggest that self-reported bodily symptoms do not have the same theoretical meaning for all individuals.

Latency to Answer the Interview Questions

Finally, we coded the latency (in seconds) to the adolescent's first reply to each of the many questions posed during the long interview. Although most adolescents answered most questions within the first 5 or 6 seconds, a small number of questions were accompanied by long response latencies (for example, "When was the last time you felt guilty?", "When was the last time you had a decision to make?", "When was the last time you experienced something beautiful?"). We computed the mean of each adolescent's four longest latencies (the range was 8 to 76 seconds with a mean of 27 and a median of 25 seconds), and divided this distribution into terciles (1-21 secs., 22-29 secs., and 30 or more secs.). The adolescents with the fastest latencies (tercile 1) had smaller beta power values than those in terciles 2 and 3 (See Figure 7). In addition, excluding the low-reactive boys, the remaining subjects in tercile 1 had the smallest I-V differences to the pictures (See Figure 8). Among the low-reactives, those with large I-V differences at age 11 had the longest latencies to answer the questions during the interview (tercile 3) ($\chi^2 = 6.6$, $p < .01$).

These data suggest that the concept of task engagement may be useful. Adolescents who engaged the interview questions more seriously should have reflected for a longer time before replying. And adolescents who engaged the ERP procedures by becoming more attentive to the invalid pictures should have produced larger I-V differences. Thus, as other investigators have reported, a cortical reaction to an event is influenced by the psychological state of the subject. A more engaged state, which should be accompanied by greater attentiveness, should have produced larger ERP responses.

Summary

The results of this investigation support the expectation that signs of tension vs. relaxation when interacting with unfamiliar adults would be preserved over time for the two temperamental groups. At every age of assessment, from 14 months to 16 years, the high-reactives were more subdued; the low-reactives more spontaneous.

The central hypothesis we have proposed to explain the differences between these two groups involves an inherited neurochemistry that affects the excitability of limbic structures to unexpected events. The fact that the high-reactive adolescents showed shallower habituation to the invalid pictures and sentences supports this explanatory position. Our ability to predict both the social behavior and biological reactions of adolescents 16 years after their classification as either high- or low-reactive infants is persuasive of the conclusion that these temperamental biases are not easily diluted by experience.

Fig 1. Correlations for Smiling

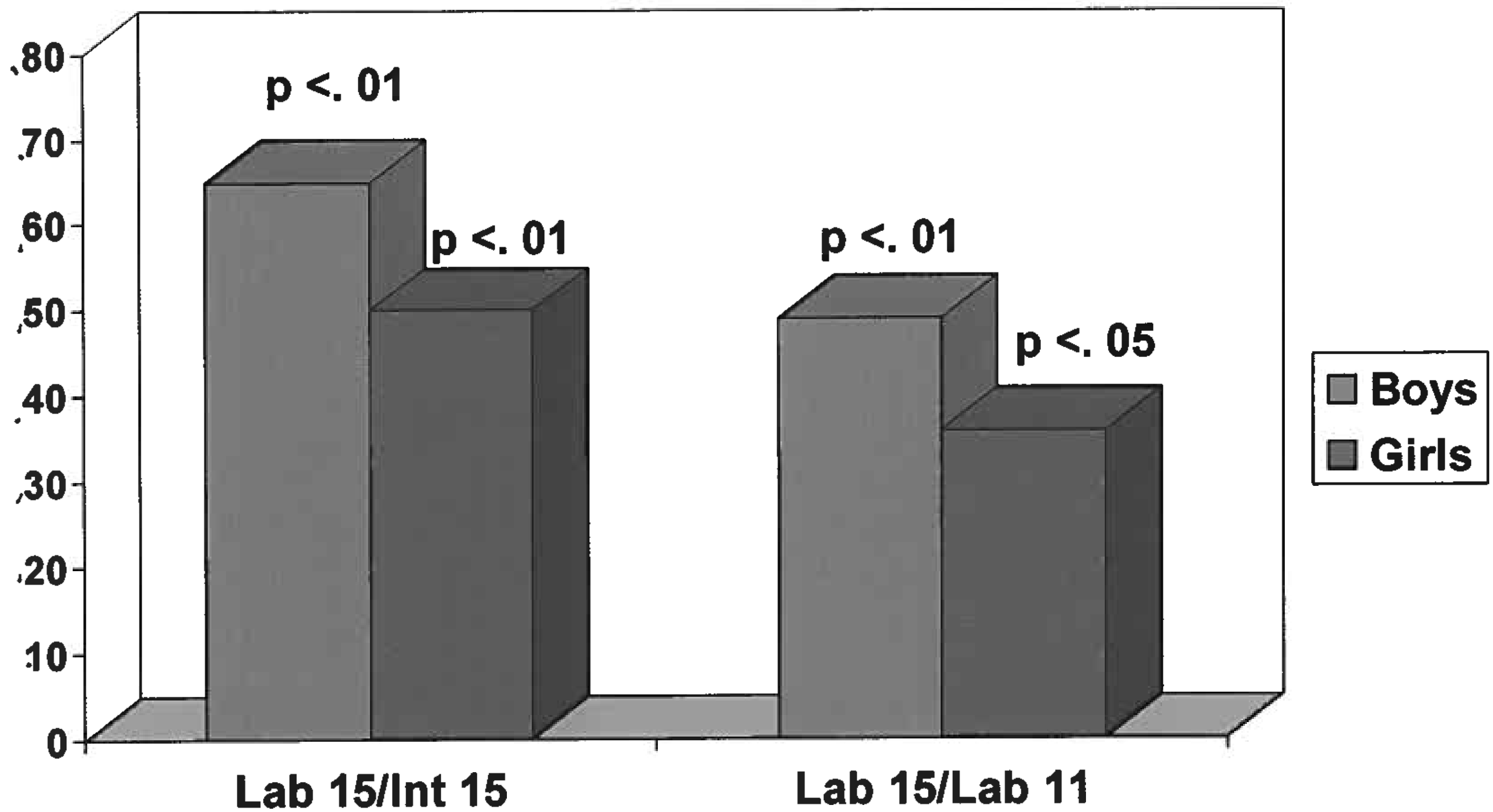

Fig 2. Difference between LR and HR in interview and Q-sort rank for "Happy" and "Easy Going"

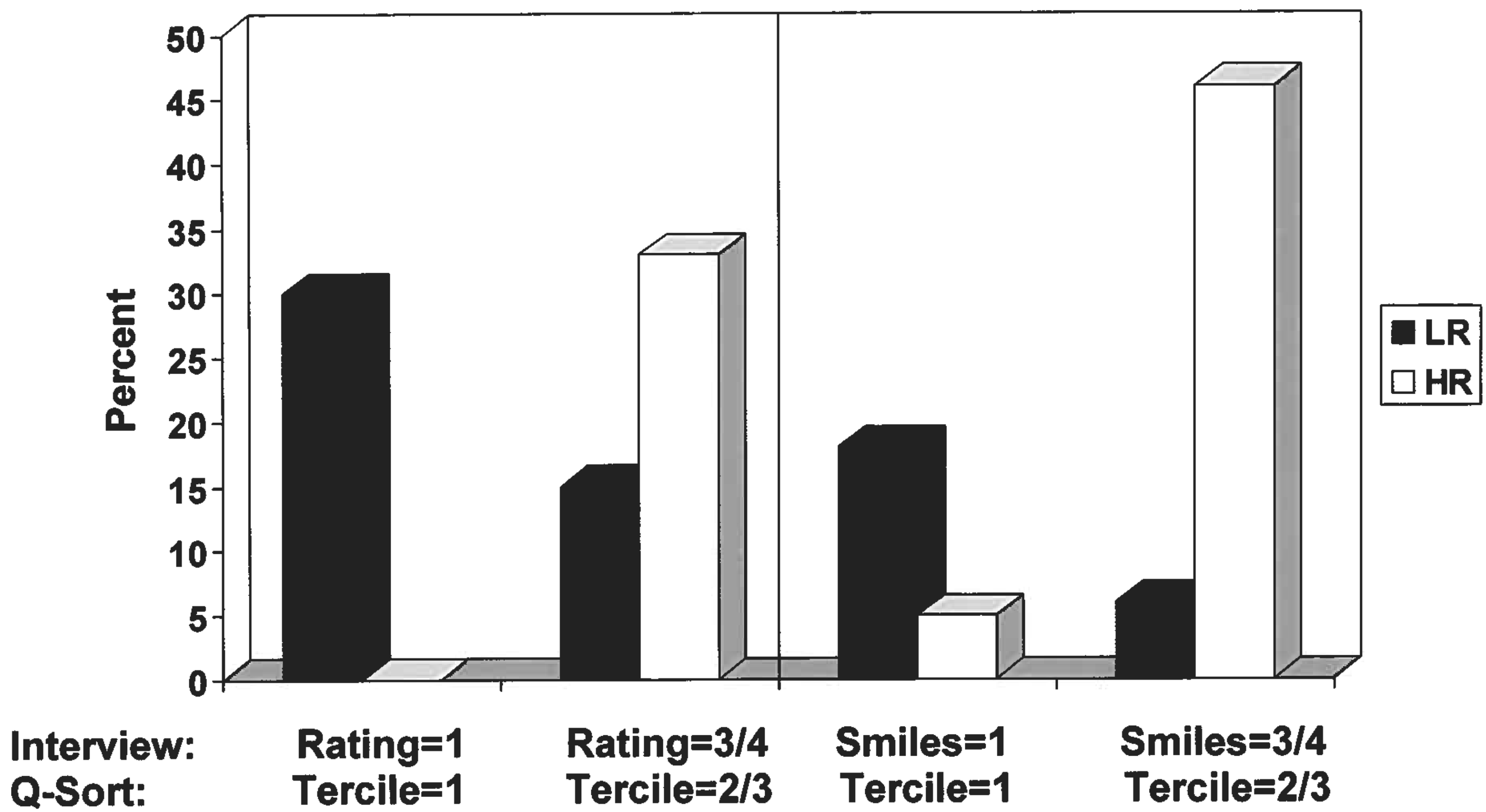

Fig 3. Temperament Differences in Beta/Alpha Ratio and Asymmetry

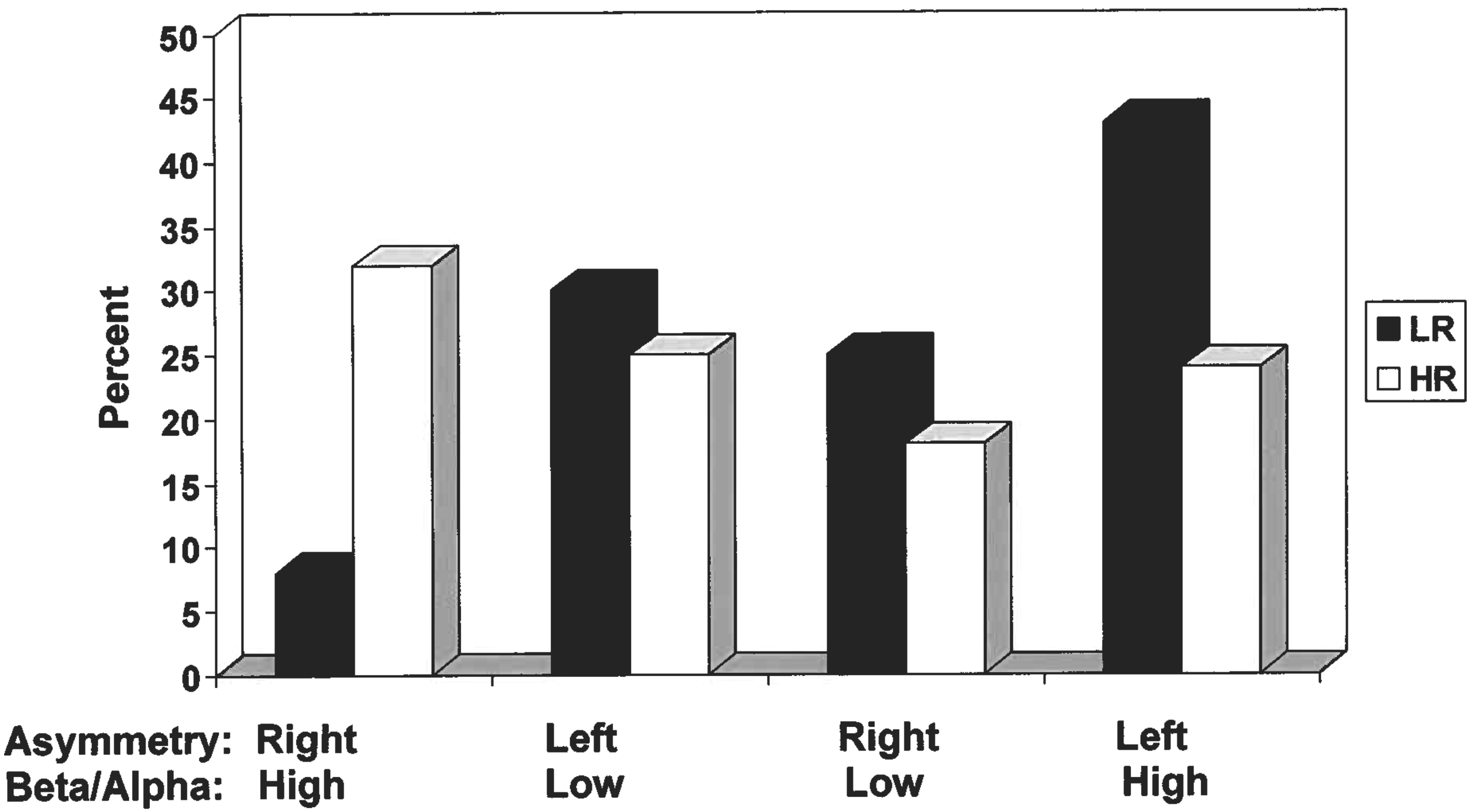

Fig 4. Difference between Low Reactive and High Reactive in I-V difference for blocks 5/6 for subjects with large N400 to pictures (> mean)

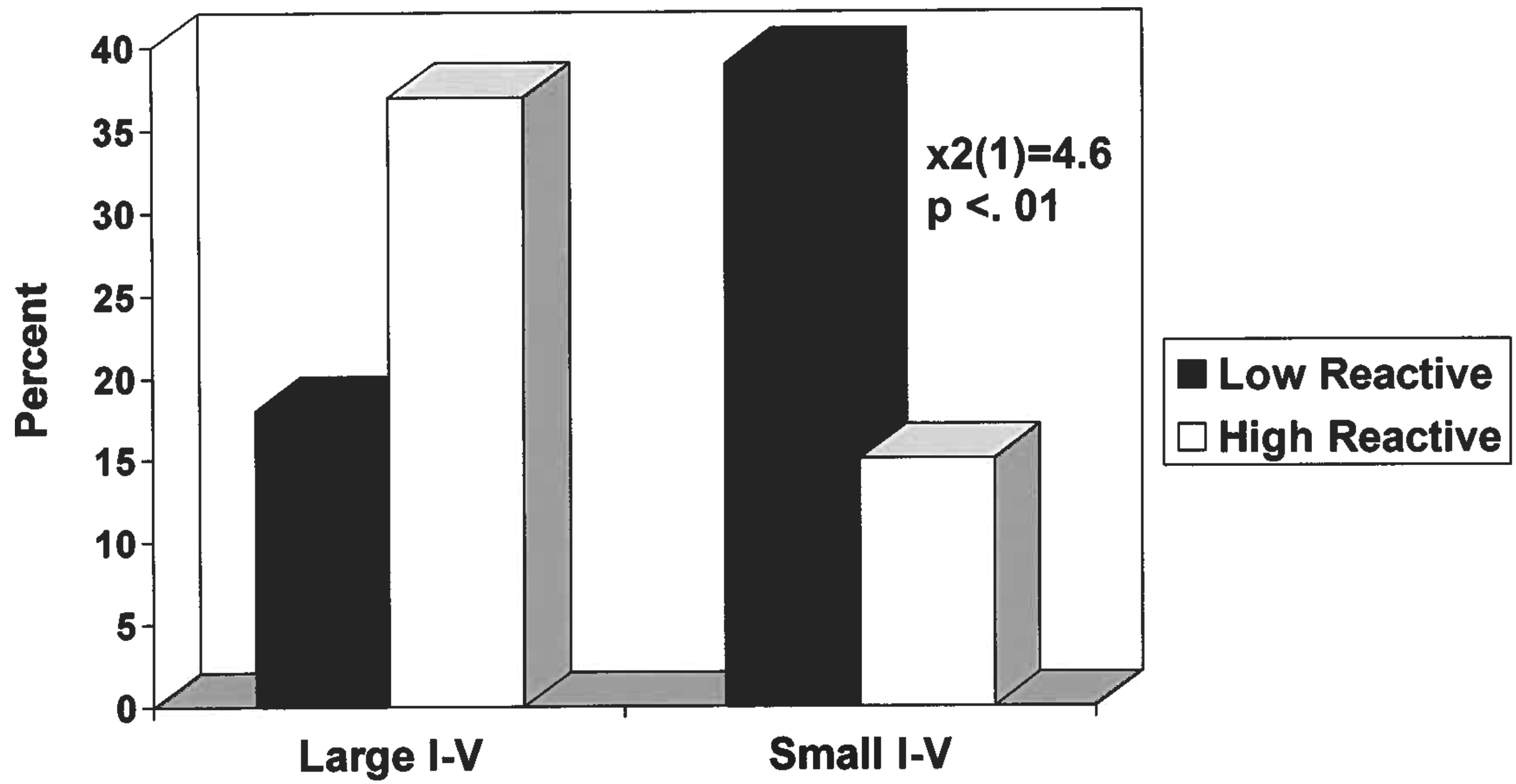

Figure 5. Ratio of subjects with F3 > F4 over F4 > F3 at age 11

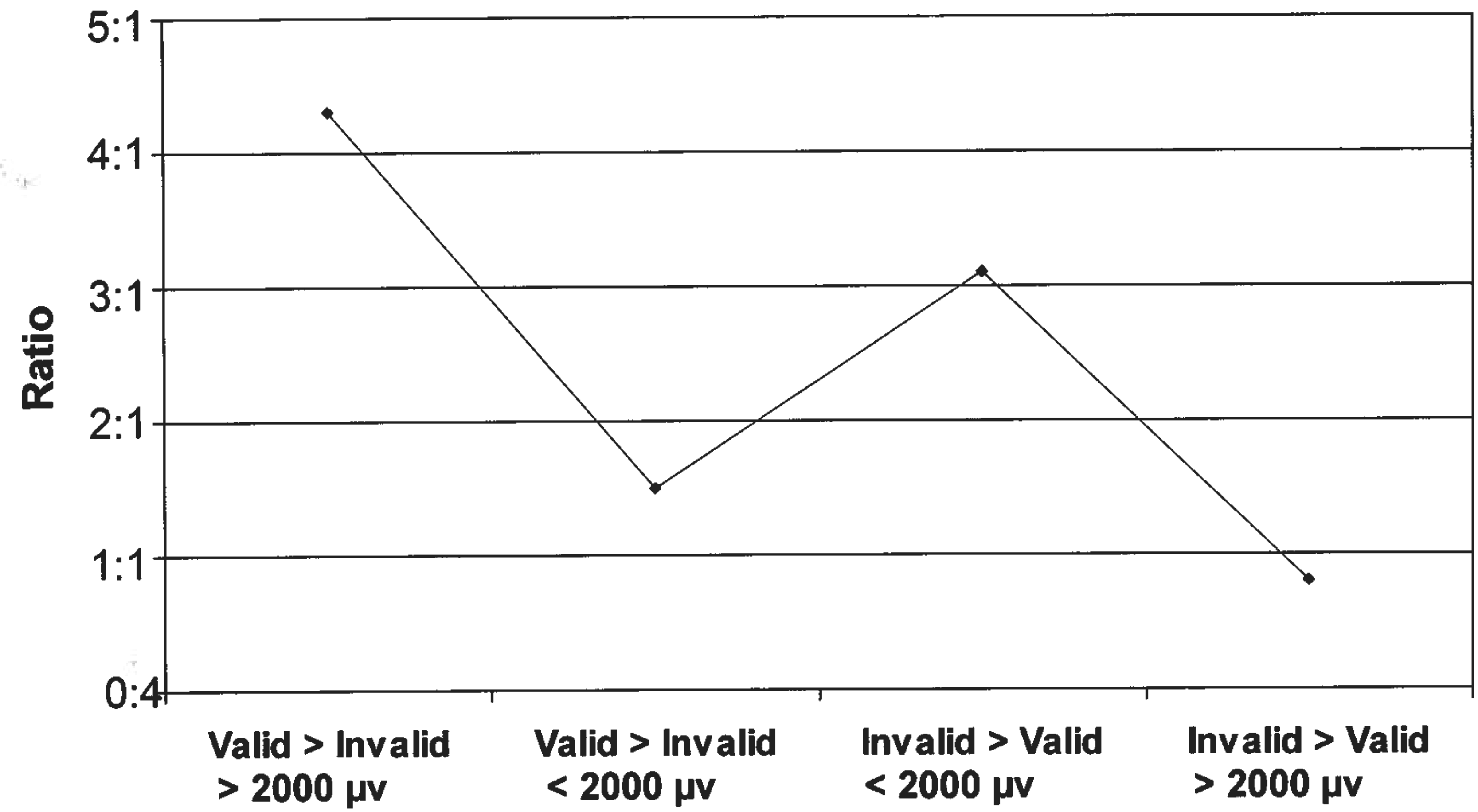

Figure 6. Integrated voltage N100-180 to pictures

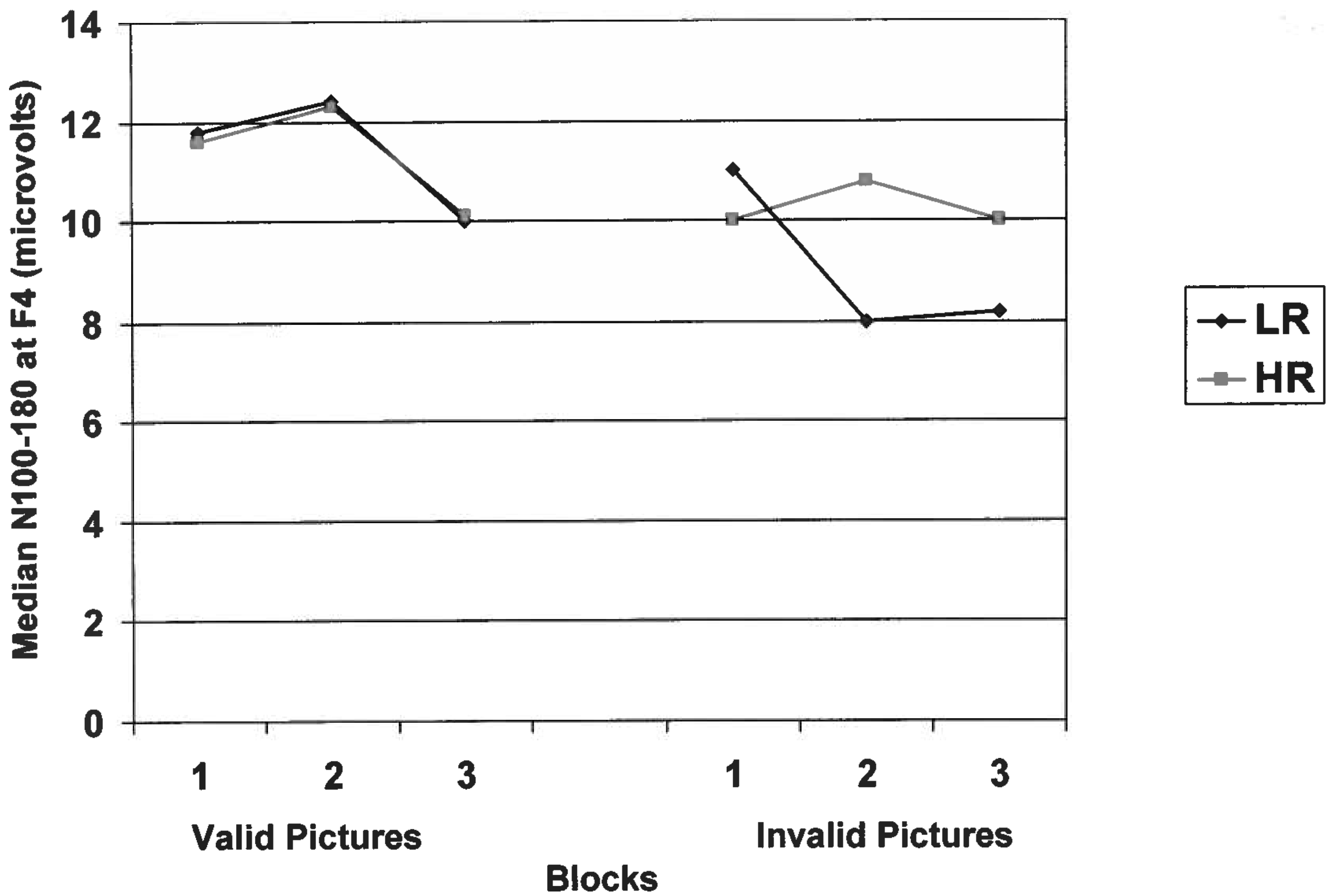

Figure 7. Relation of amount of beta power at rest to mean of 4 longest latencies in interview

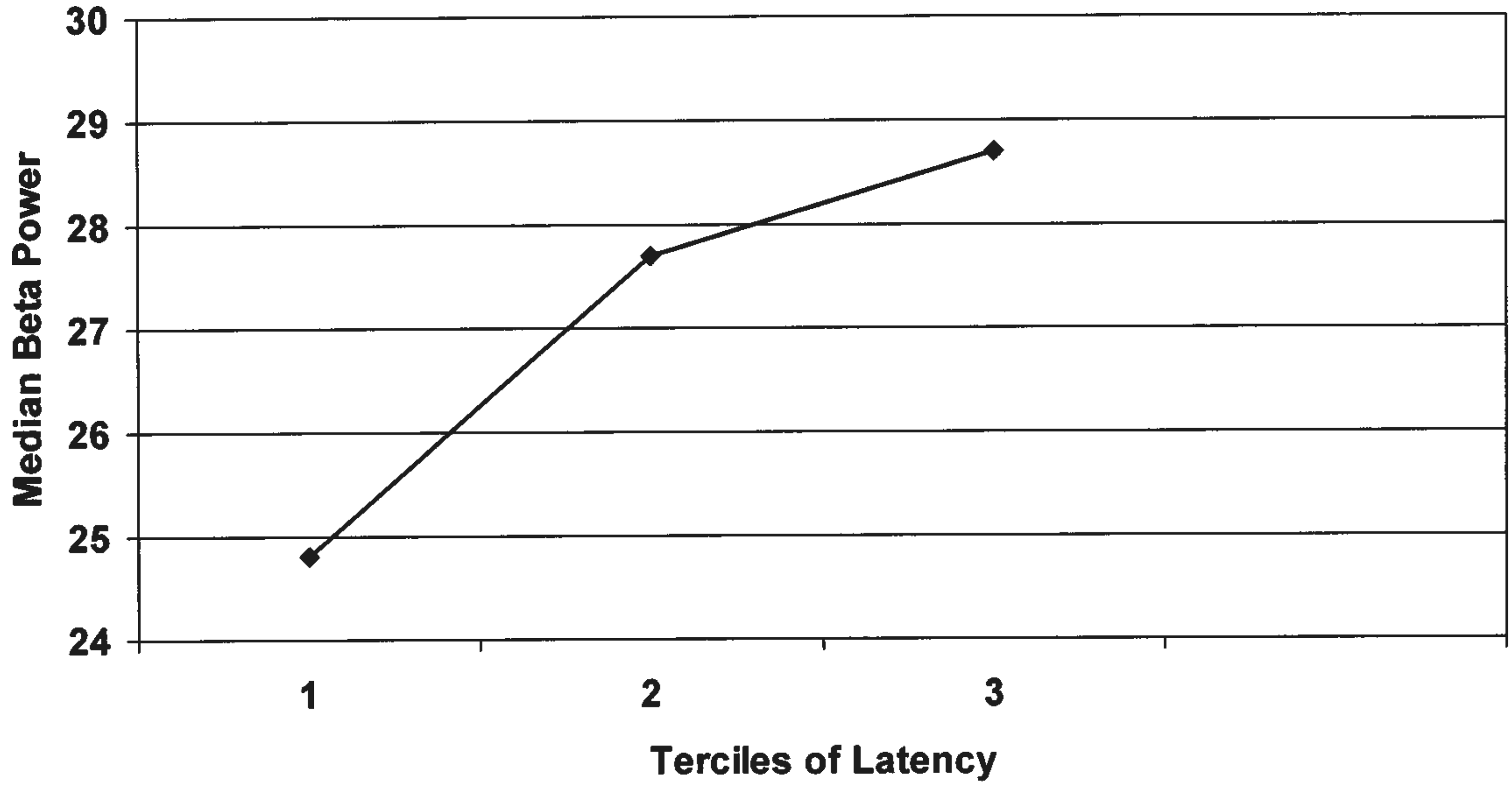

Fig 8. Relation of largest I-V difference to pictures (N400) to terciles of mean latency replies